EBRSR

HEART & STROKE FOUNDATION
Canadian Partnership for Stroke Recovery

Chapter 18: Post stroke depression

Abstract

A variety of psychological disorders may develop following stroke, namely depression. Post-stroke depression has been reported to affect approximately one-third of individuals. These rates may also be influenced by a combination of factors such as age, sex, socioeconomic status, functional independence, cognitive impairment, and stroke severity. The presence of post-stroke depression can significantly impact a wide range of outcomes and overall stroke recovery. Several studies have investigated pharmacological and non-pharmacological treatment options for post-stroke depression. However, no consensus has been reached regarding the most effective and viable treatment. This chapter explores the evidence regarding interventions for the prevention and treatment of post-stroke depression, as well as its prevalence, predictors, and consequences.

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Chapter 18: Post-stroke depression

Key Points

Omega-3 supplementation may not be beneficial for improving depression, post-stroke anxiety or quality of life post-stroke.

Nortriptyline may be beneficial for improving post-stroke depression.

The literature is mixed concerning heterocyclic antidepressants ability to improve activities of daily living.

Escitalopram or citalopram may be beneficial for improving post-stroke depression, anger, emotional lability and activities of daily living.

The literature is mixed concerning the efficacy of fluoxetine for post-stroke depression.

SNRIs may be beneficial for improving depression post stroke.

MAO inhibitors may not be beneficial for improving post-stroke depression

Methylphenidate may be beneficial for improving activities of daily living

Nefiracetam may not be beneficial for improving mood related outcomes post-stroke

Pioglitazone with fluoxetine may improve post-stroke depression more than metformin with fluoxetine, but not activities of daily living.

Free and Easy Wander Plus may be beneficial for improving post-stroke depression and activities of daily living.

Light therapy may not be beneficial for improving post-stroke depression.

Art therapy may be beneficial for improving depression, activities of daily living and quality of life post-stroke, but not anxiety.

Aquatic Therapy may be beneficial for improving depression and anxiety post-stroke.

Coordinated care and comprehensive follow-up may be beneficial for improving post-stroke depression, but not other mood related outcomes post-stroke.

Goal-setting programs or home visits may not be beneficial for improving mood related outcomes post-stroke.

The literature is mixed regarding the effectiveness of CBT for improving post-stroke depression.

CBT does not appear to improve activities of daily living or quality of life.

The literature is mixed regarding music therapies efficacy for improving post-stroke mood disorders.

The literature is mixed concerning physical activity interventions for improving depression.

Physical activity does not seem to be beneficial for improving anxiety, activities of daily living or quality of life post-stroke.

Speech therapy may improve activities of daily living, but not depression or other mood cofactors.

HBOT in combination with antidepressants may be beneficial for improving depression.

High frequency rTMS may be beneficial for improving depression and apathy post-stroke, but not activities of daily living.

Extremely low electromagnetic field therapy could be beneficial for improving post-stroke depression.

Dual tDCS could be beneficial for improving post-stroke depression.

Acupuncture may not be beneficial for improving mood related outcomes post-stroke.

Acupressure may be beneficial for improving depression and activities of daily living post-stroke.

Reiki therapy may not be beneficial for improving depression or activities of daily living.

Forest meditation may be more beneficial than urban meditation for improving depression and anxiety post-stroke.

Modified Sackett Scale

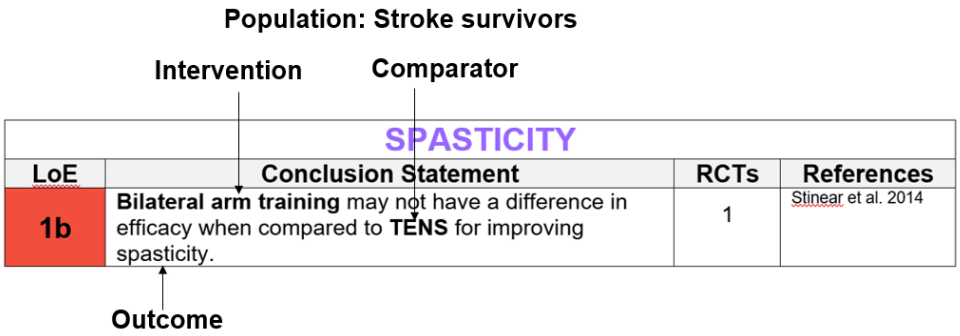
Level of evidence	Study design	Description
Level 1a	Randomized controlled trial (RCT)	More than 1 higher quality RCT (PEDro score ≥6).
Level 1b	RCT	1 higher quality RCT (PEDro score ≥6).
Level 2	RCT	Lower quality RCT (PEDro score <6).
	Prospective controlled trial (PCT)	PCT (not randomized).
	Cohort	Prospective longitudinal study using at least 2 similar groups with one exposed to a particular condition.
Level 3	Case Control	A retrospective study comparing conditions, including historical cohorts.
Level 4	Pre-Post	A prospective trial with a baseline measure, intervention, and a post-test using a single group of subjects.
	Post-test	A prospective post-test with two or more groups (intervention followed by post-test and no re-test or baseline measurement) using a single group of subjects
	Case Series	A retrospective study usually collecting variables from a chart review.
Level 5	Observational	Study using cross-sectional analysis to interpret relations. Expert opinion without explicit critical appraisal, or based on physiology, biomechanics or "first principles".
	Case Report	Pre-post or case series involving one subject.

New to the 19th edition of the Evidence-based Review of Stroke Rehabilitation

1) PICO conclusion statements

This edition of Chapter 10: Upper extremity motor rehabilitation interventions synthesizes study results from only randomized controlled trials (RCTs), all levels of evidence (LoE) and conclusion statements are now presented in the Population Intervention Comparator Outcome (PICO) format.

For example:

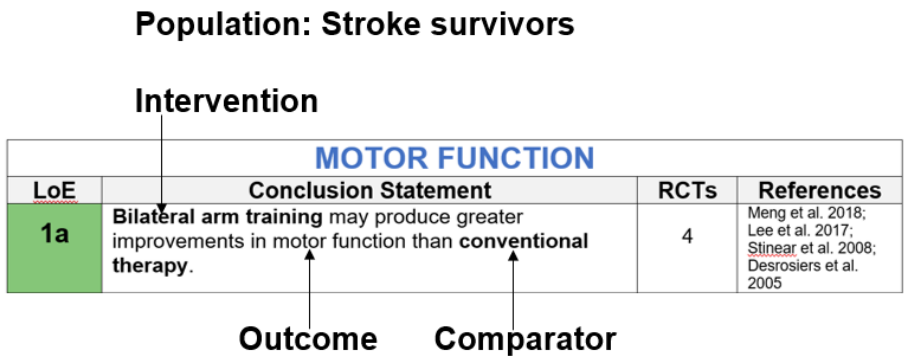


New to these statements is also the use of colours where the levels of evidence are written.

Red statements like above, indicate that the majority of study results when grouped together show no significant differences between intervention and comparator groups.

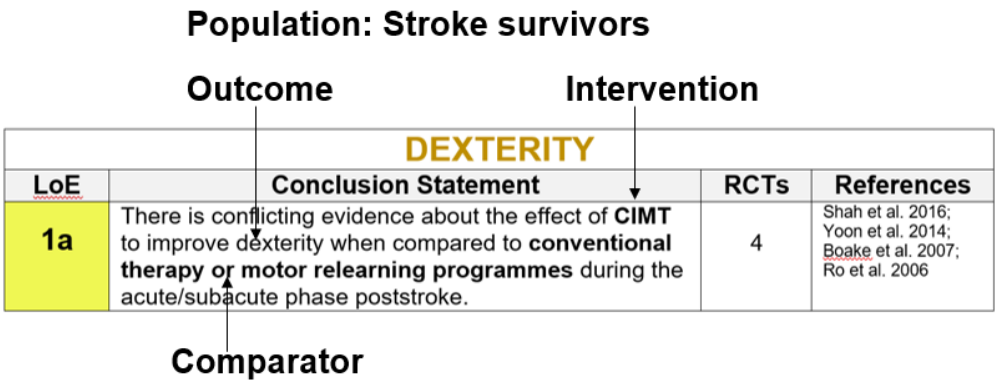
Green statements indicate that the majority of study results when grouped together show a significant between group difference in favour of the intervention group.

For example:



Yellow statements indicate that the study results when grouped together are mixed or conflicting, some studies show benefit in favour of the intervention group, while others show no difference between groups.

For example:



DEXTERITY			
LoE	Conclusion Statement	RCTs	References
1a	There is conflicting evidence about the effect of **CIMT** to improve dexterity when compared to **conventional therapy or motor relearning programmes** during the acute/subacute phase poststroke.	4	Shah et al. 2016; Yoon et al. 2014; Boake et al. 2007; Ro et al. 2006

2) Upper extremity rehabilitation outcome measures

For the studies reviewed, upper extremity rehabilitation outcome measures were classified into the following broad categories to allow for synthesis of results and formulation of PICO conclusion statements:

Depression: These measures assessed the severity and presence of major and/or minor depressive disorder and its individual symptoms.

Anxiety: These measures assessed the presence and severity of anxiety disorder, and its individual symptoms.

Activities of daily living: These outcome measures assessed performance and level of independence in various everyday tasks.

Quality of life: These outcome measures assessed an individual's overall quality of life, generally compared to their pre injury status.

Emotional liability: These outcome measures assessed the severity and frequency of emotional volatility and inappropriate emotional responses.

Mood cofactors: These outcome measures cover all the assessments examining aspects of behavior or personality which relate to, but are not directly equivalent with, mood related outcomes.

Outcome measures that fit these categories are described in the next few pages.

Outcome measures definitions

Depression

Bech-Rafaelsen Melancholia Scale: is an assessment of depression consisting of 11-items, each one relating to a different symptom of depression. Each item is scored from 0-4 for a total of 44 possible points, with higher scores relating to more severe depression. The measure has been widely used, and has shown good reliability and validity (Bech, 2002).

Beck Depression Inventory (BDI): Is a widely used instrument for the detection and assessment of the severity of depression. It can be administered by a trained interviewer or as a questionnaire. The BDI is composed of 21 multiple choice sets, each with 4 self-evaluative statements scored on a scale of 0 (least indicative of depression) to 3 (most indicative of depression). Scores are added to provide a total score from 0-63. Generally, a score >19 is associated with clinically relevant depression. The inventory is simple and easy to administer. It also assesses cognitive symptoms more than somatic, making it ideal for assessing depression in the context of stroke. The BDI is externally valid, is internally consistent and has high test-retest reliability (Aben et al. 2002; Beck, Steer & Carbin, 1988).

Beyer Six-face Rating Scale: is a rating scale commonly used for pain, or mood assessment. It is a visual analog scale of sorts, where there are a series of line drawing faces that progressively show a more painful, or sad, expression. Participants are instructed to select the face that best describes how they are feeling (Kang, Sok, Kang, 2009).

Center for Epidemiological Studies Depression Scale (CESD): Is a screening tool for depression. It is a 20-item questionnaire assessing how often patients experienced depressive symptoms within the past week. It has high internal consistency, test-retest reliability and validity. It is generalizable for use in stroke patients, however questions concerning somatic symptoms should be interpreted with caution in this population (Pickard, Dalal & Bushnell, 2006; Lewinsohn et al. 1997).

Clinical Global Impression Scale (CGI): Is a clinician-rated measure of global improvement (CGI-GI), severity (CGI-SI) or efficacy (CG-EI) pertaining to mental illness. Patients are given a single numerical rating from 1 (either normal or very much improved) to 7 (among the most ill patients or very much worse). In stroke rehabilitation, it is most often used to evaluate depression post-stroke. In this context, the CGI has good criterion validity, but poor cross-cultural validity (van Dijk et al. 2016).

Geriatric Depression Scale (GDS): Is a self-rating screening test for depression in the elderly. A long form of the scale consists of 30 yes/no questions relating to how the examinee felt over the preceding week, while the short form consists of 15 questions. One point is given for each response indicating depression symptoms. Depression severity can be categorized into mild (11-20 long form; 5-9 short form) or moderate-severe (21-30 long form; 10-15 short form). Both versions of the test have been extensively validated. They both have high internal consistency, test-retest reliability, sensitivity and specificity. The test has also been validated for use with elderly stroke patients and found to have a high predictive value (McDowel, 2006; Agrell & Dehlin, 1989; Sheikh & Yesavage, 1986).

Hamilton Rating Scale for Depression (HAM-D): Is a commonly used instrument for evaluating the severity of depression and other mood disorders that was created in 1960. The scale consists of 21 items with only 17 included in scoring. Mood, guilt, suicidal ideation,

agitation and somatic symptoms are assessed in either a structured interview or written self-report format. Test items are scored on a scale of 0-4, although some items are scored only as high as 2 or 3. There is no concrete cut-off score for depression, however a score of 7 is often the consensus. Internal reliability ranges from poor-excellent, and interrater and test-retest reliability is good-excellent. The scale's validity for evaluating post-stroke depression has been established and its sensitivity and specificity found to be within acceptable ranges (Shahid et al. 2011; Bagby et al. 2004; Aben et al. 2002).

Hospital Anxiety and Depression Scale (HADS): Is a measure of depression and anxiety symptomatology designed to detect these disorders among physically ill patients. The scale is divided into an anxiety portion (HADS-A) and a depression portion (HADS-D), each scored out of 21 points. The total test consists of 14 items (7 in each subscale), each evaluated on a 4-point scale. The HADS has been found to be sensitive, specific, have moderate-excellent internal consistency and be a valid and appropriate test for screening post-stroke depression (Aben et al. 2002; Zigmond & Snaith, 1983).

Montgomery-Asberg Depression Rating Scale: is a 10-item questionnaire meant to assess depressive symptoms. Each item is rated on a 6-point Likert scale. Higher scores are indicative of greater levels of depression. The scale has shown good psychometric properties in multiple patient groups and in multiple languages (Kang et al. 2013).

Multiple Affective Adjective Check List (depression scale): is a measure designed to assess both positive and negative affect, as a trait or a state. There are 132 adjectives that assess 5 scales (anxiety, depression, hostility, positive affect, sensation seeking). Participants are asked to check off which adjectives they are feeling 'today' (state) and 'in general' (trait). It has shown good reliability and validity (Pankratz, Glaudin & Goodmonson, 1972).

Patient Health Questionnaire: is an instrument designed to assess the severity of depression. It contains 9-items assessing the frequency of depressive symptoms, and a 10^{th} item relating to whether these difficulties are causing problems in their life. Each item is rated on a 4-point scale, with higher scores indicating more severe depression. It has been found to be both reliable and valid (Kroenke, Spitzer & Williams, 2001).

Post-Stroke Depression Rating Scale: was specifically designed to assess post-stroke depression. A semi structured interview is conducted and a trained examiner rates the individual on 10 sections (eg. Suicidal thoughts, guilt, anhedonia etc…). All sections are rated on a 6 point Likert scale with high scores corresponding to more severe depression. The measure has displayed good inter-rater reliability as well as good validity (Gainotti et al. 1997).

Present State Examination: is a semi-structured interview designed to evaluate symptoms of mental disorder. It has 140 items total, each scored on a 3 or 4-point Likert scale. It has been found to be a reliable measure for assessing a variety of mental disorders (Kendell et al. 1968).

Profile of Mood States: Is a measure of mood states and mood changes in psychiatric populations. The measure is quick and easy to administer, and can be completed in 3 to 5 minutes, however it may take longer for populations that have trouble reading due to illness or injury. The original POMS includes 65 items in total, with 58 scored items and seven unscored items designed to measure "friendliness. A shortened version of POMS was created in 1991, which removed less psychometrically sound or confusing items. This version, known as EPOMS consists of 30-items and has been adapted in other languages as well. The psychometric properties of both scales have been investigated, and the abbreviated EPOMS scale has

proven even greater reliability and validity than the full-scale POMS instrument (Bourgeois et al. 2010).

Stroke Aphasic Depression Questionnaire: is an assessment designed to measure depression in aphasic stroke patients. The questionnaire contains 21 items, and each item is scored on a 4-point scale. Higher scores indicate more severe depression. The measure has displayed good psychometric properties (Sutcliffe & Lincoln, 1998).

Stroke Inpatient Depression Inventory: is a measure of depression specifically designed for acute stroke patients. Unlike some other depression measures, this one focuses on changes since the stroke and on situations relevant to a recently injured stroke survivor. It contains 30 items in the form of questions, which require a 'yes' or 'no' response. Higher scores correspond to more severe depression. The measure has shown good reliability and validity (Rybarczyk et al. 1996).

Wakefield Depression Inventory: is a self-reported measure of depressive symptoms and behaviours. It is 12-items long and each item is scored on a 4-point Likert scale. Each item is a statement that the participant must rate based on how applicable it was to them, and their life. Higher scores indicate a more depressed individual. The scale showed good reliability and validity relative to other depression measures (Snaith et al. 1971).

Yale Self-Reported Depression Screen: is used to screen individuals who are potentially depressed and would require further assessment and testing. It is a single question, "Do you often feel sad or depressed?" to which the answer is either 'yes' or 'no'. It has shown to be accurate in identifying depressed individuals (Maboney et al. 1994).

Zung Self-Rating Depression Scale: is a tool used to assess the level of depression in individuals with depressive disorder. It has 20 items related to emotions and behaviour, and each item is rated on a 4-point Likert scale. Higher scores indicate greater levels of depression. It has shown good validity and sensitivity (Biggs, Wylie & Ziegler, 1978; Zung, 1965).

Anxiety

State-trait Anxiety Inventory: is a measure of state and trait anxiety levels. The most frequently used version contains 20 items that asses strait anxiety, and 20 items that assess state anxiety. Items are rated on a 4-point scale, with higher scores indicating greater levels of anxiety. Good reliability and validity have been previously reported (Spielberger et al. 1983).

Hospital Anxiety and Depression Scale (HADS): Is a measure of depression and anxiety symptomatology designed to detect these disorders among physically ill patients. The scale is divided into an anxiety portion (HADS-A) and a depression portion (HADS-D), each scored out of 21 points. The total test consists of 14 items (7 in each subscale), each evaluated on a 4-point scale. The HADS has been found to be sensitive, specific, have moderate-excellent internal consistency and be a valid and appropriate test for screening post-stroke depression (Aben et al. 2002; Zigmond & Snaith, 1983).

Activities of Daily Living

Activities of Daily Living Scale: is an assessment of activities of daily living. It consists of 13 items that cover eating, personal hygiene, wearing, elimination, mobility and walking. Items are scored from 1-5 with higher scores indicating a greater level of independence. The measure has good reliability, but its psychometric properties have not been strongly established (Kang, Sok & Kang, 2009).

Assessment of Life Habits: is a measure designed to assess the level of social participation in an individual with disabilities. It is based on two factors involved in the activities, 1) the difficulty of the task and 2) what sort of assistance is required for completion. It is made up of two general domains, activities, and social roles. Each domain has 6 different subscales, each with 3-8 items depending on the subscale. Each item is scored from 0-9, with lower scores indicating greater difficulty with greater assistance, and higher scores indicating less difficulty and less assistance. The test has shown good psychometric properties in stroke populations (Desrosiers et al. 2002; Noreau et al. 2004).

Barthel Index (BI): Is a measure of one's ability to perform activities of daily living. The scale consists of 10 items: personal hygiene, bathing, feeding, toilet use, stair climbing, dressing, bowel control, bladder control, ambulation or wheelchair mobility and chair/bed transfers. Each item has a five-stage scoring system and a maximum score of 100 points, where higher scores indicate better performance. The scale is suitable for monitoring on the phone, and is shown to have a high inter-rater reliability (Park 2018).

Chinese Activities of Daily Living: is a 14-item measure adapted from English activities of daily living measures intended to assess the level of independence in self-care in a Chinese population. Each item is rated on a 4-point scale, with a higher score indicating less independence and more assistance. Each item is a task (eg. Eating, dressing) that an individual would likely perform on a regular basis (Chen et al. 1995).

Frenchay Activities Index (FAI): Is a measure of activities that stroke survivors have participated in recently. The measure consists of 15 items that are in turn split up into 3 subscales (domestic chores, leisure/work and outdoor activities). These items include: preparing meals, washing clothes, light/heavy housework, social outings etc. Each task is then scored on a 4-point scale with 1 being the lowest score. This measure has been shown to have good reliability and concurrent validity in its full form (Schuling et al. 1993).

Functional Independence Measure (FIM): Is an 18-item outcome measure composed of both cognitive (5-items) and motor (13-items) subscales. Each item assesses the level of assistance required to complete an activity of daily living on a 7-point scale. The summation of all the item scores ranges from 18 to 126, with higher scores being indicative of greater functional independence. This measure has been shown to have excellent reliability and concurrent validity in its full form (Stineman et al. 1996)

Johns Hopkins Functioning Inventory: is a 10-item inventory that assesses the independence of a patient while completing activities of daily living like eating or walking. Scores range from 0-27, and items are socred from 0-3 or 0-2 depending on how necessary they are for daily living (Robinson & Szetela, 1981; Starr, Robinson & Price, 1983).

Karnofsky Performance Status: is a rating scale that classifies individuals into groups of functional ability based on their capacity to complete activities of daily living without difficulty, and their independence on those tasks. It scored from 0-100, with each increase of 10 points relating to a different 'level' of functional impairment. It has good inter-rater reliability and has been validated in several studies since its conception (Peus, Newcomb & Hofer, 2013).

London Handicap Scale: is a self-reported questionnaire intended to assess an individual's functional ability and activities of daily living. The questionnaire contains 6 domains; mobility, physical independence, occupation, social integration, social orientation and economic self-sufficiency. Each domain is rated on a 6-point Likert scale, from 'no disadvantage' to 'most severe disadvantage' on that domain. The test is scored between 0 and 1, with lower scores corresponding to a greater disadvantage (Harwood et al. 1994).

Nottingham Extended Activities of Daily Living: is a measure of activities of daily living specifically designed to assess stroke survivors. It consists of 22 questions, each with a 4-point Likert scale assessing varying levels of dependence on the task described in the item. There are four subscales (mobility, kitchen, domestic, leisure), with higher scores indicating greater independence in each area, and overall. Conclusions on its reliability and validity have been mixed (Green & Young, 2001).

Nottingham Leisure Questionnaire: is a self-rated questionnaire meant to assess leisure activity in individuals suffering from disabilities. It contains 30-items, and responses are rated on a 3-point scale based on the frequency with which they complete the activity. Total scores are from 0-60, with higher scores indicating more frequent participation in leisure activities. It has shown an acceptable test-retest reliability and validity (Drummond et al. 2001).

Stroke Impact Scale (activities of daily living): Is a patient-reported measure of multi-dimensional stroke outcomes. The measure consists of 59 functional tasks (e.g. dynamometer, reach and grab, walking, reading out loud, rating emotional regulation, word recall, number of tasks completed, and shoe tying). These tasks are then divided into 8 distinct subscales which include: strength, hand function, mobility, communication, emotion, memory, participation and activities of daily living (ADL). Each task is measured on a 5-point scale (1=an inability to complete the task, 5=not difficult at all). The measure has been shown to have good reliability and validity (Mulder et al. 2016; Richardson et al. 2016).

World Health Organization Disability Assessment Schedule II: is an instrument used to rate disability. It's measured along 6 domains (understanding/communication, getting around, self-care, getting along with others, household/work activities and participation) that encompass both physical and mental health. The scale is a 36-item self-reported questionnaire with a 5-point Likert scale for each question. Higher scores indicate a greater disability. It has shown good reliability and validity statistics (Annicchiarico et al. 2004)

Quality of Life

Assessment of Quality of Life Instrument: is a measure designed to assess an individual's health-related quality of life. It consists of 5 dimensions (illness, independent living, social relationships, physical senses and psychological wellbeing) each containing 3 items. The instrument has shown good reliability, validity, and sensitivity in comparison to other established quality of life measures (Hawthorne, Richardson & Osborne, 1999).

EuroQol Quality of Life (EQ-5D): Is a widely-used measure of quality of life. It is a brief, self-reported scale covering 5 dimensions: 1) mobility; 2) self-care; 3) usual activities; 4) pain/discomfort; and 5) anxiety/depression. There are two different versions of the scale, one with 3 levels (EQ-5D-3L) and one with 5 levels (EQ-5D-5L) in which subjects rate each dimension from 1 to 3 or 1 to 5, respectively. A "health state" is generated from the score on each dimension, generating a state of 11111 to 33333 in the EQ-5D-3L or 11111 to 55555 in the EQ-5D-5L, with lower numbers representing better health-related quality of life. A summary value can be calculated from each health state to generate a value from 0 to 1. In the second part of the test, subjects rate their current state of health from 0 (worst imaginable) to 100 (best possible) on a visual analogue scale (EQ VAS). The EuroQol scale has been extensively validated in many populations, including stroke survivors. The scale has also been shown to have good reliability (Golicki et al. 2015; Janssen et al. 2013).

McGill Quality of Life Questionnaire: is a 17-item assessment of quality of life. Each Item is a particular statement or question concerning aspects of life, and the participant rates their response from 1-7, with lower scores indicating a less desirable situation. The Measure has four subscales (physical symptoms, psychological symptoms, outlook on life, meaningful existence) that can be analysed separately. The measure has good reliability and has shown adequate validity (Cohen et al. 1995).

Medical Outcome Trusts' Short Form Health Survey (SF-36 or SF-12): Is a commonly used measure of health-related quality of life and overall health status. The test contains 36 items (or 12) encompassing 8 subscales: 1) physical functioning; 2) role limitations – physical; 3) bodily pain; 4) general health; 5) vitality; 6) social functioning; 7) role limitations – emotional; and 8) mental health. The result of each subscale is transformed to a score from 0-100 representing the lowest and highest possible scores, respectively. Two summary measures, physical and mental health, are generated by weighting the relevant subscales. The test has been validated in a wide range of populations, including stroke and traumatic brain injury patients. In stroke, the survey has demonstrated convergent validity and has high reliability (Guilfoyle et al. 2010; Hagen, Bugge & Alexander, 2003).

Nottingham Health Profile: is an assessment about an individual's perceived health status and quality of life. It contains 38 questions in 6 subdomains (energy, pain, emotional reaction, sleep, social isolation and physical abilities) that are all weighted so that the sum of their score is equal to 100. It also contains a second part, which assesses whether their health is causing problems in certain areas of life (eg. Work, vacations). It has shown good consistency and reliability, as well as sensitivity (Wann-Hansson et al. 2004).

Pictorial Thai Quality of Life: Is a measure of quality of life designed for Thai populations. The test consists of 25 items assessing 6 domains: 1) physical; 2) cognitive; 3) affective; 4) social

function; 5) economic; and 6) self-esteem. All items are in a picture format. The test has been validated in terms of construct, discriminant, and concurrent validity and good-excellent reliability demonstrated (Phattharayuttawat, Ngamthipwatthana & Pitiyawaranun, 2004).

Satisfaction with Life Scale: is questionnaire designed to assess an individual's perceived satisfaction with their life overall. It contains 5 items rated on a 7-point Likert scale. The scale has favorable psychometric properties (Diener et al. 1985).

Sickness Impact Profile: is an assessment of quality of life. It is divided into 12 subdomains, covering 3 major domains (physical, psychological, and social). There are 136 items total, each one a 'yes' or 'no' question. The measure has shown good psychometric properties (Stummer et al. 2015).

Stroke and Aphasia Quality of Life Scale-39 (SAQOL-39): Is a measure of health-related quality of life specific to stroke patients. It is an interview-administered self-report scale developed from the items from the Stroke-Specific Quality of Life Scale (SS-QoL), modified for those with aphasia. It includes 4 additional items reflecting common difficulties in patients with aphasia: speech, decision-making, and impact of aphasia on family and social life. The test has been shortened from the 49-item SS-QoL to 39 items. Similarly to the SS-QoL, each item is rated on a 5-point Likert scale with higher scores representing better function. The 39 items are divided into 4 domains: 1) physical; 2) psychosocial; 3) communication; and 4) energy. Subdomain and overall scores are obtained by averaging responses and obtaining an average score. The scale has been validated in both aphasia and general stroke patients. It also exhibits good internal consistency and test-retest reliability (Hilari et al. 2009; Hilari et al. 2003).

Stroke-Specific Quality of Life Scale (SS-QoL-12): Is a measure of health-related quality of life specific to stroke patients. The scale consists of 49-items distributed across 12 domains: mobility, energy, upper extremity function, work/productivity, mood, self-care, social roles, family roles, vision, language, thinking, and personality. Each item is rated on a 5-point Likert scale, with higher score denoting better function. The scale has demonstrated excellent internal consistency and construct validity (Williams et al. 1999).

WHO Quality of Life (WhoQol): Is a measure of quality of life using a self-administered questionnaire. The scale was developed as a comprehensive and cross-cultural measure of subjective quality of life. The initially developed scale, WhoQol-100, consists of 100 items with each rated on a 5-point Likert scale related to how the subject felt over the preceding 2 weeks. Higher scores denote greater satisfaction. The WhoQol-Bref was created to shorten the cumbersome 100-item questionnaire and contains questions concerning physical health, psychological health, social relationships, environment, and overall quality of life and general health. Both forms of the questionnaire have demonstrated validity and good reliability (Trompenaars et al. 2005).

Emotional Lability

Emotional Distress Scale: is a measure based on a more comprehensive instrument (Comprehensive Psychopathological Rating Scale), that was designed to briefly assess the domain of emotional distress without including the other outcomes involved in the comprehensive scale. It consists of 8 items, which are rated based on short interviews. It has a very high inter-rater reliability (Wilholm et al. 1984).

Emotional Incontinence – Kim's Criteria: is a purpose made criteria for assessing inappropriate/excessive laughing and crying. Both the patient, and their relatives are asked to assess the frequency of inappropriate laughing or crying since the injury. If both patient and relative agrees on either laughing or crying occurring on greater than 2 occasions, the individual is considered to have post-stroke emotional incontinence (Kim & Choi-Kwon, 2000)

Emotional Lability Questionnaire: is a measure of how emotionally unstable an individual is, assessing large changes in affect that are often inappropriate for the context. Originally, the questionnaire was given to both the patient, and their caretaker. It consists of 33-items divided between 3 subscales (laughing, crying and smiling). It has displayed good psychometric properties and has been validated in multiple languages (Palmieri et al. 2009).

Lawson Mcleod Rating Scale of Emotionalism: is a 9-point rating scale (0-8) that classifies a particular individual's emotionalism. The scale is based on observations of behavior and examining how often an individual may laugh or cry, and what stimuli trigger potentially inappropriate emotions. A score of 0 relates to no emotionalism, whereas an 8 refers to crying and laughing expressed upon initial introduction or simply the start of conversation (Brown, Sloan & Pentland, 1998).

Pathological Laughing and Crying Scale: is an 18-item long assessment of pseudobulbar affect. Each item is scored on a 3-point scale, with higher scores indicating a greater amount of emotional lability. It has shown excellent test-retest reliability and good sensitivity (Robinson et al. 1993).

Stroke Impact Scale (emotion): Is a patient-reported measure of multi-dimensional stroke outcomes. The measure consists of 59 functional tasks (e.g. dynamometer, reach and grab, walking, reading out loud, rating emotional regulation, word recall, number of tasks completed, and shoe tying). These tasks are then divided into 8 distinct subscales which include: strength, hand function, mobility, communication, emotion, memory, participation and activities of daily living (ADL). Each task is measured on a 5-point scale (1=an inability to complete the task, 5=not difficult at all). The measure has been shown to have good reliability and validity (Mulder et al. 2016; Richardson et al. 2016).

Mood Cofactors

Apathy Scale: is a 14-item observer rating scale that aims to identify apathetic individuals, and quantify apathetic behavior, separate from depression. Scores range from 0-42, with larger scores indicating a greater level of apathy. It is a modified version of the longer Marin's Apathy Evaluation Scale (Marin, Biedrzycki & Firinciogullari, 1991). The Apathy Scale has shown good reliability and validity in stroke populations and is a sensitive measure with high inter-rater reliabilities (Starkstein et al. 1993).

Coping Inventory for Stressful Situations: is a 48-item measure that covers 3 subscales (Task-, Emotion- and Avoidance-oriented coping), each containing 16 of the items. The measure asks a participating individual how frequently they would engage in different coping strategies. Each item is rated on 5-point Likert scale, where higher scores indicate they use this strategy more frequently. It has been shown to have good internal consistency, validity, and adequate test-retest reliability (McWilliams ,Cox & Enns, 2003).

General Health Questionnaire: has many different versions of various sizes, but the 28-item one is the most popular. The tool is meant to identify minor psychiatric disorders and mental health problems. The 28-item version consists of 4 subclasses (somatic symptoms, anxiety/insomnia, social dysfunction and severe depression) each with 7 items. It has been validated and found reliable in 38 different languages (Jackson, 2007).

Life Orientation Test: is a measure designed to assess differences in optimism versus pessimism. The test contains 10 items, each scored on a 5-point Likert scale from 'I Disagree A Lot' to 'I Agree A Lot'. Questions are centered around the individual's expectations for the future. The test has shown good internal consistency and test re-test reliability (Scheier, Carver & Bridges, 1994).

Perceived Stress Scale: is a questionnaire designed to assess an individuals levels of stress within the last month. The measure contains 10 items posed as questions about whether or not the participant has experienced a particular feeling. Each item is then rated on a 5-point Likert scale on the frequency that the individual experiences those particular feelings. The measure has shown good psychometric properties and is widely used for assessing stress (Coehn, Kamarck & Mermelstein, 1994).

Recovery Locus of Control Scale: is an assessment of an individual's perceived locus of control. It is made up of 40-items answered with 'yes' or 'no'. The items are based on assessing either an internal locus of external locus of control. Higher scores indicate a more internal locus, whereas lower scores indicate a more external locus of control. It has satisfactory reliability and validity (Macleod, L. & Macleod, G. 1998).

Rosenberg Self-esteem Scale: is a measure of global self-worth, assessing both positive and negative feelings the individual has toward themselves. It has 10-items, each rated on a 4-point Likert scale. Higher scores indicate higher self-esteem. It shows excellent internal consistency and reliability, and good validity (Rosenberg, 1979).

State-Trait Anger Expression Inventory: is an assessment of anger, and the traits of experiencing anger. Its most popular version has 40 items rated on a 4-point Likert scale denoting the frequency that they experience a feeling or situation denoted by the item. It has

shown adequate reliability, and good validity in psychometric assessments (Spielberger, 1989; Spielberger et al. 1983).

Utrecht Proactive Coping Competence Scale: is a self-rated measure of proactive coping mechanisms. It consists of 21 items, each assessed on a 4-point Likert scale. Each Item is posed in the form of a question relating to aspects of coping (eg. To what extent can you make realistic plans?) and the participant rates their competence. Higher scores indicate a higher perceived level of coping competency. The measure has shown good psychometric properties in multiple languages (Tielemans et al. 2014).

Introduction, prevalence and assessment of post-stroke depression

Post-stroke depression is defined by the DSM-V category, *mood disorders due to another medical condition such as stroke with depressive features, major depressive-like episode, or mixed-mood features* with the following diagnostic criteria (Eskes et al. 2015):

1. Prominent and persistent period of depressed mood or markedly diminished interest or pleasure in all or almost all activities lasting two weeks or longer.
2. Evidence from the history, physical examination, or laboratory findings that the disturbance is the direct pathophysiological consequence of a stroke.
3. Disturbance is not better explained by another mental disorder.
4. Disturbance does not occur exclusively during the course of a delirium.
5. Disturbance causes clinically significant distress or impairment in important areas of functioning.

As well, it includes the following three specifiers:

1. With depressive features: full criteria not met for major depressive episode.
2. With major depressive-like episode: full criteria met for major depressive episode, except for C.
3. With mixed features: symptoms of mania are present but do not predominate.

Approximately a third of stroke survivors will experience some form of post-stroke depression, with rates typically highest during the first year following stroke (Lanctot et al. 2019). As such it is recommended that screening for depressive symptoms be conducted at several time points during that year (e.g. during acute care, point of transition to inpatient rehabilitation, discharge from inpatient rehabilitation, and outpatient clinic visits) (Lanctot et al. 2019).

Validated screening tools with the highest sensitivities for a stroke population include: the Center of Epidemiological Studies Depression scale, the Hamilton Depression Rating scale, and the 9-item Patient Health Questionnaire (Lanctot et al. 2019). The two-item short of the version of the Patient Health Questionnaire is recommended as a feasible tool for quick screening of depressive symptoms during routine clinical assessments prior to more robust screening tools as mentioned earlier (Swartz et al. 2017).

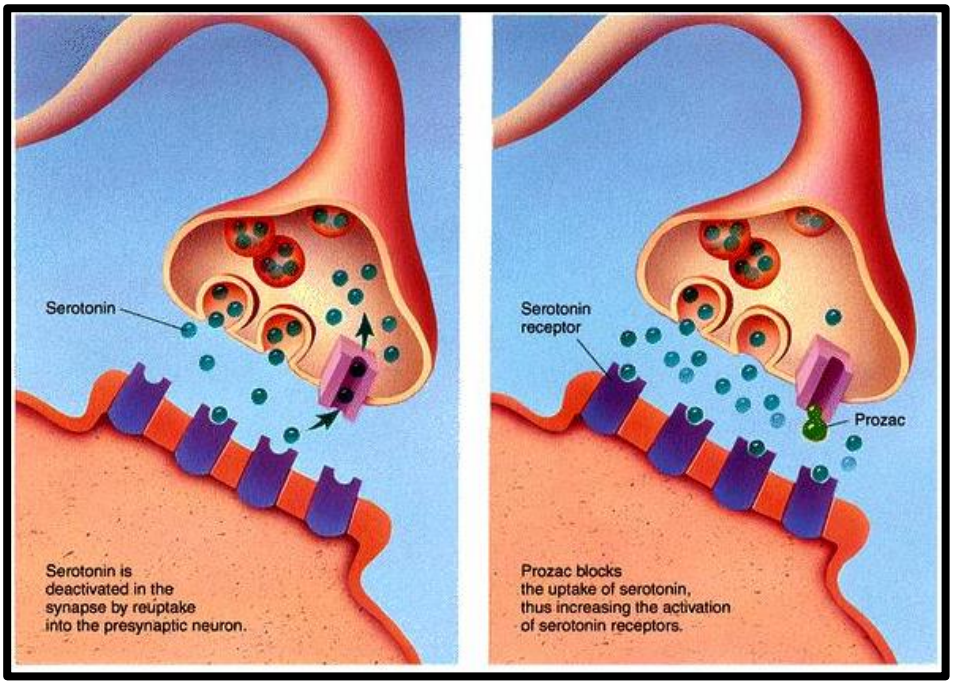
Risk factors for post-stroke depression

A comprehensive narrative review by Robinson and Jorge (2015), identified the following areas where a limited source research has elucidated potential risk factors for post-stroke depression.

1. Genetic factors such as the *5-HTTLPR* and *STin2 VNTR* polymorphisms of the serotonin transporter gene, as well as epigenetic modifications of *5-HTTLPR*.
2. Being a female.
3. A personal or familial history of depression, as well as a history of diabetes mellitus.
4. Stroke severity.
5. Having suffered a left frontal or left basal ganglia lesion.
6. Severity of impairment in activities of daily living.
7. Cognitive impairments such as executive dysfunction.
8. Communication deficits and social isolation (Lanctot et al. 2019).

Pharmacological Interventions

Selective Serotonin Reuptake Inhibitors (SSRIs)



Adopted from: http://www.psychology4a.com/treating-ocd.html

Selective serotonin reuptake inhibitors (SSRIs) selectively block the reuptake of serotonin but have weak affinity for transporters of norepinephrine and dopamine. They are commonly used to treat depressive disorders, especially those characterized by anxiety, insomnia, restlessness, hostility, and trepidation. The use of SSRIs for PSD has been thoroughly investigated, with Mead et al. (2013) identifying 52 studies in a systematic review. Their meta-analysis found that SSRIs were effective in treating symptoms of depression and anxiety, although there was significant heterogeneity between the studies. As well, the authors determined that SSRIs were associated with increased risk of adverse events and associated trial dropout

Seventeen RCTs were found evaluating an SSRI for improving mood related outcomes post-stroke. Four RCTs compared escitalopram or citalopram to a placebo (Kim et al., 2017; Robinson et al., 2008b; Andersen et al., 1994; Andersen et al., 1993). Nine RCTs were found comparing fluoxetine to a placebo or no medication (Chollet et al., 2006; Choi-Kwon et al., 2006; Fruehwald et al., 2003; Narushima et al., 2002; Robinson et al., 2000; Wiart et al., 2000; Dam et al., 1996; Gonzalez-Torrescillas et al., 1995; Brown et al., 1998). Four RCTs were found comparing sertraline to a placebo (Almeida et al., 2006; Murray et al., 2005; Rasmussen et al., 2003; Burns et al., 1999).

The methodological details and results of all 17 RCTs are presented in Table 1**.**

Table 1. RCTs evaluating SSRI antidepressants for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Escitalopram/Citalopram vs placebo		
Kim et al. 2017 RCT (8) N_{start}=478 N_{end}=405 TPS=Acute	E: Escitalopram (10mg/d) C: Placebo Duration: 12wks	• Montgomery-Asberg Depression Scale (-) • Emotional Incontinence – Kim's Criteria (+exp) • Spielberger Trait Anger Scale (+exp) • Barthel Index (-) • Stroke Specific Quality of Life Scale (-)
Robinson et al. (2008b) RCT (7) N_{Start}=176 N_{End}=134 TPS=Subacute	E1: Escitalopram (5-10mg/d) E2: Problem-solving therapy C: Placebo Duration: 1yr	E1, E2 vs C • Incidence of Depression (+exp1) • Functional Independence Measure (-)
Andersen et al. (1994) RCT (8) N_{Start}=66 N_{End}=59 TPS=Subacute	E: Citalopram (10-20mg/d, 6wk) C: Placebo Duration: 6wks	• Hamilton Depression Rating Scale (+exp) • Bech-Rafaelsen Melancholia Scale (+exp)
Andersen et al. (1993) RCT (6) N_{Start}=16 N_{End}=13 TPS=Chronic	E: Citalopram (10-20mg/d, 3wk) C: Placebo Duration: 3wks	• Crying frequency (+exp) • Hamilton Depression Rating Scale (+exp)
Fluoxetine vs placebo/no medication		
Chollet et al. (2011) RCT (9) N_{Start}=118 N_{End}=113 TPS=Acute	E: Fluoxetine (20mg/d) C: Placebo Duration: 3mo	• Montgomery-Asberg Depression Rating Scale (+exp)
Choi-Kwon et al. (2006) RCT (8) N_{Start}=152 N_{End}=125 TPS=Chronic	E: Fluoxetine (20mg/d, 3mo) C: Placebo Duration: 3mo	• Beck Depression Inventory (-) • Visual Analog Scale – Excessive Inappropriate Laughing (-) • Visual Analog Scale – Excessive Inappropriate Crying (+exp) • Visual Analog Scale – Post-stroke Anger Proneness (+exp)
Fruehwald et al. (2003) RCT (9) N_{Start}=54 N_{End}=40 TPS=Acute	E: Fluoxetine (20mg/d, 3mo) C: Placebo Duration: 12wks	• Hamilton Depression Rating Scale (-) • Beck Depression Inventory (-) • Clinical Global Impressions Scale (-) • Barthel Index (-)
Narushima et al. (2002) RCT (8) N_{Start}=48 N_{End}=32 TPS=Subacute	E1: Fluoxetine (10-40mg/d) E2: Nortrirptyline (25-100mg/d) C: Placebo Duration: 3mo	E1 vs C • Incidence of Depressive Disorder (+exp1) • Hamilton Depression Rating Scale (+exp1)
Robinson et al. (2000) RCT (8) N_{Start}=56 N_{End}=40 TPS=Subacute	E1: Nortriptyline (25-100mg/d) E2: Fluoxetine (10-40mg/d) C: Placebo Duration: 12wks	E2 vs C • Hamilton Depression Rating Scale (-) • Hamilton Anxiety rating Scale (-) • Functional Independence Measure (+con) • Johns Hopkins Functioning Inventory (-)
Wiart et al. (2000) RCT (8)	E: Fluoxetine (20mg/d, 6wk) C: Placebo	• Montgomery-Asberg Depression Rating Scale (+exp)

N_{Start}=31 N_{End}=29 TPS=Subacute	Duration: 6wks	• Functional Independence Measure (-)
Dam et al. (1996) RCT (7) N_{Start}=52 N_{End}=46 TPS=Subacute	E1: Maprotiline (150mg/d) E2: Fluoxetine (20mg/d) C: Placebo Duration: 3mo	E2 vs C • Hamilton Depression Rating Scale (-) • Barthel Index (-)
Gonzalez-Torrescillas et al. (1995) RCT (7) N_{Start}=130 N_{End}=125 TPS=Acute	E1: Nortriptyline (25-75mg/d) E2: Fluoxetine (20mg/d) C: No medication Duration: 6wks	E1,E2 vs C • Beck Depression Inventory (+exp2) • Hamilton Depression Rating Scale (+exp2) • Montgomery-Asberg Depression Rating Scale (+exp2) • Barthel Index (+exp2) • Karnofksy's Performance Status Scale (+exp2)
Brown et al. (1998) RCT (8) N_{Start}=20 N_{End}=19 TPS=Subacute	E: Fluoxetine (20mg/d, 10d) C: Placebo Duration: 10d	• Crying frequency (+exp) • Lawson & MacLeod Rating Scale of Emotionalism (+exp) • Hamilton Depression Rating Scale (-)
Sertraline vs placebo		
Almeida et al. (2006) RCT (9) N_{Start}=111 N_{End}=94 TPS= Acute	E: Sertraline (50mg/d) C: Placebo Duration: 24wks	• Hospital Anxiety & Depression Scale – Depression (-)
Murray et al. (2005) RCT (9) N_{Start}=123 N_{End}=69 TPS=Subacute	E: Sertraline (50-100mg/d, 26wk) C: Placebo Duration: 26wks	• Montgomery-Asberg Depression Rating Scale (-) • Barthel Index (-) • Clinical Global Impressions Scale – Severity (-) • Clinical Global Impressions Scale – Improvement (-) • Emotional Distress Scale (-) • Visual Analog Quality of Life Scale (+exp)
Rasmussen et al. (2003) RCT (7) N_{Start}=137 N_{End}=67 TPS=Acute	E: Sertraline (50mg/d) C: Placebo Duration: 1yr	• Hamilton Depression Rating Scale (+exp) • Geriatric Depression Scale (+exp) • Clinical Global Impression – Severity (-) • Clinical Global Impression – Improvement (-)
Burns et al. (1999) RCT (7) N_{Start}=28 N_{End}=24 TPS= Chronic	E: Sertraline (50mg/d, 8wk) C: Placebo Duration: 8wks	• Crying frequency (+) • Emotional Lability Questionnaire (+) • Clinician impression of change (+) • Montgomery-Asberg Depression Rating Scale (-) • Barthel Index (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about selective serotonin reuptake inhibitors

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Escitalopram/citalopram** may produce greater improvements in post-stroke depression than **a placebo.**	4	Kim et al., 2017; Robinson et al., 2008b; Andersen et al., 1994; Andersen et al., 1993
1a	There is conflicting evidence about the use of **fluoxetine** for improving post-stroke depression when compared to **a placebo or no medication**.	9	Chollet et al., 2006; Choi-Kwon et al., 2006; Fruehwald et al., 2003; Narushima et al., 2002; Robinson et al., 2000; Wiart et al., 2000; Dam et al., 1996; Gonzalez-Torrescillas et al., 1995; Brown et al., 1998
1a	**Sertraline** may not have a difference in efficacy when compared to **a placebo** for improving post-stroke depression.	4	Almeida et al., 2006; Murray et al., 2005; Rasmussen et al., 2003; Burns et al., 1999

ANXIETY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Fluoxetine** may not have a difference in efficacy when compared to **a placebo or no medication** for improving post-stroke anxiety.	1	Robinson et al., 2000

MOOD COFACTORS			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Escitalopram/citalopram** may produce greater improvements in anger than **a placebo.**	1	Kim et al., 2017
1b	**Fluoxetine** may produce greater improvements in anger than **a placebo or no medication.**	1	Choi-Kwon et al., 2006

EMOTIONAL LABILITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Escitalopram/citalopram** may produce greater improvements in emotional lability than **a placebo.**	2	Kim et al., 2017; Andersen et al., 1993
1a	**Fluoxetine** may produce greater improvements in emotional lability than **a placebo.**	2	Choi-Kwon et al., 2006; Brown et al., 1998
1a	There is conflicting evidence about the use of **sertraline** for improving emotional lability when compared to **a placebo**.	2	Murray et al., 2005; Burns et al., 1999

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Escitalopram/citalopram** may produce greater improvements in activities of daily living than **a placebo.**	2	Kim et al., 2017; Robinson et al., 2008b

1a	**Fluoxetine** may not have a difference in efficacy when compared to **a placebo or no medication** for improving activities of daily living.	5	Fruehwald et al., 2003; Robinson et al., 2000; Wiart et al., 2000; Dam et al., 1996; Gonzalez-Torrescillas et al., 1995
1a	**Sertraline** may not have a difference in efficacy when compared to **a placebo** for improving activities of daily living.	2	Murray et al., 2005; Burns et al., 1999

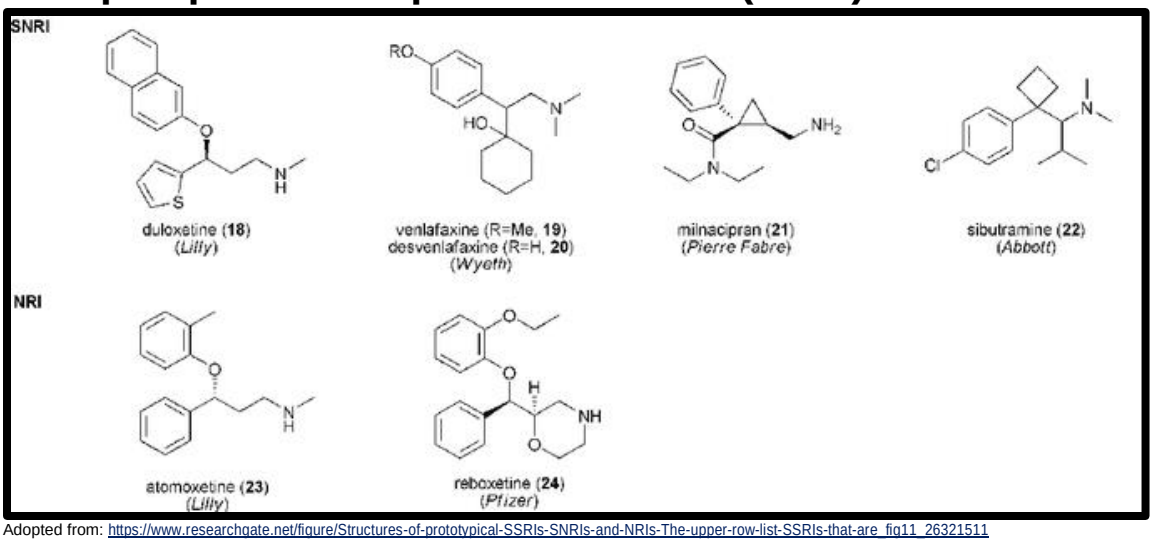
QUALITY OF LIFE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Escitalopram/citalopram** may not have a difference in efficacy when compared to **a placebo** for improving quality of life.	1	Kim et al., 2017
1b	**Sertraline** may not have a difference in efficacy when compared to **a placebo** for improving quality of life.	1	Murray et al., 2005

Key Points

Escitalopram or citalopram may be beneficial for improving post-stroke depression, anger, emotional lability and activities of daily living.

The literature is mixed concerning the efficacy of fluoxetine for post-stroke depression.

Norepinephrine Reuptake Inhibitors (NRIs)



Adopted from: https://www.researchgate.net/figure/Structures-of-prototypical-SSRIs-SNRIs-and-NRIs-The-upper-row-list-SSRIs-that-are_fig11_26321511

Serotonin- norepinephrine reuptake inhibitors (SNRI), and norepinephrine reuptake inhibitors (NRI), are reuptake channel inhibitors with specificity to norepinephrine (and in some cases serotonin as well). Norepinephrine acts on the sympathetic nervous system to increase attention, energy, and prepare the body physiologically for the 'flight or fight' response. Patients suffering from depression characterized by lethargy, anergia, hypokinesis, and hypomimia are said to be suffering from a retarded depression (Rampello et al. 2005). Selective norepinephrine reuptake inhibitors (NRIs) are proposed as an alternative to SSRIs for individuals experiencing such depression.

Three RCTs looked at an SNRI compared to a placebo or no medication for improving post-stroke depression (Zhang et al. 2013; Tsai et al. 2011; Rampello et al. 2005).

The methodological details and results of all three RCTs are presented in Table 2.

Table 2. RCTs evaluating SNRI antidepressants for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
SNRIs vs placebo		
Rampello et al. (2005) RCT (8) N_{Start}=31 N_{End}=31 TPS=Subacute	E: Reboxetine (4mg, 2x/d) C: Placebo Duration: 16wks	• Hamilton Depression Rating Scale (+exp) • Beck Depression Inventory (+exp)
Tsai et al. (2011) RCT (8) N_{Start}=92 N_{End}=56 TPS=Acute	E: Milnacipran (SNRI) (50-100mg/d) C: Placebo Duration: 1yr	• Incidence of Depression (+exp)

Zhang et al. (2013)
RCT (7)
N_{Start}=118
N_{End}=95
TPS=Acute
	E: Duloxetine (SNRI) (30-90mg/d)
	C: No medication
	Duration: 12wks
		• Incidence of Depression (+exp)
		• Hamilton Depression Rating Scale (+exp)
		• Chinese Activities of Daily Living (+exp)
		• SF-36
		  • Physical Function (+exp)
		  • Role-physical
		  • Bodily Pain
		  • General Health (+exp)
		  • Vitality
		  • Social Functioning
		  • Role-emotional (+exp)
		  • Mental Health (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about SNRIs

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Norepinephrine reuptake inhibitors** may produce greater improvements in alleviating post-stroke depression than **placebo or no medication**.	3	Zhang et al. 2013; Tsai et al. 2011; Rampello et al. 2005

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Norepinephrine reuptake inhibitors** may produce greater improvements in activities of daily living than **no medication**.	1	Zhang et al. 2013

QUALITY OF LIFE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the effect of **norepinephrine reuptake inhibitors** to improve quality of life when compared to **placebo or no medication**.	1	Zhang et al. 2013

Key Points

SNRIs may be beneficial for improving depression post stroke.

Heterocyclic Antidepressants

Adapted from: https://clearresultsdrugtest.com/detailed-drug-description/tricyclic-antidepressants-drug

Heterocyclic antidepressants may block the reuptake of both serotonin and norepinephrine to different degrees within the cerebrum, thereby increasing the levels of these neurotransmitters in the brain. Despite the risk profile associated with this class of medications, heterocyclic antidepressants have been reported to be used commonly for the treatment of depression in the elderly (Brown et al. 1995). Finklestein et al. (1987) conducted a retrospective review of 60 patients with PSD who received no pharmacotherapy or were treated with one of several cyclic antidepressant drugs (e.g. doxepine, maprotiline, trazadone, desipramine, amitriptyline, imipramine). It was found that only 17% of the untreated patients attained an improvement in depression scores compared to 40% of the drug responders. As well, drug responders showed a greater improvement in depression scores than nondrug responders or untreated patients. Despite being a retrospective study, Finklestein et al. (1987) demonstrated the potential value of cyclic antidepressants post stroke. In the aforementioned review by Xu et al. (2016), subgroup analysis of tricyclic antidepressants demonstrated a significant, large treatment effect in attenuating PSD.

Ten RCTs were found evaluating cyclic antidepressant compounds for mood disorders. Five RCTs compared nortriptyline to no treatment or a placebo (Narushima et al., 2002; Robinson et al. 2000; Gonzalez-Torrescillas et al., 1995; Robinson et al., 1993; Lipset et al., 1984), two of which also compared nortriptyline to fluoxetine (Robinson et al., 2000; Gonzalez-Torrescillas et al., 1995). Three RCTs compared a different cyclic compound to a placebo (Niedermajer et al., 2004; Palomäki et al., 1999; Dam et al., 1996), and one of these also compared it to fluoxetine (Dam et al., 1996). One RCT compared desipramine to trazodone, as well as those cyclic compounds to an SSRI (Miyai & Reding, 1998). One RCT compared 2 different combinations of cyclic antidepressants (Lauritzen et al., 1994).

The methodological details and results of all ten RCTs are presented in Table 3.

Table 3. RCTs evaluating heterocyclic antidepressants for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Nortriptyline vs placebo/no medication		
Narushima et al. (2002) RCT (8) N_{Start}=48 N_{End}=32 TPS=Subacute	E1: Fluoxetine (10-40mg/d) E2: Nortrirptyline (25-100mg/d) C: Placebo Duration: 3mo	E2 vs C • Incidence of Depressive Disorder (+exp2) • Hamilton Depression Rating Scale (+exp2)
Robinson et al. (2000) RCT (8) N_{Start}=56 N_{End}=40 TPS=Subacute	E1: Nortriptyline (25-100mg/d) E2: Fluoxetine (10-40mg/d) C: Placebo Duration: 12wks	E1 vs C • Hamilton Depression Rating Scale (+exp1) • Hamilton Anxiety rating Scale (-) • Functional Independence Measure (+exp1) • Johns Hopkins Functioning Inventory (-)
Gonzalez-Torrescillas et al. (1995) RCT (7) N_{Start}=130 N_{End}=125 TPS=Acute	E1: Nortriptyline (25-75mg/d) E2: Fluoxetine (20mg/d) C: No medication Duration: 6wks	E1 vs C • Beck Depression Inventory (+exp1) • Hamilton Depression Rating Scale (+exp1) • Montgomery-Asberg Depression Rating Scale (+exp1) • Barthel Index (+exp1) • Karnofksy's Performance Status Scale (+exp1)
Robinson et al. (1993) RCT (7) N_{Start}=82 N_{End}=81 TPS=Chronic	E: Nortriptyline (20-100mg/d, 6wk) C: Placebo Duration: 6wks	• Pathological Laughter & Crying Scale (+exp) • Hamilton Depression Rating Scale (+exp) • Present State Exam (+exp) • Johns Hopkins Functioning Inventory (-)
Lipsey et al. (1984) RCT (8) N_{Start}=39 N_{End}=34 TPS=Chronic	E: Nortriptyline (20-100mg/d) C: Placebo Duration: 4wks	• Hamilton Depression Rating Scale (+exp) • Zung Self-Rating Depression Scale (+exp) • Present State Examination (-)
Other cyclic antidepressants vs placebo/no medication		
Palomäki et al. (1999) RCT (8) N_{Start}=100 N_{End}=81 TPS=Acute	E: Mianserin (10-60mg/d) C: Placebo Duration: 1yr	• Major Depressive Disorder (-) • Hamilton Depression Rating Scale (-) • Beck Depression Inventory (-) • Clinical Global Impression – Severity (-) • Barthel Index (-)
Dam et al. (1996) RCT (7) N_{Start}=52 N_{End}=46 TPS=Subacute	E1: Maprotiline (150mg/d) E2: Fluoxetine (20mg/d) C: Placebo Duration: 3mo	E1 vs C • Hamilton Depression Rating Scale (-) • Barthel Index (-)
Niedermaier et al. (2004) RCT (5) N_{Start}=70 N_{End}=62 TPS=Acute	E: Mirtazapine (tetracyclic) (30-45mg/d) C: No medication Duration: 1yr	• Incidence of Depression (+exp) • Hamilton Depression Rating Scale (+exp)
Desipramine vs Trazodone		
Miyai & Reding (1998) RCT (6) N_{Start}=24 N_{End}=18 TPS=Subacute	E1: Desipramine (50-100mg/d) E2: Trazodone (50-100mg/d) E3: Fluoxetine (10-20mg/d) Duration: 4wks	E1 vs E2 • Functional Independence Measure (+exp2) • Hamilton Depression Rating Scale (-)
Cyclic antidepressant vs SSRI		

Robinson et al. (2000) RCT (8) N_{Start}=56 N_{End}=40 TPS=Subacute	E1: Nortriptyline (25-100mg/d) E2: Fluoxetine (10-40mg/d) C: Placebo Duration: 12wks	E1 vs E2 • Hamilton Depression Rating Scale (+exp1) • Hamilton Anxiety rating Scale (-) • Functional Independence Measure (+exp1) • Johns Hopkins Functioning Inventory (-)
Miyai & Reding (1998) RCT (6) N_{Start}=24 N_{End}=18 TPS=Subacute	E1: Desipramine (TCA) (50-100mg/d) E2: Trazodone (50-100mg/d) E3: Fluoxetine (10-20mg/d) Duration: 4wks	E1 vs E3 • Functional Independence Measure (+exp3) • Hamilton Depression Rating Scale (-) E2 vs E3 • Functional Independence Measure (-) • Hamilton Depression Rating Scale (-)
Dam et al. (1996) RCT (7) N_{Start}=52 N_{End}=46 TPS=Subacute	E1: Maprotiline (tetracyclic) (150mg/d) E2: Fluoxetine (20mg/d) C: Placebo Duration: 3mo	E1 vs E2 • Hamilton Depression Rating Scale (-) • Barthel Index (+exp2)
Gonzalez-Torrescillas et al. (1995) RCT (7) N_{Start}=130 N_{End}=125 TPS=Acute	E1: Nortriptyline (25-75mg/d) E2: Fluoxetine (20mg/d) C: No medication Duration: 6wks	E1 vs E2 • Beck Depression Inventory (-) • Hamilton Depression Rating Scale (-) • Montgomery-Asberg Depression Rating Scale (-) • Barthel Index (-) • Karnofksy's Performance Status Scale (-)
Cyclic antidepressant combinations (mianserin + imipramine vs mianserin + desipramine)		
Lauritzen et al. (1994) RCT (7) N_{Start}=20 N_{End}=15 TPS=Subacute	E1: Mianserin (10mg/d) + Imipramine (25-75mg/d) E2: Mianserin tetra (10mg/d) + Desipramine (25-75mg/d) Duration: 6wks	• Bech-Rafaelsen Melancholia Scale (+exp1) • Hamilton Depression Rating Scale (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about heterocyclic antidepressants

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Nortriptyline** may produce greater improvements in post-stroke depression than **a placebo**.	5	Narushima et al., 2002; Robinson et al. 2000; Gonzalez-Torrescillas et al., 1995; Lipset et al., 1984
1a	**Other cyclic antidepressants** may not have a difference in efficacy compared to **a placebo** for improving post-stroke depression.	3	Niedermajer et al., 2004; Palomäki et al., 1999; Dam et al., 1996
1a	**Cyclic antidepressants** may not have a difference in efficacy compared to **SSRIs** for improving post-stroke depression.	4	Robinson et al. 2000; Miyai & Reding, 1998; Dam et al., 1996; Gonzalez-Torrescillas et al., 1995
1b	**Desipramine** may not have a difference in efficacy compared to **trazodone** for improving post-stroke depression.	1	Miyai & Reding, 1998
1b	**Mianserin with imipramine** may not have a difference in efficacy compared to **mianserin with desipramine** for improving post-stroke depression.	1	Lauritzen et al., 1994

ANXIETY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Nortriptyline** may not have a difference in efficacy compared to **a placebo** for improving post-stroke anxiety.	1	Robinson et al., 2000
1b	**Cyclic antidepressants** may not have a difference in efficacy compared to **SSRIs** for improving post-stroke anxiety.	1	Robinson et al., 2000

EMOTIONAL LABILITY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Nortriptyline** may produce greater improvements in emotional lability than **a placebo or no medication.**	1	Robinson et al., 1993

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Other cyclic antidepressants** may not have a difference in efficacy compared to **a placebo** for improving activities of daily living.	2	Palomäki et al., 1999; Dam et al., 1996
1a	There is conflicting evidence about the use of **nortriptyline** for improving activities of daily living when compared to **a placebo or not medication**.	5	Narushima et al., 2002; Robinson et al. 2000; Gonzalez-Torrescillas et al., 1995; Robinson et al., 1993 Lipset et al., 1984
1a	There is conflicting evidence about the use of **cyclic antidepressants** for improving activities of daily living when compared to **SSRIs**.	4	Robinson et al. 2000; Miyai & Reding, 1998; Dam et al., 1996; Gonzalez-Torrescillas et al., 1995
1b	**Trazodone** may produce greater improvements in activities of daily living than **desipramine**.	1	Miyai & Reding, 1998

Key Points

Nortriptyline may be beneficial for improving post-stroke depression.

The literature is mixed concerning heterocyclic antidepressants ability to improve activities of daily living.

Monoamine Oxidase Inhibitors (MAOi)

	MAO-A	MAO-B
Substrates	Serotonin Norepinephrine Dopamine Tyramine	Dopamine Phenylethylamine
Tissue localization	Brain, gut, liver, placenta, skin	Brain, platelets, lymphocytes

Adapted from: https://www.mdedge.com/node/153015/path_term/48404

Monoamine oxidase (MAO) is the enzyme responsible for breaking down dopamine, noradrenaline and serotonin. MAO-A and MAO-B. MAO-A preferentially deaminates serotonin, epinephrine, norepinephrine, dopamine, and tyramine, while MAO-B primarily deaminates dopamine. MAO inhibitors have been proposed as a treatment for atypical depression, when more traditional classes of antidepressants have failed. By administering an inhibitor, greater concentrations of these neurotransmitters persist in the synapse and contribute to a greater signal strength. Over a period of several weeks this change in concentration will induce receptor-mediated pre and post synaptic changes, which are believed to have the anti-depressive effect seen with MAO inhibitors (Fiedorowicz & Swartz, 2007).

One RCT looked at MAO compared to placebo for improving post-stroke depression (Bartolo et al. 2015).

The methodological details and results of the single RCT are presented in Table 4.

Table 4. RCTs evaluating monoamine oxidase inhibitors for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Bartolo et al. (2015) RCT (5) N_{Start}=47 N_{End}=44 TPS=Acute	E: Selegiline (10mg/d) C: Placebo Duration: 6wks	• Hamilton Depression Rating Scale (-) • Functional Independence Measure (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about MAO inhibitors

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**MAO** may not have a difference in efficacy when compared to **a placebo** for improving post-stroke depression.	1	Bartolo et al. 2015

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**MAO** may not have a difference in efficacy when compared to **a placebo** for improving post-stroke activities of daily living.	1	Bartolo et al. 2015

Key Points

MAO inhibitors may not be beneficial for improving post-stroke depression

Methylphenidate

Adapted from: https://www.buymedstoday.com/product/ritalin-sr/

Methylphenidate, a psychostimulant approved for treating attention-deficit disorders, has also been used in the treatment of depression in the elderly as an alternative to other antidepressants. Depression in the elderly has been described as a "lack of interest and emotional involvement in one's surroundings", and psychostimulants have shown to be effective in treating such symptoms (Johnson et al. 1992). Methylphenidate has its effects in the cortical and subcortical areas of the brain. It is believed to heighten mood by affecting several neurotransmitter systems. It primarily acts as a dopamine and norepinephrine reuptake inhibitor. Thus, methylphenidate may affect PSD by 'correcting' the depletion of biogenic amines caused by stroke (Johnson et al. 1992).

One RCT looked at methylphenidate compared to placebo to improve post-stroke depression (Grade et al. 1998).

The methodological details and results of the single RCT are presented in Table 5.

Table 5. RCTs evaluating methylphenidate for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Grade et al. (1998) RCT (7) N_{Start}=21 N_{End}=19 TPS=Acute	E: Methylphenidate (15mg, 2x/d) C: Placebo Duration: 3wks	• Hamilton Depression Rating Scale (+) • Zung Self-Rating Depression Scale (-) • Modified Funcitonal Independence Measure (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about methylphenidate

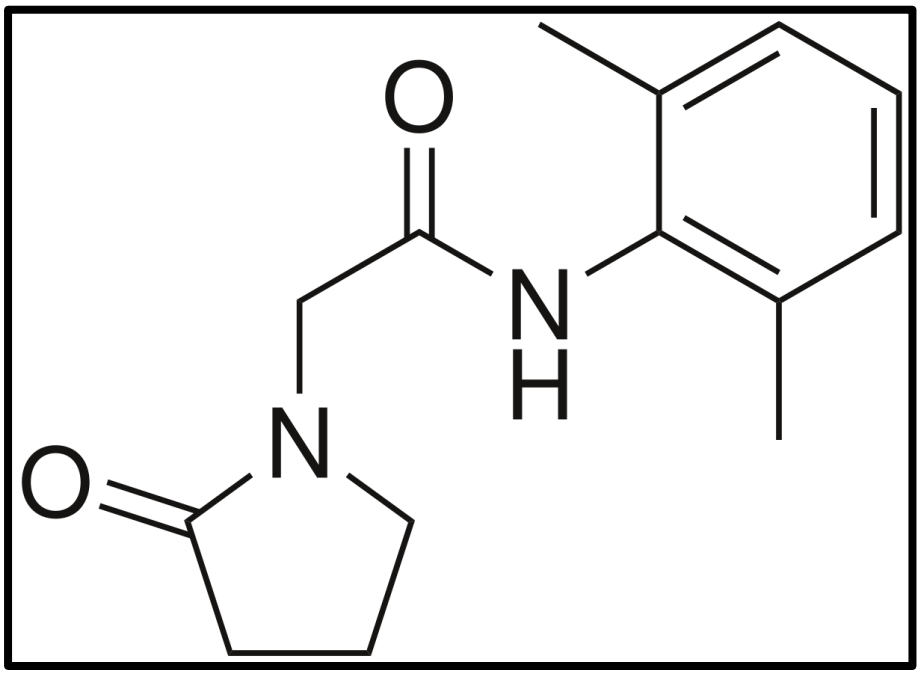
DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the effect of **methylphenidate** to improve post-stroke depression when compared to **a placebo**.	1	Grade et al. 1998

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Methylphenidate** may produce greater improvements in activities of daily living than **a placebo.**	1	Grade et al. 1998

Key Points

Methylphenidate may be beneficial for improving activities of daily living

Nefiracetam



Adapted from: https://en.wikipedia.org/wiki/Nefiracetam

In the past, the GABBAergic system has been clearly linked to anxiety, but its role in depression is less clear (Cryan & Slattery, 2010). Absence of GABA receptors in rodent models will produce antidepressant-like behaviour. Nefiracetam is a novel cyclic gamma aminobutyric acid (GABA) compound with documented effects on neurotransmission, regional blood flow, and glucose utilization. It is often sold as a nootropic compound. It has the ability to potentiate GABA signalling when GABA is in low concentrations, and supress signalling when GABA is in high concentration (Huang et al. 1996). Based on studies in rat neurons it is believed that nefiracetam may inhibit the Gi or Go subunits of the GABA signalling mechanism, or PKA, which in turn inhibits cAMP levels from rising as it normally would to supress GABA induced currents through a negative feedback loop (Cryan & Slattery, 2010). In addition, the GABA(b) receptor system has shown a significant interaction with serotonergic signalling and neurotrophic factors (eg. BDNF) (Cryan & Slattery, 2010). Consequently, although its exact mechanism of action is not yet fully understood there are a number of ways nefiracetam could help ameliorate depressive symptoms post-stroke.

Two RCTs looked at nefiracetam for improving mood post-stroke. Both compared nefiracetam to a placebo (Starkstein et al. 2016; Robinson et al. 2008a).

The methodological details and results of the two RCTs are presented in Table 6.

Table 6. RCTs evaluating nefiracetam for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Starkstein et al. (2016) RCT (8) N_{Start}=13 N_{End}=8 TPS=Subacute	E: Nefiracetam (450mg/d) C: Placebo Duration: 12wks	• Patient Health Questionnaire 9 (-) • Apathy Scale (-) • Barthel Index (-) • EuroQol-5D (-)
Robinson et al. (2008a) RCT (8) N_{Start}=159 N_{End}=139 TPS=Subacute	E1: Nefiracetam (600mg, 2x/d) E2: Nefiracetam (900mg, 2x/d) C: Placebo Duration: 12wks	E1 vs E2 vs C • Hamilton Depression Rating Scale (-) • Beck Depression Inventory (-) • Functional Independence Measure (-) • Apathy Scale (exp2)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about nefiracetam

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Nefiracetam** may not have a difference in efficacy when compared to **a placebo** for improving post-stroke depression.	2	Starkstein et al. 2016; Robinson et al. 2008a

MOOD COFACTORS			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the effect of **nefiracetam** to improve apathy when compared to **a placebo**.	1	Starkstein et al. 2016

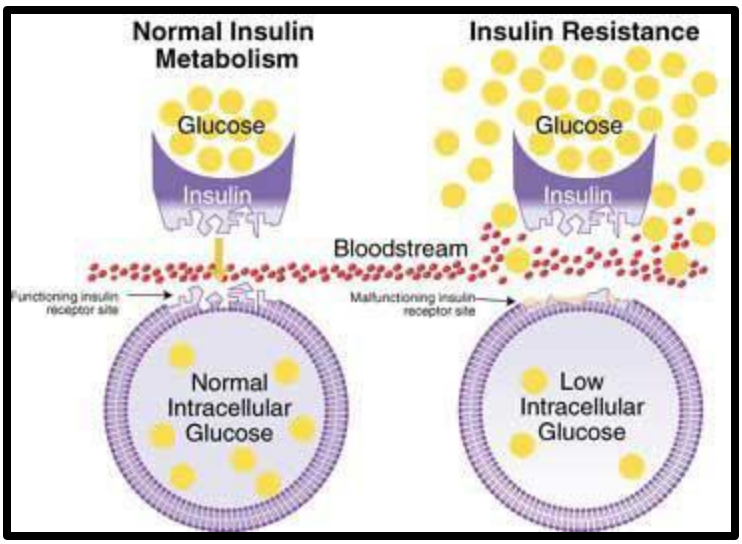
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Nefiracetam** may not have a difference in efficacy when compared to **a placebo** for improving activities of daily living.	1	Starkstein et al. 2016

QUALITY OF LIFE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Nefiracetam** may not have a difference in efficacy when compared to **a placebo** for improving quality of life.	1	Murray et al., 2005

Key Points

Nefiracetam may not be beneficial for improving mood related outcomes post-stroke.

Antidiabetics



Adapted from: https://commons.wikimedia.org/wiki/File:Insulinresistance.jpg

Antidiabetic medications, such as metformin and pioglitazone, are used to lower blood glucose levels in individuals with type II diabetes mellitus (T2DM). These are what are referred to as insulin sensitizers, and do not directly replace insulin the body but seek to make it a more effective signalling molecule. There is strong evidence to support that insulin resistance plays a role in cognitive decline (Ng et al. 2014). Therefore, insulin sensitizers could have a neuroprotective effect. Recent trials have found that pioglitazone was also associated with reduced depression in these individuals (Kashani et al. 2013; Kemp et al. 2012; Sepanjnia et al. 2012).

One RCT looked at pioglitazone with fluoxetine compared to metformin with fluoxetine for improving post-stroke depression (Hu et al. 2015).

The methodological details and results of the single RCT are presented in Table 7.

Table 7. RCTs evaluating insulin sensitizers for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Hu et al. (2015) RCT (5) N_{Start}=118 N_{End}=102 TPS=Subacute	E: Pioglitazone + Fluoxetine C: Metformin + Fluoxetine Duration: 3mo	• Hamilton Depression Rating Scale (+exp) • Activities of Daily Living (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Pioglitazone and Metformin

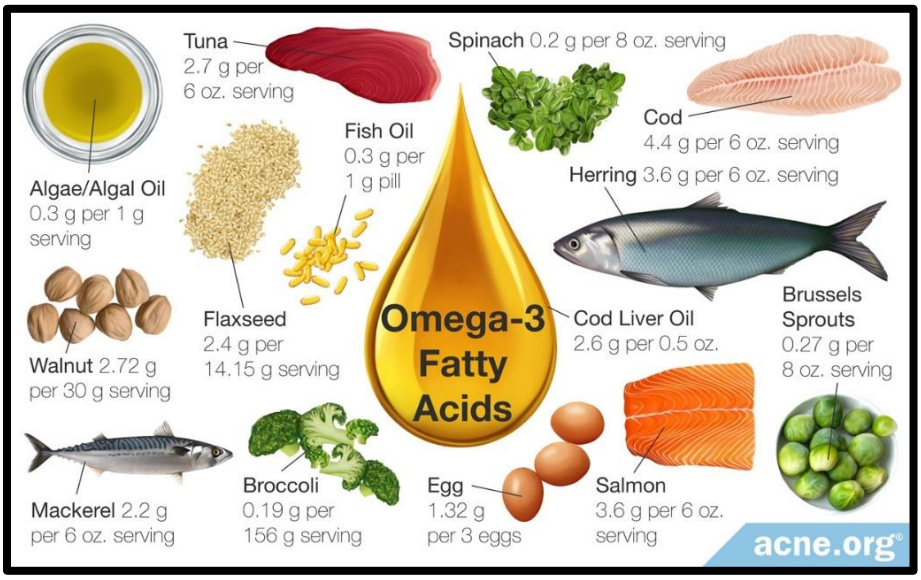
DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Pioglitazone with fluoxetine** may produced greater improvements in alleviating post-stroke depression when compared to **metformin with fluoxetine**.	1	Hu et al. 2015

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Pioglitazone with fluoxetine** may not have a difference in efficacy when compared to **metformin with fluoxetine** for improving activities of daily living.	1	Hu et al. 2015

Key Points

Pioglitazone with fluoxetine may improve post-stroke depression more than metformin with fluoxetine, but not activities of daily living

Omega-3 Supplementation



Adapted from: https://www.acne.org/omega-3-fatty-acids-and-acne.html

There has been considerable debate regarding the possible association between omega-3 polyunsaturated fatty acids (PUFAs) and depressive disorders. Hibbeln (1998) proposed a simple, correlational model demonstrating an inverse association between fish consumption and prevalence of major depression based on the results of a multinational study. While some subsequent trials provided support for such an association, other studies have shown no association between omega-3 PUFAs and depression. In a recent meta-analysis, Appleton et al. (2010) identified 35 RCTs evaluating the impact of omega-3 PUFAs on depressive symptomatology. A pooled analysis of 29 trials demonstrated a significant treatment effect in favour of the supplement but appeared to be limited to trials enrolling individuals with a diagnosed depressive disorder; the analysis also demonstrated significant heterogeneity. None of the trials in the aforementioned meta-analysis were conducted in the stroke population.

One RCT was found evaluating omega-3 fish oils for mood disorders. It compared fish oil capsules to a placebo (Poppit et al. 2009).

The methodological details and results of the single RCT are presented in Table 8**.**

Table 8. RCTs evaluating omega-3 for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Poppit et al. (2009) RCT (9) N_{Start}=102 N_{End}=95 TPS=Chronic	E: Fish oil capsules C: Placebo Duration: 12wks	• General Health Questionnaire-28 (+exp) a. Anxiety and Insomnia (-) b. Depression (-) • SF-36 (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about omega-3 supplementation

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Omega-3 supplements** may not have a difference in efficacy compared to **a placebo** for improving post-stroke depression.	1	Poppit et al., 2009

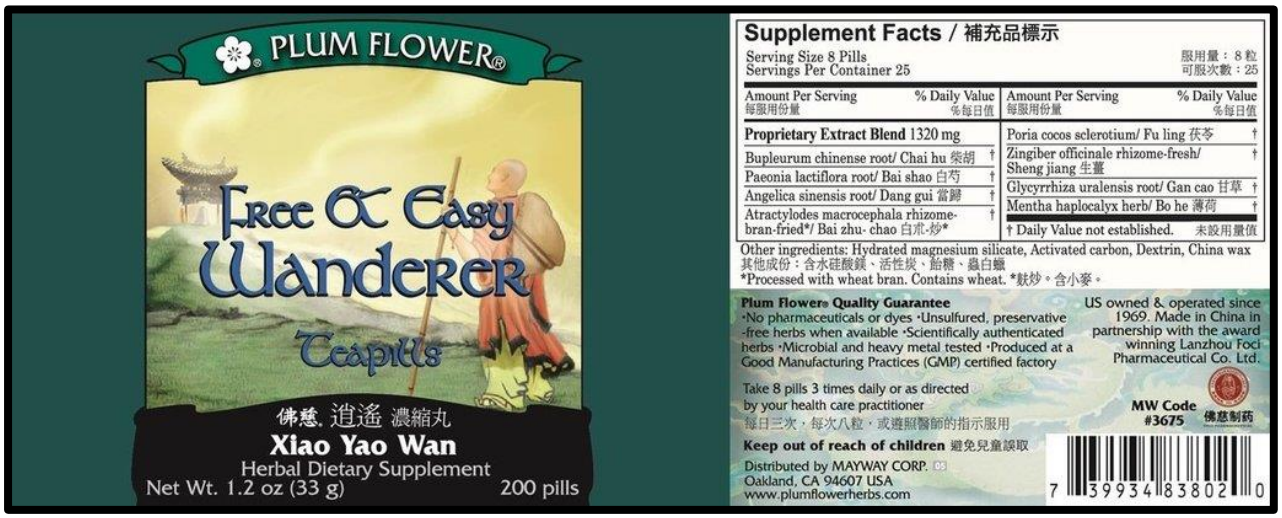
ANXIETY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Omega-3 supplements** may not have a difference in efficacy compared to **a placebo** for improving post-stroke anxiety.	1	Poppit et al., 2009

QUALITY OF LIFE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Omega-3 supplements** may not have a difference in efficacy compared to **a placebo** for improving quality of life.	1	Poppit et al., 2009

Key Points

Omega-3 supplementation may not be beneficial for improving depression, post-stroke anxiety or quality of life post-stroke.

Chinese Herbal Medicine



Adapted from: https://www.chineseherbsdirect.com/products/free-easy-wanderer-xiao-yao-wan-200-ct-plum-flower

Given concerns regarding potential side effects of antidepressants, individuals with depression may choose to self-medicate with alternative medicines, namely herbal products (Davidson & Zhang, 2008). The Chinese preparation Free and Easy Wanderer Plus (FEWP) is a combination of 11 herbal drugs that is used for the treatment of mood disorders. A recent RCT demonstrated that treatment with a standardized preparation of FEWP in individuals with depression was associated with greater reduction of depressive symptoms and higher clinical response rates when compared to placebo (Zhang et al. 2007).

One RCT looked at the Free and Easy Wanderer Plus compared to placebo and fluoxetine for improving post-stroke depression (Li et al. 2008).

The methodological details and results of the single RCT are presented in Table 9.

Table 9. RCTs evaluating free and easy wandered herbal medicine for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Li et al. (2008) RCT (8) N_{Start}=150 N_{End}=146 TPS=Subacute	E1: Free and Easy Wanderer Plus (36mg/d) E2: Fluoxetine (20-40mg/d) C: Placebo Duration: 8wks	E1 vs C • Hamilton Depression Rating Scale (+exp1) • Barthel Index (+exp1) E2 vs C • Hamilton Depression Rating Scale (+exp2) • Barthel Index (+exp2) E1 vs E2 • Hamilton Depression Rating Scale (-) • Barthel Index (+exp2)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Free and Easy Wanderer Plus

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Free and Easy Wander Plus** may produced greater improvements in alleviating post-stroke depression when compared to **a placebo**.	1	Li et al. 2008
1b	**Free and Easy Wander Plus** may not have a difference in efficacy when compared to **fluoxetine** for improving post-stroke depression.	1	Li et al. 2008

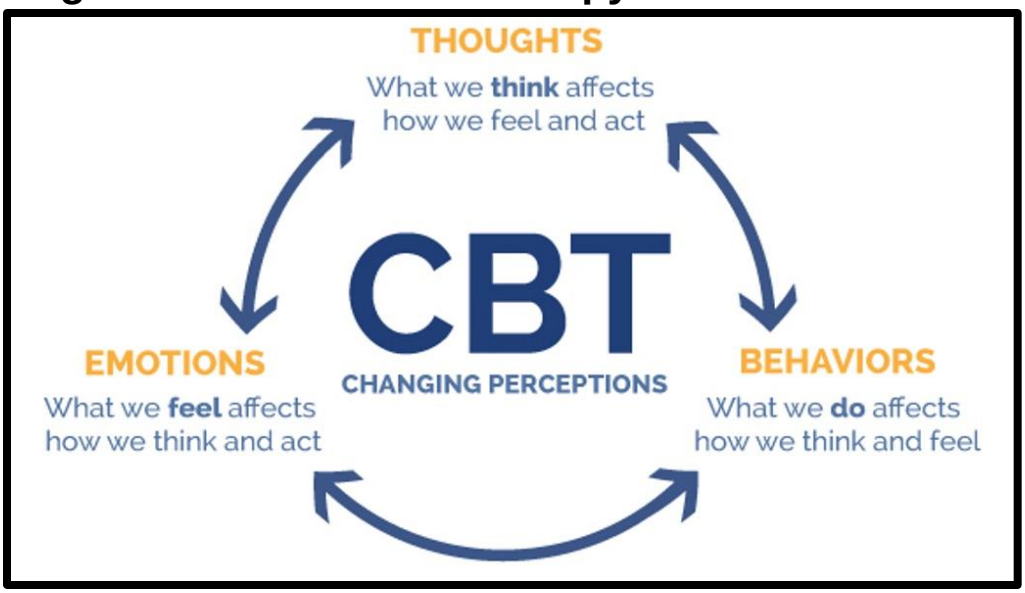
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Free and Easy Wander Plus** may produced greater improvements in activities of daily living when compared to **a placebo**.	1	Li et al. 2008
1b	**Fluoxetine** may produced greater improvements in activities of daily living when compared to **Free and Easy Wander Plus**.	1	Li et al. 2008

Key Points

Free and Easy Wander Plus may be beneficial for improving post-stroke depression and activities of daily living

Non-Pharmacologic Treatment of Post-Stroke Depression

Cognitive Behavioural Therapy



Adopted from: https://ksr-ugc.imgix.net/assets/020/753/289/40f8b80e1e9855cdd5a5cd87e1be0c5a_original.jpg?ixlib=rb-2.1.0&crop=faces&w=1024&h=576&fit=crop&v=1522698415&auto=format&frame=1&q=92&s=405b7286a751d765922b759cf91aa5e4

Cognitive behavioural therapy (CBT) has been well established as an effective intervention for depression and numerous other psychological disorders. It is founded on the notion that our thoughts affect our emotions and behaviours; whereby, dysfunctional thoughts lead to negative emotions and negative behaviours. Therefore, the aim of CBT is to evaluate, challenge and modify dysfunctional thoughts, through cognitive restructuring, to promote behavioural change and improve functioning. A psychoeducational approach is often utilized to teach individuals new ways of coping with stressful situations; however, emphasis is placed on homework assignments and activities completed outside of the therapy session (Cuijpers et al. 2013).

In a meta analysis, Cuijpers et al. (2013) identified 115 studies examining the effects of CBT on adult depression. They found that CBT is an effective treatment for adult depression; however, many of the studies were considerably poor in quality. Despite this, CBT remains the most researched form of psychotherapy for adult depression, in the general population.

Fourteen RCTs were found that evaluated CBT for improving post-stroke mood. Eight RCTs evaluated CBT compared to standard of care (Fang et al. 2017; Kirkness et al. 2017; Visser et al. 2016; Hadidi et al. 2015; Hoffman et al. 2015; Thomas et al. 2013; Chang et al. 2011; Lincoln et al. 2003). Two RCTs compared CBT to computerized cognitive training (Kookter et al. 2017; Simblett et al. 2017). One RCT compared CBT to psychoeducation (Olukolade et al. 2017). One RCT compared CBT to antidepressants (Gao et al. 2017). One RCT looked at the additive effect of CBT with antidepressants (Mitchell et al. 2009). One RCT compared motivational interviewing to standard care (Watkins et al., 2007).

The methodological details and results of these 14 RCTs are presented in Table 10.

Table 10. RCTs evaluating cognitive behavioural therapy for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Cognitive behavioural therapy vs standard care		
Fang et al. (2017) RCT (5) N_{start}=42 N_{Finish}=42 TPS=Acute	E: Constructive Integrative Psychosocial Intervention C: Standard Care Duration: 6mo	• Hospital Anxiety Depression Scale – depression (+exp) • Hospital Anxiety Depression Scale – anxiety (-)
Kirkness et al. 2017 RCT (7) N_{start}=100 N_{end}=91 TPS=Subacute	E: Telephone/In-person Psychosocial Therapy (30min, 1x/wk) C: Standard Therapy Duration: 6wks	• Hamilton Depression Rating Scale (-)
Visser et al. (2016) RCT (7) N_{Start}=166 N_{End}=151 TPS=Chronic	E: Problem-solving therapy C: Usual care Duration: 1.5h/wk for 8wk	• CES Depression Scale (-) • Coping Inventory for Stressful Situations (-) • Stroke-Specific Quality-of-Life Scale-12 (-) • EuroQol EQ-5D-5l (-)
Hadidi et al. (2015) RCT (7) N_{Start}=22 N_{End}=22 TPS=Acute	E: Problem-solving therapy C: Usual care Duration: 1.5h/wk for 10wk	• CES Depression Scale (-) • Functional Independence Measure (-)
Hoffmann et al. (2015) RCT (6) N_{Start}=36 N_{End}=33 TPS=Not reported	E1: Coping skills therapy E2: Self-management C: Usual care Duration: 1hr/wk for 8 wk	E1 vs C • Hospital Anxiety Depression Scale – Anxiety (-) • Hospital Anxiety Depression Scale – Depression (+exp) • Montgomery-Asberg Depression Rating Scale (-) • Nottingham Extended Activities of Daily Living Scale (-) • Stroke and Aphasia Quality of Life Scale (-) • Modified Barthel Index (-) E2 vs C • Hospital Anxiety Depression Scale – Anxiety (-) • Hospital Anxiety Depression Scale – Depression (-) • Montgomery-Asberg Depression Rating Scale (-) • Nottingham Extended Activities of Daily Living Scale (-) • Stroke and Aphasia Quality of Life Scale (-) • Modified Barthel Index (-)

Thomas et al. (2013) RCT (7) N_{Start}=105 N_{End}=89 TPS=Not reported	E: Behavioural therapy (aphasic) C: Usual care Duration: 20, 1h sessions over 3mo	• Stroke Aphasic Depression Questionnaire (+exp) • Visual Analogue Self-Esteem Scale (+exp) • Visual Analogue Mood Scale - Sad (+exp) • Nottingham Leisure Questionnaire (-)
Chang et al. (2011) RCT (7) N_{Start}=77 N_{End}=66 TPS=Subacute	E: Knowledge & behaviour therapy C: Usual care Duration:1-2hr/wk for 1mo	• Hamilton Depression Rating Scale (+exp) • State-Trait Anger Expression Inventory (+exp) • Hamilton Anxiety Scale (-) • Stroke-Specific Quality-of-Life Scale (+exp) • Barthel Index (+exp) •
Lincoln et al. (2003) RCT (7) N_{Start}=123 N_{End}=111 TPS=Subacute	E: Cognitive behavioural therapy C1: Attention placebo C2: Usual care Duration: 10, 1h sessions over 3mo	• Beck Depression Inventory (-) • Wakefield Depression Inventory (-) • Extended Activities of Daily Living Scale (-) • London Handicap Scale (-)
Cognitive behavioural therapy vs computer cognitive training		
Kootker et al. 2017 RCT (4) N_{start}=61 N_{end}=44 TPS=Subacute	E: Cognitive Behavioral Therapy (CBT) C: Computer Cognitive Training (CCT) Duration: 13-16 sessions (1hr, 2x/wk)	• Hospital Anxiety and Depression Scale – Depression (-) • Hospital Anxiety and Depression Scale – Anxiety (-) • Post Stroke Depression Rating Scale (-) • Stroke Specific Quality of Life Scale (-)
Simblett et al. 2017 RCT (5) N_{start}=28 N_{end}=25 TPS=Chronic	E: Computerized Cognitive Behavioural Therapy (cCBT) C: Computerized Cognitive Remediation Therapy (cCRT) Duration: 1hr, 1x/wk 8 wks	• Beck Depression Inventory (-) • Beck Anxiety Inventory (-) • Nottingham Extended Activities of Daily Living (-)
Cognitive behavioural therapy vs psychoeducation		
Olukolade et al. 2017 RCT (6) N_{start}=30 N_{end}=30 TPS=NR	E1: Cognitive Rehab Therapy (1hr, 1x/wk) E2: Psychoeducation Therapy (1hr, 1x/wk) C: Standard Care Duration: 3.5mo, 9 sessions	E1 vs E2,C • Beck Depression Inventory (+exp1)
Cognitive behavioural therapy vs antidepressants		
Gao et al. (2017) RCT (7) N_{Start}=274 N_{End}=258 TPS= Variable	E1: Placebos and participated in general discussions E2: citalopram and participated in general discussions E3: placebos and underwent cognitive behavioural therapy Duration: 3mo	E1 vs E2 • Bech-Rafaelsen Melancholia Scale (+exp2) • Hamilton Depression Scale (-) • Barthel Index (-) • Functional Independence Measure (-) E1 vs E3 • Bech-Rafaelsen Melancholia Scale (-) • Hamilton Depression Scale (-) • Barthel Index (-) • Functional Independence Measure (-)
Cognitive behavioural therapy with antidepressants vs usual care		
Mitchell et al. (2009) RCT (7) N_{Start}=101	E: Psychosocial-behavioural intervention + Antidepressants C: Usual care + Antidepressants	• Hamilton Depression Rating Scale (+exp)

N_{End}=92 TPS=Subacute	Duration: 9 sessions over 8wk	
Motivational interviewing vs usual care		
Watkins et al. (2007) Watkins et al. (2011) RCT (7) N_{Start}=411 N_{End}=340 TPS=Chronic	E: Motivational interviewing C: Usual care Duration: 1mo	• General Health Questionnaire 28 (+exp) • Yale Self-Report Screening Tool (+exp) • Barthel Index (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
$+exp_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about cognitive behavioural therapy

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **cognitive behavioural therapy** to improve post-stroke depression when compared to **standard care**.	8	Fang et al. 2017; Kirkness et al. 2017; Visser et al. 2016; Hadidi et al. 2015; Hoffman et al. 2015; Thomas et al. 2013; Chang et al. 2011; Lincoln et al. 2003
2	**Cognitive behavioural therapy** may not have a difference in efficacy when compared to **standard care** for improving depression.	2	Kookter et al. 2017; Simblett et al. 2017
1b	**Cognitive behavioural therapy with antidepressants** may produce greater improvements in alleviating post-stroke depression than **usual care with antidepressants**.	1	Mitchell et al. 2009
1b	**Motivational interviewing** may produce greater improvements in alleviating post-stroke depression than **usual care**.	1	Watkins et al. 2007

ANXIETY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Cognitive behavioural therapy** may not have a difference in efficacy when compared to **standard care** for improving post-stroke anxiety.	4	Fang et al. 2017; Visser et al. 2016; Hoffman et al. 2015; Chang et al. 2011
2	**Cognitive behavioural therapy** may not have a difference in efficacy when compared to **computerized cognitive training** for post-stroke anxiety.	2	Kookter et al. 2017; Simblett et al. 2017

MOOD COFACTORS			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Cognitive behavioural therapy** may not have a difference in efficacy when compared to **standard care** for improving coping.	1	Visser et al., 2016
1b	**Cognitive behavioural therapy** may produce greater improvements in self-esteem than **usual care**.	1	Thomas et al., 2013
1b	**Motivational interviewing** may produce greater improvements in mental health than **usual care**.	1	Watkins et al. 2007

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Cognitive behavioural therapy** may not have a difference in efficacy when compared to **usual care** for improving activities of daily living.	5	Hadidi et al. 2015; Hoffman et al. 2015; Thomas et al. 2013; Chang et al. 2011; Lincoln et al. 2003

2	**Cognitive behavioural therapy** may not have a difference in efficacy when compared to **computerized cognitive training** for improving activities of daily living.	1	Simblett et al. 2017
1b	**Motivational interviewing** may not have a difference in efficacy when compared to **usual care** for improving activities of daily living.	1	Watkins et al. 2007

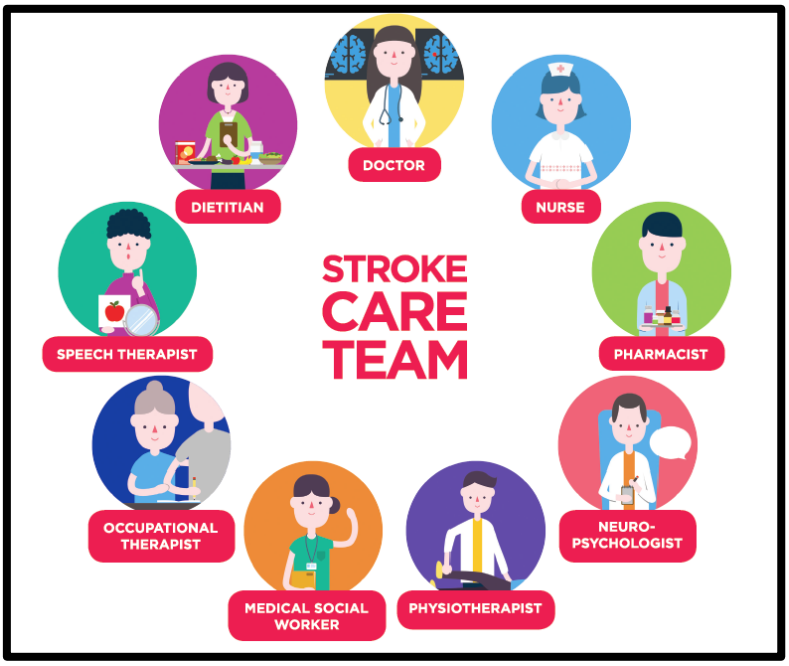
QUALITY OF LIFE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Cognitive behavioural therapy** may not have a difference in efficacy when compared to **standard care** for improving quality of life.	3	Visser et al. 2016; Hoffman et al. 2015; Chang et al. 2011
2	**Cognitive behavioural therapy** may not have a difference in efficacy when compared to **computerized cognitive training** for improving quality of life.	1	Kookter et al. 2017

Key Points

The literature is mixed regarding the effectiveness of CBT for improving post-stroke depression.

CBT does not appear improve activities of daily living or quality of life.

Care Provision and Educational Resources



Adapted from: https://www.healthhub.sg/a-z/medical-and-care-facilities/69/stroke-admission-and-stroke-care-teams

Stroke rehabilitation is not the single responsibility of any one individual, but a collaborative effort between all members in a patient's circle of care. How that care is provided is a coordinated and targeted effort that requires planning, organisation and communication both between the patient and their caregivers, and among the caregivers themselves. How that care is delivered can take on any number of forms (education, home visits, weekly phone calls). The development of depression post-stroke may be influenced by the provision of regular contact, counselling, and support within various models of care. Therefore, some research has focused on which methods of provision and support can help ameliorate mood related disorders post-stroke.

Seventeen RCTs were found evaluating care provision methods for mood disorders. Nine RCTs examined comprehensive follow up and care-coordination interventions compared to standard care (Graven et al., 2016; Wong et al., 2015; Hackett et al., 2013; Rochette et al., 2013; Joubert et al., 2008; Williams et al., 2007; Joubert et al., 2006; Claiborne, 2006; Lincoln et al., 2003). Three RCTs examined home visit interventions compared to standard care, or educational programs (Ostwald et al., 2014; Drummond et al., 2013; Burton & Gibbon, 2005). Three RCTs examined a goal-setting structured therapy against standard care (Jones et al., 2016; Sackley et al., 2015; Alexopoulus et al., 2012). One RCT examined an instructional and education DVD compared to usual care (Jones et al., 2016). One RCT compared sexual counselling to usual care (Ng et al., 2017).

The methodological details and results of all 17 RCTs are presented in Table 11.

Table 11. RCTs evaluating care provisions for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Comprehensive patient follow-up and/or care coordination programs vs standard care		
Graven et al. (2016) RCT (10) N_{Start}=110 N_{End}=94 TPS=Subacute	E: Intensive follow up + Goal Setting C: Standard care Duration: 12mo	• Geriatric Depression Scale (+exp)
Wong et al. (2015) RCT (8) N_{Start}=108 N_{End}=99 TPS=Acute	E: Dedicated care coordination and follow up C: Standard care Duration: 4wk	• CES Depression Scale (+exp) • WHO Quality of Life, Spirituality, Religion and Personal Beliefs (+exp) • SF-36 (+exp) • Modified Barthel Index (-)
Hackett et al. (2013) RCT (7) N_{Start}=201 N_{End}=164 Duration: Acute	E: Personalized postcards C: No contact Duration: 5mo	• Hospital Anxiety & Depression Scale - Depression (-) • Hospital Anxiety & Depression Scale - Anxiety (-) • Patient Health Questionnaire 9 (-)
Rochette et al. (2013) RCT (7) N_{Start}=186 N_{End}=139 TPS=Acute	E: Weekly phone calls C: Provided with contact information Duration: 6mo	• Beck Depression Inventory II (-) • Euroqual-5D (-) • Quality of Life Index (-) • Assessment of Life Habits (-)
Joubert et al. (2008) RCT (4) N_{Start}=233 N_{End}=186 TPS=Acute Note: TIA as well as Stroke	E: Integrated care program C: Usual care Duration: 12mo	• Patient Health Questionnaire 9 (+exp) • Depressive symptoms (+exp)
Williams et al. (2007) RCT (8) N_{Start}=188 N_{End}=182 TPS=Subacute	E: Activate-Initiate-Monitor intervention C: Usual care Duration: 12wks	• Hamilton Depression Rating Scale (+exp) • PHQ-9 (+exp)
Joubert et al. (2006) RCT (4) N_{Start}=97 N_{End}=80 TPS=Acute Note: TIA as well as Stroke	E: Integrated care program C: Usual care Duration: 12mo	• Patient Health Questionnaire 9 (+exp)
Claiborne (2006) RCT (5) N_{Start}=28 N_{End}=28 TPS=Acute	E: Care coordination C: Usual Care Duration: 3mo	• Geriatric Depression Scale (+exp) • SF-36 – mental component scale (+exp) •
Lincoln et al. (2003a) RCT (5) N_{Start}=250 N_{End}=187 TPS=Acute	E: Family support service C: Usual Care Duration: 9mo	• General Health Questionnaire 12 (-) • Nottingham Extended Activities of Daily Living (-)
Home visits/follow up vs usual care		
Ostwald et al. (2014) RCT (5) N_{Start}=159	E: Home visits + Resource information C: Resource information (12mo) Duration: 6mo	• Geriatric Depression Scale (-) • SF-36 (+exp) • Perceived Stress Scale (-)

N_{End}=134 TPS=Acute, Subacute, Chronic		• Functional Independence Measure (-)
Drummond et al. (2013) RCT (6) N_{Start}=93 N_{End}=86 TPS=Acute	E: Pre-discharge home visit C: Pre-discharge hospital interview Duration: Single Visit	• Stroke Aphasic Depression Questionnaire 10 (+exp) • General Health Questionnaire 28 (-) • Nottingham Extended Activities of Daily Living (-) • Barthel Index (-)
Burton & Gibbon (2005) RCT (7) N_{Start}=176 N_{End}=128 TPS= Acute	E: Home visits C: No follow-up Duration: Variable, 0-12 months	• Beck Depression Inventory (-)
Goal setting structured therapy programs vs standard care or education program		
Jones et al. (2016) RCT (6) N_{Start}=78 N_{End}=66 TPS=Subacute	E: Self-management program C: Standard care Duration: 12wk	• Hospital & Anxiety Depression Scale - Depression (-) • Hospital & Anxiety Depression Scale - Anxiety (-) • Stroke and Aphasia Quality of Life Scale (-) • Nottingham Extended Activities of Daily Living Scale (-) • Medical Outcomes Trust's Short Form 12 (-)
Sackley et al. (2015) RCT (9) N_{Start}=1042 N_{End}=1003 TPS=Not reported Note: TIA, unknown etiology included w/ stroke, designed for care home individuals	E: ADL goal focused occupational therapy program C: Standard care Duration: 3mo	• Geriatric Depression Scale (-) • Barthel Index (-) • European Quality of life-5 Dimensions (-)
Alexopoulos et al. (2012) RCT (6) N_{Start}=24 N_{End}=24 TPS=Not reported	E: Ecosystem focused therapy C: Education program Duration:45min/wk, 12wk	• Hamilton Depression Rating Scale (-) • World Health Organization Disability Assessment Schedule II (+exp)
Education and instruction DVD vs standard care		
Jones et al. 2018 RCT (6) N_{start}=66 N_{end}=55 TPS=NR	E: Instructional/Educational DVD C: Standard care Duration: 6wks	• EuroQol-5D (-) • General Health Questionnaire – 28 (-) • Centre for Epidemiological Studies – Depression (-)
Sexual counselling vs standard care		
Ng et al. 2017 RCT(4) N_{start}=68 N_{finish}=51 TPS=Acute	E: Sexual counselling C: Standard care Duration: 30min, 1 session	• Depression Anxiety Stress Scale - Depression (-) • Depression Anxiety Stress Scale – Anxiety (-) • Depression Anxiety Stress Scale - Stress (-) • Functional Independence Measure (-) • Stroke and Aphasia Quality of Life Scale (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about care coordination and education therapy

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Care coordination and follow up** may produce greater improvements in alleviating post-stroke depression than **usual care**.	8	Graven et al., 2016; Wong et al., 2015; Hackett et al., 2013; Rochette et al., 2013; Joubert et al., 2008; Williams et al., 2007; Joubert et al., 2006; Claiborne, 2006
1a	**Home visits** may not have a difference in efficacy when compared to **standard care** for improving post-stroke depression.	3	Ostwald et al., 2014; Drummond et al., 2013; Burton & Gibbon, 2005
1a	**Goal setting structured therapy** may not have a difference in efficacy when compared to **standard care or education** for improving post-stroke depression.	3	Jones et al., 2016; Sackley et al., 2015: Alexopoulus et al., 2012
1b	**Educational/Instructional DVDs** may not have a difference in efficacy when compared to **usual care** for improving post-stroke depression.	1	Jones et al., 2018
2	**Sexual counselling** may not have a difference in efficacy when compared to **usual care** for improving post-stroke depression.	1	Ng et al., 2017

ANXIETY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Care coordination and follow up** may not have a difference in efficacy when compared to **standard care** for improving post-stroke anxiety.	1	Hackett et al., 2013
1b	**Goal setting structured therapy** may not have a difference in efficacy when compared to **standard care or education** for improving post-stroke anxiety.	1	Jones et al., 2016
2	**Sexual counselling** may not have a difference in efficacy when compared to **usual care** for improving post-stroke anxiety.	1	Ng et al., 2017

MOOD COFACTORS			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Care coordination and follow up** may not have a difference in efficacy when compared to **standard care** for improving mental health.	1	Lincoln et al., 2003
1b	**Home visits** may not have a difference in efficacy when compared to **standard care** for improving mental health, or stress.	2	Ostwald et al., 2014; Drummond et al., 2013
1b	**Educational/Instructional DVDs** may not have a difference in efficacy when compared to **usual care** for improving mental health.	1	Jones et al., 2018

2	**Sexual counselling** may not have a difference in efficacy when compared to **usual care** for improving stress.	1	Ng et al., 2017

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Care coordination and follow up** may not have a difference in efficacy when compared to **usual care** for improving activities of daily living.	3	Wong et al., 2015; Rochette et al., 2013; Lincoln et al., 2003
1a	**Goal setting structured therapy** may not have a difference in efficacy when compared to **usual care or education** for improving activities of daily living.	3	Jones et al., 2016; Sackley et al., 2015: Alexopoulus et al., 2012
1b	**Home visits** may not have a difference in efficacy when compared to **usual care** for improving activities of daily living.	2	Ostwald et al., 2014; Drummond et al., 2013
2	**Sexual counselling** may not have a difference in efficacy when compared to **usual care** for improving activities of daily living.	1	Ng et al., 2017

QUALITY OF LIFE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Goal setting structured therapy** may not have a difference in efficacy when compared to **usual care or education** for improving quality of life.	2	Jones et al., 2016; Sackley et al., 2015
1a	There is conflicting evidence about the effect of **care coordination and follow up** to improve quality of life when compared to **standard care.**	3	Wong et al., 2015; Rochette et al., 2013; Claiborne et al., 2006
1b	**Educational/Instructional DVDs** may not have a difference in efficacy when compared to **usual care** for improving quality of life.	1	Jones et al., 2018
2	**Home visits** may produce greater improvements in quality of life than **usual care**.	1	Ostwald et al., 2014
2	**Sexual counselling** may not have a difference in efficacy when compared to **usual care** for improving quality of life.	1	Ng et al., 2017

Key Points

Coordinated care and comprehensive follow-up may be beneficial for improving post-stroke depression, but not other mood related outcomes.

Goal-setting programs or home visits may not be beneficial for improving mood related outcomes post-stroke.

Physical Activity

Adapted from: https://www.medicalnewstoday.com/content/images/articles/327/327021/seniors-doing-physical-activity.jpg

The neurophysiological impact of physical activity on mood states has long been established in the general population (Byrne & Byrne, 1993). In a systematic review, Eng and Reime (2014) examined 13 trials comparing exercise (e.g. resistance, aerobic, Bobath) and control conditions (e.g. passive activity, usual care) in terms of their effectiveness in reducing depressive symptoms post stroke. Exercise programs in these trials provided training by a therapist twice a week for four to twelve weeks. The authors reported that exercise was associated with a small, significant treatment effect upon program completion, but the effect was not maintained at long-term follow-up.

Physiotherapy and exercise are the primary method for regaining motor related deficits experienced after a stroke. Although it is well known that physiotherapy and exercise are effective for rehabilitation, it is still not clear as to what type is most effective (Langhorne, Wagenaar & Patridge, 1996; Cho & Cha, 2016). Besides the more obvious physical benefits associated with exercise, psycho-social benefits also exist, and attempts are made to maximize these residual benefits as well (Saunders, Greig & Mead, 2014). Many studies have shown how aerobic exercise can help improve cognitive function, and importantly protect it through ageing in healthy individuals (Quaney et al. 2009). It has also been found to significantly improve mood in non-stroke clinical populations (Fritz & O'Connor, 2016; Altmann et al. 2016). Now, more work is needed to understand how exercise can improve mood related outcomes in stroke rehabilitation.

A total of 11 RCTs were found evaluating physical exercise for post-stroke mood disorders. Seven RCTs looked at aerobic training compared to usual care (Gezer et al. 2018; Topcuoglu et al. 2015; Van de Port et al. 2012; Harrington et al. 2010; Brittle et al. 2009; Lennon et al. 2008; Lai et al. 2006). Two RCTs looked at anaerobic training compared to usual care (Sims et al. 2009; Mead et al. 2007). Two RCTs looked at aerobic training in conjunction with a technology such as robotics or virtual reality (Linder et al. 2015; Song & Park, 2015).

The methodological details and results of all 11 RCTs are presented in Table 12.

Table 12. RCTs evaluating physical activity on mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Aerobic training vs usual care		
Gezer et al. (2018) RCT (4) N_{start}=50 N_{end}=42 TPS=Subacute	E: Aerobic Exercise (30 min/d, 5x/wk) C: Usual care (1hr/d) Duration: 6wks	• Functional Independence Measure (-) • Nottingham Health Profile (-) • Beck Depression Scale (+exp)
Topcuoglu et al. (2015) RCT (6) N_{Start}=52 N_{End}=40 TPS=Subacute	E: Aerobic training (4wk) C: Usual care Duration: 4wks	• Beck Depression Inventory (+exp) • Functional Independence Measure (-) • Nottingham Health Profile (-)
Van de Port et al. (2012) RCT (8) N_{Start}=250 N_{End}=242 TPS=Subacute	E: Circuit training (24wk) C: Usual care Duration: 12wks	• Hospital Anxiety & Depression Scale - Anxiety (-) • Hospital Anxiety & Depression Scale – Depression (-) • Nottingham Extended Activities of Daily Living (-)
Harrington et al. (2010) RCT (7) N_{Start}=243 N_{End}=228 TPS=Chronic	E: Group exercise program (8wk) C: Usual care Duration: 8wks	• Hospital Anxiety & Depression Scale – Anxiety (-) • Hospital Anxiety & Depression Scale – Depression (-) • WHOQol-Bref (-) • Frenchay Activities Index (-)
Brittle et al. (2009) RCT (5) N_{Start}=56 N_{End}=46 TPS=Chronic	E: Group exercise program (5wk) C: Usual care Duration: 5wks	• Hospital Anxiety & Depression Scale - Depression (-) • Stroke Aphasic Depression Questionnaire (-)
Lennon et al. (2008) RCT (7) N_{Start}=48 N_{End}=46 TPS=Chronic	E: Aerobic training (10wk) C: Usual care Duration: 10wks	• Hospital Anxiety & Depression Scale – Anxiety (-) • Hospital Anxiety & Depression Scale – Depression (-) • Frenchay Activities Index (-)
Lai et al. (2006) RCT (8) N_{Start}=100 N_{End}=80 TPS=Subacute	E: Specialized exercise program (12wk) C: Usual care Duration: 3mo	• Geriatric Depression Scale (+exp) • Stroke Impact Scale – Emotion (+exp) • SF-36 – Emotion (+exp)
Anaerobic training vs usual care		
Sims et al. (2009) RCT (7) N_{Start}=45 N_{End}=43 TPS=Chronic	E: Resistance training (10wk) C: Usual care Duration: 10wks	• CES Depression Scale (-) • Assessment of Quality of Life Instrument (-) • Short Form-12 Health Survey (-) • Stroke Impact Scale – Emotion (-) • Satisfaction with Life Scale (-) • Life Orientation Test (-) • Self-Esteem Scale (-) • Recovery Locus of Control Scale (+exp)
Mead et al. (2007) RCT (8) N_{Start}=66 N_{End}=62 TPS=Subacute	E: Resistance training (12wk) C: Relaxation training Duration: 12wks	• Hospital Anxiety & Depression Scale – Anxiety (-) • Hospital Anxiety & Depression Scale – Depression (-) • Nottingham Extended Activities of daily Living (-) • Functional Independence Measure (-) • SF-36 – Mental Health (-)
Aerobic exercises with additional intervention		

Linder et al. (2015) RCT (8) N_{Start}=99 N_{End}=91 TPS=Subacute	E: Exercise program + Robotic device (8wk) C: Exercise program Duration: 8wks	• CES Depression Scale (-) • Stroke Impact Scale a. Activities of Daily Living (-) b. Mood (-)
Song & Park (2015) RCT (5) N_{Start}=40 N_{End}=40 TPS=Chronic	E: Aerobic training + Virtual reality (8wk) C: Aerobic training + Ergometer Duration: 8wks	• Beck Depression Inventory (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about physical activity

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **aerobic exercise** to improve post-stroke depression when compared to **usual care**.	7	Gezer et al. 2018; Topcuoglu et al. 2015; Van de Port et al. 2012; Harrington et al. 2010; Brittle et al. 2009; Lennon et al. 2008; Lai et al. 2006
1a	**Anaerobic exercise** may not have a difference in efficacy when compared to **usual care** for improving post-stroke depression.	2	Sims et al. 2009; Mead et al. 2007
1b	**Aerobic exercise with a robotic device** may not have a difference in efficacy when compared to **aerobic exercise alone** for improving post-stroke depression.	1	Linder et al. 2015
2	**Aerobic exercise with virtual reality** may produce greater improvements in alleviating post-stroke depression than **aerobic training alone**.	1	Song & Park, 2015

ANXIETY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Aerobic exercise** may not have a difference in efficacy when compared to **usual care** for improving post-stroke anxiety.	3	Van de Port et al., 2012; Harrington et al. 2010; Lennon et al. 2008
1b	**Anaerobic exercise** may not have a difference in efficacy when compared to **usual care** for improving post-stroke anxiety.	1	Mead et al. 2007

MOOD COFACTORS			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the effect of **anaerobic exercise** to improve factors related to mood management when compared to **usual care**.	1	Sims et al. 2009
1b	**Aerobic exercise with a robotic device** may not have a difference in efficacy when compared to **aerobic exercise alone** for improving mood.	1	Linder et al. 2015

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Aerobic exercise** may not have a difference in efficacy when compared to **usual care** for improving activities of daily living.	6	Gezer et al. 2018; Topcuoglu et al. 2015; Van de Port et al. 2012; Harrington et al. 2010; Lennon et al. 2008; Lai et al. 2006

1a	**Anaerobic exercise** may not have a difference in efficacy when compared to **usual care** for improving activities of daily living.	2	Sims et al. 2009; Mead et al. 2007
1b	**Aerobic exercise with a robotic device** may not have a difference in efficacy when compared to **aerobic exercise alone** for improving activities of daily living.	1	Linder et al. 2015

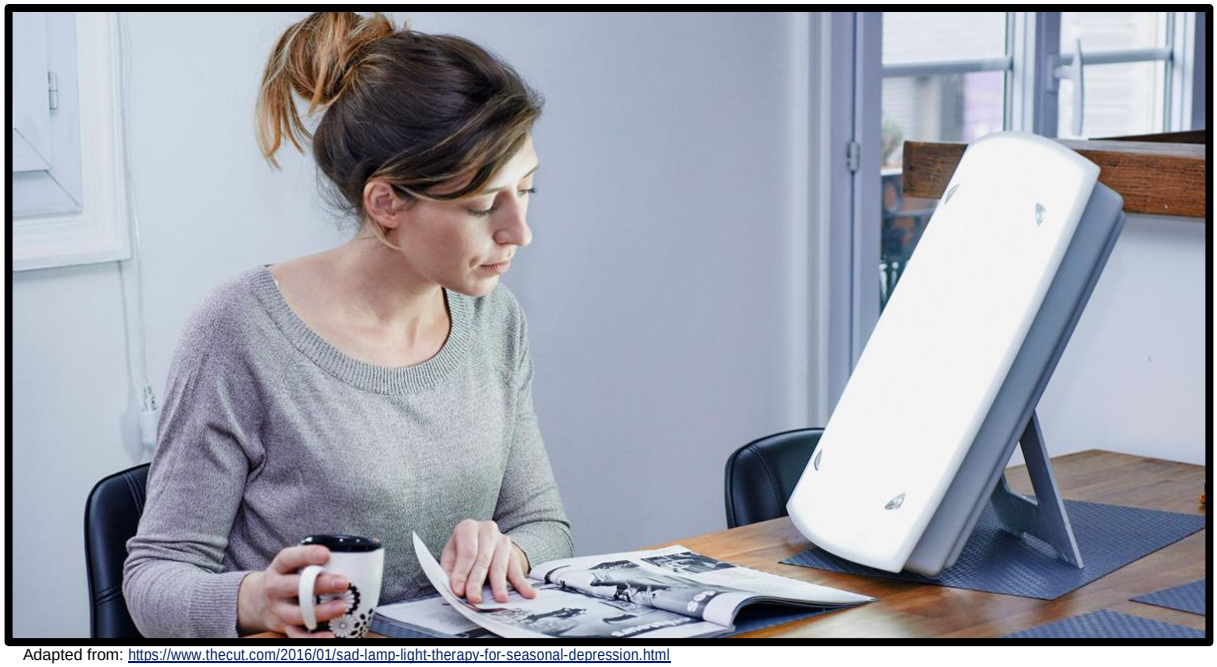
QUALITY OF LIFE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Aerobic exercise** may not have a difference in efficacy when compared to **usual care** for improving quality of life.	4	Gezer et al. 2018; Topcuoglu et al. 2015; Harrington et al. 2010; Lai et al. 2006
1a	**Anaerobic exercise** may not have a difference in efficacy when compared to **usual care** for improving quality of life.	2	Sims et al. 2009; Mead et al. 2007

Key Points

The literature is mixed concerning physical activity interventions for improving depression.

Physical activity does not seem to be beneficial for improving anxiety, activities of daily living or quality of life post-stroke.

Adjunctive Light Therapy



Adapted from: https://www.thecut.com/2016/01/sad-lamp-light-therapy-for-seasonal-depression.html

Light therapy is often used to treat seasonal affective disorder, as well as non seasonal depression. During light therapy, an individual is exposed to an artificial bright light for a given period of time. Mechanistically, the light mimics natural sunlight and is thought to affect circadian expression/activity of several neurotransmitters, which have a substantial impact on mood (Kim et al. 2015; West et al. 2019). Indeed, light therapy has been shown to increase serotonin turnover and decrease depression, in the general population (Lam et al. 2016). Likewise, several studies have reported that areas of the brain related to mood are affected by dose dependent light therapy (Alkozei et al. 2016; Fisher et al. 2014; Kim et al. 2015).

In a Cochrane review, Tuunainen et al. (2004) identified 20 studies examining the use of light therapy for depression, mostly in combination with drug treatment. Evaluation of these studies revealed a significant effect in favour of treatment over control with minimal adverse effects. A recent meta-analysis by Perera et al. (2016) supported the findings of the Cochrane review, confirming the benefit of adjunctive light therapy for depression. However, similar to the previous review, the authors noted poor quality of evidence due to high risk of bias and inconsistency.

One RCT evaluated light therapy in conjunction with citalopram for treating post-stroke depression (Sondergaard et al., 2006).

The methodological details and results of the single RCT are presented in Table 13.

Table 13. RCTs evaluating heterocyclic antidepressants for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Sondergaard et al. (2006) RCT (5) N_{Start}=73 N_{End}=63 TPS=NA*	E: High-Intensity Light Therapy (10,000 lux) + Citalopram (20mg/d) C: Moderate-Intensity Light Therapy (4,000 lux) + Citalopram (20mg/d) Duration: 4wks	• Hamilton Depression Rating Scale – 6 Item (+exp) • Hamilton Depression Rating Scale – 17 Item (-) • Bech-Rafaelsen Melancholia Scale (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about adjunctive light therapy with citalopram

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**High-intensity light therapy with citalopram** may not have a difference in efficacy when compared to **moderate-intensity light therapy with citalopram** for improving post-stroke depression.	1	Sondegaard et al. 2006

Key Points

Light therapy may not be beneficial for improving post-stroke depression.

Art Therapy

Adopted from: https://www.roydswithyking.com/wordpress/wp-content/uploads/2019/02/People-making-art-in-a-class.jpg

Art therapy emerged from the combination of visual arts and psychotherapy. Creative expression is believed to help individuals with various psychosocial outcomes such as achieving goals, solving problems, and addressing trauma. Systematic reviews have art therapy for dementia (Beard, 2011), schizophrenia (Ruddy & Milnes, 2005), post-traumatic stress (Schouten et al. 2015), and various mental health disorders (Maujean et al. 2014; Uttley et al. 2015). While these reviews generally supported the clinical effectiveness of art therapy, these findings were often based on few low-quality studies.

One RCT was found that looked at art therapy for stroke survivors (Kongkasuwan et al. 2016).

The methodological details and results of the single RCT are presented in Table 14.

Table 14. RCTs evaluating art therapy for mood

Authors (Year) **Study Design (PEDro Score)** **Sample Size$_{start}$** **Sample Size$_{end}$** **Time post stroke category**	**Interventions** **Duration: Session length, frequency per week for total number of weeks**	**Outcome Measures** **Result (direction of effect)**
Kongkasuwan et al. (2016) RCT (7) N_{Start}=118 N_{End}=113 TPS=Not reported	E: Art therapy C: Standard care Duration: 2d/wk for 4wk	• Hospital Anxiety & Depression Scale – Depression (+exp) • Hospital Anxiety & Depression Scale – Anxiety (-) • Modified Barthel Index Scale (+exp) • Pictorial Thai Quality of Life Questionnaire (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about art therapy

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Art therapy** may produce greater improvements in alleviating post-stroke depression than **standard care**.	1	Kongkasuwan et al. 2016

ANXIETY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Art therapy** may not have a difference in efficacy when compared to **standard care** for improving post-stroke anxiety.	1	Kongkasuwan et al. 2016

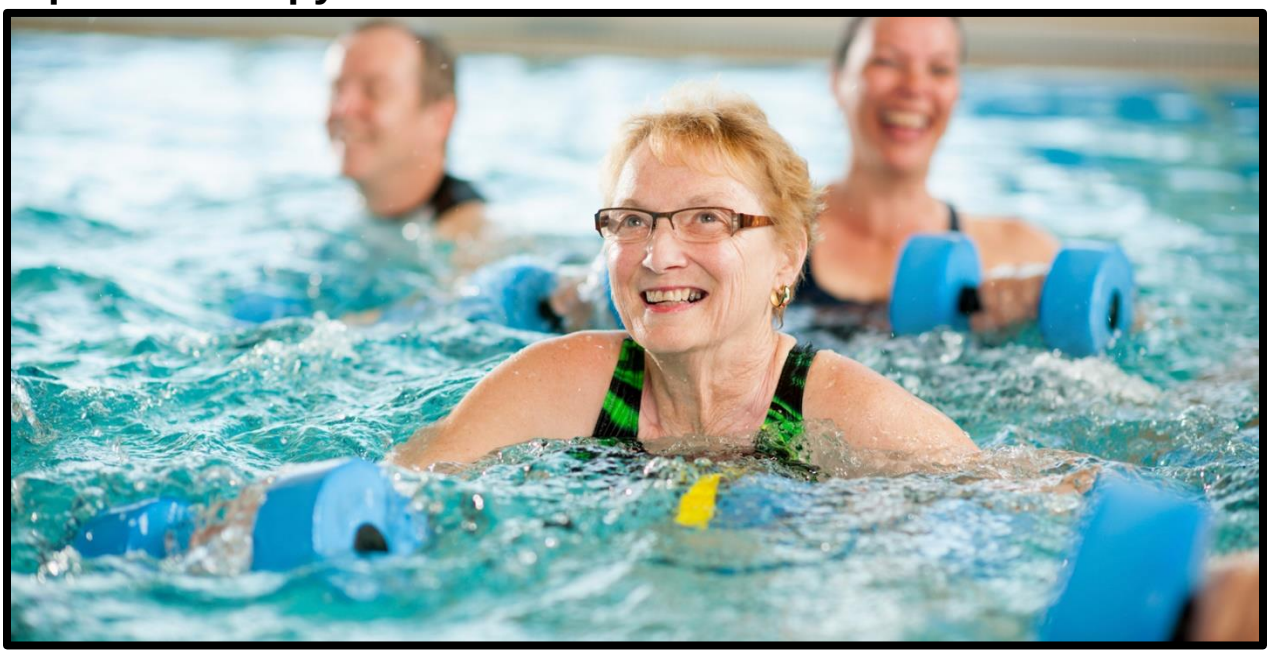
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Art therapy** may produce greater improvements in activities of daily living than **standard care**.	1	Kongkasuwan et al. 2016

QUALITY OF LIFE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Art therapy** may produce greater improvements in quality of life than **standard care**.	1	Kongkasuwan et al. 2016

Key Points

Art therapy may be beneficial for improving depression, activities of daily living and quality of life post-stroke, but not anxiety.

Aquatic Therapy



Adopted from: https://blog.soarlifeproducts.com/rehab-treatment/benefits-aquatic-therapy-aging-adults/

Aquatic therapy employs the natural properties of water (i.e. buoyancy, hydrostatic pressure, hydrodynamic forces, thermodynamics and viscosity) to act as a rehabilitation intervention in supporting weight and offsetting gravity during exercises related to balance and gait performed in water (Becker, 2009).

Aquatic therapies may vary, with some forms including traditional exercises, neurodevelopmental techniques, proprioceptive neuromuscular facilitation, and task-specific training. The Halliwick Method is an example of a motor rehabilitation program that is based on neurodevelopmental techniques, in which core stability is a major focus (Martin et al. 1981). The Bad Ragaz Ring Method is an example of a motor rehabilitation program that is based on proprioceptive neuromuscular facilitation techniques, in which improving range of motion is a major focus (Boyle et al. 1981). Alternative and complementary medicine techniques have also been integrated into aquatic therapy programs, examples include Ai chi, which is derived from tai chi, as well as Watsu, which is derived from shiatsu (Ross & Presswalla 1998; Lutz 1999).

One RCT looked at aquatic therapy for post-stroke depression and anxiety (Aidar et al. 2018).

The methodological details and results of the single RCT are presented in Table 15.

Table 15. RCTs evaluating aquatic therapy for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Aidar et al. (2018) RCT (3) N_{Start}=43 N_{End}=36 TPS= Chronic	E: Aquatic Exercise Program (2x/wk, 45-60min) C: Waiting List Group Duration: 12wks	• Beck Depression Inventory (+exp) • State-trait Anxiety Inventory (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about aquatic therapy

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Aquatic therapy** may produce greater improvements in alleviating post-stroke depression than a **waiting list group**.	1	Aidar et al. 2018

ANXIETY			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Aquatic therapy** may produce greater improvements in alleviating post-stroke anxiety than a **waiting list group**.	1	Aidar et al. 2018

Key Points

Aquatic Therapy may be beneficial for improving depression and anxiety post-stroke.

Music Therapy

Adopted from: http://static.guim.co.uk/sys-images/Guardian/Pix/pictures/2014/6/29/14040632906 57/music-in-mind-therapy-012.jpg

The benefits of music therapy have been well established in a variety of chronic diseases (Umbrello et al. 2019). However, in recent years the use of music therapy for stroke rehabilitation has gained attention. In stroke rehabilitation, music therapists utilize instruments, voice and music to address functional goals in areas such as emotion, communication, cognition, physical abilities and behaviour. In combination with the psychosocial benefits of music therapy, music has been shown to activate areas of the brain related to attention, affective processing, memory and motor control (Särkämö & Soto, 2012). As such, activation and engagement of these brain regions likely contributes to the rehabilitating effect of music after stroke. A recent Cochrane review reported that music therapy significantly improves gait and upper extremity functioning, communication and overall quality of life following stroke (Magee et al. 2017).

Three RCTs were found that evaluated music therapy for improving post-stroke mood disorders. All three RCTs compared music therapy to a standard care (Raglio et al., 2017; Jun et al., 2013; Sarkamo et al., 2008).

The methodological details and results of the single RCT are presented in Table 16.

Table 16. RCTs evaluating music therapy for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Raglio et al. 2017 RCT (6) N_{start}=38 N_{end}=38 TPS=Acute	E: Interactive Music Therapy (30min, 3x/wk) C: Standard Care Duration: 7wks	• Functional Independence Measure (+exp) • Hospital Anxiety and Depression Scale – Anxiety (-) • Hospital Anxiety and Depression Scale – Depression (+exp) • Mcgill Quality of Life Questionnaire (-)
Jun et al. (2013) RCT (4) N_{Start}=40 N_{End}=30 TPS=Not reported	E: Music-movement therapy C: Usual care Duration: 60min, 3d/wk for 8wk	• CES Depression Scale (-) • Barthel Index (-) • Profile of Mood States (+exp)
Sarkamo et al. (2008) RCT (6) N_{Start}=60 N_{End}=55 TPS=Acute	E1: Music-listening therapy E2: Language-listening therapy C: Usual care Duration: 1h/d for 2mo	E1 vs C • Profile of Mood States – Depression (+exp1) E2 vs C • Profile of Mood States – Depression (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about music therapy

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **music therapy** to improve post-stroke depression than **standard care**.	3	Raglio et al. 2017; Jun et al. 2013; Sarkamo et al. 2008

ANXIETY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Music therapy** may not have a difference in efficacy when compared to **standard care** for improving post-stroke anxiety.	1	Raglio et al. 2017

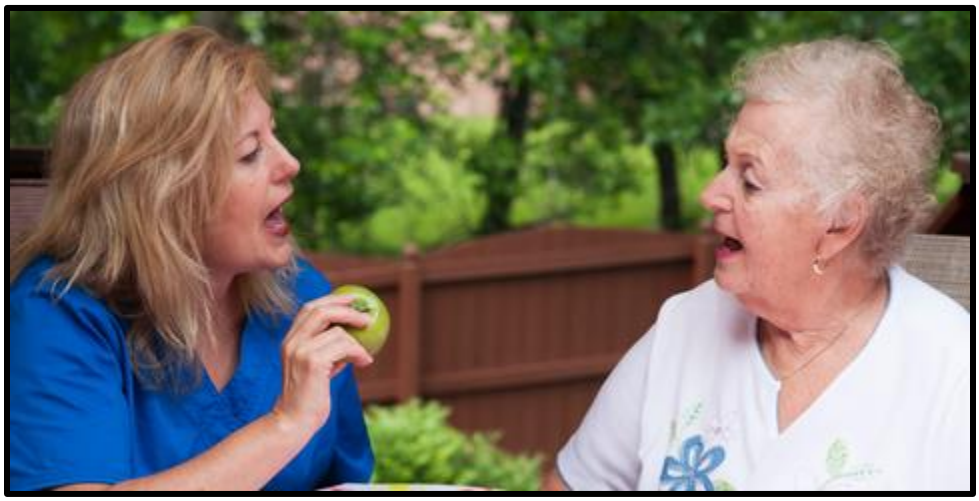
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	There is conflicting evidence about the effect of **music therapy** to improve performance of activities of daily living than **standard care**.	2	Raglio et al. 2017; Jun et al. 2013

QUALITY OF LIFE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Music therapy** may not have a difference in efficacy when compared to **standard care** for improving quality of life.	1	Raglio et al. 2017

Key Points

The literature is mixed regarding music therapies efficacy for improving mood related outcomes post-stroke.

Speech Therapy



Adopted from: https://www.saundershouse.org/sites/default/files/styles/large/public/field/image/SH_StrokeSpeech_Blog.png?itok=1KYoIY_S

Speech and language therapy can take on many different forms, but the underlying principles remain relatively the same. Because of the different types of aphasia and varying levels of severity, treatment is often individualized. Depending on the nature of their deficits, certain tactics can be employed, and certain aspects of language and speech focused on more intensely. The counselling role of speech therapists is thought to help patients adapt to their communication disturbances and better express their needs, which in return may alleviate emotional problems (Lincoln et al. 1985). In fact, participants in a community-based speech therapy program demonstrated improved psychological wellbeing (Hoen et al. 1997).

Two RCTs were found that looked at speech therapy for treating post-stroke depression. One RCT compared speech therapy to usual care (Lincoln et al. 1985). One RCT compared speech therapy with orofacial therapy to speech therapy (Konecny et al. 2014).

The methodological details and results of the two RCTs are presented in Table 17.

Table 17. RCTs evaluating speech therapy on mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Konecny et al. (2014) RCT (4) N_{Start}=99 N_{End}=99 TPS=Subacute	E: Speech therapy + Orofacial therapy C: Speech therapy Duration: 4wk	• Beck Depression Inventory (+exp) • Barthel Index (+exp)
Lincoln et al. (1985) RCT (5) N_{Start}=168 N_{End}=149 TPS=Acute	E: Speech therapy C: Usual care Duration: 1hr, 2d/wk for 24wk	• MAACL Depression (-) • General Health Questionnaire (-) • Wakefield Depression Inventory (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about speech therapy

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Speech therapy** may not have a difference in efficacy when compared to **usual care** for improving post-stroke depression.	1	Lincoln et al. 1985
2	**Speech therapy with orofacial therapy** may produce greater improvements in alleviating post-stroke depression than **speech therapy**.	1	Konecny et al. 2014

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Speech therapy** may produce greater improvements in activities of daily living than **standard care**.	1	Konecny et al. 2014

MOOD COFACTORS			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Speech therapy** may not have a difference in efficacy when compared to **usual care** for improving mental health.	1	Lincoln et al. 1985

Key Points

Speech therapy may improve activities of daily living, but not depression or other mood cofactors.

Hyperbaric Oxygen Therapy

Adopted from: https://cdn-prod.medicalnewstoday.com/content/images/articles/313/313155/hbot.jpg

Hyperbaric oxygen therapy (HBOT) administers patients with 100% oxygen at high atmospheric pressure in an isolated treatment chamber. While it is an established treatment for medical conditions, such as decompression illness and carbon monoxide poisoning, it has been suggested that HBOT may treat certain mental health issues.

Two RCTs looked at HBOT. One RCT examined HBOT in combination with fluoxetine (Yan et al. 2015), and another RCT examined HBOT with dexamethasone (Cao et al. 2013) for treating post-stroke depression.

The methodological details and results of the two RCTs are presented in Table 18.

Table 18. RCTs evaluating hyperbaric oxygen therapy (HBOT) for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Yan et al. (2015) China RCT (6) N_{Start}=90 N_{End}=90 TPS=Acute	E1: HBOT + Fluoxetine (20mg/d) E2: Fluoxetine (20mg/d) E3: HBOT Duration: 1 session, 5d/wk	E1 vs E2 • Hamilton Depression Rating Scale (+exp) E1 vs E3 • Hamilton Depression Rating Scale (+exp) E2 vs E3 • Hamilton Depression Rating Scale (-)
Cao et al. (2013) RCT (6) N_{Start}=60 N_{End}=60 TPS=Subacute	E: HBOT (45min/d) + Dexamethasone (5mg/d) C: Deanxit (combination of flupentixol and melitracen) (10mg/d) Duration: 4wk	• Hamilton Depression Rating Scale (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

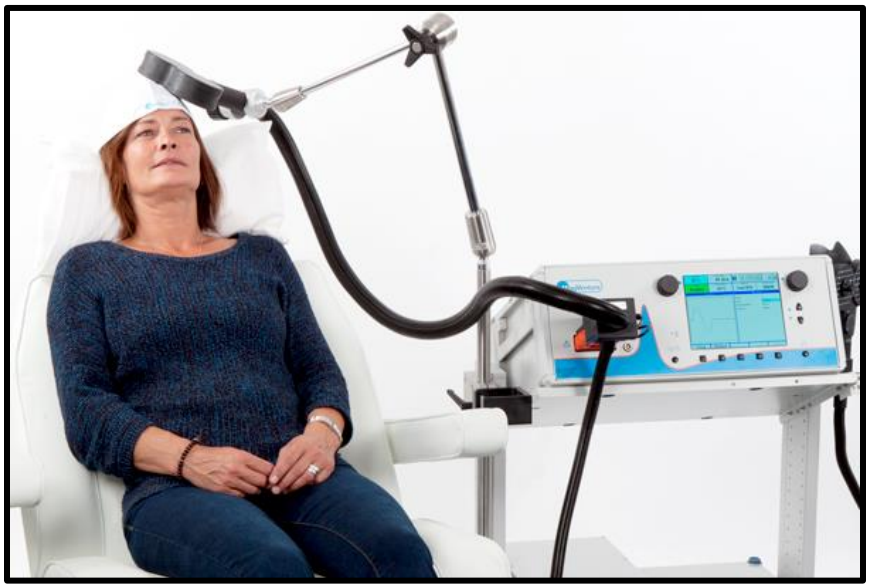
Conclusions about hyperbaric oxygen therapy

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Hyperbaric oxygen therapy** may not have a difference in efficacy when compared to **fluoxetine** for improving post-stroke depression.	1	Yan et al. 2015
1b	**Hyperbaric oxygen therapy with fluoxetine** may produce greater improvements in alleviating post-stroke depression than **hyperbaric oxygen therapy or fluoxetine alone**.	1	Yan et al. 2015
1b	**Hyperbaric oxygen therapy with dexamethasone** may produce greater improvements in alleviating post-stroke depression than **Deanxit, a combinatory antipsychotic and tricyclic antidepressant**.	1	Yan et al. 2015

Key Points

HBOT in combination with antidepressants may be beneficial for improving depression.

Repetitive Transcranial Magnetic Stimulation



Adopted from: http://bipolarnews.org/wp-content/uploads/2015/11/rtms.png

Repetitive transcranial magnetic stimulation (rTMS) applies a magnetic field to the head, inducing an electric current at the brain and delivering a series of magnetic pulses. Initially developed as an alternative non-invasive stimulation treatment for disorders of the CNS, it has since been shown effectiveness as a treatment for major depressive disorder (Grunhaus et al. 2003; Janicak et al. 2002) and treatment-resistant depression (George & Post, 2011; Loo et al. 2003). In a recent systematic review, McIntyre et al. (2016) evaluated rTMS for the treatment of depression due to cerebrovascular disease (i.e. vascular depression and PSD). The authors reported that active rTMS demonstrated a greater decrease in depressive symptoms than sham stimulation. rTMS was also associated with greater rates of response and remission, without any significant side effects or adverse events.

Four RCTs were found evaluating rTMS for post-stroke depression. All four evaluated high frequency (10Hz) rTMS to sham stimulation (Sasaki et al. 2017; Gu et al. 2016; Kim et al. 2010; Jorge et al. 2004).

The methodological details and results of the four RCTs are presented in Table 19.

Table 19. RCTs evaluating repetitive transcranial magnetic stimulation (rTMS) for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
High frequency rTMS vs sham		
Sasaki et al. (2017) RCT (6) N_{Start}=13 N_{End}=13 TPS=Chronic	E: High frequency rTMS (10Hz) C: Sham group Duration: 1x/d, 5d	• Apathy Scale (+exp) • Quick Inventory of Depressive Symptomology (-)
Gu et al. 2016 RCT (9) N_{start}=24 N_{end}=24 TPS=Chronic	E: High frequency rTMS (10Hz) C: Sham stimulation Duration: 2.5hrs 6d/wk, 2wks	• Beck Depression Inventory (+exp) • Hamilton Depression Rating Scale (+exp)
Kim et al. (2010) RCT (8) N_{Start}=18 N_{End}=18 TPS=Chronic	E1: High-frequency rTMS (10Hz) E2: Low-frequency rTMS (1Hz) C: Sham rTMS Duration: 5d/wk for 2wk	E1 vs E2 vs C • Beck Depression Inventory (+exp) • Barthel Index (-)
Jorge et al. (2004) RCT (7) N_{Start}=20 N_{End}=20 TPS=Chronic	E: High frequency rTMS (10Hz) C: Sham rTMS Duration: 10 sessions over 2wk	• Hamilton Depression Rating Scale (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about high frequency (10Hz) rTMS

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**High frequency (10Hz) rTMS** may produce greater improvements in alleviating post-stroke depression than **sham stimulation**.	4	Saskai et al. 2017; Gu et al. 2016; Kim et al. 2010; Jorge et al. 2004

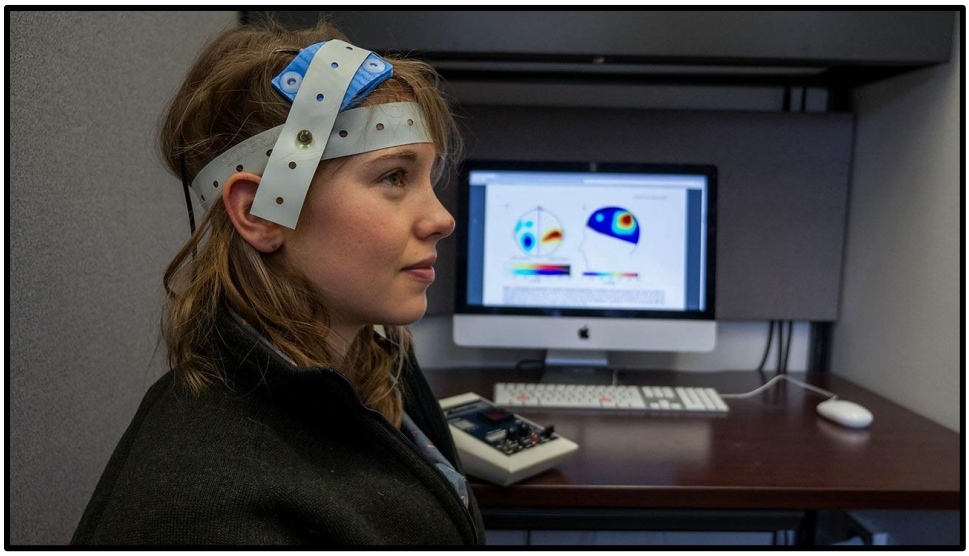
MOOD COFACTORS			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**High frequency (10Hz) rTMS** may produce greater improvements in alleviating apathy than **sham stimulation**.	1	Saskai et al. 2017

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**High frequency (10Hz) rTMS** may not have a difference in efficacy when compared to **sham stimulation** for improving activities of daily living.	1	Kim et al. 2010

Key Points

High frequency rTMS may be beneficial for improving depression and apathy post-stroke, but not activities of daily living.

Transcranial Direct Current Stimulation



Adopted from: https://www.sciencemag.org/sites/default/files/styles/article_main_large/public/images/sn-handednessREV.jpg?itok=qCzi7XjO

Another form of non-invasive brain stimulation is transcranial direct-current stimulation (tDCS). This procedure involves the application of mild electrical currents (1-2 mA) conducted through two saline-soaked, surface electrodes applied to the scalp, overlaying the area of interest and the contralateral forehead above the orbit. Anodal stimulation is performed over the affected hemisphere and increases cortical excitability, while cathodal stimulation is performed over the unaffected hemisphere and decreases cortical excitability (Alonso-Alonso et al., 2007). Additionally, tDCS can be applied on both hemispheres concurrently, this is known as dual tDCS. In contrast to TMS, tDCS does not induce action potentials, but instead modulates the resting membrane potential of the neurons (Alonso-Alonso et al., 2007). It is a relatively newer form of non-invasive stimulation that has demonstrated efficacy and tolerability in treating major depressive episodes (Meron et al. 2015; Shiozawa et al. 2014).

A single RCT was found evaluating tDCS for post-stroke depression. It compared dual tDCS to a sham condition (Valiengo et al. 2017).

The methodological details and results of the single RCT are presented in Table 20.

Table 20. RCTs evaluating tDCS for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Valiengo et al. 2017 RCT (8) N_{start}=48 N_{end}=43 TPS=Chronic	E: Dual tDCS stimulation C: Sham stimulation Duration: 12 sessions, 30min, 5d/wk (first 2 weeks) then 7d/wk	• Hamilton Depression Rating Scale (+exp) • Montogmery-Asberg Depression Rating Scale (+exp) • Clinical Global Impression – Severity (-) • Barthel Index (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about transcranial direct current stimulation (tDCS)

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Dual tDCS** may produce greater improvements in alleviating post-stroke depression than **sham stimulation**.	1	Valiengo et al. 2017

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Dual tDCS** may not have a difference in efficacy when compared to **sham stimulation** for improving activities of daily living.	1	Valiengo et al. 2017

Key Points

Dual tDCS could be beneficial for improving post-stroke depression.

Extremely Low Frequency Electromagnetic Field

Adopted from: https://www.dotmed.com/listing/magnetic-field-therapy-/magnetronic/mf-10/2916977

Extremely low frequency electromagnetic field is an emerging treatment in stroke rehabilitation. The treatment is based on the principles of regeneration, osteogenesis, analgesics, and anti-inflammatory action (Cichon et al. 2017).

Two RCTs looked at this intervention for post-stroke depression (Cichon et al. 2017; Cichon et al. 2017b).

The methodological details and results of the two RCTs are presented in Table 21.

Table 21. RCTs evaluating extremely low frequency electromagnetic field for mood

Authors (Year) **Study Design (PEDro Score)** **Sample Size$_{start}$** **Sample Size$_{end}$** **Time post stroke category**	**Interventions** **Duration: Session length, frequency per week for total number of weeks**	**Outcome Measures** **Result (direction of effect)**
Cichon et al. 2017 RCT (6) N_{start}=48 N_{end}=48 TPS=Acute	E: Magnetic Field Therapy (ELF-EMF) C: Standard Care Group Duration: 15min/d, 4wk	• Geriatric Depression Scale (+exp) • Barthel Index (-)
Cichon et al. 2017b RCT (6) N_{start}=57 N_{end}=57 Tps=Acute	E: Magnetic Field Therapy (ELF-EMF) C: Standard Care Group Duration: 15min/d, 4wk	• Barthel Index (+exp) • Geriatric Depression Scale (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about extremely low frequency electromagnetic field therapy

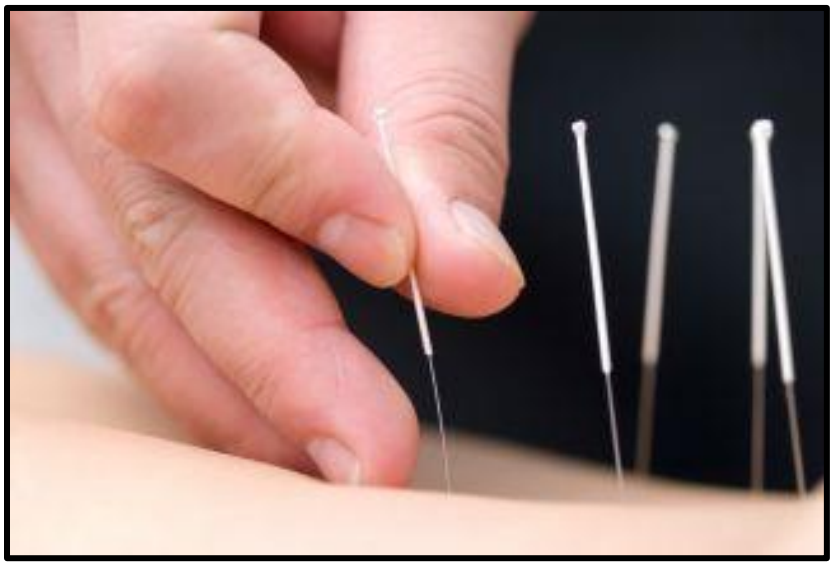
DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Extremely low frequency electromagnetic field** may produce greater improvements in alleviating post-stroke depression than **standard care**.	2	Cichon et al. 2017; Cichon et al. 2017b

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	There is conflicting evidence about the effect of **extremely low frequency electromagnetic field** to improve activities of daily living when compared to **standard care**.	2	Cichon et al. 2017; Cichon et al. 2017b

Key Points

Extremely low electromagnetic field therapy could be beneficial for improving post-stroke depression.

Acupuncture and Electroacupuncture



Adopted from: https://cdn.mos.cms.futurecdn.net/pSubdkTXtC6J8GZLJnkX9k-320-80.jpg

Acupuncture is a form of traditional Chinese medicine that has been used to treat musculoskeletal issues and relieve various types of pain. It is based upon a theoretical network of channels ("meridians") that are connected to different body parts and through which life-energy ("chi") is believed to flow. Practitioners insert needles into specific places in the body ("acupoints") in order to manipulate the meridian system. While it is often considered part of complementary and alternative medicine, acupuncture has more recently become integrated into mainstream biomedicine. A systematic review by Chan et al. (2015) found that acupuncture in combination with antidepressant medications was an effective and safe treatment for depression. In a stroke-specific review, Yang et al. (2016) reported that acupuncture was associated with a large, significant effect in reducing depressive symptoms.

Ten RCTs were found evaluating acupuncture for improving post-stroke mood disorders. Two RCTs evaluated acupuncture against a sham (Liao et al. 2017; Wayne et al. 2005). Five RCTs compared acupuncture to antidepressant medication (Lin et al. 2018; Wang et al. 2018; Li et al., 2017; Zhang et al. 2016; Qian et al., 2015). One RCT compared acupuncture with herbal medicine to standard care (Fang et al. 2016). One RCT compared acupuncture with music therapy to acupuncture alone and antidepressant medication (Lin et al. 2017). One RCT compared dense cranial acupuncture and electroacupuncture with non-invasive acupuncture and electroacupuncture (Man et al. 2014).

The methodological details and results of the ten RCTs are presented in Table 22.

Table 22. RCTs evaluating acupuncture and electroacupuncture for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Acupuncture vs sham		
Liao et al. (2017) RCT (7) N_{start}=52 N_{end}=33 TPS=Acute	E: Chinese acupuncture C: Sham acupuncture Duration: 20 min 3x/wk for 8 wk	• Barthel Index (-) • Instrumental Activities of Daily Living (-) • Hamilton Depression Rating Scale (-)
Wayne et al. (2005) RCT (9) N_{Start}=33 N_{End}=24 TPS=Chronic	E: Acupuncture C: Sham acupuncture Duration: 20, 60min session over 10.5wk	• Center for Epidemiological Studies Depression Scale (-) • Barthel Index (-) • Nottingham Health Profile (-)
Acupuncture vs antidepressants		
Lin et al. (2018) RCT (5) N_{Start}=105 N_{End}=90 TPS=Acute	E: Acupuncture (1mo only, 5d/wk, 30min/d) + Tai Ji (5d/wk, 40min/d) C: Citalopram (20mg/d) Duration: 12mo	• Hamilton Depression Rating Scale (+exp) • Barthel Index (-)
Wang et al. 2018 RCT (6) N_{start}=64 N_{end}=64 TPS=Subacute (>4wks)	E: Traditional acupuncture C: escitalopram (10mg, 1/d) Duration: 30 min, 5d/wk, 8wk	• Hamilton Depression Scale (-) • Hamilton Anxiety Scale (+exp) • Barthel Index (-)
Li et al. 2017 RCT (8) N_{start}=58 N_{end}=46 TPS=Subacute	E: Tiaoshen Kaiqiao acupuncture plus starch tablets C: Body acupuncture plus fluoxetine (10mg, 2x/d) Duration 30 min, 3x/wk, 12wks	• Hamilton Depression Rating Scale (-) • Clinical Global Impression Scale – Severity (-) • Clinical Global Impression Scale – Improvement (-)
Zhang et al. (2016) RCT (5) N_{Start}=70 N_{End}=65 TPS=Subacute	E: Acupuncture C: Escitalopram (10mg/d) Duration: 30min, 5d/wk for 8wk	• Montgomery-Asberg Depression Rating Scale (-) • Hamilton Depression Rating Scale (-) • Barthel Index (-)
Qian et al. (2015) RCT (8) N_{Start}=68 N_{End}=65 TPS=Subacute	E: Acupuncture + Placebo C: Sham acupuncture + Fluoxetine (20mg/d) Duration: 6wk	• Hamilton Depression Rating Scale (-)
Acupuncture with herbal medicine vs standard care		
Fang et al. (2016) RCT (9) N_{Start}=360 N_{End}=348 TPS=Subacute	E: Acupuncture + Herbal medicine C: Standard care Duration: 20wk	• Hamilton Depression Rating Scale (+exp) • Self-Rating Depression Scale (+exp) • Modified Barthel Index (+exp) • Zung Self-reported Depression Scale (+exp)

Acupuncture with music therapy vs acupuncture vs sertraline		
Lin et al. 2017 RCT (6) N_{start}=92 N_{end}=90 TPS=Subacute	E1: Needling/accupoint injection (30 min 5x/wk) E2: Needling/accupoint plus music therapy (20 min 2x/d, 5x/wk) C: Sertraline hydrochloride (50mg/d) Duration: 3wks	E1 vs E2 • Hamilton Depression Rating Scale (exp2) • Instrumental Activities of Daily Living Scale (exp2) E2 vs C • Hamilton Depression Rating Scale (exp2) • Instrumental Activities of Daily Living Scale (-)
Dense cranial acupuncture + electroacupuncture vs non-invasive acupuncture + electroacupuncture		
Man et al. (2014) RCT (8) N_{Start}=43 N_{End}=33 TPS=Chronic	E1: Dense cranial acupuncture + Body electroacupuncture E2: Non-invasive cranial acupuncture + Body electroacupuncture Duration: 3d/wk for 4wk	• Hamilton Depression Rating Scale (-) • Clinical Global Impression-Severity Scale (+exp) • Barthel Index (+exp2)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp_2 indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about acupuncture

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1a	**Acupuncture** may not have a difference in efficacy when compared to **sham** for improving post-stroke depression.	2	Liao et al. 2017; Wayne et al. 2005
1a	**Acupuncture** may not have a difference in efficacy when compared to **antidepressants** for improving post-stroke depression.	5	Lin et al. 2018; Wang et al. 2018; Li et al., 2017; Zhang et al. 2016; Qian et al., 2015
1b	**Acupuncture with herbal medicine** may produce greater improvements in alleviating post-stroke depression than **usual care**.	1	Fang et al. 2016
1b	**Acupuncture with music therapy** may produce greater improvements in alleviating post-stroke depression than **a selective serotonin reuptake inhibitor**.	1	Lin et al. 2017
1b	**Dense cranial acupuncture with electroacupuncture** may not have a difference in efficacy when compared to **non-invasive cranial electroacupuncture with electroacupuncture** for improving post-stroke depression.	1	Man et al. 2014

ANXIETY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Acupuncture** may produce greater improvements in alleviating post-stroke anxiety than **antidepressants**.	1	Wang et al. 2018

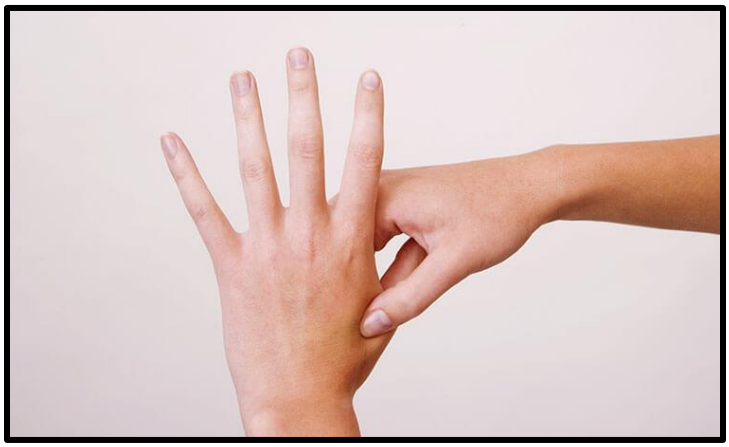
ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Acupuncture** may not have a difference in efficacy when compared to **sham** for improving activities of daily living.	2	Liao et al. 2017; Wayne et al. 2005
1b	**Acupuncture** may not have a difference in efficacy when compared to **antidepressants** for improving activities of daily living.	3	Lin et al. 2018; Wang et al. 2018; Zhang et al. 2016
1b	**Acupuncture with herbal medicine** may produce greater improvements in activities of daily living than **usual care**.	1	Fang et al. 2016
1b	**Acupuncture with music therapy** may not have a difference in efficacy when compared to **a selective serotonin reuptake inhibitor** for improving activities of daily living.	1	Lin et al. 2017
1b	**Non-invasive cranial electroacupuncture with electroacupuncture** may produce greater improvements in activities of daily living than **non-invasive cranial electroacupuncture with electroacupuncture**.	1	Man et al. 2014

QUALITY OF LIFE			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Acupuncture** may not have a difference in efficacy when compared to **sham** for improving quality of life.	1	Wayne et al. 2005

Key Points

Acupuncture may not be beneficial for improving mood related outcomes post-stroke.

Acupressure



Adopted from: https://cdn.massagemag.com/wordpress/wp-content/uploads/3_1_Accupressure-1.jpg

Acupressure is a form of massage in traditional Chinese medicine in which movement of qi or life energy is encouraged through various the channels or meridians inside the body (Chen et al. 2007). Acupressure makes use of the same meridians and acupoints as acupuncture with the same goal of encouraging energy flow throughout the body (Chen et al. 2007; Di et al. 2017).

Massage is the practice of applying structured pressure, tension, motion or vibration — manually or with mechanical aids — to the soft tissues of the body, including: muscles, connective tissue, tendons, ligaments, joints and lymphatic vessels, to achieve a beneficial response (Holland & Pokorny, 2001). The benefits of massage therapy are suggested to be increased blood flow, relief of muscle spasms and release of β-endorphins (Wei-Chun et al. 2017). One of the more common forms of massage therapy is the traditional Chinese massage therapy also known as Tui Na (Yang et al. 2017).

One RCT was found evaluating acupressure compared to usual care for improving post-stroke depression (Kang et al. 2009).

The methodological details and results of the single RCT are presented in Table 23.

Table 23. RCTs evaluating acupressure for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Kang et al. (2009) RCT (5) N_{Start}=56 N_{End}=56 TPS=Acute	E: Meridian acupressure (10min, 7d/wk) C: Usual care Duration: 2wks	• Beyer Six-Face Rating Scale (+exp) • Activities of Daily Living Scale (+exp)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about acupressure

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Acupressure** may produce greater improvements in alleviating post-stroke depression than **usual care**.	1	Kang et al. 2009

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
2	**Acupressure** may produce greater improvements in activities of daily living than **usual care**.	1	Kang et al. 2009

Key Points

Acupressure may be beneficial for improving depression and activities of daily living post-stroke.

Reiki Treatment

Adopted from: https://cdn.mos.cms.futurecdn.net/h7qZKtvpyhYpENYhEpmSVZ-320-80.jpg

Reiki is a form of alternative medicine that originated in Japan. It is based on the theory that 'life energy' is transferred to patients when practitioners place their hands on or directly above the body, which promotes physical or psychological healing (Borang, 2001).

One RCT examined Reiki treatment for post-stroke depression. It compared Reiki treatment to a sham condition, and no treatment (Shiflett et al. 2002).

The methodological details and results of the single RCT are presented in Table 24.

Table 24. RCTs evaluating Reiki for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Shiflett et al. (2002) RCT (7) N_{Start}=50 N_{End}=44 TPS=Acute	E1: Reiki C1: Sham reiki C2: No treatment Duration: 10, 30min sessions over 2.5wk	E1 vs. C1 vs. C2 • CES Depression Scale (-) • Functional Independence Measure (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about Reiki treatment

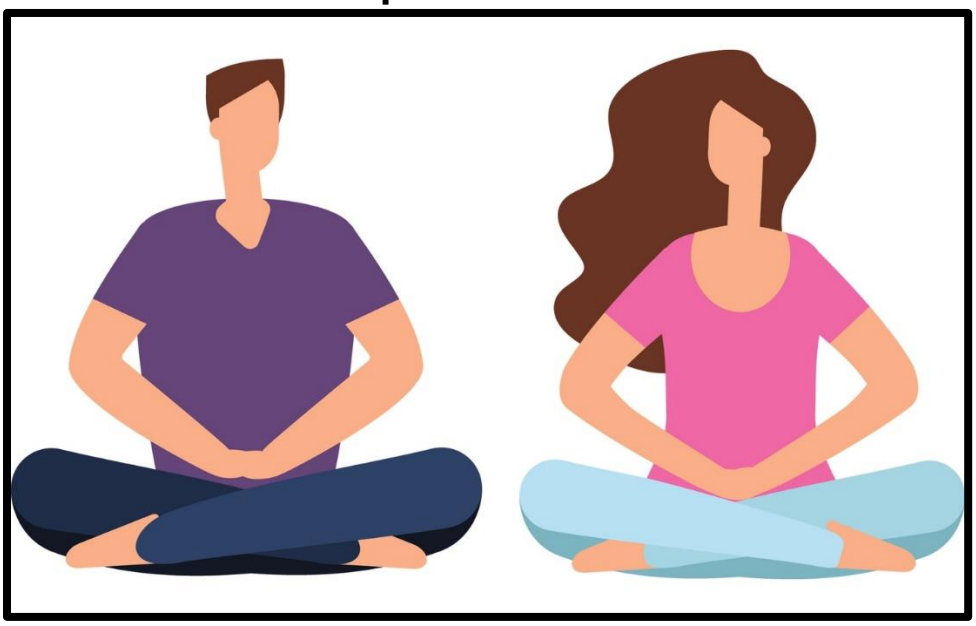
DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Reiki treatment** may not have a difference in efficacy when compared to **sham or no treatment** for improving post-stroke depression.	1	Shiflett et al. 2002

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Reiki treatment** may not have a difference in efficacy when compared to **sham or no treatment** for improving activities of daily living.	1	Shiflett et al. 2002

Key Points

Reiki therapy may not be beneficial for improving depression or activities of daily living.

Mindfulness Therapies



Adopted from: https://www.mindful.org/mindfulness-how-to-do-it/

Pharmacological methods that are frequently used to manage post-stroke mood disorders may come with adverse side effects for some people. Finding alternative, non-pharmacological methods of treatment are important for improving patient outcomes and providing more accessible care opportunities. Meditation and other mindfulness-oriented therapies provide a behavioural method for improving mood related outcomes. These types of interventions are not only easily accessible for all levels of ability post-stroke but can be completed by the patient on there own, as frequently as desired. Previous work has shown that meditation-based interventions can create significant improvements in depressive symptoms in both clinical and healthy populations (Britton, 2006). There is however, very little work done specifically for post-stroke depression.

Three RCTs were found evaluating a mindfulness technique for improving mood. One RCT looked at the use of relaxation CDs (Golding et al. 2018), another the effects of meditating in the forest or at home (Chun et al. 2017), and the effects of Yoga (Immink et al. 2014) to improve post-stroke depression.

The methodological details and results of the three RCTs are presented in Table 25.

Table 25. RCTs evaluating mindfulness therapies for mood

Authors (Year) Study Design (PEDro Score) Sample Size$_{start}$ Sample Size$_{end}$ Time post stroke category	Interventions Duration: Session length, frequency per week for total number of weeks	Outcome Measures Result (direction of effect)
Golding et al. 2018 RCT (6) N_{start}=21 N_{end}=20 TPS=Chronic	E: Autogenic relaxation CD C: Standard care Duration: 5x/wk for 1 mo	• Hospital Anxiety and Depression Scale – Depression (-)
Chun et al. 2017 RCT (6) N_{start}=59 N_{end}=59 TPS=Chronic	E: Forest meditation C: Urban meditation Duration: 4 day/3 night program	• Beck Depression Inventory (+exp) • Hamilton Depression Rating Scale (+exp) • Spielberg State-trait Anxiety Inventory (+exp)
Immink et al. (2014) RCT (7) N_{Start}=25 N_{End}=22 TPS=Chronic	E: Yoga (10wk) C: Usual care Duration: 10wks	• Geriatric Depression Scale (-) • State Trait Anxiety Inventory (-) • Stroke Impact Scale (-)

Abbreviations and table notes: C=control group; D=days; E=experimental group; H=hours; Min=minutes; RCT=randomized controlled trial; TPS=time post stroke category (Acute: less than 30 days, Subacute: more than 1 month but less than 6 months, Chronic: over 6 months); Wk=weeks.
+exp indicates a statistically significant between groups difference at α=0.05 in favour of the experimental group
+exp$_2$ indicates a statistically significant between groups difference at α=0.05 in favour of the second experimental group
+con indicates a statistically significant between groups difference at α=0.05 in favour of the control group
- indicates no statistically significant between groups differences at α=0.05

Conclusions about mindfulness therapies (relaxation, meditation, yoga)

DEPRESSION			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Forest meditation** may produce greater improvements in alleviating post-stroke depression than **urban meditation**.	1	Chun et al. 2017
1b	**Autogenic relaxation CDs** may not have a difference in efficacy when compared to **usual care** for improving post-stroke depression.	1	Golding et al. 2018
1b	**Yoga** may not have a difference in efficacy when compared to **usual care** for improving post-stroke depression.	1	Immink et al. 2014

ANXIETY			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Forest meditation** may produce greater improvements in post-stroke anxiety than **urban meditation**.	1	Chun et al. 2017
1b	**Yoga** may not have a difference in efficacy when compared to **usual care** for improving post-stroke anxiety.	1	Immink et al. 2014

ACTIVITIES OF DAILY LIVING			
LoE	**Conclusion Statement**	**RCTs**	**References**
1b	**Yoga** may not have a difference in efficacy when compared to **usual care** for improving activities of daily living.	1	Immink et al. 2014

Key Points

Forest meditation may be more beneficial than urban meditation for improving depression and anxiety post-stroke.

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