18 Post-Stroke Depression and Mood Disorders
Evidence Tables

Katherine Salter PhD (cand.), Swati Mehta PhD (cand.), Andreea Cotoi MSc, Robert Teasell MD, Norine Foley MSc, Jonathan Serrato MSc, Mark Speechley PhD

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Dr. Robert Teasell
Parkwood Institute, 550 Wellington Road, London, Ontario, Canada, N6C 0A7
Phone: 519.685.4000 ● Web: www.ebrsr.com ● Email: Robert.Teasell@sjhc.london.on.ca
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## 18.3 Risk Factors for Post-Stroke Depression

### 18.3.1.2 Stroke Location and Depression

#### Table 18.3.1.2 Stroke Location and Depression

<table>
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<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Folstein et al. (1977)</td>
<td>USA</td>
<td>Observational</td>
<td>No Score</td>
<td>TPS=acute</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=20 N&lt;sub&gt;End&lt;/sub&gt;=20</td>
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<tr>
<td></td>
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<td></td>
<td><strong>Intervention:</strong> Stroke patients admitted 30d after stroke onset and 10 orthopaedically disabled patients admitted at the same time were assessed for depression.</td>
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<td></td>
<td><strong>Outcomes:</strong> Hamilton Rating Scale; Visual Analogue Mood Scale; Present State Exam; Mini-Mental State Exam and Activities of Daily Living.</td>
</tr>
<tr>
<td>Robinson &amp; Szetela (1981)</td>
<td>USA</td>
<td>Observational</td>
<td>No Score</td>
<td>TPS&lt;sub&gt;Mean&lt;/sub&gt;=NA</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=18</td>
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<td><strong>Intervention:</strong> Patients with left hemispheric stroke were compared to 11 patients with traumatic brain injury for frequency and severity of depression.</td>
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<td></td>
<td></td>
<td><strong>Outcomes:</strong> Visual analog mood scale; Zung Self Rating Depression Scale; Hamilton Depression Rating Scale.</td>
</tr>
<tr>
<td>Robinson et al. (1983)</td>
<td>USA</td>
<td>No Score</td>
<td>TPS=acute</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;=103</td>
<td></td>
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<td></td>
<td><strong>Intervention:</strong> Stroke patients capable of undergoing psychiatric interview and not exhibiting decreased consciousness and/or aphasia with severe comprehension deficits were evaluated for mood disorders. All examinations were done in late morning or early afternoon to avoid effects of diurnal mood variation.</td>
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<td></td>
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<td><strong>Outcomes:</strong> Zung Self Rating Depression Scale; Hamilton Depression Scale; Present State Examination; General Health Questionnaire.</td>
</tr>
</tbody>
</table>

1. Patients with right hemisphere stroke seemed to be particularly vulnerable and displayed a syndrome of irritability, loss of interest and difficulty in concentration in addition to depression of mood.

2. More than 60% of the stroke patients had clinically significant depression compared with about 20% of the trauma patients.

3. Both groups were comparable in impairment in activities of daily living and global cognitive function.

4. Two groups had similar-sized lesion, but areas of ischemic injury were more anterior than the traumatic lesion.

5. Severity of depression was directly correlated with the closeness of the lesion to the frontal poles.

6. Nearly 50% of patients had clinically significant depression and one fourth had symptom clusters typically found in major depression disorders.

7. Lesion location was found to be most important in determining the frequency and severity of depression.

8. Functional physical impairment, intellectual impairment, quality of social support and age contributed to or modified depression.

9. Distance of lesion on CAT scan from the frontal pole in patients with left anterior infarcts was significantly associated with severity of depression at 3mo and 6mo post-stroke.

10. Intellectual functioning and functional physical impairment in-hospital were significantly correlated with severity of depression and social functioning scores at 3mo and 6mo post-stroke.
Patients developing depression during the first 6mos post-stroke might be responding to severity of their impairment whereas patients who develop depression during acute post-stroke may have a neuroanatomical and neurophysiological basis for the relationship.

| Ebrahim et al. (1987) | Intervention: Acute stroke survivors underwent mood assessment. | 1. The prevalence of depression was 23% for the study sample.  
2. No difference in depression was found between right and left hemisphere strokes.  
3. Affective illness was strongly associated with functional ability.  
4. Only 15% of those with high depression scores were receiving antidepressant drugs. |
|---|---|---|
| UK  
TPS=acute  
N\text{start}=149 | Outcomes: General Health Questionnaire. |  |
| Eastwood et al. (1989) | Intervention: Stroke patients were assessed over 18mo to examine the effect of a specific brain lesion or consequent disability on depression. | 1. Depression affected 50% of the patients.  
2. Previous psychiatric disorder and previous cerebrovascular accident appeared to be important risk factors.  
3. There were hemispheric differences with both site-of-lesion and reactive depression viewpoints confirmed. |
| Canada  
Case Control  
No Score  
TPS=chronic  
N\text{start}=8 | Outcomes: Schedule for Affective Disorders and Schizophrenia; Zung Self-Rating Depression; Geriatric Depression Scale; Hamilton Depression Rating Scale. |  |
| Aström et al. (1993) | Intervention: Major depression, functional ability and social networks were repeatedly assessed for 3yr in 80 acute stroke patients. Cerebral atrophy and brain lesion parameters were determined from CT scans. | 1. At discharge, depression was noted to be significantly more frequent in those patients with left hemisphere lesions.  
2. By 3mos post-stroke there was a significant increase in the frequency of depression among patients with right hemispheric lesions.  
3. Lesion location in the left anterior hemisphere was significantly associated with depression with a rate 3 times higher than that with lesions in the right hemisphere. However, after 3mos this was no longer significant and after 3yr, depression occurred more often in right than in left hemisphere lesions. |
| Sweden  
Observational  
No Score  
TPS=acute  
N\text{start}=80 | Outcomes: Diagnostic and Statistical Manual of Mental Disorders (DSM-III). |  |
| Herrmann et al. (1995) | Intervention: Patients with single demarcated unilateral lesions were selected for study. Clinical examination, CT scan examination and psychiatric assessment were performed within a 2mo period after the acute stroke. | 1. No significant differences in depression scores noted between patients with left and right hemisphere lesions.  
2. No correlation was noted between the severity of depression and the anteriority and the volume of the lesion or brain atrophy.  
3. Major depression was exhibited in nine patients with left hemispheric strokes all involving the basal ganglia. |
| Germany  
No Score  
TPS=acute  
N\text{start}=47 | Outcomes: Cornell Depression Scale; Montgomery-Asberg Depression Rating Scale; Modified Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R). |  |
<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Score</th>
<th>TPS</th>
<th>Start</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morris et al. (1996)</td>
<td>USA</td>
<td>No</td>
<td>acute</td>
<td>193</td>
<td>First time stroke patients were selected from the National Stroke Data Bank in order to examine the relationship between post-stroke lesion size and location, and depressed mood.</td>
<td>CT scans; Center for Epidemiologic Studies Depression Scale.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Score</td>
<td></td>
<td></td>
<td>1. None of the patients with right hemispheric strokes exhibited a major depression.</td>
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<td></td>
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<td>2. Lesion size or location was not associated with depression; however, among patients with comparable small-sized lesions, depression was more frequent among those with left hemispheric stroke than those with right hemispheric stroke.</td>
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<td>3. Among patients with small lesions, those with hemispheric lesions had a significantly higher frequency of depression than right hemispheric lesions.</td>
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<td></td>
<td>4. Patients with predominantly left cortical lesions had a higher rate of depression than right cortical lesions.</td>
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<td>5. The difference in the rate of depression was greatest, albeit non-significantly, between left and right posterior cortical lesions.</td>
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</tr>
<tr>
<td>Morris et al. (1996)</td>
<td>Australia</td>
<td>No</td>
<td>NA</td>
<td>44</td>
<td>First-ever stroke patients with single lesions on CT were examined for the presence of post-stroke depression, severity of depression and its relationship to lesion location.</td>
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<tr>
<td></td>
<td>Canada</td>
<td>No</td>
<td>NA</td>
<td>35</td>
<td>Depression was assessed in 16 stroke patients with localized right hemisphere lesions and 19 with localized left hemisphere lesions. All psychological tests were administered between 10 a.m. and 3 p.m. to control for diurnal variations in mood. All patients underwent computerized tomography of the brain.</td>
<td>Zung Depression Scale (ZDS); Beck Hopelessness Scale; Hopkins Symptom Checklist; Composite Depression Index.</td>
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<td>1. Patients with left hemisphere prefrontal or basal ganglia structures had a significantly higher frequency of depressive disorder than other left hemispheric lesions or those with right hemispheric lesions.</td>
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<td>2. There was a significant positive relationship between ZDS scores and the most posterior point location of the lesion in right hemisphere patients.</td>
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<td>3. In left hemisphere patients, severity of depression tended to be greater with increasing proximity of the lesion to the frontal pole.</td>
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<tr>
<td>MacHale et al. (1998)</td>
<td>UK</td>
<td>No</td>
<td>chronic</td>
<td>55</td>
<td>Patients with a single lesion on CT were assessed for depression 6mos post stroke.</td>
<td>Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV).</td>
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<td>1. 26% of patients met DSM-IV criteria for an anxiety or depressive disorder with 20% being depressed.</td>
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<td>2. Depression was significantly associated with larger lesions involving the right cerebral hemisphere.</td>
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<tr>
<td>Sato et al. (1999)</td>
<td>USA</td>
<td>Observational</td>
<td>NA</td>
<td></td>
<td>Patients were assessed to determine the relationship between MRI infarcts in the basal ganglia and non-basal-ganglia areas, potential functional consequences of the lesion and depressive symptomatology.</td>
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<td></td>
<td>1. The CES-D scores were independently associated with non-basal-ganglia lesions but not independently associated with basal ganglia lesions.</td>
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<tr>
<td>Study Reference</td>
<td>Country</td>
<td>Study Type</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;</td>
<td>N&lt;sub&gt;End&lt;/sub&gt;</td>
<td>Population</td>
<td>Intervention</td>
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<tr>
<td>Kim &amp; Choi-Kwon (2000)</td>
<td>Korea</td>
<td>Observational</td>
<td>148</td>
<td>148</td>
<td>Mean age=62yr; Gender: Males=94, Females=54.</td>
<td>Studied 148 patients with single, unilateral stroke for the presence of post-stroke depression and post stroke emotional incontinence at 2 to 4mos post-stroke.</td>
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<td>Aben et al. (2006)</td>
<td>Netherlands</td>
<td>Observational</td>
<td>190</td>
<td>NA</td>
<td>Patients with first infarct were followed for a period of 1yr. CT was performed during the acute admission. 75 patients also received MRI. Depression was assessed at 1, 3, 6, 9 and 12 mo post stroke.</td>
<td>Structured Clinical Interview for Diagnostic and Statistical Manual Disorders.</td>
</tr>
<tr>
<td>Santos et al. (2009)</td>
<td>Switzerland</td>
<td>Observational</td>
<td>41</td>
<td>41</td>
<td>An autopsy series of 41 stroke patients, 20 of whom had been diagnosed with post-stroke depression (PSD). Macrionfarcit site was recorded and cortical microinfarcts and lacunes were assessed in 10 sections/area using a semi-quantitative scale. Total scores for each of these lesion types were obtained by adding scores for each area.</td>
<td></td>
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<tr>
<td>Study</td>
<td>Country</td>
<td>TPS</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;</td>
<td>Interference</td>
<td>Lesion Location</td>
<td>Outcomes</td>
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<tr>
<td>Chatterjee et al. (2010)</td>
<td>UK</td>
<td>No Score</td>
<td>103</td>
<td>Identified individuals with major depression (experimental group, EG) (Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria + Montgomery-Asberg Depression Rating Scale (MADRS) scores &gt;17; n=33) for comparison with control participants (control group, CG) (no major or minor depressive symptoms, no treatment for depression within 6mos and MADRS scores ≤7; n=70). CT scans performed acutely were assessed for chronic changes and a rating scale for white matter changes applied.</td>
<td>Basal ganglia and thalamic lacunes, white matter lesions</td>
<td>Diagnostic and Statistical Manual of Mental Disorders; Clinical Dementia Rating Scale.</td>
</tr>
<tr>
<td>Nishiyama et al. (2010)</td>
<td>Japan</td>
<td>No Score</td>
<td>134</td>
<td>Examined the relationship between lesion location and the presence of depressive symptoms 1mo following stroke in 134 patients. All patients received an MRI scan or CT to determine lesion location.</td>
<td>Lenticulocapsular lesions</td>
<td>Zung Self Rating Depression Scale.</td>
</tr>
<tr>
<td>Tang et al. (2011)</td>
<td>China</td>
<td>No Score</td>
<td>591</td>
<td>Individuals admitted to the medical wards of a university-affiliated regional hospital were assessed by a psychiatrist for depression at 3mo post-stroke. MRIs were obtained during the acute period (99.8% during the first wk following the stroke event).</td>
<td>Frontal subcortical infarcts</td>
<td>Kim’s and House’s criteria.</td>
</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>Study Type</td>
<td>Score</td>
<td>TPS Range</td>
<td>Start</td>
<td>End</td>
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<tr>
<td>Rajashekaran et al.</td>
<td>India</td>
<td>Observational</td>
<td>No Score</td>
<td>2wk-6mo</td>
<td>62</td>
<td>62</td>
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<tr>
<td>Rashid et al. (2013)</td>
<td>United Kingdom</td>
<td>Observational</td>
<td>No Score</td>
<td>NA</td>
<td>120</td>
<td>120</td>
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**Population:**

**Mean age=57.89±7.12yr; Gender: Males=49, Females=13.**

**Intervention:**

Patients with first ever stroke were interviewed and diagnosed with depression by using a semi-structured Mini International Neuropsychiatric Interview (MINI) Plus Interview and Statistical Manual of Mental Disorders Fourth edition Text Revision (DSM-IV-TR) guidelines, in addition to completing a set of questionnaires. Assessments were conducted only once.

**Outcomes:**

MINI Plus Interview; Mini-Mental State Examination (MMSE); Barthel Index (BI).

**Population:**

Patients (N=60): Mean age=67.35±11.08yr; Gender: Males=43, Females=17. Spouses (N=60): Mean age=65.67±10.84yr; Gender: Males=16, Females=44.

**Intervention:**

Five sites within England recruited patients and their spouses to participate in completing a set of questionnaires as part of a home visit. The assessments were completed by both patients and spouses, and conducted once only.

**Outcomes:**

Post Stroke Depression Rating Scale (PSDRS); Level of Expressed Emotion Scale (LEE).

1. A total of 45.16% (n=28) patients were diagnosed with depression, of which 18 qualified for a major depression diagnosis according to the MINI Plus interview.
2. Of the remaining 34 patients, 13 qualified for a diagnosis of Adjustment disorder, of which 61% were diagnosed with lower mean BI scores within the first 5wk of stroke onset compared to the group diagnosed with depression (no p-value provided).
3. Among those with depression, left sided lesions were significantly more prominent (p=0.002) however, no statistically significant correlation could be made with the site of lesion and diagnosis of depression.
4. MMSE scores did not differ significantly between those with a diagnosis of depression and those without (no p-value provided).

5. Patients with a left hemisphere stroke reported significantly higher PSDRS scores than patients with a right hemisphere stroke (p=0.02).
6. No significant difference was found between patients with right or left hemisphere stroke on the LEE (p=0.595).
7. A significant relationship was found between lesion laterality and Post-Stroke Depression (PSD) according to PSDRS score (p=0.028) (for left hemisphere).
8. As the levels of spouse/partner LEE scores increased, the levels of patient PSD also increased (p=0.039).
9. The LEE scores illustrated a significant interaction between lesion laterality and level of expressed emotion on PSD (p=0.005).
10. The interaction between lesion laterality and levels of partner/spouse expressed emotion according to LEE results on PSDRS scores was not statistically significant (p=0.63).
### Shi et al. (2014)

**China**  
**Case Series**  
**No Score**  
**TPSOverall=14d**  
**NStart=1067**  
**NEnd=1067**

**Population:** Mean age=61.5±11.5yr; Gender: Males=691, Females=376.  
**Intervention:** Data collected from patients admitted between April 2008 and April 2010 as part of the Incidence and Outcome of Patients with Post Stroke Depression in China study were reanalyzed. Assessments were conducted at baseline, 14d, 3mo, 6mo and 1yr follow-ups.  
**Outcomes:** Hamilton Rating Scale for Depression-17 (HAMD-17); Modified Rankin Scale (MRS).

1. A decreasing trend in rates of depression diagnosed by HAMD-17 were reported with 303 (28.4%), 220 (20.6%), 166 (15.6%), and 154 (14.4%) patients reporting symptoms of depression at 14d, 3mo, 6mo and 1yr respectively.  
2. Patients with frontal lobe lesions were significantly more likely to experience persistent or recurrent depression than patients with non-frontal lobe lesions (p=0.028).  
3. Patients with frontal lobe lesions had significantly higher rates of depression than patients with non-frontal lobe lesions at 3mo and 6mo post stroke (p=0.017 and p=0.042 respectively).  
4. Persistent and recurrent depression was significantly associated with lower functional outcome compared to transient depression according to MRS scores for patients with frontal lobe lesions and non-frontal lobe lesions (both p<0.001).

### Tang et al. (2014)

**China**  
**Longitudinal**  
**No Score**  
**TPSShort=3mo**  
**NStart=213**  
**NEnd=135**

**Population:** Mean age=65.7±11.0yr; Gender: Males=66, Females=69.  
**Intervention:** The association between post-stroke depression (PSD) and cerebral microbleeds (CMBs) was prospectively analyzed. Assessments for depression were conducted at 3mo and 15mo after index stroke.  
**Outcomes:** Geriatric Depression Scale 15-item version (GDS); Number of CMBs according to MRI scan.

1. 65.9% (n=89) of the 135 patients who attended the 1-year follow-up still had PSD (non-remitters), while 34.1% (n=46) no longer had PSD (remitters).  
2. Non-remitters were significantly more likely than remitters to have CMBs (p=0.049), specifically lobar CMBs (p=0.024).  
3. Lobar CMBs were the only significant MRI indicators for non-remission of PSD (p=0.039).  
4. Frontal (p=0.298), Temporal (p=1.000), Parietal (p=0.097), Occipital (p=0.094), Deep (p=0.771), and Infratentorial (p=0.493) CMB’s were not significant indicators of non-remission of PSD.

### Wu et al. (2014)

**China**  
**Observational**  
**No Score**  
**TPSShort=NA**  
**NStart=243**  
**NEnd=243**

**Population:** Depression group (N=60): Mean age=66.45±9.95yr; Gender: Males=15, Females=45. Non-Depression group (N=183): Mean age=67.16±9.09; Gender: Males=81, Females=102.  
**Intervention:** Patients with silent lacunar infarction (SLI) were divided into depression and non-depression groups depending on their diagnosis during a clinical examination and interview. The presence and location of SLI were evaluated using magnetic resonance imaging. Patients donated blood samples for analysis and blood pressure was recorded by questionnaire over the previous 3mos.

1. 24.7% of the 243 participants were classified as depressed.  
2. Number of patients with SLI in the basal ganglia was significantly higher in the depression group compared to the non-depression group (p<0.001).  
3. No statistically significant differences were noted for blood pressure, blood lipid levels, coronary artery disease, diabetes, fasting insulin, or other locations of SLI (i.e. thalamus, deep white matter, brainstem) between the depression and the non-depression groups.
**Outcomes:** Patient Health Questionnaire-9 (PHQ-9); Physiological variables (physical activity, BMI, Blood pressure, coronary artery disease, diabetes, fasting insulin, blood lipid, inflammation markers, location of lacunar infarction).

4. SLI in the basal ganglia was a significant independent imaging predictor of depression with an OR of 3.12 (95% CI [1.221,8.015]), along with mild to moderate and vigorous physical activity (OR 0.21, 95% CI [0.05,0.82]; OR 0.28, 95% CI [0.10,0.80] respectively), BMI (overweight: OR 3.56, 95% CI [1.27,9.94]; obese: OR 8.94, 95% CI [2.41,33.17]), TNF-α (OR4.59, 95% CI [1.91,11.06]), IL-6 (OR 3.38, 95% CI [1.29,8.90]), and CRP (4.63, 95% CI [1.85,11.61]).

5. Women (p=0.013) and those with high school or less than high school education (p=0.044) exhibited more symptoms of depression.

6. Both overweight and obese patients (p<0.001) and physically inactive participants (p<0.001) displayed more symptoms of depression.

7. Those with high levels of inflammation markers including CRP (p<0.001), hs-CRP (p=0.005), IL-6 (p=0.002), and TNF-α (p<0.001) exhibited significant symptoms of depression.

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### 18.4 Assessment of Post-Stroke Depression

**Table 18.4.1 Detection and Diagnosis of Post-Stroke Depression**

<table>
<thead>
<tr>
<th>Author, Year Country Observation PEDro Score TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>da Rocha e Silva et al. (2013) Brazil Observational No Score TPS&lt;sub&gt;Mean&lt;/sub&gt;=NA TPS&lt;sub&gt;Start&lt;/sub&gt;=64 N&lt;sub&gt;End&lt;/sub&gt;=64</td>
<td><strong>Population:</strong> Experimental Group 1 (EG1, N=14): Mean age: Males=50.7±8.0yr, Females=56.0±19.4yr; Gender: Males=3, Females=11. Experimental Group 2 (EG2, N=33): Mean age: Males=61.9±9.9yr, Females=61.9±14.8yr; Gender: Males=20, Females=13. Experimental Group 3 (EG3, N=17): Mean age: Males=50.5yr, Females=51.1±7.0yr; Gender: Males=2, Females=15. <strong>Intervention:</strong> Participants were divided into three groups: stroke patients with Post-Stroke Depression (PSD) (EG1), stroke patients without PSD (EG2), and patients diagnosed with major depression but without stroke (CG). Patients were diagnosed according to the Structured</td>
<td>1. BDI, HAM-D, HAM-A, and HADS scores were significantly higher in the CG group compared to the other two groups (p&lt;0.05), thereby indicating that a diagnosis of PSD is not comparable to CG. 2. BDI scores revealed greater severity of depressive symptoms among CG group patients compared to the Stroke+PSD and Stroke-PSD groups.</td>
</tr>
</tbody>
</table>
Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and completed a set of questionnaires. **Outcomes:** Beck Depression Inventory (BDI); Hospital Anxiety and Depression General Scale (HADS); Hamilton Depression Rating Scale (HAM-D); Hamilton Rating Scale for Anxiety (HAM-A).

### de Man-Van Ginkel et al. (2013)
The Netherlands Observational No Score
TPS<sub>Exp</sub>=1wk
TPS<sub>Con</sub>=1wk
N<sub>Start</sub>=410
N<sub>Exp</sub>=382

**Population:** Experimental Group (EG, N=54): Mean age=70.2±14yr; Gender: Male=26, Female=28. Control Group (CG, N=328): Mean age=66.2±17.3yr; Gender: Male=181, Female=137.

**Intervention:** Both the EG (patients with depression) and the CG (patients without depression) provided data at 1wk post stroke followed by a diagnostic interview at 6-8wks post stroke. This data was then used to develop a new diagnostic tool, the Post-Stroke Depression Prediction Scale. Assessments were completed at 1wk and 6-8wks post-stroke.

**Outcomes:** Post-stroke Depression Prediction Scale (DePreS: Sensitivity, Specificity, Positive Predicted Value, Negative Predicted Value); Composite International Diagnostic Interview (CIDI); Barthel Index (BI); Social Support List-6 (SSL-6).

1. A cut-off score ≥2 was found to be most accurate for the DePreS with a Sensitivity of 0.73 (95% CI, 0.60–0.83).
2. Specificity of the DePreS was 0.75 (95% CI, 0.70–0.80).
3. The Positive Predicted Value was 0.94 (95% CI: 0.91–0.97).
4. The Negative Predicted Value was 0.33 (95% CI: 0.25–0.42).
5. DePreS with cutoff scores of ≥3, ≥6, and ≥11 were tested but were not found to be as accurate.
6. Ratings of needing help on the BI: Dressing subscale (p<0.03) and CIDI diagnoses of depression (p<0.001) were significant predictors of depression.
7. SSL-6 scores differed significantly between the EG and CG at baseline (p<0.05).

### Kang et al. (2013)
South Korea Longitudinal No Score
TPS<sub>Mean</sub>=2wks
N<sub>Start</sub>=423
N<sub>Exp</sub>=288

**Population:** Intervention Group (N=423): Mean age=64.5±10.0yr; Gender: Male=244, Female=179.

**Intervention:** Patients were assessed for depression according to Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) criteria by a psychiatrist and then completed a set of assessment questionnaires for depression 2wks post stroke. Comparisons were then made between DSM-IV diagnoses of depression and the assessment questionnaires. Assessments were conducted at baseline and at 1yr follow-up.

**Outcomes:** Beck Depression Inventory (BDI); Hospital Anxiety and Depression Scale (HADS: Depression); Hamilton Rating Scale for Depression (HAMD); Montgomery-Asberg Depression Rating Scale (MADRS); Barthel Index (BI); Mini Mental State Examination (MMSE).

1. BDI, HADS, HAMD and MADRS all demonstrated high discriminating abilities (AUC 0.88–0.92) but generally lower values were found for sensitivity (0.83–0.85) and specificity (0.72–0.80) for all variations of depression.
2. Misclassification of depression on the BDI, HADS, and MADRS was associated with female gender at 2wks post-stroke.
3. Misclassification of depression on the BDI, HADS, MADRS and HAMD were associated with lower BI and lower MMSE scores at 2wks post-stroke.
4. Misclassification of depression on the HAMD and the BDI were associated with female gender and lower BI scores respectively at 1yr follow-up but no other associations with misclassifications were found.

### White et al. (2013)
Australia Observational No Score
TPS<sub>Mean</sub>=NA
N<sub>Start</sub>=62
N<sub>Exp</sub>=62

**Population:** (Demographic data available for only 49 patients) Intervention Group (N=62): Mean age=65±13yr; Gender: Male=27, Female=22.

**Intervention:** Patients completed an electronic depression screening tool followed by a survey on acceptability. Clinicians were also interviewed in regards to acceptability of an electronic screening tool.

1. The acceptability survey revealed that 95% of patients found the electronic screening easy to complete, 87% stated it was easy to understand, 73% thought the questions were important, and almost 97% believed it was a good way to pass on information.
2. Clinicians reported that electronic depression screening tool only provided...
Outcomes: Custom acceptability survey; Qualitative themes concerning depression.

summarised results but encouraged them to monitor and discuss depressive symptoms more frequently.

3. Clinicians also noted that screening for depression does not occur frequently due to time-constraints and that the screening tool would be beneficial.

D’Aniello et al. (2014)
Italy
Observational
No Score
TPS Mean = 4.0 ± 4.6 yr
N Start = 81
N End = 81

Population: Mean age = 62.0 ± 12.6 yr; Gender: Males = 48, Females = 33.
Intervention: Patients completed a set of questionnaires assessing psychological and cognitive well-being during chronic stroke. Assessments were conducted at a mean of 4 yr post-stroke.
Outcomes: Hospital Anxiety and Depression Scale (HADS: Depression, Anxiety); Medical Outcomes Study 36-item Short Form Questionnaire (SF-36: General Health, Mental Health); Psychological General Well-Being Index (PGWBI: Total, Positive Well-Being, Vitality, General Health, Anxiety, Depression, Self-Control).

1. Mean scores for HADS Depression and HADS Anxiety scales were 2.44 and 5.66 respectively with depression and anxiety prevalence rates of 19.7% and 55.6% respectively.
2. HADS Depression was significantly correlated with the PGWBI Total score, PGWBI Positive Well-Being, PGWBI Vitality, PGWBI Depression, PGWBI Anxiety (all p < 0.001), PGWBI General Health (p = 0.008), SF-36 Mental Health (p = 0.04), and SF-36 General Health (p = 0.046).
3. HADS Anxiety was significantly correlated with the PGWBI Positive Well-Being, Vitality, General Health, Anxiety, Depression, Self-Control subscales (all p < 0.001).

Lees et al. (2014)
United Kingdom
Longitudinal
No Score
TPS Overall ≤ 1 d
N Start = 69
N End = 61

Intervention: Patients completed a set of questionnaires on the day of admission followed by a telephone interview at follow-up. Assessments were completed at baseline and at 1 mo follow-up.
Outcomes: Hospital Anxiety and Depression Scale (HADS: Anxiety, Depression); Depression Intensity Scale Circles (DISCs).

1. HADS Depression scores reported a prevalence of 9 patients (13%) with depression but DISCs found a prevalence of 25 patients (37%) with depression at baseline, revealing a significant difference between the two measures (p = 0.021).
2. HADS Anxiety and HADS Depression scores decreased significantly (p < 0.0001 and p = 0.04 respectively) from baseline to follow-up.
3. HADS Anxiety and HADS Depression both showed poor sensitivity (0.33 [95% CI: 0.10–0.70] and 0.33 [95% CI: 0.12–0.65] respectively) but good specificity (0.92 [95% CI: 0.82–0.97] and 0.96 [95% CI: 0.86–0.99] respectively) for prediction of relevant anxiety and depression disorders at 1 mo follow-up.

18.5 Consequences Associated with Post-Stroke Depression

18.5.1 Functional Impairment and Depression Post-Stroke

Table 18.5.1 Functional Ability and Depression Post-Stroke
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robinson et al. (1983)</td>
<td>USA</td>
<td>Longitudinal</td>
<td>No Score</td>
<td>TPS=acute</td>
<td>$N_{start}=103$</td>
</tr>
<tr>
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<td><strong>Intervention:</strong> Stroke patients capable of undergoing psychiatric interview and not exhibiting decreased consciousness and/or aphasia with severe comprehension deficits were evaluated for mood disorder. All examinations were done in late morning or early afternoon to avoid effects of diurnal mood variation.</td>
<td>1. Nearly 50% of patients had clinically significant depression and one fourth had symptom clusters found in major depression disorders. 2. Functional physical impairment, intellectual impairment, quality of social support and age contribute to or modify depression. 3. Functional physical impairments in-hospital was significantly correlated with severity of depression and social functioning scores at 3 and 6mos post-stroke. 4. The authors concluded patients developing depression during the first 6mos post-stroke may be responding to severity of their impairment whereas patients who develop depression during acute post-stroke may have a neuroanatomical and neurophysiological basis for their relationship.</td>
</tr>
<tr>
<td>Sinyor et al. (1986)</td>
<td>USA</td>
<td>No Score</td>
<td>TPS=NA</td>
<td>$N_{start}=64$</td>
<td></td>
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<td></td>
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<td><strong>Intervention:</strong> Patients were screened from 166 consecutive stroke admissions to a rehabilitation hospital. Patients were assessed in hospital and 6wks post-discharge.</td>
<td>1. Moderate to severe depression was identified in 22% of patients; mild depression in 25%. 2. Depression scores were not correlated with functional status scores on discharge, change in functional status over the rehabilitation stay or with length of stay. 3. When comparing depressed patients to non-depressed patients, depressed patients had lower functional status scores. 4. Both groups of patients improved significantly over time and there were no significant differences between groups regarding the degree of improvement.</td>
</tr>
<tr>
<td>Ebrahim et al. (1987)</td>
<td>UK</td>
<td>No Score</td>
<td>TPS=acute</td>
<td>$N_{start}=149$</td>
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<td><strong>Intervention:</strong> Acute stroke survivors underwent mood assessment.</td>
<td>1. Found that the prevalence of depression was 23% for study sample. 2. Affective illness was strongly associated with functional ability. 3. Only 15% of those with high depression scores were receiving antidepressant drugs.</td>
</tr>
</tbody>
</table>
### Robinson et al. (1987)
**USA**  
No score  
TPS=NA  
N_start=NA

Refer to Robinson et al. (1983).

1. All follow-up patients with major depression scores in-hospital improved by 2yr, with a significant reduction in mean depression scores and improvement in activities of daily living (ADLs).  
2. There was no significant improvement in mean depression scores or ADL for dysthymic patients.  
3. 34% of patients not depressed in hospital had developed major or minor depression by 2yr with their mean depression scores significantly elevated.

### Bacher et al. (1990)
**Canada**  
No Score  
TPS=NA  
N_start=48

**Intervention:** Stroke patients were followed for 12mo in order to identify the course of post-stroke depression among rehabilitation patients and the relationship of depression with physical and cognitive impairment. Patients with known history of psychiatric illness and or stroke, dementia or comprehension disorders were excluded. Clinical depression was defined as a score $>50$ and moderate to severe $>60$ on the Zung Self-Rating Scale (ZDS).  

**Outcomes:** ZDS.

1. By 12mos more than half the patients were clinically depressed.  
2. Functional level improved for all patients, but was higher for non-depressed patients.

### Parikh et al. (1990)
**USA**  
No Score  
TPS=NA  
N_start=36

**Intervention:** Patients with acute thrombotic or hemorrhagic stroke were followed for 2yr.

1. In hospital all patients had comparable scores on all measures; however, rate of recovery was different with depressed patients being more impaired at 2yr.  
2. Among patients with major depression, the difference in impairment recovery was present even after depression had subsided.

### Morris et al. (1992)
**USA**  
No Score  
TPS=subacute  
N_start=49

**Intervention:** Inpatients with stroke initially at 2mos after stroke and then again 14mos post-stroke were studied to examine the effect of clinical depression on recovery from stroke.

1. At initial assessment, 41% of patients were depressed. There were no significant differences in demographic, clinical, stroke or lesion characteristics.  
2. Depressed patients improved less than non-depressed patients in functional status and cognitive functioning.  
3. Mean recovery of activities of daily living (ADLs) was not different between the two groups. Depressed patients tended to deteriorate over time on ADLs.

### Sharpe et al. (1994)
**UK**  
No Score  
TPS=chronic  
N_start=60

**Intervention:** Stroke survivors 3 – 5yr post stroke were interviewed.  

**Outcomes:** Diagnostic and Statistical Manual of Mental Disorders-Revised.

1. Presence of depression was associated with physical and cognitive impairment, increased age, institutionalization, absence of close relationships and large brain lesion.  
2. When controlling for the effects of all other variables, the association between depression...
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Outcomes</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loong et al. (1995)</td>
<td>Prospective study assessing the outcomes of rehabilitation (mood and physical recovery) for 52 patients with post-stroke depression. Patients assessed to have rehabilitative potential were admitted to the rehabilitation unit and all those with severe motor deficits or comprehension deficits were not admitted if there was a shortage of beds. Patients with aphasia, dementia or delusion were excluded.</td>
<td>Diagnostic and Statistical Manual of Mental Disorders-Revised; Hamilton Rating Scale for Depression.</td>
<td>1. 55% of patients were assessed as depressed on admission and 98% had physical impairment. 2. Patients less functionally impaired on discharge were less likely to be depressed. Patients less depressed were also found to be less likely to be depressed at time of discharge. 3. Patients who were more depressed on admission were more likely to be functionally impaired on discharge. 4. The association between depression and functional impairment was found to be strong and accounted for 48% of the variance.</td>
</tr>
<tr>
<td>Herrmann et al. (1998)</td>
<td>Of 436 consecutive admissions to a regional stroke center, 150 were available for assessment at 3mos and 136 at 1yr post-stroke.</td>
<td>Montgomery Asberg Depression Rating Scale (MADRS); Zung Self-rating Depression Scale (ZDS); Functional Independence Measure (FIM); Oxford Handicap Scale (OHS).</td>
<td>1. At 3 mos marked symptoms of depression were assessed in 22% of patients using the ZDS and 27% using the MADRS. 2. Depression was significantly associated with FIM scores and OHS scores both at 3mos (p&lt;0.0001 and p&lt;0.0001, respectively) and at 1yr (p&lt;0.001 and p&lt;0.0001, respectively).</td>
</tr>
<tr>
<td>Pohjasvaara et al. (1998)</td>
<td>Stroke patients were assessed at 3 – 4mo post-stroke to evaluate the frequency and clinical correlates of post-stroke depression.</td>
<td>Montgomery-Asberg Depression Rating Scale; Beck Depression Inventory; Zung Self-Rating Anxiety Scale; Symptom Checklist-90; Barthel Index.</td>
<td>1. On logistic regression, dependence in activities of daily living was associated with the diagnosis of major depression (OR = 2.9) or depression (OR = 1.8).</td>
</tr>
<tr>
<td>Pohjasvaara et al. (1998)</td>
<td>Stroke patients were assessed 3mos following stroke and again at 15mos to examine the influence of depression on long-term outcome. 390 patients completed the Beck Depression Inventory (BDI) at 3mos and 276 at 15mos.</td>
<td>BDI; Barthel Index (BI); Rankin Scale (RS).</td>
<td>1. Patients with major depression or classified as depressed using the BDI were more likely to have poor functional outcome (dependence) at 15 mos assessed on the BI and RS.</td>
</tr>
<tr>
<td>Kotila et al. (1999)</td>
<td>Post-stroke depression and functional outcome was examined in 594 patients in four different districts. Depression was defined by a Beck depression inventory (BDI) score of ≥ 10.</td>
<td>BDI; Barthel Index; Rankin Scale.</td>
<td>1. 47% of the 321 surviving patients were depressed at 3mos and 47.3% of 311 surviving patients were depressed at 12mos. 2. Depressed patients needed more help on activities of daily living than did non-depressed patients. 3. 68.9% of depressed patients were in institutional care compared to 57.6% of non-depressed patients.</td>
</tr>
<tr>
<td>Reference</td>
<td>Country</td>
<td>Score</td>
<td>TPS</td>
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<td>-----------------------------------------</td>
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<tr>
<td>Paolucci et al. (1999)</td>
<td>Italy</td>
<td>No Score</td>
<td>TPS=NA</td>
</tr>
<tr>
<td>Van de Weg et al. (1999)</td>
<td>Netherlands</td>
<td>No Score</td>
<td>TPS=acute</td>
</tr>
<tr>
<td>Gillen et al. (2001)</td>
<td>USA</td>
<td>No Score</td>
<td>TPS=acute</td>
</tr>
<tr>
<td>Cully et al. (2005)</td>
<td>USA</td>
<td>No Score</td>
<td>TPS=NA</td>
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<tr>
<td>Study Reference</td>
<td>Country</td>
<td>Score</td>
<td>TPS</td>
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<tr>
<td>Nannetti et al. (2005)</td>
<td>Italy</td>
<td>No Score</td>
<td>TPS=acute</td>
</tr>
<tr>
<td>Paolucci et al. (2006)</td>
<td>Italy</td>
<td>No Score</td>
<td>TPS=NA</td>
</tr>
<tr>
<td>Van de Port et al. (2006)</td>
<td>Netherlands</td>
<td>No Score</td>
<td>TPS=1-3 yr</td>
</tr>
<tr>
<td>Hama et al. (2007)</td>
<td>Japan</td>
<td>No Score</td>
<td>TPS=NA</td>
</tr>
<tr>
<td>Saxena et al. (2007)</td>
<td>Singapore</td>
<td>Intervention: 6 mo prospective cohort study of 141 stroke patients admitted to two rehabilitation hospitals.</td>
<td>1. Linear regression demonstrated that greater change in BI scores from rehabilitation</td>
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<tr>
<td>Study</td>
<td>Intervention</td>
<td>Outcomes</td>
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<tr>
<td>Rehabilitation hospitals. Patients were assessed on admission and again at 6mos post-stroke. <strong>Outcomes:</strong> Barthel Index (BI).</td>
<td>Admission to 6mo was associated with better mood status at baseline and greater improvement in depressive symptoms ($p&lt;0.02$ and $p&lt;0.001$, respectively). 2. Other significant predictors of functional recovery included baseline neurological status, neurological improvement, baseline functional status and age.</td>
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<tr>
<td><strong>Goodwin &amp; Devanand</strong> (2008) USA</td>
<td><strong>Intervention:</strong> Data from the Midlife Development in the United States Study (MIDUS) ($n=3032$) were analysed to determine the relationship between stroke, depression and functional outcome in community-dwelling individuals. <strong>Outcomes:</strong> MIDUS.</td>
<td>1. Of the 3,032 participants (aged 25-74 years), only 24 (0.8%) reported having a stroke within the past 12mos. 2. Participants with stroke were significantly older than those without. 3. Stroke and depression were both independently associated with impairment in physical functioning (adjusted for sociodemographic and personality characteristics). 4. In addition, having both depression and stroke at the same time was associated with greater limitations than either condition alone.</td>
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<tr>
<td><strong>Donnellan et al.</strong> (2010) Ireland</td>
<td><strong>Intervention:</strong> Patients with stroke were assessed 1mo and 1yr following the stroke event. Probable depression was identified with a cut-off score on the depression scale of ≥8. Previous history of depression was determined using a single, self-report question. <strong>Outcomes:</strong> Hospital Anxiety and Depression Scale; Nottingham Extended Activities of Daily Living; Stroke-Specific Quality of Life scale.</td>
<td>1. Prevalence of depression was 35% at 1mo and 36% at 1yr. 22% of individuals identified with depression at 1mo continued to experience symptoms at 1yr. 2. There was a significant association between depression and functional outcome at both assessment points ($r=-0.29$, $p&lt;0.01$ and $r=-0.19$, $p&lt;0.05$ at 1mo and 1yr, respectively) such that greater depression was associated with poorer function. 3. Presence of depression was also associated with poorer health-related quality of life at 1mo and 1yr assessment points ($r=0.56$, $p&lt;0.001$ and $r=-0.41$, $p&lt;0.001$).</td>
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<tr>
<td><strong>Feigin et al.</strong> (2010) Australia</td>
<td><strong>Intervention:</strong> As part of the Auckland Stroke Outcomes Study (ASTRO), 418 5yr stroke survivors were included in an analysis of association between functional outcomes and potential predictors such as depression. <strong>Outcomes:</strong> Geriatric Depression Scale; Barthel Index; Frenchay Activities Index (FAI); London Handicap Scale (LHS).</td>
<td>1. At 5 yr, 29.6% of survivors reported symptoms suggestive of depression. 2. Depression was independently associated with greater odds for dependency (OR = 4.58, 95% CI 2.48-8.46) as well as reduced instrumental activities of daily living activity (FAI; OR = -4.55, 95% CI -6.29 to -2.81) and lower levels of participation (LHS OR = -7.48, 95% CI -11.06 to -3.9).</td>
<td></td>
</tr>
<tr>
<td><strong>West et al.</strong> (2010) UK</td>
<td><strong>Intervention:</strong> As part of the Stroke Outcomes Study, physical function and psychological symptoms were assessed at baseline (2-6wks post-stroke) and 9, 13, 26 and 52 wks. Symptom trajectories were analysed and</td>
<td>1. Most psychological distress occurred within the first wks of stroke. 2. In general, individuals with more psychological symptoms had poor initial physical function.</td>
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</tbody>
</table>
logistic regression was used to model poor functional outcome.

Outcomes: 28-item General Health Questionnaire; Modified Barthel Index.

3. At 1yr, individuals with more psychological symptoms had poor outcomes.
4. On logistic regression, patients at greatest risk for poor physical outcome were those who were older, had more severe disability early after stroke and had persistent psychological symptoms over the first 26wks following stroke.

**Willey et al. (2010)**
USA
No Score
TPS=7-10d
NStart=340

**Intervention:** In the Northern Manhattan Stroke Study (NOMASS), a single question was used to identify the presence of “depressed mood” within 7 – 10d post-stroke (n=340). Patients were followed-up every 6mos for 2 yr and every yr up to 5 yr following enrolment. Disability was categorized as no disability, moderate, or severe.

**Outcomes:** Barthel Index.

1. At 7 – 10d post-stroke, 40.9% of individuals reported feeling depressed.
2. Analysis adjusted for sociodemographic variables, stroke severity, diabetes, physical inactivity and CAD, there was significant association between depressed mood and functional ability such that the presence of depressed mood was associated with greater odds of severe disability at 1 and 2yr (when compared to no disability) (OR=2.91, 95% CI 1.07-7.91 and OR=3.72, 95% CI 1.29-10.71).
3. Depressed mood was not associated with moderate disability when compared to no disability on any of the analyses.

**Schmid et al. (2011)**
USA

**Intervention:** Secondary data analysis from the Activate-Initiate-Monitor (AIM) study to examine the association between depression and functional outcomes. Participants were categorized as depressed vs. non-depressed. A change in depression was assessed by change in Patient Health Questionnaire (PHQ-9) scores. Improvement was defined as a decrease in PHQ-9 scores from baseline to 12wks of at least 50% (or a score of less than 10 at 12 wks). Participants scoring 0-2 on the modified Rankin Scale were considered independent.

**Outcomes:** Structured clinical interview; PHQ-9; mRS.

1. Participants who were classified as dependent at 12wks had significantly greater baseline depression scores than individuals classified as independent (p=0.026).
2. Depressed individuals who met the criteria for improvement over the 12wk period were more often independent at 12wks (p=0.012) than those who did not improve.
3. Independent predictors of 12wk function in the depressed group were medical co-morbidity, stroke severity and depression severity.
4. In the non-depressed group, baseline depression was not independently associated with dependency at 12wks.

**Brown et al. (2012)**
Sweden
No Score
TPS=NA
NStart=181

**Intervention:** Individuals with stroke were assessed at discharge from hospital, then again at 3mos and 12mos post-stroke. Presence of depression was defined as Center for Epidemiologic Studies Depression Scale (CES-D) score ≥16. On the Barthel Index (BI), scores of ≤60 were indicative of lower levels of independence.

**Outcomes:** Barthel Index (BI); Center for Epidemiologic Studies Depression Scale (CES-D).

1. At all three assessment points, individuals who were identified as depressed using the CES-D had lower BI scores than individuals who were not depressed – although these differences reached statistical significance at discharge and 3mos only (p<0.05).
2. At all three assessment points, individuals with lower levels of independence in function had significantly higher CES-D scores than individuals who were considered independent on the BI (p<0.05).
3. Regression analysis demonstrated that, at all three time periods, function as assessed on the
Brodaty et al. (2013) Australia Observational No Score TPSOverall≤1wk NStart=330 NEnd=253

Population: Experimental Group (EG, N=152): Mean age=72.1±8.9yr; Gender: Male=88, Female=64. Control Group (CG, N=101): Mean age=71.1±6.1yr; Gender: Male=49, Female=52.

Intervention: EG patients admitted to inpatient stroke units and a CG consisting of community-dwelling volunteers with no history of stroke were asked to complete a set of questionnaires. Assessments were conducted at baseline, 3-6mo, 1yr, 3yr and 5yr follow-up.

Outcomes: Apathy Evaluation Scale (AES); Geriatric Depression Scale (GDS); Activities of Daily Living Scale (ADL); Instrumental ADL Scale (IADL).

1. EG demonstrated significantly higher AES scores throughout the study (p<0.0001) and greater increases in AES score over time (p=0.007) compared to the CG at 5yr follow-up.
2. GDS and ADL/IADL score for the EG were found to be significant predictors of higher AES scores over the course of the 5yr study period (both p<0.01).
3. ADL/IADL score for the CG was found to be a significant predictor of higher AES scores over the course of the 5yr study period (p<0.05).

De Ryck et al. (2014b) Belgium Case Series No Score TPSOverall≤7d NStart=186 NEnd=125

Population: Intervention Group (N=125): Mean age=70.1±12.7yr; Gender: Males=76, Females=49.

Intervention: Data was collected and analysed from patients admitted between 2005 and 2012 as part of the Middelheim Interdisciplinary Stroke Study. Assessments were conducted at baseline, 1mo, 3mos, 6mos, 12mos, and 18mos follow-up.

Outcomes: Cornell Scale for Depression (CSD); Montgomery and Åsberg Depression Rating Scale (MADRS); Functional Independent Measure (FIM: Total, Motor, Cognitive); Stroke Impact Scale (SIS: Total); Modified Rankin Scale (mRS); Barthel Index (BI); National Institute of Health Stroke Scale (NIHSS).

1. The mean CSD score increased significantly from baseline to 18mos follow-up (p=0.024) with 35 patients (28%) diagnosed as depressed compared to 21 patients (16.8%) at baseline.
2. Patients diagnosed as depressed scored significantly higher on the mRS (p=0.001) and significantly lower in FIM Total (p<0.001), FIM Cognitive (p=0.032) and SIS (p<0.001) scores compared to patients without a diagnosis of depression at 18mos follow-up.
3. FIM Total, FIM Motor, FIM Cognitive, SIS Total, mRS, BI, and NIHSS scores were all significantly associated with CSD and MADRS scores (all p<0.05).
4. Patients who stated they had experienced persistent relationship difficulties at 18mos follow-up were almost four times more likely to be depressed than non-depressed (17.1% vs 4.4%, p=0.028).

De Ryck et al. (2014a) Belgium Longitudinal No Score TPSOverall≤7d NStart=201 NEnd=156

Population: Intervention Group (N=201): Mean age=70.1±13.1yr; Gender: Males=115, Females=86.

Intervention: This longitudinal epidemiological study was conducted between 2005 and 2012, where patients admitted to the stroke unit with first or recurrent stroke participated in an interview and completed questionnaires. Assessments for Post-Stroke Depression (PSD) were conducted at 1mo, 3mos, 6mos, 12mos, and 18mos.

Outcomes: Functional Independent Measure Scale; Barthel Index (BI); National Institute of Health Stroke Scale (NIHSS).

1. Prevalence rates were 24.5% (23/94) at 1mo, 27.1% (46/170) at 3mos, 28.3% (28/99) at 6mos, 19.8% (23/116) at 12mos, and 26.3% (41/156) at 18mos post-stroke.
2. There was no significant difference regarding gender, education, employment, marital status, family composition, vascular risk factors, history of depression, use of psychotropic medication, and stroke localization between PSD and non-PSD patients at any of the five time points.
3. Patients with PSD were significantly younger than non-PSD patients at 6mos post-stroke (62.4±15.7yr vs. 70.2±13.7yr; p=0.016).
Post-Stroke Depression and Mood Disorders

Health Stroke Scale; modified Rankin Scale; Stroke Impact Scale; Mini Mental State Examinations (MMSE); Presence/absence of confusion, agnosia, aphasia, dysarthria, apraxia, unilateral neglect; Cornell Scale for Depression; Montgomery-Asberg Depression Rating Scale.

4. Patients with PSD at 3mos were significantly more dependent with regard to activities of daily living functions, had more functional impairment, were participating significantly less in daily social activities and were more cognitively impaired (all p<0.05).

5. At 6mos post-stroke, depressed patients were significantly more cognitively impaired and participated significantly less in daily social activities than non-depressed patients (all p<0.05).

6. At 12mos, the mean scores of the functional scales were significantly different between the depressed and the non-depressed patients.

7. At 18mos, all functional scales were significantly different in the depressed compared to the non-depressed individuals (all p<0.05) except for the BI and MMSE.

8. PSD was significantly associated with stroke severity, physical disability, cognitive impairment, and stroke outcome during the 18mos of the study (all p<0.05).

9. Reduced social activities and the presence of apraxia were consistently associated with PSD whereas aphasia was only significantly associated in the first 6mos after stroke (p<0.05).

Rabi Zikic et al. (2014) Serbia
Observational
No Score
TPS\textsubscript{Exp}=2wks
TPS\textsubscript{Con}=2wks
N\textsubscript{Start}=60
N\textsubscript{End}=60


Intervention: Both the EG (patients with depression) and the CG (patients without depression) completed a set of questionnaires at 2wks post-stroke followed by a second set of questionnaires at 6wks post-stroke. Assessments were completed at baseline and at follow-up.

Outcomes: Hamilton Depression Rating Scale (HAMD); Barthel Index (BI); Medical Outcomes Study 36-Item Short Form Questionnaire (SF-36: Bodily Pain).

1. HAMD scores were significantly higher in the EG compared to the CG at baseline and at follow-up (both p<0.001).

2. HAMD scores at follow-up revealed that 26.7% of patients initially diagnosed with depression experienced spontaneous recovery (p=0.008) but no patients diagnosed with major depression experienced remission.

3. HAMD scores were not significantly correlated with BI scores at baseline (p=0.253) or at follow-up (p=0.065) indicating depression cannot be predicted by BI performance.

4. BI scores were significantly higher in the EG compared to the CG at baseline and at follow-up (both p<0.001).

5. BI scores improved significantly within both groups with the EG mean score improving by 31.9 and the CG improving by a mean of 10.8 (both p<0.001).

6. SF-36 scores were significantly higher in the CG compared to the EG on all SF-36 subscores (p<0.001) with a lesser but still significant difference on the SF-36 Bodily Pain subscale (p=0.011).
### Population
No demographic data available.

### Intervention
Data from patients undergoing rehabilitation therapy 5/wk for 8wks at a rehabilitation institution in the Gyeonggi-do province from 2008-2009 was analyzed.

### Outcomes
- Korean modified Barthel Index (K-MBI: activities of daily living (ADL)); Mini Mental State Examination (MMSE); Beck Depression Inventory (BDI).

1. After 8wks of rehabilitation, change in BDI scores revealed a significant positive association (p<0.05).
2. Change in BDI score was significantly and positively associated with improved ADL according to BI and cognitive function according to MMSE scores (p<0.05).
3. Cardiac disorder, depression, high improvements in ADL and cognitive functions were significant predictors of change in depression (p<0.05).

### 18.5.2 Depression and Social Activities Post-Stroke

#### Table 18.5.2 Depression and Social Activities Post Stroke

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labi et al. (1980)</td>
<td>USA</td>
<td>No Score</td>
<td>TPS Mean=NA</td>
<td>NStart=262</td>
<td><strong>Intervention:</strong> 121 stroke survivors and 141 controls with a minimum score of 20 on the Kenny self-care evaluation (KSCE) were tested on three parameters of social function – socialization in the home, socialization outside the home and hobbies and interests – to determine social reintegration of long-term survivors of stroke. <strong>Outcomes:</strong> KSCE.</td>
</tr>
<tr>
<td>Feibel &amp; Springer (1982)</td>
<td>USA</td>
<td>No Score</td>
<td>TPS Mean=NA</td>
<td>NStart=91</td>
<td><strong>Intervention:</strong> Stroke patients were assessed for physical independence in activities of daily living, mobility, and depression by nurses’ observation, patient’s mood, behaviour, somatic complaints and number of social activities. <strong>Outcomes:</strong> Katz Index.</td>
</tr>
<tr>
<td>Robinson et al. (1983)</td>
<td>USA</td>
<td>No Score</td>
<td>TPS=chronic</td>
<td>NStart=103</td>
<td><strong>Intervention:</strong> Stroke patients capable of undergoing psychiatric interview and not exhibiting decreased consciousness and/or aphasia with severe comprehension deficits were evaluated for mood disorder at 6mos. All examinations were done in late morning or early afternoon to avoid effects of diurnal mood variation. <strong>Outcomes:</strong> Zung Self Rating Depression Scale; Hamilton Depression Scale; Present State Examination; General Health Questionnaire.</td>
</tr>
</tbody>
</table>

1. A significant proportion of survivors manifested social disability, despite complete physical recovery. Most of the disability could not be accounted for by age, physical impairment or specific neurological deficits.
2. The greatest social functioning impairments were seen in women and those of higher educational background.
3. Incidence of depression was 26% 6mos after stroke.
4. Depression was significantly correlated with failure to resume premorbid social activities.
5. Depressed patients lost a mean of 67% of their previous activities.
6. Depression status was not significantly correlated to age, sex, marital status or side of brain involvement.
**Andersen et al.** (1995)  
Denmark  
No Score  
TPS\text{Mean}=\text{NA}  
N\text{Start}=285  

**Population:** Median age=69yr.  
**Intervention:** Patients with stroke admitted to hospital or referred to a hospital-based outpatient clinic were included. Patients were assessed at 7d, 1mo, 6mos and 1yr post-stroke to study the correlation between risk factors and 1yr incidence of post-stroke depression (PSD).  
**Outcomes:** Hamilton Rating Scale for Depression; Beck Depression Inventory.  

1. 1yr incidence of PSD was reported to be 41%. Most cases developed in the first mo post-stroke.  
2. The presence of PSD was associated with social distress in the 6mos preceding stroke (p<0.01), few social activities at home visits and a decrease in the social activities index scores at 1mo and 1yr (p<0.001 and p<0.05, respectively).

**Baseman et al.** (2010)  
USA  
No Score  
TPS=chronic  
N\text{Start}=48  
N\text{End}=48  

**Intervention:** Individuals with stroke (6mos prior to enrolment) were assessed via mailed survey. Centre for epidemiologic studies depression scale (CES-D) scores >10 were considered indicative of depression.  
**Outcomes:** Demographic questionnaire; Subjective Index of Physical and Social Outcome; CES-D.  

1. Depression was significantly, and inversely, correlated with social integration (r=−0.74, p=0.01), function (r=−0.33, p=0.026) and perceived overall stroke recovery (r=−0.49, p=0.001).  
2. In a linear regression model, these three factors could account for 62% of the variance in social integration; although, only functional ability and depression were significant predictors.

**Sienkiewicz-Jarosz et al.** (2010)  
Poland  
No Score  
TPS=acute  
N\text{Start}=242  

**Intervention:** Individuals with first ever stroke were evaluated 3mo following the stroke event to assess the association between demographic, socioeconomic, and clinical factors on the severity and presence of post-stroke depression as well as on their social functioning. A cut-off Geriatric Depression Scale (GDS) score of >5 was used to indicate probable depression.  
**Outcomes:** National Institutes of Health Stroke Scale (NIHSS); Rankin Scale; Barthel Index; Mini-Mental State Examination (MMSE); Boston Diagnostic Aphasia Examination; self-report of frequency and satisfaction with social contact; GDS.  

1. Individuals with a GDS score >5 reported fewer positive assessments of family relationships (p=0.03) and less satisfaction with the frequency of contact with family members (p=0.0004).  
2. In addition, more individuals with depression reported seeing friends only rarely or occasionally (p=0.002), and they reported less satisfaction with frequency of contact (p<0.01).  
3. 66.2% of individuals with GDS score >5 reported reduction of social contacts following stroke (vs. 31.4% in the non-depressed group).

**Hinojosa et al.** (2011)  
USA  
Longitudinal  
No Score  
TPS=NA  
N\text{Start}=77  

**Intervention:** Individuals with stroke were enrolled in a longitudinal study at discharge from inpatient care in order to explore the relationship between social isolation, depression, and management of activities of daily living post-stroke. Geriatric Depression Scale (GDS) scores <10 were considered normal.  
**Outcomes:** Connectedness-Isolation Scale; Frenchay Activities Index; GDS.  

1. Approximately 60% of participants experienced no change in their sense of connectedness or isolation over 1yr post-stroke.  
2. Approximately 7% of individuals who reported connectedness at 1mo were isolated at 6mos and remained isolated for the duration of the study.  
3. On multivariate regression analysis, depression was significantly associated with social isolation such that increased symptomatology was associated with...
<table>
<thead>
<tr>
<th>Reference</th>
<th>Country</th>
<th>Study Design</th>
<th>No Score</th>
<th>TPS Range</th>
<th>N Start</th>
<th>N End</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcomes</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jean et al. (2013)</td>
<td>France</td>
<td>Longitudinal</td>
<td>No Score</td>
<td>4-10d</td>
<td>36</td>
<td>36</td>
<td>Mean age=61.31±12.94yr; Gender: Male=19, Female=17.</td>
<td>Patients were given a personal digital assistant upon discharge and used an Ecological Momentary Assessment (EMA) tool for monitoring and recording behaviours and social environments. The intervention was provided for 1wk and the EMA consisted of 5/d electronic interviews performed randomly. Assessments were conducted at baseline and at 3mo follow-up.</td>
<td>HAMD scores were significantly lower at 3mos follow-up among patients who reported being at their partner’s home (p&lt;0.001) or a relative’s home (p&lt;0.01) during the intervention. HAMD scores were significantly lower at 3mos follow-up for patients who socialized with friends during the intervention (p&lt;0.01). HAMD scores were significantly higher at 3mos follow-up among patient who returned to work or played sports (both p&lt;0.05) during the intervention while patients who reported passive activities such as listening to music experienced significantly lower HAMD scores at 3mos follow-up (p&lt;0.05).</td>
<td></td>
</tr>
<tr>
<td>Lewin et al. (2013)</td>
<td>Germany</td>
<td>Observational</td>
<td>No Score</td>
<td>6.6±4.4wk</td>
<td>96</td>
<td>96</td>
<td>Mean age=67.1±10.6yr; Gender: Males=50, Females=46.</td>
<td>Ischemic stroke patients residing at a rehabilitation centre completed an interview in which demographic data and questionnaires were completed. Assessments were completed once only.</td>
<td>35.28% of patients were considered depressed with a mean score of 5 on the GDS. Gender (p=0.72), age (p=0.82) and marital status (p=0.23) were not significantly related to depressive symptoms. Low levels of depressive symptoms on the GDS were associated with high scores on the GSES (p&lt;0.00). High levels of cognitive functioning (MMSE) were associated with high levels of self-efficacy (GSES) (p=0.00), and low levels of depressive symptoms (p=0.00). The following variables accounted for a total of 60% variance in depressive symptoms: activities of daily living according the BI (6%), MMSE (9%), pre-stroke depression (16%), perceived social support (14%), SSEQ (5%) and GSES (10%).</td>
<td></td>
</tr>
<tr>
<td>Obembe et al. (2013)</td>
<td>Nigeria</td>
<td>Observational</td>
<td>No Score</td>
<td>2.2±1.2yr</td>
<td>90</td>
<td>90</td>
<td>Mean age=58.3±7.8yr; Gender: Males=56, Females=34.</td>
<td>Stroke survivors attending the physiotherapy clinics of selected hospitals were assessed to determine the association of community reintegration with motor function and post-stroke depression (PSD). Assessments were conducted at a mean of 2.2yr post-stroke.</td>
<td>Community reintegration had a significant correlation with age (r=-0.221, p=0.036), motor function (r=-0.084, p=0.001), and PSD (r=-0.0373, p=0.006). Age (p=0.016), motor function (p=0.000), and depression (p=0.008) were significant predictors of community reintegration, accounting for 41% of the variance in the RNLI scores (p&lt;0.001).</td>
<td></td>
</tr>
</tbody>
</table>
| Van Puymbroeck et al.  | (2014)           |                   |          |           |         |       | Mean age=64.06±8.78yr; Gender: Males=58, Females=19. | Age, gender, education level, race, ethnicity, and perceived general health did
Intervention: Patients completed a set of questionnaires during a one-time visit to a local clinic, stroke support group, or a university campus. Assessments were completed at 6mos post-stroke. Outcomes: Generalized Anxiety Disorder Scale (GAD); 9-Item Patient Health Questionnaire (PHQ-9); Orientation to Life Questionnaire (OLQ; sense of coherence); ICF Measure of Participation and Activities Screener (IMPACT-S); Modified Rankin Scale (mRS).

not have a significant relationship with the level of activity or participation (all p>0.05).
2. The activity portion of the IMPACT-S correlated significantly with mRS scores (r=0.341, p<0.01), PHQ-9 (r=0.576, p<0.01), GAD (r=0.582, p<0.01), and negatively with the OLQ (r=-0.553, p<0.01).
3. The participation portion of the IMPACT-S correlated significantly with the PHQ-9 (r=0.567, p<0.01), GAD (r=0.561, p<0.01), and negatively with the OLQ (r=-0.493, p<0.01).
4. Disability (mRS), depression (PHQ-9), and anxiety (GAD) were all found to be independent predictors of activity (all p=0.000), and accounted for 68% of the variance in the model. This indicated that those with less disability, depression and anxiety have higher levels of activity.
5. PHQ-9 and GAD scores were found to be independent predictors of participation (both p=0.000), and accounted for 58% of the variance in the model. This indicated that those with less depression and anxiety had higher levels of participation.
6. GAD score was found to be a significant predictor of coherence (p=0.000), thus indicating that those with lower anxiety had a higher sense of coherence.

18.5.3 Cognitive Impairment and Depression Post-Stroke

Table 18.5.3 Cognitive Impairment and Depression Post Stroke

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robinson et al. (1986)</td>
<td>USA</td>
<td>No Score</td>
<td>TPS=NA</td>
<td>NStart=184</td>
<td><strong>Intervention</strong>: Patients with ischemic lesions of the left cerebral hemisphere were examined for depression and intellectual impairment. All examinations were done in late morning or early afternoon to avoid effects of diurnal mood variation. <strong>Outcomes</strong>: Zung Self Rating Depression Scale; Hamilton Depression Scale; Present State Examination; General Health Questionnaire.</td>
</tr>
<tr>
<td>Bacher et al. (1990)</td>
<td>Canada</td>
<td>No Score</td>
<td>TPS=chronic</td>
<td>NStart=184</td>
<td><strong>Intervention</strong>: Stroke patients were followed for 12mos in order to identify the course of post-stroke depression among rehabilitation patients and the relationship of depression with physical and cognitive impairment. Patients with a known history of</td>
</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>Score</td>
<td>Type of TPS</td>
<td>Start N</td>
<td>Intervention</td>
</tr>
<tr>
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</tr>
<tr>
<td>N_start=48</td>
<td>Start=48</td>
<td>psychiatric illness, stroke, dementia and/or comprehension disorders were excluded.</td>
<td>Outcomes: Self Rating Depression Scale; Zung Self Rating Scale (Clinical depression was assigned a score &gt;50 and moderate to severe &gt;60); Mini-Mental State Examination.</td>
<td>2. Functional level improved overall, but was significantly greater for patients who were not depressed initially.</td>
<td></td>
</tr>
<tr>
<td>Morris et al. (1992) USA</td>
<td>USA</td>
<td>No Score</td>
<td>TPS=chronic N_start=48</td>
<td>Intervention: This study followed 49 patients over 14mos to assess the effects of clinical depression on stroke recovery.</td>
<td>Outcomes: Structured clinical interview; Diagnostic and Statistical Manual of Mental Disorders.</td>
</tr>
<tr>
<td>Start=48</td>
<td>Start=48</td>
<td>41% (n=20) of the study sample was depressed at initial assessment.</td>
<td>1. At follow-up, depressed patients improved less than non-depressed patients in functional status (p=0.001) and cognitive performance (p=0.096).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start=48</td>
<td>Start=48</td>
<td>Mean recovery in activities of daily living did not differ between the two groups but more depressed patients deteriorated over time (20% vs. 0%) (p=0.047).</td>
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<tr>
<td>Andersen et al. (1995) Denmark</td>
<td>No Score</td>
<td>TPS=acute N_start=285</td>
<td>Population: Median age=69yr.</td>
<td>Intervention: Patients with stroke admitted to hospital or referred to a hospital-based outpatient clinic were included. Patients were assessed at 7d, 1mo, 6mos and 1yr post-stroke to study the correlation between risk factors and 1yr incidence of post stroke depression (PSD).</td>
<td>Outcomes: Beck Depression Inventory; Hamilton Rating Scale for Depression.</td>
</tr>
<tr>
<td>Start=285</td>
<td>Start=285</td>
<td>1yr incidence of PSD was reported to be 41%. Most cases developed in the first mo post-stroke.</td>
<td>2. The presence of PSD was associated with social distress in the 6mos preceding stroke (p&lt;0.01), few social activities at home visits and a decrease in the social activities index scores at 1mo and at 1yr (p&lt;0.001 and p&lt;0.05, respectively).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Den (2001)</td>
<td>Denmark</td>
<td>No Score</td>
<td>TPS=chronic N_start=127</td>
<td>Intervention: 99 stroke patients, 7yr post-stroke, and 28 control patients participated. Subjects were questioned regarding changes in concentration, memory, fatigue, mood and irritability.</td>
<td>Outcomes: Research Diagnostic Criteria; Hamilton Depression Rating Scale; Beck Depression Inventory; Raven Matrices A+B; Mini-Mental State Examination (MMSE); Word Pair Learning (WPL).</td>
</tr>
<tr>
<td>Start=127</td>
<td>Start=127</td>
<td>No differences were reported between depressed and non-depressed stroke patients on the MMSE, Raven Matrices A+B and WPL.</td>
<td>2. Stroke patients experienced more lability of mood and irritability during the 7yr period than control subjects.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start=127</td>
<td>Start=127</td>
<td>However, stroke survivors who were depressed reported significantly more concentration (p=0.006) and memory difficulties (p=0.01) than non-depressed survivors.</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>House et al. (2001) UK</td>
<td>UK</td>
<td>No Score</td>
<td>TPS=acute N_start=448</td>
<td>Intervention: Stroke inpatients were seen 1mo post-stroke and reassessed at 12 and 24mos to assess the association between early mood symptoms and mortality.</td>
<td>Outcomes: International Classification of Diseases-10th Revision (ICD-10); Present State Examination; General Health Questionnaire.</td>
</tr>
<tr>
<td>Start=448</td>
<td>Start=448</td>
<td>Mood symptoms on a self-report rating scale were associated with 12 and 24mo mortality after stroke, after adjustment for factors associated with stroke severity.</td>
<td>2. Psychiatric disorders such as major depression (ICD-10) were not statistically significantly associated with increased mortality at 12 or 24 mos.</td>
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</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>Score</td>
<td>TPS</td>
<td>Start N</td>
<td>Intervention</td>
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<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Spalletta et al. (2002)</td>
<td>Italy</td>
<td>No</td>
<td>&lt;1yr</td>
<td>153</td>
<td>Individuals who had experienced first-ever stroke within the past year and were admitted to a specialized rehabilitation facility were included. Patients were assessed on day 7 and 14 of their rehabilitation admission to evaluate sociodemographic and clinical predictors of cognitive level and depression in subjects with different lesion laterality. <strong>Outcomes:</strong> Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders; Hamilton Rating Scale for Depression (HAMD); Hamilton Anxiety Rating Scale; State Trait Anger Expression Inventory; Barthel Index; Mini-Mental State Examination (MMSE).</td>
</tr>
<tr>
<td>Verdelho et al. (2004)</td>
<td>France</td>
<td>No</td>
<td>acute</td>
<td>202</td>
<td>Patients admitted consecutively for acute stroke were included. Patients were assessed periodically over a 3yr period (1, 6, 12, 24 and 36mos) to assess factors of post-stroke depressive symptoms and their relationship with dementia. <strong>Outcomes:</strong> Cambridge Mental Disorders for the Elderly examination; Montgomery-Asberg Depression Rating Scale; Mini-Mental State Examination; Mattis Dementia Rating Scale; Orgogozo Scale; modified Rankin Scale; Informant Questionnaire on Cognitive Decline in the Elderly.</td>
</tr>
<tr>
<td>Barnes et al. (2006)</td>
<td>USA</td>
<td>Longitudinal</td>
<td>chronic</td>
<td>2220</td>
<td>A prospective, longitudinal study (6yr) of community dwelling adults having no cognitive impairment and aged 65 or over at baseline. 799 participants had MRI evidence of vascular disease (large or small infarcts, or high white matter grade ≥4). 106 presented with a history of vascular disease at baseline. <strong>Outcomes:</strong> Standard clinical criteria.</td>
</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>Score</td>
<td>TPS</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;</td>
<td>N&lt;sub&gt;End&lt;/sub&gt;</td>
</tr>
<tr>
<td>-------</td>
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</tr>
<tr>
<td>Saxena et al. (2008)</td>
<td>India &amp; Singapore</td>
<td>No Score</td>
<td>chronic</td>
<td>252</td>
<td></td>
</tr>
<tr>
<td>Bour et al. (2010)</td>
<td>Netherlands</td>
<td>No Score</td>
<td>chronic</td>
<td>190</td>
<td>138</td>
</tr>
<tr>
<td>Hosking &amp; Marsh (2013)</td>
<td>New Zealand</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

1. On admission, depressive symptomatology was identified in 60% of patients while CIND was identified in 54%.
2. By the time of discharge, there was a significant decrease in both the symptoms of depression and of cognitive impairment (p<0.05). However, corresponding improvement was not noted at 6mos.
3. Baseline variables significantly associated with depression at 6mos were dependence in activities of daily living (OR = 5.28), cognitive impairment on admission (OR=4.78) and recurrent stroke (OR=3.34). Baseline variables significantly associated with CIND at 6mos were age ≥76yr (OR=8.07), cognitive impairment on admission (OR=6.94), depression (OR=3.50) and dysphagia (OR=4.58).
<table>
<thead>
<tr>
<th>Observational No Score</th>
<th>TPS\text{Mean}=367±5d</th>
<th>N\text{Start}=67</th>
<th>N\text{End}=67</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention:</strong></td>
<td>Patients were selected from consecutive admissions, over a 12mo period to Waikato Hospital for ischemic stroke or intracerebral hematoma. Patients participated in an interview along with their relatives and completed a set of questionnaires at a post-stroke 1yr follow-up.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Outcomes:</strong></td>
<td>Geriatric Depression Scale (GDS); Barthel Activities of Daily Living; Nottingham Extended ADL Index (NEADL); Wechsler Adult Intelligence Scale—Revised (WAIS-R: Vocabulary &amp; Block Design, Digit Span, Verbal Paired Associates, Controlled Oral Word Association test).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prokopenko et al. (2013)</th>
<th>Russia RCT PEDro=8 TPS\text{Exp}=2wk TPS\text{Cont}=2wk N\text{Start}=43 N\text{End}=43</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention:</strong></td>
<td>EG received 15hr of individual computer program training consisting of Schulte’s table tasks and figure-background tests in addition to standard treatment and CG received standard treatment only. The intervention was provided for 30min/d, 7d/wk over a period of 2wk. Assessments were conducted at baseline and at post-treatment.</td>
</tr>
<tr>
<td><strong>Outcomes:</strong></td>
<td>Hospital Anxiety and Depression Scale (HADS: Anxiety, Depression); Montreal Scale of Cognitive Assessment (MoCA); Clock Drawing Test (CDT); Mini Mental State Examination (MMSE); Frontal Assessment Battery (FAB); Schulte's Test (ST).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sibolt et al. (2013)</th>
<th>Finland Longitudinal No Score TPS\text{Mean}=NA N\text{Start}=223 N\text{End}=223</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population:</strong></td>
<td>Mean age=71yr; Gender: Males=116, Females=107.</td>
</tr>
<tr>
<td><strong>Intervention:</strong></td>
<td>Patients from the Helsinki Stroke Aging Memory cohort with first-time stroke completed a medical examination, a psychiatric examination, and a set of cognitive assessments. The study aimed to focus on a subtype of depression known as Depression-Executive Dysfunction Syndrome (DES). Assessments were conducted 12-20wks post-stroke and follow-ups were conducted up to 12yr post-stroke.</td>
</tr>
<tr>
<td><strong>Outcomes:</strong></td>
<td>Montgomery-Asberg Depression Rating Scale (MADRS); Schedules for Clinical Assessment in Neuropsychiatry (SCAN) interview; Trail Making (TMT); Stroop Color Naming Test (SCNT); Wechsler</td>
</tr>
</tbody>
</table>

1. Higher GDS scores occurred for those patients who had experienced a previous stroke ($r=0.46$, $p=0.001$), had greater impairment on the NEADL ($r=-0.32$, $p=0.027$) and were more impaired on the Digit Span subtest of complex attention ($r=-0.40$, $p=0.005$).
2. Of the 61 patients that completed the PD experimental group, 28% displayed impairment in basic cognitive functioning.
3. The estimated premorbid IQ according to the Vocabulary & Block Design subtest was significantly higher than the mean IQ score obtained during the study ($p<0.0005$).
4. Demographic variables, medical variables, physical variables, and cognitive variables in total accounted for 40% of the variance in GDS scores.
5. The strongest predictors of depression at 1yr post-stroke were previous stroke (22%) and level of functional independence (8%).

1. HADS Anxiety and HADS Depression scores at baseline and at post-treatment did not differ significantly between the EG and CG.
2. Although not statistically significant, HADS Depression scores reduced for both the EG and CG from baseline to post-treatment.
3. CDT ($p=0.05$), FAB ($p=0.02$) and ST ($p=0.01$) scores improved significantly for the EG from baseline to post-treatment compared to the CG.
4. Within group analyses revealed significant improvements on the MoCA ($\Delta=+4$), MMSE ($\Delta=+3$), FAB ($\Delta=+2$), CDT ($\Delta=+1.5$) and ST ($\Delta=+20$) for the EG from baseline to follow-up (all $p<0.01$) but the CG did not improve significantly on any measures.

1. Of the 223 patients, 37% were diagnosed with depression according to SCAN and MADRS scores, and 40% were found to have executive dysfunction according to TMT, WMS, WMS, WMS, WMS, WMS.
2. DES was reported in 17% of patients.
3. Patients with executive dysfunction or DES were older than those without executive dysfunction and DES (both $p=0.01$).
4. The cumulative recurrence risk of ischemic stroke during the 12yr follow-up was higher in patients with depression ($p=0.04$) than in those without depression.
5. Patients with executive dysfunction ($p=0.02$) and patients with DES ($p<0.01$) reported...
### 18.5.4 Mortality and Depression Post-Stroke

Table 18.5.4 Mortality and Depression Post-Stroke

<table>
<thead>
<tr>
<th>Yang et al. (2013)</th>
<th>China</th>
<th>Case Series</th>
<th>No Score</th>
<th>TPS Overall</th>
<th>N_Start=75</th>
<th>N_End=75</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population:</strong></td>
<td>Intervention Group (N=75): Mean age=66.7+9.3yr; Gender: Males=47, Females=28.</td>
<td><strong>Intervention:</strong></td>
<td>Medical charts of patients admitted between December 2010 and December 2011 were reviewed. Assessments were conducted within 2wks post-stroke.</td>
<td><strong>Outcomes:</strong></td>
<td>Hamilton Depression Scale (HAMD); Apathy Evaluation Scale Clinician Version (AES-C); Montreal Cognitive Assessment (MoCA); Mini-Mental State Examination (MMSE); Mattis Dementia Rating Scale (MDRS: Initiation/Perseverance Subscale); Frontal Assessment Battery (FAB).</td>
<td></td>
</tr>
</tbody>
</table>

1. A total of 12 patients (16%) were found to be depressed according to the HAMD.
2. HAMD scores were significantly higher in patients who demonstrated post-stroke apathy compared to patients who did not (p=0.046).
3. Patients without post-stroke depression (PSD) had a significantly higher score on the MDRS Initiation/Perseverance Subscale compared to patients with PSD (p=0.009).
4. Patients who did not demonstrate post-stroke apathy according to AES-C scored significantly higher on the MMSE (p<0.001), MoCA, and MDRS Initiation/Perseverance Subscale (both p=0.001) compared to patients who did demonstrate post-stroke apathy.
5. FAB scores were significantly associated with AES-C scores (p=0.05) but not with HAMD scores (p=0.976).

<table>
<thead>
<tr>
<th>Arauz et al. (2014)</th>
<th>Mexico</th>
<th>Observational</th>
<th>No Score</th>
<th>TPS Overall</th>
<th>N_Start=165</th>
<th>N_End=110</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population:</strong></td>
<td>Intervention Group (N=165): Mean age=56.0+17.8yr; Gender: Males=68, Females=42.</td>
<td><strong>Intervention:</strong></td>
<td>Patients who had been admitted into a previous study at onset of stroke returned for a follow-up to complete a battery of cognitive tests and undergo a neuropsychological evaluation. Assessment was completed at 3mos post stroke only.</td>
<td><strong>Outcomes:</strong></td>
<td>Prevalence of depression.</td>
<td></td>
</tr>
</tbody>
</table>

1. Depression was reported in 56% of the sample and 14% reported both depression and executive dysfunction.
2. Patients with vascular cognitive impairment and vascular dementia reported symptoms of depression significantly more frequently compared to patients without cognitive impairment.
3. Depression was significantly associated with a decline in performance on a battery of cognitive tests (p=0.001).
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Morris et al. (1993) | USA | No Score | TPS=acute | N_{Start}=103 \ N_{End}=91 | **Intervention:** Patients were assessed for major or dysthymic depression 2wks post-stroke. Life status was determined for 91 patients 10yr later.  
**Outcomes:** Structured mental examination; Diagnostic and Statistical Manual of Mental Disorders. | 1. 53% (n=48) of the patients died.  
2. Those with either major or minor depression were 3.4 times more likely to die than non-depressed patients during the follow-up period.  
3. Patients who were depressed and socially isolated seemed to be most vulnerable (>90% mortality rate). |
| House et al. (2001) | UK | No Score | TPS=acute | N_{Start}=448 | **Intervention:** Stroke inpatients were seen 1mo post-stroke and reassessed at 12 and 24mo post-stroke.  
**Outcomes:** Present State Examination; General Health Questionnaire. | 1. Mood symptoms on a self-report rating scale were associated with 12 and 24mo mortality after stroke, after adjustment for factors associated with stroke severity.  
2. Psychiatric disorders such as major depression, (according the International Classification of Disease, 10th Revision), were not statistically significantly associated with increased mortality at 12 or 24mos. |
| Lewis et al. (2001) | UK | No Score | TPS=NA | N_{Start}=272 | **Intervention:** Stroke patients were observed to determine whether attitude toward illness was associated with survival after stroke.  
**Outcomes:** Mental Adjustment to Stroke Scale; Hospital Anxiety and Depression Scale; General Health Questionnaire 30. | 1. Fatality and helplessness/hopelessness were both associated with decreased survival (p=0.03 and 0.04, respectively) while fighting spirit, anxious preoccupation and denial/avoidance were not.  
2. Mood was not associated with survival. |
| Williams et al. (2004) | USA | No Score | TPS=NA | N_{Start}=51119 | **Intervention:** From the US Veteran’s Affairs administrative database, 51,119 patients hospitalized with ischemic stroke between 1990 and 1998 were identified. 55 patients with depression were identified and matched with 47 patients with other mental or substance abuse diagnoses and 95 patients with no recorded mental disorders or diagnoses. Using data extracted for the subset of patients, the relationship between the presence of post-stroke depression (PSD), other mental disorders, substance abuse, and mortality was examined. Admission stroke severity was not significantly different between patients with and without PSD.  
**Outcomes:** International Statistical Classification of Diseases and Related Health Problems-9 codes; Cox regression models. | 1. After controlling for cardiovascular risk factors and mortality risk associated with co-morbid conditions (assessed via the Charlson Index), the presence of PSD increased the risk of death by 13% (HR = 1.13, 95% CI 1.06 – 1.21). The presence of other mental disorder or substance abuse diagnosis also increased the risk of death (HR = 1.13, 95% CI 1.07 – 1.22). |
<p>| Almeida &amp; Xiao (2007) | Australia | Cohort | No Score | | <strong>Intervention:</strong> Administrative records of individuals with first –ever stroke and no previous mental health disorder were identified and followed for 10yr following the index stroke event. 287 individuals for whom mental health disorders were recorded in the | 1. Cumulative incidence rates for mental health disorders were calculated using 1008 stroke patient records. |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reynolds et al. (2008)</td>
<td>Data from the first three waves of the Asset and Health Dynamics Among the Oldest Old study were analysed to determine the relationship between depression, chronic disease and total life expectancy (TLE), disabled life expectancy (DLE) and active life expectancy (ALE = TLE - DLE) in men and women aged 70 and 85.</td>
<td>Outcomes: Center for Epidemiological Studies Depression scale, 8-item version (CES-D).</td>
</tr>
<tr>
<td>Ellis et al. (2010)</td>
<td>Data was collected from 10,025 participants in the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study who were alive and interviewed in 1982 and had completed the depression assessment. Respondents were placed into one of 4 groups; 1) no stroke or depression, 2) no stroke with depression, 3) stroke, no depression and 4) stroke and depression present. Presence of depression was defined as Center for Epidemiological Studies Depression scale (CES-D) score ≥16 points. Mean follow-up=8yr. The main outcome was all-cause mortality.</td>
<td>Outcomes: CES-D; Mortality rate.</td>
</tr>
</tbody>
</table>
| Naess et al. (2010) | Patients with stroke were screened for prior history of depression and use of selective 1. Using individuals in group one as the reference, and adjusting for sociodemographic variables and clinical comorbidities, individuals with both stroke and depression had the greatest risk for mortality (HR = 1.88, 95% CI 1.27-2.79). 2. Individuals with depression, but no stroke had the lowest risk relative to the reference group (HR=1.23 (95% CI 1.08-1.40). 3. Individuals with stroke but no depression also had an elevated risk (HR=1.74, 95% CI 1.06-2.85). 4. Having both stroke and depression created the greatest risk, but the combination of each of these factors was not additive. | 1. On logistic regression analysis, PSD was independently, and significantly, associated...
| Peters et al. (2010) | UK | Population: An analysis of data from the Hypertension in the Very Elderly Trial in which participants completed the Geriatric Depression Scale (GDS) at baseline and annually thereafter. For the purposes of this study, depression was defined as GDS score ≥6 points.  
**Intervention:** Analysis of data from the Hypertension in the Very Elderly Trial in which participants completed the Geriatric Depression Scale (GDS) at baseline and annually thereafter. For the purposes of this study, depression was defined as GDS score ≥6 points.  
**Outcomes:** GDS. |
|---|---|---|
| Pan et al. (2011) | International Cohort | Population: Age range=54-79yr.  
**Intervention:** An analysis of women from the Nurses’ Health Study, aged 54-79 at baseline in 2000, were followed up until 2006. Associations between depression, diabetes and mortality were examined. Depression was defined as self-reported depression diagnosis, treatment with antidepressants or a Mental Health Index score ≤52.  
**Outcomes:** Mortality Rate. |
| No Score TPS=acute N<sub>start</sub>=771 | serotonin reuptake inhibitor medications. As inpatients all patients had CT or MRI and the National Institute of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) was administered. Patients received a postal questionnaire 6mos following stroke. Presence of post-stroke depression (PSD) was defined as Hospital Anxiety and Depression Scale score ≥11 points (HADS-D).  
**Outcomes:** NIHSS; mRS; Barthel Index (BI); HADS-D. | with prior depression, being unmarried, having a stroke in progression. There was a trend toward a significant association with higher age and a history of previous stroke.  
2. Among those individuals that returned completed questionnaires, mortality was significantly and independently associated with the presence of PSD (HR=4.4, p=0.002) and age (HR=1.08, p<0.001), but not with gender (p=0.28).  
3. For individuals who did not complete questionnaires (and therefore could not be assessed for PSD), mortality was significantly and independently associated with prior depression (HR=1.7, p=0.01), age (HR=1.06, p<0.001), mRS scores (HR=1.7, p<0.001) and BI (HR=2.2, p=0.001). | 1. 40.8% of individuals with previous cardiovascular disease were identified as depressed.  
2. Overall, GDS=6 at baseline was associated with increased risk of all-cause mortality (HR=1.8, 95% CI 1.4-2.3), all stroke (HR=1.9, 95% CI 1.3-2.8), cardiovascular mortality (HR=2.2, 95% CI 1.6-3.1) and all cardiovascular events (HR=1.7, 95% CI 1.3-2.2). These relationships did not lose significance when examined by subgroups, including those individuals with previous history of cardiovascular disease.  
3. Controlling for comorbidities (including stroke) resulted in an attenuation of effect; however, both depression and diabetes are risk factors for stroke and other cardiovascular disease which may have resulted in an "over-adjustment." | 1. Age-adjusted relative risk for all-cause mortality in women with depression only was 1.76 (1.64-1.89) and 3.11 (2.7-3.58) in women reporting both diabetes and depression.  
2. Age adjusted relative risks for cardiovascular disease-related mortality were 1.81 for individuals with depression (1.54-2.13) and 5.38 for those with both conditions (4.19-6.91).  
3. Controlling for comorbidities (including stroke) resulted in an attenuation of effect; however, both depression and diabetes are risk factors for stroke and other cardiovascular disease which may have resulted in an "over-adjustment." |
### Hornsten et al. (2013)

**Sweden**  
**Case Series**  
**No Score**  
**TPS Mean = NA**  
**N start = 452**  
**N end = 452**

**Population:** Mean age ≥ 85 yr; Gender: Unspecified.  
**Intervention:** Data was collected from interviews with patients, staff and relatives, or medical charts that had been completed as part of a previous study from 2005 to 2007. The aim of the study was to investigate the relationship between depression and mortality among patients over the age of 85 yr with or without a history of stroke.  
**Outcomes:** Geriatric Depression Scale 15-item version (GDS).

1. 38 of 88 patients with a history of stroke were depressed compared with 91 of 364 patients without stroke (p = 0.001).
2. After 5 yr, 62 of the 88 patients with stroke had died, while 198 of the 364 without stroke had died (p = 0.009).
3. A history of stroke and depression was associated with increased 5 yr mortality when compared with patients having only stroke, only depression, or neither stroke or depression.
4. The 5 yr mortality rate did not increase for patients with a history of stroke without depression when compared with patients having neither stroke nor depression.

### Naess et al. (2013)

**Norway**  
**Observational**  
**No Score**  
**TPS Mean = 6 yr**  
**N start = 190**  
**N end = 190**

**Population:** Experimental Group (EG, N = 158): Mean age = 47.2 ± 8.3 yr; Gender: Males = 87, Females = 71. Control Group (CG, N = 32): Mean age = 51.2 ± 6.6 yr; Gender: Male = 22, Females = 10.  
**Intervention:** Young ischemic stroke patients aged 15-50 yr at the time of stroke were invited to a follow-up interview to complete a set of questionnaires after a previous follow-up of 6 yr after the index stroke. Assessments for the present study were conducted at a mean of 12 yr after the index stroke.  
**Outcomes:** Fatigue Severity Scale (FSS); Montgomery-Asberg Depression Rating Scale (MADRS); Mortality rate.

1. MADRS score was significantly higher among deceased patients compared to living patients (p = 0.004).
2. Mortality was significantly associated with FSS (p = 0.005) after adjusting for age (p = 0.06) and sex (p = 0.19).
3. Mortality was significantly associated with MADRS score (p = 0.006) after adjusting for age (p = 0.10) and sex (p = 0.11).
4. MADRS was significantly correlated with smoking, alcoholism, being unmarried, unemployment and stroke severity (all p < 0.05).
5. FSS was significantly correlated with diabetes mellitus, myocardial infarction, alcoholism, unemployment, depression and stroke severity (all p < 0.05).

### Ayerbe et al. (2014)

**UK**  
**Case Series**  
**No Score**  
**TPS Mean = NA**  
**N start = 3240**  
**N end = 1101**

**Population:** Age range < 64 yr = 393, Age Range > 65 yr = 708; Gender: Males = 595, Females = 506.  
**Intervention:** Data from patients registered on the South London Stroke Register between 1997 and 2010 was analyzed. Assessments within the study were conducted at 3 mo follow-up.  
**Outcomes:** Hospital Anxiety and Depression Scale (HADS); Medical Outcomes Study 12-Item Short Form Questionnaire (SF-12); Medical Outcomes Study 36-Item Short Form Questionnaire (SF-36); Barthel Index (BI); Mortality rates.

1. 32.8% of patients were found to be depressed at 3 mo according to the HADS.
2. Mortality was significantly higher at year 5 for patients depressed at 3 mo post-stroke compared to non-depressed patients (p = 0.0015).
3. Depression at 3 mo was associated with: increased mortality (HR 1.27, 95% CI [1.04, 1.55]), disability according to BI (RR up to 4.71, 95% CI [2.96, 7.48]), anxiety according to HADS (OR up to 3.49, 95% CI [1.71, 7.12]), and lower quality of life according to SF-12 and SF-36 (coefficients up to -8.16, 95% CI [-10.23, -6.15]) up to 5 yr.  
4. Recovery from depression by 1 yr did not alter these risks at 5 yr.
5. Depression at 5 yr was associated with anxiety (OR up to 4.06, 95% CI [1.92, 8.58]) and quality of life according to SF-12 and
### 18.6 Prevention of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nishida et al.</strong> (2015) Japan Case Control No Score TPS_Exp=30.0±23.4d TPS_Con=47.5±18.5d N_Start=24 N_End=24</td>
<td></td>
<td></td>
<td>Population: Experimental Group (EG, N=11): Mean age=81.2±9.3yr; Gender: Male=5, Female=6. Control Group (CG, N=13): Mean age=76.2±12.0yr; Gender: Male=9, Female=4.</td>
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</tbody>
</table>

1. There were 32 patients with SI and 486 patients without SI.
2. The SI group had a significantly greater GDS score (10.47±3.17 vs. 4.24±3.71, p<0.001) and frequency of NPI Apathy (31.2% vs. 5.3%, p<0.001) than the Non-SI group.
3. GDS (p<0.001) and NPI Apathy (p=0.025) were both significant predictors of SI.

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**Table 18.6 Prevention of Post-Stroke Depression**
<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Design</th>
<th>PEDro</th>
<th>N Start</th>
<th>N End</th>
<th>Intervention</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palomäki et al. (1999)</td>
<td>Finland</td>
<td>RCT</td>
<td>8</td>
<td>100</td>
<td>81</td>
<td>Stroke patients were involved in a double blind RCT of either 60 mg/d of mianserin or placebo for 1yr.</td>
<td>Barthel Index (BI); Hamilton Depression Rating Scale (HAMD); Beck Depression Inventory (BDI).</td>
<td>1. No significant difference between groups was found on any of the outcome measures (BI, HAMD, BDI).</td>
</tr>
<tr>
<td>Narushima et al. (2002)</td>
<td>USA &amp; Japan</td>
<td>RCT</td>
<td>8</td>
<td>48</td>
<td>29</td>
<td>Non-depressed stroke patients were randomly allocated to receive treatment with nortriptyline or with fluoxetine or placebo for 3mos.</td>
<td>Present State Examination.</td>
<td>1. During the treatment period, one minor depression was seen in nortriptyline group, three in the fluoxetine group and five in the placebo condition. 2. Intention-to-treat analysis of active vs. placebo conditions revealed no significant difference between these two conditions. 3. When treatment was discontinued, nortriptyline patients were more likely to develop depression and had significantly severe depression symptoms during the next 6mos compared to patients in the other two groups although there were no significant differences in prevalence of depression. 4. At 9mos, active treatment groups had significantly greater frequency of depression than placebo. 5. There was no significant group difference at 12 and 24mos.</td>
</tr>
<tr>
<td>Rasmussen et al. (2003)</td>
<td>Denmark</td>
<td>RCT</td>
<td>7</td>
<td>137</td>
<td>67</td>
<td>Non-depressed stroke patients were randomized to receive either sertraline or placebo for the prevention of post-stroke depression.</td>
<td>Hamilton Rating Scale for Depression.</td>
<td>1. Kaplan-Meier analysis demonstrated that sertraline has a significantly superior prophylactic efficacy compared to placebo. 2. Overall, after 52wks of treatment, 8.2% of the sertraline-treated group developed depression compared to 22.8% of the placebo treated group.</td>
</tr>
<tr>
<td>Niedermaier et al. (2004)</td>
<td>Germany</td>
<td>RCT</td>
<td>5</td>
<td>70</td>
<td>70</td>
<td>Patients with acute ischemic stroke with no depression or use of antidepressants in the immediate pre-stroke period were randomly allocated to treatment with mirtazapine (experimental group, EG) (n=35) or control (control group, CG) (N=35).</td>
<td></td>
<td>1. 40% of patients in the CG developed post-stroke depression vs. 5.7% of the EG (p&lt;0.001). 2. Of the 16 patients that developed post-stroke depression, 15 demonstrated remission of symptoms following treatment with mirtazapine.</td>
</tr>
<tr>
<td>Almeida et al. (2006)</td>
<td>Australia</td>
<td>RCT</td>
<td>9</td>
<td></td>
<td></td>
<td>Stroke patients were randomly assigned to receive either treatment with sertraline (50 mg once per day) (experimental group, EG) or matching placebo (control group, CG). Treatment commenced within 2wks of a recent stroke event and continued for</td>
<td></td>
<td>1. By 24wks, 21.6% of patients in the CG and 16.7% of patients in the EG were diagnosed with depression (OR = 0.8, p=0.59).</td>
</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>Design</td>
<td>PEDro</td>
<td>N&lt;sub&gt;Start&lt;/sub&gt;</td>
<td>N&lt;sub&gt;End&lt;/sub&gt;</td>
<td>Intervention</td>
<td>Outcomes</td>
<td>Results</td>
</tr>
<tr>
<td>-------</td>
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</tr>
<tr>
<td>Robinson et al. (2008)</td>
<td>USA</td>
<td>RCT</td>
<td>7</td>
<td>176</td>
<td>134</td>
<td>Patients with no depression were randomly assigned to receive one of three treatments within 3mos of stroke onset; i) escitalopram 10 mg/d (if &lt;65 yr, 5 mg/d for patients ≥ 65) ii) matching placebo or iii) problem-solving therapy (six treatment sessions over 12wks + six reinforcement sessions over 9mos). Patients were evaluated at 3, 6, 9 and 12mos</td>
<td>Hospital Anxiety and Depression Scale (HADS-D).</td>
<td>1. Patients with a history of mood disorders were 5.2 times more likely to develop depression than those without (p&lt;0.001). 2. Adjusted for previous history of mood disorders, patients assigned to the placebo condition were more likely to develop depression than individuals receiving either therapy with escitalopram (adj. HR= 4.5, 95% CI 2.4-8.2, p&lt;0.001) or problem-solving therapy (adj. HR=2.2, 95% CI 1.4-3.5, p&lt;0.001). 3. On intention-to-treat analysis that included 27 patients who did not receive any treatment and assumed all untreated patients developed depression, escitalopram was still associated with a significantly reduced risk for depression (23.1% vs. 34.5%, HR = 2.2 95% CI 1.2-39, p=0.007); however, problem-solving therapy was not (30.5% vs. 34.5%, HR=1.1, 95% CI 0.8-1.5, p=0.51).</td>
</tr>
<tr>
<td>Chollet et al. (2011) (FLAME study)</td>
<td>France</td>
<td>RCT</td>
<td>9</td>
<td>118</td>
<td>118</td>
<td>Patients were randomly assigned to receive either 20 mg/d fluoxetine (experimental group, EG) or matching placebo (control group, CG) within 5-10d of stroke onset. Treatment continued for 3mos. All patients received usual rehabilitation care delivered by organised stroke teams. Assessments were conducted at baseline, 30d and 90d.</td>
<td>Fugl-Meyer scale (FMS); Montgomery-Asberg Depression Rating Scale.</td>
<td>1. Frequency of depression was significantly greater in the CG when compared to the EG (4 pts vs. 17, p=0.002). 2. There was a significant between group difference reported in mean change in symptoms of depression over 90d (p=0.032). 1. Over the course of treatment, there was no change in depressive symptomatology in the EG (adjusted mean change = -0.1, 95% CI -2.1 to 1.9) while there was a significant increase in symptoms in the CG (adj. Mean change = 3.2, 95% CI 1.1-5.3). Change was adjusted for age, history of previous stroke and FMS score at baseline.</td>
</tr>
<tr>
<td>Tsai et al. (2011)</td>
<td>China</td>
<td>RCT</td>
<td>8</td>
<td>118</td>
<td>118</td>
<td>92 patients with first or recurrent ischemic stroke (within the preceding 4wks) and no depression were randomly assigned to receive either 50 mg/d milnacipran (titrated to 100 mg) (experimental group, EG), or matching placebo (control group, CG).</td>
<td>Frequency of depression was 2.22% in the EG and 15.22% in the CG. 2. Side effects were reported by both groups – there was no significant between group</td>
<td></td>
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</tbody>
</table>

24wks. Primary endpoint was development of significant symptoms of depression. Patients were assessed at baseline, 24wk and 52wk. **Outcomes:** Hospital Anxiety and Depression Scale (HADS-D).
post-stroke depression and mood disorders

Individuals with previous depression, those taking antidepressants or with possible, undiagnosed depression (Hamilton Depression Rating Scale (HAMD) ≥10) were excluded from the study. Evaluation was administered at 3, 6, 9, and 12mo follow-up visits.

**Outcomes**: HAMD (modified to remove item 14 – sexual behaviour); Barthel Index; National Institutes of Health Stroke Scale.

There was a statistically significant benefit associated with milnacipran over placebo (p=0.048).

**Populations**:

| Population | Experimental Group 1 (EG1, N=51): Mean age=60.8±14.0yr; Gender: Males=35, Females=16. Experimental Group 2 (EG2, N=56): Mean age=67.6±11.3yr; Gender: Males=29, Females=27. Control Group (CG, N=47): Mean age=62.7±13.3yr; Gender: Males=29, Females=18. | Population: | }

1. The mean time from baseline to onset of apathy was 6.0mo for EG1, 6.3mo for EG2, and 5.1mo for CG but no significant differences were found between groups (p=0.79).
2. The CG were 3.47 times more likely to develop apathy than EG1 (p<0.0001) and 1.84 times more likely to develop apathy than EG2 (p<0.0001).
3. There was no significant difference among patients who developed apathy compared to those who did not on the FIM (p=0.32) and the RBANS (p=0.17).
4. No significant differences were reported between EG1 and both EG2 and CG regarding adverse events.

### 18.6.1 Care Provision and the Prevention of Post-Stroke Depression

**Table 18.6.1 Impact of Care Provision Interventions on Post-Stroke Depression**

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lincoln et al.</strong> (2003) UK RCT PEDro=5 TPSExp1≤3mo TPSExp2≤3mo NStart=250 NEnd=187</td>
<td><strong>Intervention</strong>: Stroke patients and their informal caregivers were randomized to receive either Stroke Family Support Organiser service which provided support, information to patients and carers and liaised with hospital (experimental group, EG) or standard care (control group, CG). Intervention was provided for up to 9mos and participants were assessed at 4 and 9mos.</td>
<td></td>
<td>1. There were no significant differences between groups on patients’ mood, independence in personal or instrumental activities of daily living, caregivers’ mood, strain or independence. 2. The EG had better knowledge of stroke and was more satisfied with the service they received than the CG.</td>
<td></td>
</tr>
<tr>
<td><strong>Burton and Gibbon</strong> (2005) UK RCT PEDro=7 NStart=176</td>
<td><strong>Intervention</strong>: Inpatients with stroke were recruited from two district hospitals. Patients were randomly assigned to receive either extended stroke nurse follow-up post discharge (experimental group, EG) (n=87) or usual care (control group, CG) (n=89). Intervention included a single visit from a stroke nurse</td>
<td></td>
<td>1. Patients in the EG were less likely to experience deterioration on the BI when compared to the CG (p=0.049) over 12mos. 2. Intervention patients experienced greater improvement in perceived health than control patients (NHP, p=0.039).</td>
<td></td>
</tr>
</tbody>
</table>
### Claiborne (2006)
USA  
RCT  
PEDro=5  
TPS=NA  
N<sub>Start</sub>=28  

**Intervention:** Patients with stroke were randomly allocated to intervention (experimental group, EG) (n=16) or control conditions (control group, CG) (n=12). The EG received care coordination provided by a social worker consisting of a home visit (1-2wks following discharge from rehabilitation) followed by weekly telephone appointments 20min-1hr in length over a 3mo period. The CG received usual care.  

**Outcomes:** Barthel Index (BI); Nottingham Health Profile (NHP); Beck Depression Inventory; Frenchay Activities Index; Caregiver Strain Index.  

1. There were no significant between group differences on the SF-36 physical components scale.  
2. However, significant differences were reported for the MCS (p<0.001), GDS (p<0.001) and adherence to prescribed regimens (p<0.05).  

### Joubert et al. (2006)
Australia  
RCT  
PEDro=6  
TPS=NA  
N<sub>Start</sub>=97  

**Intervention:** Stroke patients, who returned to their GPs for ongoing care management, were assigned to receive either integrated care (experimental group, EG) (n=46) or the control condition (control group, CG) (n=51). Integrated care patients received shared care: visits with the GPs at 2wk, 3mo, 6mo, 9mo and 1yr, ongoing consultations between GP and the patient’s neurologist, telephone calls prior to GP visits from the study coordinator in order to assess patient progress and screen for depression, transmission of information from telephone contact to the GP and follow-up telephone contact to discuss changes to medication and management, ongoing progress tracking to ensure that best-practice standards were being met and provisions to the GP of options for review, testing and treatment. Control patients were told that they would be contacted at 12mo to review test results and clinical data.  

**Outcomes:** London Handicap Scale; Carer Strain Index; Person-in-Environment assessment; clinical status; Rankin Scale; Mini-Mental State Examination; Barthel Index; Medical Outcomes Study Social Support Survey; Functional Assessment Staging.  

1. 80 of 97 patients remained for analysis at 12mos. More patients in EG than the CG reached target BP, though this trend was not significant (p=0.11).  
2. Similarly, the mean cholesterol for patients in the EG was lower than the CG (p=0.16).  
3. Exercise participation increased significantly among individuals in the EG vs. CG (p=0.048).  
4. At 12mos, 45% of individuals assigned to the CG screened positively for depression vs. 20% of the EG (p=0.06).  
5. A later report from Joubert et al. (2008) provided additional results from ongoing enrolment. Based on data from 186 patients (91 in the EG, 95 in the CG), the authors reported that individuals receiving integrated care demonstrated significantly fewer symptoms of depression (p=0.006) as assessed on the Patient Health Questionnaire (a 9-item self-report tool). At 12mos, 33% of patient in the treatment condition reported depressive symptoms compared with 55% of individuals receiving standard care.  

### Watkins et al. (2007)
UK  
RCT  
PEDro=7  
TPS=NA  

**Intervention:** Stroke patients were randomly allocated to either the treatment (n=207) or the control conditions (n=204). All patients received usual stroke care. Patients in the treatment condition also received 4/wk individual sessions of motivational interviewing. Sessions were conducted by the same  

1. A significant benefit on mood was associated with the treatment condition over usual care at 3mos (OR for normal mood = 1.60, p=0.03).  

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**N<sub>End</sub>=126**  
within 2d following discharge to plan further follow-up. CG participants received no further contact from the stroke nurse following discharge. Assessments were administered at 3 and 12mos post-stroke.  

**Outcomes:** Barthel Index (BI); Nottingham Health Profile (NHP); Beck Depression Inventory; Frenchay Activities Index; Caregiver Strain Index.  

1. At 3 and 12mos, patients in the EG reported lower levels of emotional distress (p=0.01, p=0.037) and social isolation (p=0.045 and p=0.002) than the CG.  

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N\textsubscript{Start}=411 therapist and lasted 30-60min each. Baseline assessments were conducted between 5-28d following the stroke event. Outcomes were assessed via mailed questionnaire at 3mos. **Outcomes:** General Health Questionnaire-28.

2. Using a self-report (Yale) screening tool for depression, a protective effect of motivational interviewing was also identified (OR = 1.65, p=0.03).

3. Motivational interviewing was not associated with reduced risk for dependency or morality.

Watkins et al. (2011) UK

(follow-up study)

**Population:** Experimental Group (EG, N=100): Mean age=68±16y; Gender: Male=52, Female=48. Control Group (CG, N=101): Mean age=72±14y; Gender: Male=63, Female=38.

**Intervention:** 125 patients assigned to the control group (CG) and 164 assigned to the intervention (experimental group, EG) participated in the 12mo follow-up to Watkins et al. (2007). Analysis was conducted on an intention to treat basis.

**Outcomes:** General Health Questionnaire-28.

1. At 12mos, the significant benefit associated with motivational interviewing appeared to be maintained (OR for normal mood = 1.66, 95% CI 1.08-2.55, p=0.02).

2. The previously identified protective effect vs. depression (based on the Yale screening tool) was not present at 12mos (OR = 1.1, 95% CI 0.74-1.64, p=0.80).

Hackett et al. (2013) Australia

RCT

PEDro=7

TPS\textsubscript{exp}=20.8±24.0d

TPS\textsubscript{con}=17.5±19.0d

N\textsubscript{Start}=201

N\textsubscript{End}=164

**Population:** Experimental Group (EG, N=100): Mean age=68±16y; Gender: Male=52, Female=48. Control Group (CG, N=101): Mean age=72±14y; Gender: Male=63, Female=38.

**Intervention:** The EG received personalised postcards wishing the patients well and inviting patients to contact the hospital should they feel the need to. The CG did not receive postcards. Postcards were sent to the EG at 1mo, 2mo, 3mo, 4mo and 5mo post-stroke. Assessments were conducted at baseline, 3mo and 6mo follow-ups.

**Outcomes:** Hospital Anxiety and Depression Scale (HADS: Depression, Anxiety); Patient Health Questionnaire (PHQ-9); Australian Quality of Life (AQoL).

1. HADS Depression and Anxiety scores did not differ between groups (p=0.9357 and p=0.7408, respectively) when 3mo and 6mo follow-up mean scores were combined.

2. PHQ-9 scores did not differ between groups (p=0.8082) when 3mo and 6mo follow-up mean scores were combined.

3. AQoL scores did not differ significantly between groups at 6mo follow-up (p=0.73).

Rochette et al. (2013) Canada

RCT

PEDro=7

TPS\textsubscript{Overall}=6mo

N\textsubscript{Start}=186

N\textsubscript{End}=139

**Population:** Experimental Group (EG, N=92): Mean age=61.7±12.7y; Gender: Male=57, Female=35. Control Group (CG, N=94): Mean age=63.2±12.4y; Gender: Male=50, Female=44.

**Intervention:** Participants were recruited from 11 acute care hospitals located in urban and rural areas across four Canadian provinces. The EG received a multimodal support intervention (WE CALL group) in the form of 1/wk phone calls and follow-ups for the first 2mo, 2/wk during the third month and monthly for the remaining 3mo of the 6mo trial. The CG (YOU CALL group) were provided with the name and phone number of a trained healthcare professional and asked to call when patients felt they needed to. Assessments were conducted at baseline, post-treatment, and at 1yr follow-up.

**Outcomes:** Unplanned and planned use of health services (participant diaries); EuroQOL-5D (EQ-5D); Quality of Life Index (QOLI); Beck Depression Inventory II (BDI-II); Assessment of Life Habits (LIFE-H).

1. No significant differences were found between the two groups regarding planned use of health services (p=0.24), BDI-II (p=0.27), and LIFE-H (p=0.61), however a significant improvement in both groups was found from baseline to 6mo on the BDI-II (time effect p<0.001) and on the LIFE-H (time effect p<0.001).

2. At 1yr assessment, the only significant change from 6mo for both groups was in the social domains (relationships, work, and recreation) of the LIFE-H (p<0.05).

3. There were no significant differences between the two groups on unplanned use of health services (p=0.15), EQ-5D (p=0.27), and QOLI (p=0.57), however both groups improved significantly from baseline to 6mo on the EQ-5D (time effect p<0.001), and on the QOLI (time effect p=0.005).
**Drummond et al.**
(2013)  
UK  
RCT and Cohort  
PEDro=6  
TPS\text{Mean}=NA  
RCT: N\text{Start}=93  
RCT: N\text{End}=86  
Cohort: N\text{Start}=33  
Cohort: N\text{End}=31  

**Population:** RCT (N=173): Experimental Group (EG, N=47): Mean age=70.6±14.3yr; Gender: Males=26, Females=21. Control Group (CG; N=46): Mean age=73.7±15.1yr; Gender: Males=24, Females=22. Cohort Study (N=33): Mean age=71.7±12.7yr; Gender: Males=15, Females=18.

**Intervention:** Patients recruited to the RCT were allocated either to the EG whereupon patients received a pre-discharge home assessment visit by occupational therapist or to the CG where patients received a pre-discharge hospital interview. Patients in the cohort study received a home visit under the same protocol as patients in the RCT EG. Assessments were conducted at 1wk and 1mo post-discharge from hospital.

**Outcomes:** Nottingham Extended Activities of Daily Living Scale (NEADL); Stroke Aphasic Depression Questionnaire (SADQ-10); Quality of Life (EQ-5D); Number of patients readmitted to hospital; Mean cost of home visits.

1. SADQ-10 scores were significantly lower in the EG compared to the CG at 1wk post-discharge (p=0.05).
2. SADQ-10 scores did not differ significantly between the EG and CG at 1mo post-discharge (p=0.05).
3. No significant differences were reported between the EG and CG on the NEADL at both 1wk (p=0.75) and 1mo (p=0.52) post-discharge.
4. EQ-5D scores did not differ significantly between the EG and CG at 1mo post-discharge (p=0.74).
5. A greater proportion of participants in the EG were readmitted to hospital within 1mo after discharge when compared to the CG (p=0.04).
6. On average, the main resource use associated with home visits (amount of staff time required) was greater for the Cohort study patients than the RCT study patients.
7. The mean total cost per home visit for the Cohort study group was £243, whilst the RCT study group cost less at £183 per home visit.

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**Ostwald et al.**
(2014)  
USA  
RCT  
PEDro=5  
TPS\text{Exp1}≤12mo  
TPS\text{Exp2}≤12mo  
N\text{Start}=159  
N\text{End}=134  

**Population:** Experimental Group (EG, N=80): Mean age=66.98±9.04yr; Gender: Male=55, Female=25. Control Group (CG, N=79): Mean age=65.75±9.26yr; Gender: Male=64, Female=15.

**Intervention:** EG received mailed letters with information on stroke, resources and advice plus home visits from nurses and therapists. CG received mailed letters with information on stroke, resources and advice only. The intervention was provided 1/mo for both groups but EG1 was also provided with a mean of 16 home visits lasting 70min each for the first 6mo of the study. Assessments were conducted at baseline, 3mo, 6mo, 9mo and 12mo follow-ups.

**Outcomes:** Geriatric Depression Scale (GDS); Perceived Stress Scale (PSS); Medical Outcomes Study 36-Item Short Form Questionnaire (SF-36); Stroke Impact Scale (SIS: Memory, Social Participation); Functional Independence Measure (FIM: Cognitive).

1. GDS and PSS scores did not differ significantly between groups at any time point but when both groups were combined, a significant decreases in depression and stress were found (p<0.05).
2. SF-36 improved significantly for EG1 from baseline to 6mo (p=0.03) but no improvements were reported from 6mo to 12mo follow-ups.
3. SF-36 improved significantly for caregivers of both EG1 and CG (both p=0.041) at 6mo follow-up but no significant improvement was noted at 12mo.
4. FIM Cognitive improved for both groups from baseline to 6mo (both p=0.03) but no differences were reported between groups.
5. The SIS Memory and Social Participation subscales revealed significant improvements for all patients combined (both p<0.05) at 6mo and 12mo but no significant differences were found between groups for either subscale.
18.6.2.1 Omega-3 Fish Oil

Table 18.6.2.1 Omega-3 Fish Oil Supplementation and Mood

<table>
<thead>
<tr>
<th>Author, Year Country PEDro Score TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poppit et al. (2009) Australia/New Zealand RCT PEDro=9 TPS=NA NStart=102 NEnd=102</td>
<td><strong>Intervention:</strong> Stroke patients were randomly assigned to receive either 3 g/d encapsulated fish oil or a matching placebo oil (palm and soy oils). Assigned treatments were taken daily for a period of 12wk. Assessments were performed at baseline and 12wk. <strong>Outcomes:</strong> Serum triglycerides; total cholesterol; lipoproteins; inflammatory and haemostatic markers; General Health Questionnaire-28 (GHQ-28); Health Related Quality of Life.</td>
<td>1. Compliance to treatment was approximately 90%. 2. There were no significant effects reported for the primary study outcomes of serum triglycerides, lipids, inflammatory or haemostatic markers. 3. There was a significant difference between groups reported for the total score of the GHQ-28 (p&lt;0.04); however, this was attributable to a decrease in scores for the placebo condition. 4. There was no effect of treatment on the depression subscale of the GHQ-28.</td>
</tr>
</tbody>
</table>

18.6.2.2 B-Vitamins

Table 18.6.2.2 B-Vitamin Supplementation in the Treatment of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year Country PEDro Score TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almeida et al. (2010) VITATOPS-DEP Study Australia RCT PEDro=10 TPS=NA NStart=563</td>
<td><strong>Intervention:</strong> This was an added substudy of the VITATOPS trial (a large multicenter RCT to evaluate the impact of B-vitamin therapy on risk for secondary stroke). Patients (n=563) with previous stroke/TIA were randomly allocated to treatment (n=284) with folic acid (2.0 mg/d), vitamin B6 (25 mg/d) and vitamin B12 (0.5 mg/d) (experimental group, EG) or to treatment with matching placebo (n=279) (control group, CG). The depression substudy included only individuals who did not fulfill criteria for a depressive disorder at baseline. Assessments were conducted every 6mo following baseline. <strong>Outcomes:</strong> Mini-International Neuropsychiatric Interview.</td>
<td>1. Mean length of follow-up was 6.9yr in the CG and 7.3yr in the EG (p=0.3). Compliance to treatment was approximately 80% in both groups. 2. During the trial, more episodes of major depression occurred within the CG than in the group receiving vitamin therapy (23.3% vs. 18.4%; HR=0.48, 95% CI 0.27-0.86). 3. At the final assessment, there were no between group differences in prevalence of depression; however, on logistic regression (adjusted for age, gender, antidepressant use, handicap, recurrence of stroke and presence of cognitive impairment), there was a non-significant trend toward reduced risk for major or minor depression associated with vitamin therapy (OR=0.58, 95%CI = 0.31-1.09) using intention-to-treat analysis. On per protocol analysis, the</td>
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</table>
18.7 Pharmacologic Treatment of Post-Stroke Depression

Table 18.7.1 Heterocyclic Antidepressants in the Treatment of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipsey et al. (1984)</td>
<td>USA</td>
<td>RCT</td>
<td>PEDro=8</td>
<td>TPS=NA</td>
<td>NStart=39</td>
</tr>
<tr>
<td><strong>Intervention:</strong> Stroke patients partook in a double blind, placebo controlled randomized trial evaluating the efficacy of nortriptyline in treatment of post-stroke depression for 6wks with a single bedtime dose of 20mg during week 1, 50mg during week 2; late-starters received 70mg at week 1 and 100mg at week 2.</td>
<td><strong>Outcomes:</strong> Hamilton Depression Rating Scale (HAM-D); Zung Self-Rating Depression Scale (ZDS); Overall Depression Scores (ODS).</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Lauritzen et al. (1994)</td>
<td>Denmark</td>
<td>RCT</td>
<td>PEDro=7</td>
<td>TPS=NA</td>
<td>NStart=58</td>
</tr>
<tr>
<td><strong>Intervention:</strong> This study involved a 6wk double blind RCT of imipramine + mianserin and desipramine + mianserin in 58 thromboembolic stroke patients with post-stroke depression. 25mg imipramine and 25mg desipramine were given 2/d for the first wk and thereafter dosage changed on basis of side effects to max dosage of 75mg 2/d. A fixed dose of 10mg mianserin was given the first wk and adjusted thereafter to a max of 30mg.</td>
<td><strong>Outcomes:</strong> Bech-Rafaelsen Melancholia Scale (MES).</td>
<td></td>
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<tr>
<td>Robinson et al. (2000)</td>
<td>USA &amp; Argentina</td>
<td>RCT</td>
<td>PEDro=8</td>
<td>TPS=NA</td>
<td>NStart=104</td>
</tr>
<tr>
<td><strong>Intervention:</strong> Double blind, placebo controlled randomized crossover trial. Patients were randomly assigned to either fluoxetine (10 mg/d gradually increased to 40 mg/d) or nortriptyline (dose of 25 mg/d gradually increased to 100 mg/d) or identical placebo given over 12 wk. Patients received 12wk of active treatments and cross-over for 12wk of placebo treatment.</td>
<td><strong>Outcomes:</strong> Hamilton Depression Rating Scale (HAM-D); Functional Independence Measure (FiM).</td>
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</tbody>
</table>

1. Patients who were treated with nortriptyline showed significantly greater improvement on the HAM-D, ZDS; and on the ODS than those who received the placebo treatment.

1. A significant mean improvement was noted on the MES in favour of imipramine + mianserin.

1. A significant time-by-treatment interaction was found on the repeated measure analysis of variance of the mean HAMD score.

2. Nortriptyline treated group showed significantly greater improvement on the HAMD than the other 2 groups.

3. Nortriptyline produced a significantly higher rate than fluoxetine or placebo in treating post-stroke depression, in improving anxiety symptoms and in improving recovery of activities of daily living as measured by the FiM.

18.7.2 Selective Serotonin Reuptake Inhibitors (SSRIs)

Table 18.7.2 Selective Serotonin Reuptake Inhibitors in the Treatment of Post-Stroke Depression

reduction in risk did reach significance (OR=0.48, 95% CI 0.25-0.91).
<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andersen et al. (1994)</td>
<td>Denmark</td>
<td>RCT</td>
<td>PEDro=8 TPS=2-52wk N_{start}=66 N_{end}=56</td>
<td><strong>Intervention:</strong> Stroke patients with depression 2-52wk after stroke participated in a double blind RCT of citalopram. Patients received either 20 mg/d of citalopram before bedtime if younger than 66yr old (10 mg/d in patients &gt;66yr old) or received a placebo. <strong>Outcomes:</strong> Hamilton Depression Rating Scale (HAMD); Bech-Rafaelsen Melancholia Scale (MES).</td>
<td>1. Significant improvement was noted on the HAMD and the MES with citalopram when compared to placebo.</td>
</tr>
<tr>
<td>Robinson et al. (2000)</td>
<td>USA &amp; Argentina</td>
<td>RCT</td>
<td>PEDro=8 TPS=NA N_{start}=104 N_{end}=78</td>
<td><strong>Intervention:</strong> Double-blind, placebo controlled RCT. Patients randomly assigned to either fluoxetine (10mg/d gradually increased to 40 mg/d) or nortriptyline (dose of 25 mg/d gradually increased to 100 mg/d) or identical placebo given over 12wk. Patients received 12wk of active treatments and crossed-over to 12wk of placebo treatment. <strong>Outcomes:</strong> Response rate of treatment; Weight loss.</td>
<td>1. There was no significant difference between fluoxetine and placebo. 2. Response rate of treatment was not significantly different between fluoxetine and placebo. 3. Fluoxetine induced significant weight loss in elderly patients.</td>
</tr>
<tr>
<td>Wiart et al. (2000)</td>
<td>France</td>
<td>RCT</td>
<td>PEDro=8 TPS=NA N_{start}=31 N_{end}=31</td>
<td><strong>Intervention:</strong> Patients with post-stroke depression participated in a double blind RCT of 20mg/d of fluoxetine or a placebo treatment. <strong>Outcomes:</strong> Montgomery-Asberg Depression Rating Scale (MADRS).</td>
<td>1. A significant improvement was noted on the MADRS in favour of the fluoxetine treatment group.</td>
</tr>
<tr>
<td>Fruehwald et al. (2003)</td>
<td>Austria</td>
<td>RCT</td>
<td>PEDro=9 TPS=acute N_{start}=54 N_{end}=40</td>
<td><strong>Intervention:</strong> Patients suffering from moderate to severe post-stroke depression were randomized within 2wk of stroke to either treatment with fluoxetine or to placebo control (control group, CG). <strong>Outcomes:</strong> Beck Depression Inventory (BDI).</td>
<td>1. Significant improvement was seen in both groups within 4wk; however no advantage of fluoxetine was noted at this time. 2. BDI scores of patients treated with fluoxetine decreased until the follow-up at 12wk whereas the scores increased in the CG. 3. At long-term follow up, 18mo after inclusion, patients treated who had been treated with fluoxetine were significantly less depressed than CG patients.</td>
</tr>
<tr>
<td>Murray et al. (2005)</td>
<td>Sweden</td>
<td>RCT</td>
<td>PEDro=9 TPS=NA N_{start}=123</td>
<td><strong>Intervention:</strong> Stroke patients with either a major or minor depressive episode (defined according to the Diagnostic and Statistical Manual of Mental Disorders) were assigned to either the treatment (experimental group, EG) or placebo (control group, CG) conditions. 62 patients received sertraline (50-100 mg/d) and 61 received a matching placebo. Assessments were recorded at baseline, 6wk and 26wk. <strong>Outcomes:</strong> Montgomery Asberg Depression Rating Scale (MADRS); Emotional Distress Scale (EDS).</td>
<td>1. Both groups demonstrated significant improvements over the study period. 2. There were no significant between group differences on the primary study outcomes whether the patient was diagnosed with major or minor depression. 3. There was a significant difference between groups favouring treatment identified on the EDS (p&lt;0.05). 4. Improvement in global quality of life was greater for those patients treated with...</td>
</tr>
</tbody>
</table>
Choi-Kwon et al. (2006) Korea RCT PEDro=7 TPS=NA N_{start}=152 N_{end}=125

**Intervention:** Stroke patients with one of post-stroke depression (PSD) (average=14 mos post-stroke), emotional incontinence or anger proneness were randomly assigned to receive either fluoxetine 20 mg/d (n=76) (experimental group, EG) or matching placebo (n=79) (control group, CG). Treatment continued for a period of 3 mo.

**Outcomes:** Beck Depression Inventory (BDI); Visual Analogue Scale (VAS) for emotional incontinence and anger proneness.

1. A total of 32 patients in the EG and 19 patients in the CG were diagnosed with PSD. The severity of PSD was judged to be mild (mean BDI = 19).
2. Treatment with fluoxetine was not associated with a significant improvement in depression when compared to the placebo condition.

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### 18.7.2.1 Adjunctive Light Therapy

**Table 18.7.2.1 Adjunctive Light Therapy in the Treatment of Post-Stroke Depression**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sondergaard et al. (2006)</td>
<td>Denmark RCT</td>
<td>PEDro=5</td>
<td>TPS=acute</td>
<td>N_{start}=63</td>
<td>Intervention: Patients with acute stroke who were diagnosed with major depression (Diagnostic and Statistical Manual of Mental Disorders) were included in the study. All patients were treated with 20 mg/d citalopram for 4wk. At baseline, participants were randomly assigned to high or moderate light conditions. Intensity was manipulated via distance from the light source. High intensity conditions were 10,000 lux (30 cm) while moderate light was 4,000 lux (60 cm). Light therapy was conducted every morning for 30min over 14d. <strong>Outcomes:</strong> Hamilton Depression Rating Scale (HADS-17 or -6); Bech-Rafaelsen Melancholia Scale.</td>
</tr>
</tbody>
</table>

1. All patients experienced similar reductions in reported symptoms of depression over the first 2wk of treatment.
2. At 2wk, there were no significant between group differences reported.
3. However, at 4wk there was a statistically significant reduction in depressive symptomatology on the HADS-6 in favour of the high intensity light treatment vs. moderate intensity (p<0.05).
4. There were no significant side effects reported and no patients left the study due to side effects.

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### 18.7.3 Selective Noradrenaline Reuptake inhibitors (NARI)

**Table 18.7.3 Reboxetine in the Treatment of Post-Stroke Depression**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rampello et al. (2005)</td>
<td>Italy RCT</td>
<td>PEDro=8</td>
<td>N_{start}=125</td>
<td>N_{end}=119</td>
<td>Intervention: Patients who had experienced stroke within the preceding 12mo and were diagnosed with major or minor depression according to the Diagnostic and Statistical Manual of Mental Disorders criteria and who presented with the characteristics of retarded</td>
</tr>
</tbody>
</table>

1. Patients in the EG experienced significant improvement from baseline to 4, 8 and 16wk on both the HAMD and the BDI (p<0.01). There was no significant change
depression were randomly allocated to treatment (experimental group, CG) or control (control group, CG) conditions. Treatment consisted of 4 mg/d of reboxetine (n=16) while the control condition received a matching placebo. Treatment continued for 16wk. **Outcomes**: Hamilton Depression Rating Scale (HAM-D); Beck Depression Inventory (BDI).

2. At each assessment time, comparisons to the CG revealed significant improvement on the part of patients enrolled in the EG (p<0.01).

3. The most commonly reported side effects associated with reboxetine treatment were dryness of fauces, constipation and hyperperspiration.

### 18.7.4 Serotonin and Noradrenaline Reuptake Inhibitors (SNRIs)

#### Table 18.7.4.1 Venlafaxin and Duloxetine in the Treatment of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year Country PEDro Score TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dahmen et al. (1999) Germany No Score TPS=acute N&lt;sub&gt;Start&lt;/sub&gt;=12</td>
<td><strong>Intervention</strong>: Patients with recent stroke (within 2wk) and depression (Diagnostic and Statistical Manual of Mental Disorders) were treated for 5wk with venlafaxine (75 mg/d for first 2d, 150 mg/d for rest of the treatment period). Depressive symptomatology was assessed at baseline, after 2wk and at end of treatment. <strong>Outcomes</strong>: Hamilton Depression Rating Scale (HAM-D); Montgomery-Asberg Depression Rating Scale (MADRS).</td>
<td>1. Treatment was well tolerated and treatment was not discontinued in any cases. 2. There were no cardiovascular or hepatic disturbances recorded with the exception of one case of elevated liver enzymes in one patient with chronic hepatitis. 3. At 2wk, there was a positive treatment response recorded in 10/12 patients (reduction of ≥ 50% on HAMD). Scores on the MADRS showed a similar response.</td>
</tr>
<tr>
<td>Kucukalic et al. (2007) Bosnia &amp; Herzegovina No Score TPS=acute N&lt;sub&gt;Start&lt;/sub&gt;=30</td>
<td><strong>Intervention</strong>: Patients with post-stroke depression (within 3mo of the stroke event) were treated with venlafaxine over a period of 3mo. Assessments were performed at baseline, 1mo and at end of treatment. <strong>Outcomes</strong>: Hamilton Depression Rating Scale (HAM-D).</td>
<td>1. There were significant reductions in depressive symptomatology at 1 and 3mo (p&lt;0.001). 2. At 1mo, there was notable improvement in 80% of patients and after 3mo of treatment, there was a clinical response (reduction of ≥ 50%) in 53.3% of patients and remission of depression in 26.6%. 3. Two patients reported side effects (increase in blood pressure), but these were mild and transient.</td>
</tr>
<tr>
<td>Zhang et al. (2013) China RCT PEDro=7 TPS=NA N&lt;sub&gt;Start&lt;/sub&gt;=118</td>
<td><strong>Intervention</strong>: Participants were randomly allocated to a control group (CG) or a duloxetine group (experimental group, EG). The EG received a daily dose of 30mg which was increased to up to 90mg/d (according to clinical need) for 12wk. Outcomes were assessed at 2, 4, 12 and 24wk post-treatment.</td>
<td>1. Duloxetine was shown to significantly reduce the incidence of minor and major depression among individuals in the EG compared to the CG (p&lt;0.05). 2. The study reported improvement in the health domains on the SF-36 among individuals in the EG (&lt;0.05).</td>
</tr>
</tbody>
</table>
Outcomes: National Institute of Health Stroke Scale; Hamilton Depression Rating Scale; Medical Outcomes Study 36-Item Short Form Questionnaire (SF-36).

18.7.5 Gamma Aminobutyric Acid Compounds (GABA)

Table 18.7.5 Nefiracetam in the Treatment of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year Country PEDro Score TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robinson et al. (2008) USA/Canada RCT PEDro=8 TPS=NA NStart=159 NEnd=159</td>
<td>Intervention: Patients with post-stroke depression were randomly assigned to receive 1 of 34 treatments: i) 600 mg nefiracetam (n=55), ii) 900 mg nefiracetam (n=48) or iii) matching placebo. Patients were evaluated at baseline, 4, 9 and 12wk (end of treatment).</td>
<td>1. There was no significant time X treatment effect of 600 mg or 900 mg nefiracetam when compared with placebo. 2. There were no significant effects identified on an item-by-item analysis of the HAMD. 3. A post hoc analysis identified a significant effect of treatment among the most severely depressed quintile of patients treated with 900 mg nefiracetam compared with placebo (p=0.05).</td>
</tr>
</tbody>
</table>

18.7.6 Psychostimulants

Table 18.7.6 Psychostimulants in the Treatment of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year Country PEDro Score TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lingam et al. (1988) USA No Score TPS=NA NStart=25</td>
<td>Intervention: Retrospective review of 25 stroke patients with a diagnosis of major depression by the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) criteria who were treated with methylphenidate. Only patients who showed complete remission of depression symptoms were rated as responders. Patients who showed partial response, no response, or worsening of depressive symptoms were considered non-responders.</td>
<td>1. 52% of patients recovered completely from their depression. These responders did not differ significantly from the 12 non-responders on demographic characteristics, location of stroke and other variables. 2. Mood usually improved within 48hr with only three patients experiencing side effects.</td>
</tr>
<tr>
<td>Masand et al. (1991) USA No Score TPS=NA NStart=17</td>
<td>Intervention: Hospital charts of 17 patients with post-stroke depression who were treated with either dextroamphetamine or methylphenidate during a 5yr period were examined. Patients rated as markedly improved showed complete or nearly complete remission of all depressive symptoms. Those rated as moderately improved showed decided improvement in several symptoms without complete remission and those rated minimally improved showed a minor</td>
<td>1. 82% of patients showed improvement after psycho-stimulant treatment. 47% of all patients showed marked or moderate improvement in depressive symptoms. 2. There were no significant differences between the two psycho-stimulants across the diagnostic categories for depression.</td>
</tr>
<tr>
<td>Study</td>
<td>Intervention</td>
<td>N Start</td>
</tr>
<tr>
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<tr>
<td>Johnson et al. (1992)</td>
<td>Stroke patients were placed on methylphenidate for treatment of post-stroke depression. Dose range of methylphenidate was 5mg (q.a.m.) to 15 mg (b.i.d.) and length of therapy ranged from 5d to 1mo. Eight patients had an adjustment disorder with depressed mood, one with major depression, one had a combination of major depression and anxiety disorder and eight had concomitant attention depression. All patients were observed to have cognitive deficits on initial evaluation. <strong>Outcomes:</strong> Medical records.</td>
<td>10</td>
</tr>
<tr>
<td>Lazarus et al. (1992)</td>
<td>Patients meeting Diagnostic and Statistical Manual of Mental Disorders, Text Revision criteria for major depression were followed up during a 3wk efficacy and side-effect trial of methylphenidate. Methylphenidate was begun at a dose of 2.5 mg or 5 mg p.o. q. a.m. and q. noon that was slowly increased to as much as 40 mg/d. Mean dosage used, approximately at the 10th day, was 17.0 mg/d.</td>
<td>10</td>
</tr>
<tr>
<td>Lazarus et al. (1994)</td>
<td>Hospital charts of elderly stroke patients with major depression (Diagnostic and Statistical Manual of Mental Disorders, Text Revision criteria (DSM-III-R)) that were treated with either methylphenidate (n=28) or nortriptyline (n=30) were reviewed retrospectively. <strong>Outcomes:</strong> DSM-III-R; Hospital charts.</td>
<td>58</td>
</tr>
<tr>
<td>Grade et al. (1998)</td>
<td>A double blind RCT of stroke patients comparing the efficacy of methylphenidate during stroke rehabilitation. Patients were randomized to receive either 5mg in the morning and 30mg before bedtime of methylphenidate or a placebo treatment. <strong>Outcomes:</strong> Hamilton Depression Rating Scale (HAMD); Zung Self-Rating Depression Scale (ZDS); Functional Independence Measure (FIM); Fugl-Meyer Scale (FMS).</td>
<td>21</td>
</tr>
</tbody>
</table>

18.7.7 Melatonin Agonist
### Table 18.7.7 Melatonin Agonist in the Treatment of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year Country PEDro Score</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Bogolepova et al.</em>, (2011) Russia Pre-Post No Score TPS=NA N_{Start}=40</td>
<td><strong>Intervention</strong>: Individuals post-stroke, aged 55-85yr were prescribed 25mg/d of valdoxan for 3mo. Outcomes were measured at baseline, 14, 30, 60 and 90d of treatment. <strong>Outcomes</strong>: Hamilton Depression Rating Scale (HAMD); Hospital Anxiety and Depression Scale (HADS).</td>
<td>1. Significant improvement in depressive symptoms were seen on the HAMD and HADS by 2wk and continued to show improvement throughout follow-up (p&lt;0.05). 2. The HADS also found significant improvement in anxiety symptoms post treatment (p&lt;0.05).</td>
</tr>
</tbody>
</table>

### 18.7.8 Statins

### Table 18.7.8 Statins in the Treatment of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year Country PEDro Score TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Kim et al.</em>, (2014) South Korea Cohort No Score TPS=mean=12.3±3.0d N_{Start}=423 N_{End}=288</td>
<td><strong>Population</strong>: Experimental Group (EG, N=251): Mean age=64.2±9.6yr; Gender: Male=142, Female=109. Control Group (CG, N=172): Mean age=64.8±10.7yr; Gender: Male=102, Female=70. <strong>Intervention</strong>: The EG consisted of patients who had been prescribed statins and the CG had not received statins between 2006 and 2010. Statins prescribed to patients included atorvastatin, fluvastatin, lovastatin, mevastatin, pravastatin, and rosuvastatin. Assessments were completed at baseline and at 1yr follow-up. <strong>Outcomes</strong>: Hamilton Depression Rating Scale (HAMD); Hospital Anxiety and Depression Scale (HADS: Depression).</td>
<td>1. HADS Depression scores between the EG and CG revealed a significant Group x Time interaction with the EG exhibiting no change but CG scores increasing from baseline to 1yr follow-up (p=0.05). 2. HADS Depression scores for depressed patients only in the EG revealed a significant Group x Time interaction with scores decreasing from baseline to 1yr follow-up whilst scores for depressed CG patients increased slightly (p=0.007). 3. HAMD scores between the EG and CG revealed a significant Group x Time interaction with the EG exhibiting a decrease in scores but CG scores increased slightly from baseline to 1yr follow-up (p=0.042). 4. HAMD scores for depressed patients only in the EG revealed a significant Group x Time interaction with scores decreasing from baseline to 1yr follow-up whilst scores for depressed CG patients increased slightly (p=0.036).</td>
</tr>
</tbody>
</table>

### 18.7.9 Alternative Medicine

### Table 18.7.9 Herbal Medicine in the Treatment of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
<td>PEDro Score</td>
<td>Methods</td>
</tr>
<tr>
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<td>---------</td>
</tr>
<tr>
<td>Li et al. (2008)</td>
<td>China</td>
<td>RCT</td>
</tr>
<tr>
<td>TPS=acute</td>
<td>Nstart=151</td>
<td>Nend=146</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Williams et al. (2007)</td>
<td>USA</td>
<td>RCT</td>
</tr>
<tr>
<td>TPS=acute</td>
<td>Nstart=188</td>
<td><strong>Intervention:</strong> Patients with depression 1-2mo post-stroke were randomly allocated to receive either the Activate-Initiate-Monitor (AIM) intervention or control conditions. The AIM intervention consisted of 3 steps: 1) activate stroke survivors to understand and accept the diagnosis of depression and its treatment 2) initiate antidepressant medication 3) monitor treatment</td>
</tr>
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</table>
effectiveness (including dose adjustment and medication change as necessary). The control condition consisted of usual care plus an identical number of baseline and telephone sessions as were received by the treatment condition in order to control for an attention effect. The primary study outcome was proportion of patients who had achieved significant response (Hamilton Depression Rating Scale (HAMD) <8 or 50% decline in score) following 12wk of treatment. **Outcomes:** HAMD.

### 18.8 Impact of Pharmacologic Treatment of PSD on Rehabilitation Outcomes

#### 18.8.2 Mortality and Pharmacologic Treatment of Post-stroke Depression

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Jorge et al.</strong> (2003)</td>
<td>USA</td>
<td>RCT</td>
<td>PEDro=7</td>
<td>TPS&lt;6mo</td>
<td>N_start=104 N_end=81</td>
</tr>
</tbody>
</table>
| **Ayerbe et al.** (2014) | | | | | | **Population:** Intervention Group (N=1354): Mean age=Unspecified; Gender: Male=731, Female=623. | 1. Mortality rates at 5yr follow-up were significantly higher for patients classified as...
18.9 Non-Pharmacologic Treatment of Post-Stroke Depression

### Table 18.9 Electroconvulsive Therapy in the Treatment of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year Country PEDro Score</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| **Murray et al.** (1986) USA No Score TPS=NA N_{Start}=14 | **Intervention:** Medical records of 14 patients who received ECT for post-stroke depression were reviewed. **Outcomes:** Medical records. | 1. 12 patients demonstrated marked improvement in depression after ECT. 
2. A transitory cardiac arrhythmia developed in 1 patient but none of the patients had an exacerbation of stroke or a worsening of neurologic status. |
| **Currier et al.** (1992) USA No Score TPS=NA N_{Start}=20 | **Intervention:** Medical records of 20 medically ill geriatric patients who received ECT for post-stroke depression was retrospectively reviewed. **Outcomes:** Medical records. | 1. 19 of 20 patients demonstrated a marked or moderate response to ECT. Only 1 patient did not improve with ECT. 
2. 7 of the 20 patients experienced a relapse approximately 4mo following ECT. 5 patients (25%) experienced significant ECT-related complications. An additional 3 patients experienced minor ECT-related complications. 
3. No patients experienced worsening of neurological deficits and ECT therapy was not associated with development of new neurological deficits. |

### Table 18.9.2 Repetitive Transcranial Magnetic Stimulation in the Treatment of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year Country PEDro Score</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
</table>

18.9.2 Repetitive Transcranial Magnetic Stimulation
18. Post-Stroke Depression and Mood Disorders

TPS

**Jorge et al.** (2004)
USA
RCT
PEDro=7
TPS=NA
NStart=20
NEnd=20

**Intervention:** Patients with stroke and Diagnostic and Statistical Manual of Mental Disorders diagnosis of depression were randomised to receive either active left prefrontal repetitive Transcranial Magnetic Stimulation (rTMS) or sham stimulation to duplicate the appearance/sensation of treatment. Patients had failed to respond to >2 trials of antidepressants. Treatments consisted of 10 sessions of active or sham stimulation over a 2wk period. Final assessment was performed 1wk following the last treatment. Cognitive and neuropsychological assessments were conducted to monitor for possible adverse effects.

**Outcomes:** Hamilton Depression Rating Scale (HAMD); Mini-Mental State Examination (MMSE); National Institute of Health Stroke Scale.

1. Active rTMS treatment was associated with a significant reduction in depressive symptomatology on the HAMD (p<0.0006).
2. MMSE scores in the active treatment group increased by a mean 1.5 points, though this was not significantly different from the sham treatment group.
3. There were no significant neuropsychological differences between the sham and active treatment groups demonstrated.
4. All adverse events registered during the course of treatment were mild and included mild headache (six patients), local discomfort at the stimulation site due to cap tightness (five patients) and exacerbation of insomnia (one patient).

**Kim et al.** (2010)
Korea
RCT
PEDro=8
TPS=NA
NStart=18
NEnd=18

**Intervention:** Individuals with stroke were randomly assigned to one of three treatment groups; low-frequency (1 Hz), high-frequency (10Hz) or sham (control) repetitive Transcranial Magnetic Stimulation (rTMS) to the left dorsolateral prefrontal cortex. Patients received 10 treatment sessions; 5/wk over a 2wk period. During the study period, all participants also received conventional cognitive rehabilitation 2/ or 3/week. Assessment was conducted at baseline and immediately following end of treatment (2wk).

**Outcomes:** Computerized Neuropsychological Test (digit span, visual span, verbal learning, visual learning, visual continuous performance, auditory continuous performance and word-colour tests); Tower of London Test (TLT); modified Barthel Index; Beck Depression Inventory (BDI).

1. Treatment at either frequency was not associated with any significant difference on any cognitive assessment including TLT reaction time when compared to the control group.
2. However, treatment was associated with lower scores on the BDI.

### 18.9.3 Cognitive Behavioural Therapy

**Table 18.9.3 Cognitive Behavioural Therapy in the Treatment of Post-Stroke Depression**

<table>
<thead>
<tr>
<th>Author, Year Country PEDro Score</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lincoln et al.</strong> (1997) UK No Score</td>
<td><strong>TPS</strong>=NA NStart=19</td>
<td><strong>TPS</strong>=NA NEnd=19</td>
</tr>
</tbody>
</table>

**Intervention:** 19 stroke patients who had scored >13 on the Beck Depression Inventory (BDI) or >10 on the Hospital Anxiety and Depression Scale partook in an AB single case design where they received cognitive behaviour therapy administered by a community. Four patients showed benefits from the treatment, six showed some benefits and nine showed no benefits during the treatment period.

[www.ebrsr.com](http://www.ebrsr.com)
psychiatric nurse or by an assistant psychologist during the treatment period.  

**Outcomes:** BDI.

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Outcomes</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lincoln et al. (2003)</td>
<td>Stroke patients admitted to hospital with &gt;10 score on Beck Depression Inventory (BDI) or &gt;18 on Wakefield Depression Inventory (WDI) were randomly assigned to receive cognitive behaviour psychotherapy (10, 1hr sessions over 3mo) (n=39), standard care (n=41) or “attention placebo” (n=41; patients offered 10 visits over 3mo, but no formal therapy). Assessments were completed at 3 and 6mo.</td>
<td><strong>BDI; WDI; Extended Activities of Daily Living; London Handicap Scale; satisfaction with care.</strong></td>
<td>2. For the group as a whole, there was a significant decrease (p=0.02) in depression during the treatment period on the BDI.</td>
</tr>
</tbody>
</table>
| Chang et al. (2011)            | Individuals with hemiplegic stroke were randomly assigned to receive either conventional care (prescribed medications + rehabilitation training) (control group, CG) or conventional care in addition to counselling (experimental group, EG). Counselling/behaviour therapy was provided 1/wk in sessions 1-2hr in length for 1mo and included belief change and forgiveness and anger management training. Education was also provided re: lifestyle risks and lifestyle changes to reduce risk for subsequent stroke. Assessments were conducted before and after the intervention. | **Hamilton Depression Rating Scale (Chinese Versions); Hamilton Anxiety Scale; Stroke specific Quality of Life scale; Barthel Index; State-Trait Anger Expression Inventory.** | 1. No significant differences were reported on any measure.  
2. Individuals assigned to the intervention group demonstrated significant improvements in state-anger, hostility, anger-out, anger control, anxiety, depression, quality of life (QOL) and functional ability over time (p<0.001 for all).  
3. When effect sizes for change were compared between groups, the authors reported that the EG demonstrated significantly greater improvement than the CG in terms of state anger, anger control, depression, QOL and functional ability.  
4. On analysis of variance, there were significant group X time interactions identified for state anger (F=24.57, p<0.001), anger-out (F=24.87, p<0.001), anger control (F=21.24, p<0.001), depressive symptoms (F=27.64, p<0.001), QOL (F=41.96, p<0.001) and functional ability (F=24.2, p<0.001). |
| Johansson et al. (2012)        | Individuals with mental fatigue for at least 1yr were included. Participants were randomized to a mindfulness based stress reduction training group (experimental group, EG) or a control waitlist group (control group, CG). Individuals in the EG received eight weekly 2.5hr sessions with guided instructions and CDs for home practice. Outcomes were assessed at baseline and post intervention. | **Mental fatigue (MFS); Comprehensive Psychopathological Rating scale.** | 1. Significant improvement in the MFS outcomes were seen at 8wk between the EG compared to the CG (p=0.008).  
2. Furthermore, a significant decrease in depression and anxiety symptoms were seen based on time in individuals receiving treatment (p<0.002). |
| Thomas et al. (2013)           | Aphasic stroke patients with low mood based on the Stroke Aphasic Depression Questionnaire (SADQ) were randomly allocated to behavioural therapy or usual care group. Patients in the treatment group received 20 sessions of treatment over 3mo with focus | **After controlling for baseline factors and communication impairments, a significant improvement in the SADQ and VAS self-esteem scale was seen (p<0.05).**  
2. These results remained significant for up to 6mo post-intervention. |
on mood elevating activities such as activity scheduling and education. Outcomes were assessed at 3 and 6mo. **Outcomes**: SADQ; Visual Analogue Self Esteem Scale (VAS Self Esteem); Nottingham Leisure Questionnaire (NLQ).

Humphreys et al. (2015) UK RCT PEDro=8 TPSExp=NA TPSCon=NA NStart=105 Nest=87

**Population**: Experimental Group (EG, N=51): Mean age=Unspecified; Gender: Unspecified. Control Group (CG, N=54): Mean age=Unspecified; Gender: Unspecified.

**Intervention**: EG received behavioural therapy and CG received usual care. Therapy for the EG was tailored to each patient’s individual needs and included activity monitoring, activity scheduling, and graded task assignments. The intervention was provided over 3mo with up to 20, 1hr behavioural therapy sessions. Assessments were conducted at baseline, and at 3mo and 6mo follow-ups.

**Outcomes**: Stroke Aphasic Depression Questionnaire 21-item Hospital Version (SADQH-21); Intervention costs.

1. SADQH-21 scores did not differ significantly between the EG and CG at baseline (p=0.723), 3mo (p=0.737) and 6mo (p=1.000).
2. SADQH-21 scores changed significantly with a decrease in the EG (mean change=6) to a mean of 20.4 and an increase in the CG (mean change=0.7) to a mean of 17.3 from baseline to 6mo follow-up (p=0.003).
3. The total cost of the intervention per patient was £1961.
4. The difference in the cost of the intervention per patient at 3mo follow-up was significantly higher in the EG compared to the CG (p<0.001), however, prior to accounting for the £1961 intervention cost, the EG saved £139.24 compared to £11.59 in the CG.
5. Intervention cost according to 24mo projection would be cheaper for the EG compared to the CG (£1,388.90 vs £1,541.70) but this was not statistically significant (p=0.26).

Hoffmann et al. (2015) Australia RCT PEDro=6 TPSMean=NA NStart=36 Nest=33

**Population**: Coping Skills (CS, n=11): Mean age=63.6±13.0yr; Gender: Male=7, Female=4. Self-Management (SM, n=12): Mean age=60.8±11.7yr; Gender: Male=9, Female=3. Usual Care (UC, n=10): Mean age=57.0±14.2yr; Gender: Male=6, Female=4.

**Intervention**: Patients were randomized to receive CS, SM or usual care interventions for eight 1hr sessions. CS consisted of performing cognitive and behavioural exercises with the goal of restructuring cognitions, and improving self-monitoring and coping skills. SM taught problem-solving skills, the ability to communicate with healthcare professionals and how to adjust to life post-stroke in addition to addressing individualized concerns. UC comprised of multidisciplinary assessment and treatment in addition to basic education and advice.

**Outcomes**: Stroke Knowledge Questionnaire (SKQ); Hospital Anxiety and Depression Scale (HADS); Modified Barthel Index (MBI); Montgomery and Asberg Depression Rating Scale (MADRS); Self-efficacy questionnaire; Nottingham Extended Activities of Daily Living scale (NEADL); Stroke and Aphasia Quality of Life Scale (SAQoL: Psychosocial, Physical, Communication).

1. Depressive symptoms according to HADS were significantly more prevalent in the CS group compared to the UC group at post-treatment (mean UC=6.4±0.5, CS=7.9±0.5) (p=0.034).
2. SKQ scores post-treatment were significantly greater in the CS group compared to the UC group (mean UC=19.9±0.4, CS=21.2±0.4) (p=0.036).
3. MBI scores at post-treatment did not differ significantly in the SM group compared to the UC group (mean UC=69.2±2.6, SM=75.4±2.5) (p=0.099).
4. MADRS, NEADL, and SAQoL scores did not differ significantly between the CS and UC group, and the SM and UC group at post-treatment.
5. No significant differences were observed between the CS and UC groups and the SM and UC groups at 3-5mo follow-up.
### 18.9.3.1 Combined Therapy

#### Table 18.9.3.1 Combined Therapy in the Treatment of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year Country PEDro Score TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sondergaard et al. [2006]</strong> Denmark RCT PEDro=6 TPS=NA NStart=73 NEnd=53</td>
<td><strong>Population</strong>: High intensity group (N=34): Mean age=74.9±8.2yr; Gender: Males=16, Females=18. Low intensity group (N=29): Mean age=74.9±9.5yr; Gender: Males=3, Females=26. <strong>Intervention</strong>: Participants were randomized to receive either high-light intensity therapy plus Citalopram, or to receive medium-light intensity plus Citalopram. The intervention period lasted 6wk. Assessments were conducted post intervention. <strong>Outcomes</strong>: Hamilton Depression Scale-6 items (HAM-D6); Hamilton Depression Scale-17 items; Bech-Rafaelsen Melancholia Scale (MES).</td>
<td>1. After 2wks of treatment, no statistically significant differences between the two groups were found regarding any of the measures. 2. After 4wks of treatment, significant differences between groups were seen on the HAM-D6 (p&lt;0.05).</td>
</tr>
<tr>
<td><strong>Mitchell et al. [2009]</strong> USA RCT PEDro=7 TPS&lt;4mo NStart=101 NEnd=101</td>
<td><strong>Intervention</strong>: Individuals with stroke (within the past 4mo) and diagnosed with clinical depression were randomly assigned to receive either a brief psychosocial, problem-solving intervention + possible antidepressant medication (experimental group, (EG) or usual care + possible antidepressant medication (control group, CG). The psychosocial intervention consisted of 9 sessions over 8wk of problem-solving therapy and increased pleasant social and physical activity provided by a study interventionist. Usual care were treated by their primary care physician. Patients in both groups could be prescribed antidepressant medication as deemed appropriate. In the treatment condition, sertraline was the recommended first choice of possible medications. Medication use was tracked using a medication diary. Outcomes were assessed at 9wk, 21wk, 12mo and 24mo. <strong>Outcomes</strong>: Hamilton Depression Rating Scale (HAMD); Stroke Impact Scale; Barthel Index (BI).</td>
<td>1. At baseline, 60% of patients in each group were receiving antidepressant therapy. This rose to 77% in both groups at 8wk. Type of drug and dose were not standardized. 2. There were significantly greater reductions in HAMD scores in the EG than in the CG at 9wk (p&lt;0.001) and at 12mo (p=0.023), though not at 6wk or 24mo. 3. The percentage of patients in remission from depression (HAMD≤9) was larger in the EG vs. the CG at 9wk (p&lt;0.001) and at 12mo (p=0.023), though not at 6wk or 24mo. 4. Remission from depression was associated with better physical function (strength p&lt;0.001, mobility p&lt;0.001, and activities of daily living p=0.004) and improved social participation (communication p=0.005, work and recreation p&lt;0.001) at 12mo. BI scores demonstrated a trend toward improved recovery associated with depression remission (p=0.09).</td>
</tr>
<tr>
<td><strong>Cao et al. [2013]</strong> China RCT PEDro=6 TPSExp=2-6mo TPSCon=2-6mo NStart=60 NEnd=60</td>
<td><strong>Population</strong>: Experimental Group (EG, N=30): Mean age=57±13yr; Gender: Male=11, Female=19. Control Group (CG, N=30): Mean age=56±17yr; Gender: Male=12, Female=18. <strong>Intervention</strong>: EG received hyperbaric oxygen therapy (HBOT) 45min/d with 2.5-5mg of Dexamethasone administered prior to each HBOT session. The CG received two doses of Deanxit (0.5mg depixol and</td>
<td>1. HAMD scores were significantly lower for the EG compared to the CG at post-treatment (p&lt;0.05). 2. HAMD scores improved significantly within both the EG and CG (both p&lt;0.01) from baseline to post-treatment. 3. HAMD score reduction rates were 83.3% and 60.0% for the EG and CG respectively</td>
</tr>
</tbody>
</table>
10mg Melitracen), 2/d with a reduction to 1/d if improvement was noted. The interventions for both groups were provided for 4wk with EG receiving 10 HBOT treatment sessions. Assessments were conducted at baseline and at post-treatment. **Outcomes:** Hamilton Depression Scale (HAMD); National Institutes of Health Stroke Scale (NIHSS).

4. NIHSS scores were significantly lower for the EG compared to the CG at post-treatment (p<0.05).
5. NIHSS scores improved significantly within both the EG and CG (both p<0.01) from baseline to post-treatment.

**Population:** Experimental Group 1 (EG1, N=30): Mean age=65±7.9yr; Gender: Male=17, Female=13. Experimental Group 2 (EG2, N=30): Mean age=63±8.1yr; Gender: Male=16, Female=14. Experimental Group 3 (EG3, N=30): Mean age=66±5.9yr; Gender: Male=18, Female=12.

**Intervention:** EG1 were administered 20mg of Fluoxetine 1/d, EG2 received hyperbaric oxygen therapy 1/d for 45min and EG3 received both hyperbaric oxygen therapy (HBOT) and Fluoxetine using the same protocols as described above. The interventions were all provided for a total of 4wk. Assessments were conducted at baseline and at post-treatment.

**Outcomes:** Hamilton Depression Rating Scale (HAMD); Scandinavian Stroke Scale (SSS).

1. HAMD scores for EG3 were significantly lower than both EG1 and EG2 (p<0.05) at post-treatment.
2. HAMD score reduction rates for EG1, EG2 and EG3 were 70%, 76.7% and 90% respectively, indicating that EG3 exhibited significantly greater success rates of patients being cured or making progress with depressive symptoms compared to EG1 and EG2 (p<0.05).
3. HAMD scores improved significantly within all three groups (all p<0.05).
4. SSS scores did not differ significantly between groups at post-treatment (all p>0.05).
5. SSS scores improved significantly within all three groups (all p<0.05).

### 18.9.4 Music Therapy

**Table 18.9.4 Music Therapy in the Treatment of Post-Stroke Depression**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purdie et al. (1997)</strong></td>
<td>Scotland</td>
<td>No Score</td>
<td>TPS=NA</td>
<td>Intervention: In this quasi-randomised trial, Patients received either 12 sessions of music therapy 1/wk (experimental group, EG) or standard care (no music therapy) (control group, CG). Assessments were administered at baseline, 6wk and 12wk. <strong>Outcomes:</strong> Hamilton Depression Rating Scale (HAMD); Functional Assessment Staging; behaviour rating scales.</td>
<td>1. Only 15 participants completed all assessments. 2. Both the CG and EG demonstrated a decline in depression over the study period. However, the EG demonstrated a greater decline than the CG (-1.65 ±1.59 vs. -1.57 ±1.59).</td>
</tr>
<tr>
<td><strong>Nayak et al. (2000)</strong></td>
<td>USA</td>
<td>No Score</td>
<td>TPS=NA</td>
<td>Intervention: Patients with traumatic brain injury or stroke were assigned to receive music therapy 2-3/wk (experimental group, EG) for the duration of their stay in the hospital and received a maximum of 10 treatment sessions in addition to their standard therapy or to receive standard therapies that are part of inpatient rehabilitation regimen only. Patients rated</td>
<td>1. Significant difference between groups on social interaction scale was noted in favour of the EG. 2. Staff rated participants’ social interaction in music as more actively involved in therapy and were more motivated to participate.</td>
</tr>
</tbody>
</table>
their own mood on the Faces Scale (McDonnell & Newell, 1996). Family and therapists rated patients’ mood on a 7-point visual analogue scale (7-VAS) with “not depressed at all” on one end and “very depressed” on the other end. Higher scores indicated more depression.

**Outcomes:** Faces Scale; 7-VAS.

**Sarkamo et al. (2008) Finland**
RCT
PEDro=6
TPS=NA
N_start=60
N_end=55

**Intervention:** Patients with middle cerebral artery stroke were randomly allocated to music listening (ML), language listening (LL) or control groups (CG) as soon as possible following discharge from acute care. Patients in the ML and LL groups both received portable CD players and CD’s of either music or narrated audio books as appropriate and independently listened for a minimum of 1 hr/d for a period of 2mo. Patients assigned to the CG received no listening material. 54 patients completed the trial (music = 18, language = 19, control = 17). Follow-up assessments were performed at 3mo and 6 mo post stroke.

**Outcomes:** Neuropsychological assessments; Profile of Mood States (POM); Health Related Quality of Life Assessment.

1. Although not statistically significant, self-report, family and therapists’ rating of patients’ mood improved.

2. At baseline, there were no significant differences between groups on cognitive or mood assessments. However, at 3mo there were significant between group differences on the depression subscale of the POM, such that depression scores were significantly lower in the ML group (p=0.024).

3. At the 6mo assessment, the ML group still demonstrated a significant trend toward lower depression scores (p=0.071).

**Kim et al. (2011) Korea**
No Score
TPS<6mo
N_start=18
N_end=18

**Intervention:** Patients (with Mini-Mental State Examination scores >20) within 6mo of stroke onset received either regular rehabilitation treatment (RRT) (physiotherapy (PT), occupational therapy (OT), SLP + psychotherapy) or regular rehabilitation treatment plus music therapy (MT). MT sessions were 40min/session. A total of eight sessions were provided (2/wk over 4 wk). Assessments were administered pre- and post-intervention for both groups.

**Outcomes:** Beck Depression Inventory (BDI); Beck Anxiety Inventory (BAI).

1. Over the course of the intervention BDI scores improved significantly in the MT group (p=0.048), but not in the RRT group.

2. The authors do not report between group comparisons.

3. There were no significant changes reported for scores on the BAI in either group.

4. 77.8% of patients and 66.7% of caregivers reported that they perceived MT to be associated with a positive psychological change.

**Jun et al. (2013) Korea**
RCT
PEDro=4
TPS=Overall≤2wk
N_start=40
N_end=30

**Population:** Experimental Group (EG, N=15): Mean age=60.70±8.59yr; Gender: Males=6, Females=9. Control group (CG, N=15): Mean age=55.10±17.23yr; Gender: Males=9, Females=6.

**Intervention:** Patients were randomized either to the EG where they received music-movement therapy in their wheelchairs, or to the CG who received routine treatment. The intervention was provided 3/wk for 8wk with each session lasting 60min. Assessments were conducted at baseline and post-treatment.

**Outcomes:** Centre for Epidemiologic Studies Depression Scale (CES-D); Range of Motion (ROM); Medical Research Council Scale (muscle strength); Korean-modified Barthel Index (K-MBI).

1. The change in mood state was significantly different between the two groups (EG Δ=9.46; CG Δ=2.08; p=0.04) however, the change in CES-D scores was not significantly different between the two groups (p=0.280).

2. The mean difference between baseline and post-treatment was significantly different between the EG and the CG regarding the ROM during shoulder flexion (EG Δ=9.33±12.79; CG Δ=0.66±15.79; p=0.03) and during elbow joint flexion (EG Δ=9.33±14.37; CG Δ=1.00±10.38; p=0.04), but not during hip joint flexion.

3. The change in muscle strength was not significantly different between the two groups for either the upper arm muscle...
strength or the lower leg muscle strength (p=0.360; p=0.150).
4. The change in K-MBI activities of daily living were not significantly different between the two groups (p=0.799).

### 18.9.5 Speech Therapy

#### Table 18.9.5 Speech Therapy and Emotional Outcomes in Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lincoln et al.</strong> (1985)</td>
<td>UK</td>
<td>RCT PEDro=5</td>
<td>TPS=10wk</td>
<td>NStart=168 NEnd=149</td>
</tr>
<tr>
<td><strong>Hoen et al.</strong> (1997)</td>
<td>Canada</td>
<td>No Score</td>
<td>TPS=NA</td>
<td>NStart=47</td>
</tr>
<tr>
<td><strong>Konecny et al.</strong> (2014)</td>
<td>Czech Republic</td>
<td>RCT</td>
<td>PEDro=4</td>
<td>TPSExp=2d TPSCon=2d NStart=99 NEnd=99</td>
</tr>
</tbody>
</table>

**Intervention:** At 10wk post-stroke, patients were randomized to receive either two 1hr sessions/wk of speech therapy for 24wk or to receive no speech therapy. All other rehabilitation carried out as usual.

**Outcomes:** Multiple Adjective Checklist (Depression, Anxiety and Hostility) (MAACL).

1. No significant differences were found between treatment and control patients on MAACL scores on anxiety, depression and hostility.

**Intervention:** Evaluation of the York-Durham Aphasia Centre’s community-based programme. Psychological well-being of 35 patients and 12 family members was evaluated.

**Outcome:** Ryff Psychological Well-Being Scale.

1. Patients showed significant positive change on five of six measures of well-being: self-acceptance, purpose of life, personal growth, autonomy, and environmental mastery.

**Population:** Experimental Group (EG, N=50): Mean age=Unspecified; Gender: Male=26, Female=24. Control Group (CG, N=49): Mean age=Unspecified; Gender: Male=27, Female=22.

**Intervention:** The EG received orofacial therapy to relax spasticity, restore orofacial functions, eating functions, communication mimicry, and facial mimicry in addition to speech therapy and physical rehabilitation. The CG received speech therapy and physical rehabilitation only. The intervention was provided 1/d over a 4wk period, speech therapy was provided 1/d and physical rehabilitation provided 2/d. Assessments were conducted at baseline and at post-treatment.

**Outcomes:** House-Brackmann Grading System (HBGS); Beck Depression Inventory (BDI); Barthel Index (BI); Modified Rankin Scale (mRS).

1. BDI improved significantly for the EG from baseline to post-treatment (p<0.001) but no significant change was noted for the CG.
2. HBGS improved within both groups but a statistically significant improvement in mimicry was found for the EG (p<0.001) at post-treatment.
3. BI improved significantly within the EG from baseline to post-treatment (p<0.001) but no significant change was noted for the CG.
4. mRS improved significantly within the EG from baseline to post-treatment (p<0.001) but no significant change was noted for the CG.
5. HBGS and BDI scores were positively and significantly correlated (p<0.001).

### 18.9.6 Physical Activity

#### Table 18.9.6 Impact of Physical Activity on Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
</table>

18. Post-Stroke Depression and Mood Disorders  
[www.ebrsr.com](http://www.ebrsr.com)
| **PEDro Score** | **TPS** | **Intervention**: Patients with stroke were randomized to receive a structured, progressive, physiologically based exercise program (experimental group, EG) or usual care (control group, CG) in a single blinded RCT. The program consisted of 36, 90min sessions over 12wk targeting flexibility, strength, balance, endurance and upper-extremity function. Assessments were conducted at baseline, 3mo and 9mo after enrollment. **Outcomes**: Geriatric Depression Scale (GDS); Stroke Impact Scale (SIS); Medical Outcomes Study 36-Item Short Form Questionnaire (SF-36). | **1.** At baseline, 18% vs. 22% of participants in the EG vs. CG had GDS scores ≥6 (presence of significant depressive symptoms).  
**2.** GDS scores and rates of significant symptomatology were significantly lower in the EG vs. the CG immediately following the intervention (0.01 < p < 0.05).  
**3.** At 9mo, GDS scores were still significantly lower in the EG (p < 0.05).  
**4.** Individuals in the EG also demonstrated higher SIS scores and higher SF-36 emotional subscale scores.  
**5.** Use of antidepressant medication was comparable in both groups.  
**6.** Overall gains in impairments and functional limitations were greater in the EG vs. CG and did not appear to be limited by the presence of depressive symptomatology. |
|---|---|---|
| Lai *et al.* (2006) secondary analysis of Duncan *et al.* 2003 USA RCT PEDro=8 TPS=NA N_{Start}=100 N_{End}=80 | **Intervention**: Ambulatory stroke patients who had completed inpatient rehabilitation were randomized to receive a 12wk outpatient program of strength and resistance exercise (n=32) or relaxation (n=34). Treatments were provided for 1.5 hr, 3/wk. Outcomes were assessed at 3 and 7mos. **Outcomes**: Functional Independence Measure; Nottingham Extended Activities of Daily Living; Rivermead Mobility Index; functional reach; sit-to-stand; elderly mobility score; timed up-and-go; Medical Outcomes Study 36-Item Short Form Questionnaire, version 2 (SF-36); Hospital Anxiety and Depression Scale; aspects of physical fitness (comfortable walking speed, walking economy, and explosive leg extensor power). | **1.** At 3mos, the role-physical component of the SF-36, timed up-and-go and walking economy were significantly better among patients in the exercise group compared with the relaxation group.  
**2.** By 7mos, the only difference that remained between groups was the role physical component of the SF-36.  
**3.** At 3 and 7mos, assessment of depression identified no significant within-group change over time (ES=0.008, 0.001, respectively) and no significant between group differences (p=0.56, 0.82, respectively). |
| Mead *et al.* (2007) UK RCT PEDro=8 TPS>12wk N_{Start}=66 N_{End}=62 | **Intervention**: Individuals with stroke, living within the community, were assigned randomly to receive either regular physiotherapy and occupational therapy services in addition to a cardiac rehabilitation program (experimental group, EG) or just the regular therapy services alone (control group, CG). If assigned to the CRP, participants attended 30min cycle ergometry (aerobic training) exercise sessions for either the upper or lower limbs 2/wk for 10wk. In addition, they were provided with two life skills classes. Assessments were conducted at baseline and after 10wks. **Outcomes**: Battery of physical performance measures; Frenchay Activities Index; Hospital Anxiety and Depression Scale (HADS). | **1.** Pre- and post-assessment HADS scores improved significantly over time within the EG (p<0.001), but not in the CG.  
**2.** However, when the difference in change of HADS scores between groups was examined, there was no significant difference (p=0.22). |
<table>
<thead>
<tr>
<th>Study Authors</th>
<th>Country</th>
<th>Study Design</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>N Start</th>
<th>N End</th>
<th>Intervention</th>
<th>Outcomes</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Macko et al. (2008)           | Italy   | No Score     | NA          | NA  | 20      | 20    | Intervention: Patients with chronic hemiparesis following stroke were enrolled in a 2mo group exercise program focused on mobility, balance and stretching exercises consisting of 1hr sessions 2/wk. A home regimen of walking, stair climbing and stretching was also provided. Evaluations were conducted at baseline, 1mo and 2mo after starting the program.  | Outcomes: Motricity Index (MI); Short Physical Performance Battery (SPPB); 6-minute walk test (6-MWT); Berg Balance Scale (BBS); Barthel Index (BI); Stroke Impact Scale (SIS); Geriatric Depression Scale (GDS). | 1. 79% of individuals had scores >6 on the GDS at baseline.  
2. There was significant improvement in depression (p=0.01) over time, although the mood score of the SIS did not show similar improvement (p=0.33).  
3. The proportion of individuals with GDS>6 did not change significantly over time (15/19 vs. 12/19, p=0.2).  
4. Scores on the MI (upper and lower limb), 6-MWT, BBS, SPPB and BI all demonstrated significant improvements over time. |
| Smith and Thompson (2008)     | USA     | PCT          | NA          | NA  | 20      | 20    | Intervention: Participants with previous ischemic stroke (at least 3mos prior to baseline) were enrolled in a matched pair controlled trial to examine the effectiveness of a 12-session treadmill training intervention on depression. 20 individuals were assigned to the intervention condition (experimental group, EG) and 20 to the control group (CG). EG received 12 sessions of treadmill training over a 4wk period (20 min/session). The CG received weekly phone calls and were encouraged to record life events in a personal log. Assessments were conducted at baseline, 4wks (after the intervention) and at 6wks (follow-up).  | Outcomes: Beck Depression Inventory (BDI); Stroke Impact Scale. | 1. Within groups analysis demonstrated a significant reduction of symptoms of depression reported on the BDI in the EG over time (p<0.05) – both by the end of intervention and at the end of follow-up.  
2. There was no significant difference in BDI score over time reported within the CG. In addition, there was a significant group X time interaction reported (F=2.61, p<0.01). |
| Brittle et al. (2009)          | UK      | RCT          | 5           | NA  | 56      | 56    | Intervention: Residents in five long-term care homes received either group exercise (experimental group, EG) or usual care (control group, CG). Randomization was by facility. Group exercise training focused on flexibility, sitting balance, posture, coordination, strengthening and cardiovascular fitness. Sessions were 40min to 60min, 2/wk for 5wks. The usual care group received no exercise training or regular physiotherapy. Assessments were conducted at baseline, 3mos (after the intervention) and 6mos (follow-up).  | Outcomes: Rivermead Mobility Index; Hospital Anxiety and Depression Scale; Stroke Aphasic Depression Questionnaire. | 1. Approximately one-quarter of all participants had a history of at least one stroke (21% and 25% of individuals in the CG and EG, respectively).  
2. There were no significant improvements reported, for any of the outcomes assessed, in favour of the exercise intervention.  
3. Individuals with severe cognitive impairments had difficulty participating in the program and some were disruptive. |
| Sims et al. (2009)             | Australia | RCT         | 7           | NA  | 45      | 43    | Intervention: Patients >6mo post-stroke and diagnosed with post-stroke depression were randomly assigned to either progressive resistance training (experimental group, EG) 2/wk for 10wks or to a waiting list (control group, CG) condition. Sessions were provided in small groups within a community setting. Outcomes were assessed at 10wks (end of treatment) and 6mos by mailed self-report questionnaires.  |  | 1. At baseline, individuals in the CG had more severe depression as assessed on the CES-D (p=0.003).  
2. At 10wks and at 6mos, individuals assigned to the EG had fewer symptoms of depression (p=0.08 and p=0.004, respectively); however, these between |
Outcomes: Center for Epidemiologic Studies Depression Scale (CES-D).

Group differences were non-significant when controlling for baseline depression.

3. Approximately 50% of patients in each group experienced a clinically significant (>5 pts on the CES-D) reduction in depressive symptoms, and at 6mos, this reduction was maintained in 30% of individuals in the EG vs. 15% in the CG. This difference was not statistically significant.

Stuart et al. (2009)
Italy
No Score
TPS=NA
NStart=78

Intervention: Individuals with stroke made up the experimental group (EG), participating in the Adaptive Physical Activity (APA) program. 38 individuals, from neighbouring communities, served as a control group (CG) and did not participate in the program. The APA program provides walking, strength and balance exercises in a group/class setting and is specifically designed for individuals who have experienced stroke. The exercises increase in duration and intensity over the course of the 3mo program. Assessments were conducted at baseline and 6mos.

Outcomes: Mini-Mental State Examinaton; Hamilton Depression Rating Scale; Motricity Index; 6-minute walk test; Berg Balance Scale; Barthel Index; Stroke Impact Scale.

1. In a within-groups analysis (including only those individuals with symptoms of depression at baseline), there was a significant improvement in symptoms of depression demonstrated in the EG (p<0.01) over time, but not in the CG (p=0.88).

2. The APA intervention was associated with significantly greater improvement in depression when compared to the control condition (p<0.003).

Harrington et al. (2010)
UK
RCT
PEDro=7
TPS=NA
NStart=243
NEnd=243

Intervention: Individuals with stroke were randomly assigned to receive either standard care (control group, CG) or a peer-volunteer-facilitated exercise and education intervention (experimental group, EG). Intervention sessions were conducted 2/wk for 8wks. Each session consisted of 1hr exercise (with qualified instructors) followed by a short break and 1hr of interactive education. Control participants received standard care + an information sheet about local groups. Study outcomes were assessed at baseline, 9wks and 6mos.

Outcomes: Subjective Index of Physical and Social Outcome; Frenchay Activities Index; Rivermead Mobility Index; social care and personal costs; Hospital Anxiety and Depression Scale; World Health Organization Quality of Life-BREF (WHOQoL-BREF).

1. Although there was a significantly greater improvement in the psychological domain of the WHOQoL-Bref at 6mos in the EG vs. CG (p=0.01), there were no significant between group differences at 9wks, 6mos or 1yr for any of the secondary outcomes assessed, including depression.

Van de Port et al. (2012)
Netherlands
RCT
PEDro=8
TPS=NA
NStart=126
NEnd=126

Intervention: A multi-centered study in which individuals with stroke discharged home from inpatient rehabilitation (and able to walk 10m unassisted) were randomly assigned to participate in either a group-based, task-oriented circuit training program (experimental group, EG) (n=126) or usual care (control group, CG) (n=124). The circuit training program was 90min in length (warm-up, circuit training, evaluation, short break and group game) and offered 2/wk for 24wks. Usual care

1. Individuals in the EG received a mean of 72min (±39min) per session compared with 34min (±10min) in the CG (p<0.05).

2. There was no significant group X time interaction for the mood and emotions domain of the SIS from baseline to 12wks assessment (p=0.41) or from 12 to 24wks assessment points (p=0.41).
consisted of one-to-one physiotherapy treatments over the same period of time. All outcomes were assessed by blinded observers lasting 24wks. Secondary outcomes were performed at baseline, 12wk and 24wk.

**Outcomes:** Stroke Impact Scale (SIS); Rivermead Mobility Index; falls efficacy; Nottingham Extended Activities of Daily Living Scale; Hospital Anxiety and Depression Scale (HADS); fatigue severity.

**Batcho et al. (2013)**
Belgium
Pre-Post TPS
Mean=37.7mo NStart=44 NEnd=34

**Population:** Mean age=58.0±11.0yr; Gender: Males=24, Females=10.

**Intervention:** Participants followed an intervention consisting of a 3/wk group-based brisk walking programme for 3mos. Assessments consisted of three periods: pre-intervention period of 1mo (two baselines measures), an intervention period of 3mos (baseline to post-treatment), and a follow-up period of 3mos (post-treatment to follow-up).

**Outcomes:** Hospital Anxiety and Depression Scale (HADS); 6-Minute Walk Test (6MWT); Berg Balance Scale (BBS); ACTIVLIM-Stroke Questionnaires; Stroke Impairment Assessment Set (SIAS).

1. No significant change in the HADS score was found during the intervention period (p=0.058).
2. No significant change in scores were found for any of the outcome measures during the pre-intervention period.
3. A significant improvement in the ACTIVLIM-Stroke questionnaire (p=0.008), 6MWT (p<0.001), SIAS (p<0.001), and on the BBS (p=0.001) from baseline to post-treatment was found.
4. Only the SIAS (p=0.002), and the BBS (p=0.001) scores were maintained from post-treatment to follow-up.

**Taylor-Piliae et al. (2013)**
USA
Case Series
No Score
TPS Mean=39.4±48.9mo NStart=100 NEnd=100

**Population:** Mean age=70±1yr; Gender: Males=54, Female=46.

**Intervention:** Baseline data collected between 2009 and 2011 from stroke patients enrolled in a randomized clinical trial (the “Tai Chi for Stroke Survivors Study”) was analyzed. Patients completed a set of questionnaires at a mean of 3.3yr (39.4mos) post-stroke.

**Outcomes:** Centre for Epidemiological Studies-Depression scale (CES-D); Medical Outcomes Study Short Form-36 Questionnaire (SF-36); Pittsburgh Sleep Quality Index (PSQI); Multidimensional Scale of Perceived Social Support (MSPSS); Mini-Mental State Examination (MMSE); Modified Rankin Scale (mRS).

1. The prevalence of depressive symptoms according to CES-D scores among patients was 35%.
2. Depressive symptoms were significantly associated with quality of life (SF-36), sleep quality (PSQI), social support (MSPSS), and history of depression (all p≤0.05).
3. Approximately 64% of the variance in depressive symptoms could be explained by the 12 independent variables: quality of life (SF-36 Physical and Mental Health subscores), sleep quality (PSQI), social support (MSPSS), cognitive function (MMSE), functional disability (mRS), time since stroke, age, gender, history of major depression, and lesion location.
4. Depressive symptoms decrease by 0.6 points with each point increased in the quality of life (mental health), accounting for 20% of the variance (p<0.01).
5. Social support was significant (p=0.04), indicating that depressive symptoms decrease by 1.53 points on average with each point increased in social support, accounting for 1.9% of the variance (p=0.04).

**Immink et al. (2014)**
Australia
RCT

**Population:** Experimental Group (EG, N=12): Mean age=56.1±13.6yr; Gender: Male=6, Female=5.

1. GDS scores decreased for both groups but no significant differences or improvements were found.
Control Group (CG, N=13): Mean age=63.2±17.4yr; Gender: Male=3, Female=8.

**Intervention**: The EG group received yoga classes and the CG were assigned to a waiting list. The intervention was provided for 90min/d, 1d/wk over a course of 10wks with patients also asked to complete additional home practice sessions 6d/wk with each home session lasting 35-45mins. Assessments were conducted at baseline and post-treatment.

**Outcomes**: Geriatric Depression Scale (GDS); Stroke Impact Scale (SIS: Physical, Memory); State Trait Anxiety Inventory-Form Y (STAI-Y: State Anxiety, Trait Anxiety).

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**Baek et al. (2014)**

**Korea**

**PCT**

No Score

TPS<sub>Exp</sub>=8.4±1.9mo

TPS<sub>Cont</sub>=7.9±2.6mo

N<sub>Start</sub>=40

N<sub>End</sub>=40

**Population**: Experimental Group (EG, N=20): Mean age=57.2±10.8yr; Gender: Males=7, Females=13.

Control Group (CG, N=20): Mean age=58.7±9.7yr; Gender: Males=7, Females=13.

**Intervention**: The EG received gradual task-oriented circuit class training (80min/session), while the CG performed stretching exercises and weight bearing exercises (80min/session). Both groups performed the exercise 3/wk for 8wk. Levels of branched-chain amino acids and free-tryptophan levels were observed to investigate the potential effects of CCT on depression. Depression was assessed at baseline and at post-treatment.

**Outcomes**: Beck Depression Inventory II (BDI-II), Levels of branched-chain amino acids (BCAAs) and free-tryptophan (f-Trp).

---

**McDonnell et al. (2014)**

**Australia**

Cohort

No Score

TPS<sub>Exp</sub>=8.9±6.9yr

TPS<sub>Cont</sub>=NA

TPS<sub>Cont</sub>=1.6±0.7yr

N<sub>Start</sub>=40

N<sub>End</sub>=40

**Population**: Experimental Group 1 (EG1, N=17): Mean age=70±10yr; Gender: Male=12, Female=5.

Experimental Group 2 (EG2, N=13): Mean age=69±7yr; Gender: Male=4, Female=9.

Control Group (CG, N=10): Mean age=65±9yr; Gender: Male=8, Female=2.

**Intervention**: EG1 and EG2 consisted of patients and healthy adults respectively who participated in low to moderate intensity exercise classes. The CG did not participate in any exercise training. The intervention was provided 60min/d, 1d/wk for 12wks. Assessments were conducted at post-treatment.

**Outcomes**: Depression, Anxiety, Stress Scale (DASS: Depression, Stress, Anxiety); Assessment of Quality of Life Scale (AQoL).

---

**Ploughman et al. (2014)**

**Population**: Mean age=57.7±13.6yr; Gender: Male=17, Female=10.

1. No significant improvements from baseline to post-treatment were reported for the...
Intervention: All patients were enrolled into the NeuroFIT training program. The NeuroFIT program consisted of 90 min/d, 2/wk sessions for 10 wks where patients engaged in circuit training and learned how to use standard fitness equipment. The circuit training used 10 stations and focused on improving the walking balance and functional ability of patients. Assessments were conducted at baseline, post-treatment and at 4 mos follow-up.

Outcomes: Hospital Anxiety and Depression Scale (HADS); Frenchay Activities Index (FAI); Timed Up and Go Test (TUG); 6 Minute Walk Test (6MWT); Health Related Quality of Life (HRQoL); Self-reported functional improvement; Proportion of patients participating in structured exercise at follow-up.

Population: Experimental Group (EG, N=126): Mean age=71.8±10.5 yr; Gender: Males=85, Females=41. Control Group (CG, N=103): Mean age=70.1±10.7 yr; Gender: Males=62, Females=41.

Intervention: Patients with mild to moderate hemiparesis were referred to two physical medicine and rehabilitation units. The EG received 16 sessions of Adapted Physical Activity for 1 hr/d, 2/wk over 8 wks followed by three sessions of Therapeutic Patient Education with both caregivers and families. The CG received usual care. Assessments were conducted at baseline and post-treatment.

Outcomes: 6-Minute Walk Test (6MWT: Gait Endurance, Gait Velocity); Short Physical Performance Battery (SPPB); Berg Balance Scale (BBS); Motricity Index (MI); Barthel Index; Geriatric Depression Scale (GDS); Medical Outcomes Study 12-Item Short Form Questionnaire (SF-12: Physical, Mental); Caregiver Strain Index (CSI); Visual Analog Scale (VAS).

1. GDS scores differed significantly at baseline with the EG revealing significantly lower scores compared to the CG (p<0.001).
2. GDS scores for the EG improved significantly from baseline to post-treatment GDS (Δ=-0.8±1.7, p<0.001), but no significant improvement was noted for the CG (Δ=-0.3±2.0, p=0.384).
3. The level of change in GDS scores from baseline to post-treatment did not differ significantly between groups (p=0.384).
4. There was a significant improvement in the EG from baseline to post-treatment regarding the 6MWT (Gait Endurance: Δ=23.4±71.5 m, p=0.002; Gait Velocity: Δ=6.5±19.9 m/s, p=0.002), BBS (Δ=2.5±6.1, p<0.00), SPPB (Δ=1.2±2.1, p<0.001), MI (Δ=3.7±10.7, p=0.001), VAS (Δ=8.5±17.7, p<0.001), and SF-12 (Physical: Δ=4.0±8.3, p<0.001; Mental: Δ=4.8±10.0, p<0.001).
5. The CG did not exhibit any significant improvement on any of the outcome measures from baseline to post-treatment.
6. There were no significant changes in either of the groups on the CSI (EG: p=0.755; CG: p=0.394) from baseline to post-treatment.
TPS_{\text{Con}}=125.6\pm47.2\text{d}
N_{\text{Start}}=99
N_{\text{End}}=91

**Intervention:** EG was provided with a home exercise program focusing on upper extremity recovery with a robotic assistive device and the CG was provided with the home exercise program only. The interventions were to be completed 3hr/d, 5d/wk, for a total of 8wks. Assessments were conducted at baseline and at post-treatment.

**Outcomes:** Center for Epidemiological Studies-Depression Scale (CES-D); Stroke Impact Scale (SIS: Strength, Memory, Communication, activities of daily living (ADL)/instrumental activities of daily living (IADL), Mobility, Hand Function, Mood, Meaningful Activities, Stroke Recovery).

$(p=0.001$ and $p=0.17$, respectively) from baseline to post-treatment.

3. Changes in SIS scores did not differ significantly between the EG and CG on all subscale measures from baseline to post-treatment.

4. Within group analyses revealed that the EG improved significantly on the SIS; ADL/IADL, Mobility, Hand Function, Mood, Meaningful Activities, Stroke Recovery (all $p<0.001$), Strength ($p=0.001$), Mood ($p=0.002$), and Communication ($p=0.007$) from baseline to post-treatment except for the Memory subscale ($p=0.324$).

5. Within group analyses revealed that the CG improved significantly on all SIS subscales (all $p<0.05$) from baseline to post-treatment except for the Mood subscale ($p=0.324$).

**Population:**

Topcuoglu et al. (2015)
Turkey
RCT
PEDro=6
TPS_{\text{Exp}}=75.30\pm29.3\text{d}
TPS_{\text{Con}}=81.40\pm36.3\text{d}
N_{\text{Start}}=52
N_{\text{End}}=40

**Intervention:** Stroke patients with complex regional pain syndrome type I were randomly allocated either to the EG and received upper extremity aerobic exercise in addition to physiotherapy, or to the CG and received physiotherapy only. The intervention was provided 5d/week for 4wks. Assessments were conducted before and after the intervention.

**Outcomes:** Nottingham Health Profile (NHP); Beck Depression Scale (BDS).

1. The mean changes in NHP and BDS scores between groups were statistically significantly ($p<0.05$).

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**18.9.7 Ecosystem Focused Therapy**

**Table 18.9.7 Ecosystem Focused Therapy in the Treatment of Post-Stroke Depression**

<table>
<thead>
<tr>
<th>Author, Year Country PEDro Score TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alexopoulos et al.</strong> (2012) USA RCT PEDro=6 TPS=NA N_{\text{Start}}=24 N_{\text{End}}=24</td>
<td><strong>Intervention:</strong> Individuals diagnosed with post-stroke depression (via SCI for the Diagnostic and Statistical Manual of Mental Disorders) were randomly assigned to receive either ecosystem focused therapy (EFT) (experimental group, EG) or education on stroke or depression (control group, CG). EFT was provided in 12 weekly sessions of approximately 45mins in length. Inpatients had the first session prior to discharge; the remaining sessions were conducted in the participants’</td>
<td>1. Group X time analysis revealed an interaction suggesting that there was a greater decline in symptoms of depression associated with EFT vs. education ($p=0.054$). 2. The mean HAMD score at 12wks was 8.2 ($sd=6.63$) for individuals in the EG and 13.2 ($sd=5.37$) for individuals assigned to the CG. In addition, remission of depression was recorded for 8/12 participants receiving EFT</td>
</tr>
</tbody>
</table>

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homes. Outcome was assessed over the course of the 12wk intervention.  
**Outcomes:** Hamilton Depression Rating Scale (HAMD).  
(66.7%) vs. 2/12 (16.7%) participants in the CG (OR = 10, 95% CI 1.44, 69.26).

### 18.9.8 Acupuncture

#### Table 18.9.8 Acupuncture in the Treatment of Post-Stroke Depression

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wayne et al. (2005)</td>
<td></td>
<td></td>
<td><strong>Intervention:</strong> Patients with chronic stroke were randomized to receive an average of 17 real (experimental group, EG) or sham acupuncture (control group, CG) treatments over an average of 10.5wks. All outcomes were measured at baseline, at 12wks and 6mos. <strong>Outcomes:</strong> Fugl-Meyer Assessment; Modified Ashworth Scores; grip strength; range of motion; Barthel Index; Nottingham Health Profile; depression; mood.</td>
<td></td>
</tr>
<tr>
<td>USA RCT PEDro=9 TPS=chronic NStart=33 NEnd=24</td>
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</tbody>
</table>

1. On intention-to-treat analyses, there were no statistically significant differences in outcomes between the EG and CG at 12wks.
2. 13/16 patients completed the active treatment arm, 11 per protocol. 11/17 completed the sham treatment arm, 8 per protocol.
3. Analyses of protocol-compliant subjects revealed significant improvement in wrist spasticity (P<0.01) and both wrist (P<0.01) and shoulder (P<0.01).
4. The results from 6mo outcomes were not reported.

<table>
<thead>
<tr>
<th>Youn et al. (2013)</th>
<th>South Korea</th>
<th>PCT</th>
<th>No Score</th>
<th>TPSExp=74.79±10.35d TPSExp=77.00±10.79d NStart=28 NEnd=28</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population:</strong> Experimental Group 1 (EG1, N=14): Mean age=64.73±7.08yr; Gender: Male=7, Female=7. Experimental Group 2 (EG2, N=14): Mean age=62.36±6.97yr; Gender: Male=5, Female=9. <strong>Intervention:</strong> Both EG1 (patients with good motor function) and EG2 (patients with poor motor function) received electro-acupuncture with all acupuncture points receiving 2Hz. The intervention was provided 1/d for 16wks with each session lasting 20mins. Assessments were completed at baseline and at 4wks, 8wks, 12wks and 16wks into the study. <strong>Outcomes:</strong> Beck Depression Inventory II (BDI); Hamilton Depression Rating Scale (HAMD).</td>
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</tbody>
</table>

1. BDI scores at 8wks, 12wks and 16wks of treatment were significantly lower when compared to baseline for both EG1 and EG2 (all p<0.01).
2. BDI scores were significantly lower for EG1 compared to EG2 at 12wks and 16wks (both p<0.05).
3. HAMD scores at 4wks, 8wks, 12wks and 16wks of treatment were significantly lower when compared to baseline for both EG1 and EG2 (all p<0.01).
4. HAMD scores were significantly lower for EG1 compared to EG2 at 12wks and 16wks (both p<0.05).
5. ANOVA analyses of BDI and HAMD revealed a significant main effect of time (both p<0.001) but no effect for Group x Time (p=0.158 and p=0.302, respectively).

| Man et al. (2014) | Hong Kong | RCT | PEDro=8 TPS=7.7±11.6mo TPSCon=10.2±14.9mo NStart=43 NEnd=33 |
|--------------------|------------|-----|----------|-----------------|
| **Population:** Experimental Group [EG, N=23]: Mean age=66.7±13.6yr; Gender: Male=9, Female=14. Control Group (CG, N=20): Mean age=66.5±11.9yr; Gender: Male=7, Female=13. **Intervention:** EG received cranial acupuncture with electrical stimulation, and CG received non-invasive cranial acupuncture with electrical stimulation. The intervention was provided 3d/wk for 4wks. |

1. HAMD-17 scores improved significantly for the EG at 1wk compared to the CG (p=0.007) but not at any other assessment time.
2. CGI-S scores improved significantly for the EG compared to the CG at 1wk and 4wks (both p=0.001) but not at any other assessment time.
Assessments were conducted at baseline, 1wk, 2wks and 4wks during treatment. **Outcomes:** 17-item Hamilton Rating Scale for Depression (HAMD-17); Barthel Index (BI); Clinical Global Impression-Severity Scale (CGI-S); Adverse events.

3. CGI-S scores were significantly different on the intercept of a linear mixed-effects model (p=0.0002) between the EG and CG.

4. BI scores improved significantly for the CG compared to the EG at 4wks (p<0.001) but not at any other assessment time.

5. BI scores were significantly different on the slope of a linear mixed-effects model (p=0.0002) between the EG and CG.

6. The number of adverse events experienced did not differ significantly between groups.

### 18.9.9 Reiki Treatments

**Table 18.9.9 Reiki Treatments in the Treatment of Post-Stroke Depression**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shiflett et al. (2002)</td>
<td>USA</td>
<td>RCT PEDro=7 TPS=NA NStart=50 NEnd=44</td>
<td><strong>Intervention:</strong> A modified double-blind, placebo controlled clinical trial. Patients were assigned to receive either Reiki master, Reiki practitioner or sham Reiki. A no-treatment historic control group (CG) was also included. Subjects received up to 10 treatments over a 2.5wk period in addition to standard rehab. <strong>Outcomes:</strong> Functional Independence Measure (FIM); Center for Epidemiologic Studies Depression Measure (CES-D).</td>
<td>1. No significant effects of Reiki were found on the FIM or CES-D. 2. Post hoc analysis suggested that Reiki may have had limited effects on mood and reported energy levels.</td>
</tr>
</tbody>
</table>

### 18.9.9.1 Meridian Acupressure

**Table 18.9.9.1 Meridian Acupressure in the Treatment of Post-Stroke Depression**

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kang et al. (2009)</td>
<td>Korea</td>
<td>RCT PEDro=5 TPS&lt;2wk NStart=56 NEnd=56</td>
<td><strong>Intervention:</strong> Patients admitted to hospital within 2wks of stroke were randomized to receive Meridian acupressure for 10min/d for 2wks (n=28) or routine care only (n=28). Outcomes were assessed before and after treatment. <strong>Outcomes:</strong> Hand dynamometer; 15-point Graphic Rating Scale; Distance Around Index Finger; Electrogoniometry; Activity of Daily Living Scale; Beyer Six-Face Rating Scale.</td>
<td>1. At the end of treatment, there were significantly greater improvements on all outcomes assessed, favoring the acupressure group.</td>
</tr>
</tbody>
</table>

### 18.9.10 Massage Therapy

**Table 18.9.10 Massage Therapy in the Treatment of Post-Stroke Depression**

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### 18.9.11 Relaxation and Stroke Recovery

#### Table 18.9.11 Relaxation Therapy in Stroke Recovery

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mok &amp; Woo</td>
<td>Hong Kong</td>
<td>RCT</td>
<td>PEDro=5</td>
<td></td>
<td>Intervention: Stroke patients were randomly allocated to a massage group (MG) or a control group (CG). The MG received 10mins of slow-stroke back massage for seven successive evenings. Outcomes: Anxiety level; Heart rate; Systolic blood pressure; Diastolic blood pressure; Pain score; State-Trait Anxiety Inventory.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TPS=NA</td>
<td></td>
<td>1. Significant improvements in all five variables at post-test and 3d post-test were seen for the MG compared to the CG (p&lt;0.05).</td>
</tr>
<tr>
<td>Kneebone et al.</td>
<td>United Kingdom</td>
<td>Pre-Post</td>
<td>No Score</td>
<td>Population: Mean age=74±14yr; Gender: Males=27, Females=28. Intervention: The intervention group (IG) received autogenic relaxation training, a technique that requires patients to silently repeat statements being read to them. Statements included &quot;my right arm is very heavy&quot; and &quot;my fingers are heavy, limp and relaxed&quot;. Autogenic relaxation sessions were 30min in duration and were provided 1/wk. Assessments were conducted at baseline and at post-treatment. Outcomes: Tension Rating Scales (TRC); Practical issues.</td>
<td></td>
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<tr>
<td>Marshall et al.</td>
<td>USA</td>
<td>PCT</td>
<td>No Score</td>
<td>Population: Experimental Group 1 (EG1, N=6): Mean age=58.2yr; Gender: Male=5, Female=1. Experimental Group 2 (EG2, N=5): Mean age=52.4yr; Gender: Male=4, Female=1. Intervention: EG1 (aphasic stroke patients) and EG2 (non-aphasic stroke patients) received unilateral nostril breathing (UNB) training which required patients to close one nostril and breathe through the other. The intervention was provided for 10wks, with the first 4wks consisting of instruction for 1hr/wk and the remaining 6wks consisting of practice performed for 5-40min, 6-7d/wk. Assessments were conducted at baseline, at 4wks, and at post-treatment.</td>
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<tr>
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<td></td>
<td>TPSExp1=27.5±23.8mo</td>
<td></td>
<td>1. The IG reported a significant reduction in self-reported tension according to the TRC from baseline to post-treatment (p&lt;0.001).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TPSExp2=32.0±37.8mo</td>
<td></td>
<td>2. A separate analysis of TRC scales for patients who only attended one session (n=21) was conducted and a significant reduction in self-reported tension was still evident (p&lt;0.01).</td>
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<tr>
<td></td>
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<td>NStart=55</td>
<td></td>
<td>3. Practical issues were reported by staff in regards to the level of staffing required, training patients with communicative, hearing or cognitive disabilities, and treating larger groups with greater variation in disability.</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>NEnd=55</td>
<td></td>
<td>4. BAI scores significantly decreased for both groups at 4wk assessment (p=0.0069) but no difference was reported between groups for baseline and post-treatment scores.</td>
</tr>
<tr>
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<td>2. A significant main effect of time was reported for BAI scores between EG1 and EG2 (p=0.0092).</td>
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<tr>
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<td>3. BDI scores revealed no significant differences between EG1 and EG2 from baseline to post-treatment.</td>
</tr>
<tr>
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<td>4. ADP scores for alternative communication, personal information, information units, phrase length, ADP severity (all p&lt;0.05) and lexical retrieval</td>
</tr>
</tbody>
</table>
18.9.12 Art Therapy in Stroke Recovery

Table 19.9.12 Art Therapy in Stroke Recovery

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ali et al. (2014)</td>
<td>United Kingdom</td>
<td>Pre-Post No Score</td>
<td>TP=NA N\text{\textsubscript{Start}}=6 N\text{\textsubscript{End}}=6</td>
<td>Population: Mean age=69yr; Gender: Males=6, Females=0. Intervention: The intervention group (IG) received art therapy which included activities such as drawing, painting, sculpting and collaborating in the production of a short animated film. The intervention was provided 2/wk for 6wks with each session lasting 50min. Assessments were conducted at baseline and post-treatment. Outcomes: Hospital Anxiety and Depression Scale (HADS); Therapy Outcome Measure (TOM).</td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td>1. The IG demonstrated a reduction in both depression and anxiety on the HADS from baseline with scores of 10 and 8 respectively to 4 and 6 at post-treatment; indicating a shift from borderline abnormal levels to normal range. 2. TOM score also increased from 9 to 10.5. 3. Feedback was positive in all but one patient.</td>
<td></td>
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18.10 Post-Stroke Emotionalism

18.10.3 Treatment of Post-Stroke Emotionalism

Table 18.10.3 Pharmacologic Treatment of Post-Stroke Emotionalism

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<th>Author, Year</th>
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<th>PEDro Score</th>
<th>TPS</th>
<th>Methods</th>
<th>Outcomes</th>
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<tr>
<td>Andersen et al. (1993)</td>
<td>Denmark</td>
<td>RCT</td>
<td>PEDro=6 TPS=NA</td>
<td>Intervention: In a cross-over design, patients with pathological crying following stroke were randomly assigned to receive either 21d of citalopram 20 mg/d (for patients under age 65 or 10 mg/d for older patients) or matching placebo. Following first 21d treatment period, participants entered a 7d washout followed by a second baseline and then crossed over to the second 21d treatment period. Response to treatment was defined as a reduction of 50% or more in the frequency of crying episodes. Crying frequency was assessed via interview, patient diary and rating on a 5-point scale. Outcome: Crying frequency; Hamilton Depression Rating Scale (HAMD).</td>
<td>1. Frequency of crying could be assessed in 13/16 patients. Frequency of crying was reduced by 50% or more in all patients treated with citalopram, but in only 2 patients assigned to the placebo condition (p&lt;0.005). 2. When compared to baseline, treatment with citalopram resulted in a significant reduction in the mean number of episodes/d (p&lt;0.05). 3. Although no patients were diagnosed with depression during baseline, treatment with citalopram was also associated with reduction in scores on the HAMD (p&lt;0.005).</td>
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4. All patients experienced a relapse of crying episodes when treatment was stopped. No significant side effects were detected, however, transient orthostatic dizziness, insomnia and increased spasticity were all reported in a global assessment.

Robinson et al. (1993) USA RCT PEDro=7 TPS=NA NStart=28 NEnd=26

**Intervention**: Individuals with stroke and who self-referred for treatment of pathological laughing or crying were randomly allocated to receive either treatment with nortriptyline (20mg/d for 1wk, 50mg/d for 2wks, 70mg/d for 1wk and 100mg/d for the last 2wks) or matching placebo. Total treatment time was 6wks. Evaluations took place at 2wk intervals.

**Outcomes**: Pathological Laughter and Crying Scale (PLCS); Mini-Mental State Examination; Hamilton Depression Rating Scale; John Hopkins Functioning Inventory.

1. 8/13 patients receiving nortriptyline and 11/13 patients receiving a matching placebo were diagnosed with major depression prior to the commencement of treatment.

2. Both groups experienced improvement in depression over the period of treatment; however, significantly greater improvement was associated with treatment with nortriptyline.

3. On the PLCS, patients treated with nortriptyline demonstrated greater improvement than those receiving placebo (p=0.008). While both groups experienced improvement over time, patients in the nortriptyline group improved more quickly than those in the placebo condition (p<0.001).

4. When a subgroup of patients from each condition were matched for depression, patients treated with nortriptyline demonstrated greater improvement than those who were not (p=0.002).

5. Comparison of depressed vs. non-depressed patients demonstrated a significant treatment effect (vs. placebo) that was not affected by depression.

Brown et al. (1998) UK RCT PEDro=8 TPS=NA NStart=20 NEnd=19

**Intervention**: Patients with at least a 4wk history of emotionalism following stroke were randomly assigned to receive either 20mg/d fluoxetine for 10d (n=10) (experimental group, EG) or matching placebo (n=10) (control group, CG). One subject withdrew from the EG. Significant change was defined as a ≥50% reduction in frequency of outbursts.

**Outcomes**: Lawson and MacLeod Rating Scale (LMRS); Patient interview; Patient ratings (5-point scale).

1. By the third day, ratings of emotionalism on the LMRS had improved substantially among EG when compared to CG (p=0.017). At day 10, these results remained constant.

2. Similarly, on self-ratings of change in emotionalism, by day three, patients in the EG reported improvements of at least 2 points, more often than patients in the CG (p=0.0049). This difference also remained constant by day 10 (p=0.0049).

3. At day three, more patients in the EG (8/9) than the placebo group (3/10) reported a ≥50% reduction in outbursts (p=0.015). By day 10, this difference between groups remained significant (p=0.0007), with 7/9 patients receiving fluoxetine and 2/10...
### Burns et al. (1999) UK RCT
PEDro=7 TPS<1mo N\text{Start}=28 N\text{End}=24

**Intervention:** Patients with emotionalism at least 1mo post-stroke were randomly assigned to treatment with 50mg sertraline/d (n=14) (experimental group, EG) or matching placebo (n=14) (control group, CG). Patients participated in a single-blind run-in phase (2wks), followed by a double-blind treatment phase (8wks) and a follow-up placebo phase (2wks).

**Outcomes:** Frequency of outbursts; Ratings of emotionalism (criteria of House et al. (House et al. 1989)); Clinician’s interview-based impression of change (CIBIC).

1. Following the first 2wk run-in phase, 50% of patients in the CG demonstrated improvement in tearfulness compared with 97% of patients receiving sertraline.
2. By 8wks, the EG demonstrated greater improvements on the CIBIC as well as improvements in emotional lability and frequency of episodes of tearfulness when compared to patients in the CG (p=0.41).
3. Following the final 2wk washout period, all between group differences became non-significant.

### Choi-Kwon et al. (2006)
Korea RCT PEDro=8 TPS=14mo N\text{Start}=152 N\text{End}=125

**Intervention:** Stroke patients with one of post-stroke depression, emotional incontinence or anger proneness were randomly assigned to receive either fluoxetine 20mg/d (n=76) (experimental group, EG) or matching placebo (n=79) (control group, CG). Treatment continued for a period of 3mos.

**Outcomes:** Beck Depression Inventory (BDI); Percentage change in Visual Analogue Scale (VAS: emotional incontinence, anger proneness).

1. Overall, 110 patients demonstrated emotional incontinence at baseline. 51 patients in the EG and 55 in the CG exhibited emotional incontinence for crying. 13 in the CG and 18 in the EG exhibited emotional incontinence for laughter.
2. By 3mos, treatment with fluoxetine was associated with significant reduction in emotional incontinence (crying) when compared to the CG (p<0.01).
3. At 1, 3 and 6mos, the percentage change in VAS score for emotional incontinence (crying) was significantly greater among patients in the EG than in the CG (p<0.01).
4. There was significant differences demonstrated between EG and CG for BDI or VAS (emotional incontinence-laughing).
5. Subjective reports of improvement were greater for patients with emotional incontinence of both types when receiving treatment vs. placebo (p<0.05 at all assessments).

### Choi-Kwon et al. (2008)
Korea RCT PEDro=8 TPS=NA N\text{Start}=158 N\text{End}=107

**Intervention:** A secondary analysis of data collected from Choi-Kwon et al. (2006). Assessments were performed at 3 and 6mos as well as at 12mos (6mos after study was opened for open-label continuation). Evaluations at 12mos included assessments of health-related quality of life and emotional dysfunction. 107 patients provided data at 12mo follow-up.

**Outcomes:** Medical Outcomes Study 36-Item Short Form Questionnaire (SF-36).

1. Treatment was associated with significantly higher SF-36 mental health scores at 3mos (p<0.01), 6mos (p<0.05) and 12mos (p<0.01) compared to the placebo condition.
2. At 12mos, individuals in the fluoxetine group had significantly higher scores on the general health (p<0.01) and social function (p<0.05) subscales vs. placebo.
3. For individuals with emotional disturbances following stroke, treatment with the
| | antidepressant, fluoxetine may improve the mental health aspects of health-related quality of life. |
References


Spalletta, G., Guida, G., De, A. D., Caltagirone, C. (2002). Predictors of cognitive level and depression severity are different in patients with left and right hemispheric stroke within the first year of illness. *J.Neurol., 249*(11), 1541-1551.


