

Question 50 evidence tables

**Question 50: Do interventions aimed at treating post-stroke apathy improve outcomes?**

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

DT imaging = diffusion tensor imaging, MOT-Q = Motivation for Traumatic Brain Injury Rehabilitation Questionnaire, PHQ-9 = Patient Health Questionnaire-9, MRI = magnetic resonance imaging, VCI = vascular cognitive impairment, PSD = post-stroke depression, PSA = post-stroke anxiety, MCI = mild cognitive impairment, FAS = Fatigue Assessment Scale, PASE = physical Activity Scale for the Elderly, SB = sedentary behaviour, AI-C = Apathy Inventory-Clinician Version, MADRS = Montgomery-Asberg Depression Rating Scale, FMA = Fugl-Meyer motor scale, MCA = middle cerebral artery, AS = Apathy Scale, QIDS = Quick Inventory of Depressive Symptomatology, OT = occupational therapist, SR = systematic review, MA = meta-analysis, RCT = randomised controlled trial, IPDMA = individual patient data meta-analysis, MDT = multidisciplinary team, PICO = patient/population, intervention, comparison and outcomes, OR = odds ratio, CI = confidence interval, QoL = quality of life, ADL = activities of daily living, OR = odds ratio, RR = relative risk, aOR = adjusted odds ratio, cOR = crude odds ratio, CI = confidence interval, RoB = risk of bias, I2 = heterogeneity statistic.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
254	W.-L. Bickerton et al. (2015) The BCoS cognitive profile screen: Utility and predictive value for stroke. <i>Neuropsychology</i> , 29: 4 638-648	<ul style="list-style-type: none"> <li>- Study was conducted between 2006-2011:</li> <li>- 657 participants within sub-acute stage after stroke.</li> <li>- All assessed at time 1, 331 re-assessed after 9 months</li> <li>- Cross-section observational study</li> <li>- Demographics of 1<sup>st</sup> vs 2<sup>nd</sup> stroke indicated similarity between the groups;</li> <li>- Left sided vs right sided groups differed sign re lower level of cognition of left .s stroke patients</li> <li>- Psychological variables were controlled for</li> </ul>	<ul style="list-style-type: none"> <li>- Detailed analysis of cognitive profiles</li> <li>- cognitive predictors for recovery defined</li> </ul>	<ul style="list-style-type: none"> <li>- Patients re-tested at 9months were similar re demographics regardless of 1<sup>st</sup>/2<sup>nd</sup> stroke or left/right sided lesion; sign. differences were found in that patients in the follow-up group were higher educated and more depressed (not sure if both co-existed in participants),</li> <li>- Neuropsychological effects differentiated patients with 1<sup>st</sup> vs. patients with 2<sup>nd</sup> stroke; left s. vs. right s. stroke;</li> </ul>	<ul style="list-style-type: none"> <li>- patients with second stroke had sign. Lower cognitive recovery at 9 month re-test than subjects who only had one stroke. This was attributed to reduced neural plasticity.</li> <li>- Patients with left s. stroke performed less well than right s. stroke patients,</li> <li>- Predictive estimates were related to attention and praxis; the BCoS provides such assessments which is an advantage over other screening tests;</li> </ul>	<p>++</p> <p>SIGN = high quality; Paper indicated the usefulness of establishing detailed cognitive profiles; -valid estimates of post-stroke recovery after 9 months were established by applying the cognitive outcomes; valid differentiation between left s. and right s. stroke outcomes were possible due to the available detailed neuropsychological profile, - the study took place between 2006-2011: it is likely that stroke population variables have changed since the implementation of specialised acute/post-acute stroke units. Most patients who were</p>

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		<ul style="list-style-type: none"> <li>- Predictive validity of the BCOS neuropsychological test of longer-term functional outcomes.</li> </ul>		<ul style="list-style-type: none"> <li>- Affective variables were considered;</li> </ul>		<p>treated as inpatients during this time, will now be seen in ESD and community rehab teams. How would such setting variables affect cognitive and functional outcomes?</p> <ul style="list-style-type: none"> <li>- Development of a new stroke specific neuropsychology battery: since then many neuropsychological tests have been validated for stroke. Due to the acuteness of stroke patients in UK stroke units recently, it is questionable whether such a comprehensive battery may be feasible as an initial measure. The assumption would be that cognitive recovery can be predicted with neuropsychological tests. There could be further studies confirming that other tests have also robust predictive validity.</li> </ul>
244	H. Boosman et al. (2016). Further validation of the Motivation for Traumatic Brain Injury Rehabilitation Questionnaire (MOT-Q) in patients with acquired brain injury. <i>Neuropsychological rehabilitation</i> , 26:1 87-102	<ul style="list-style-type: none"> <li>- Two groups: inpatients (122 subjects; 3 month post ABI) vs outpatients, 92 subjects 9months post ABI)</li> <li>- Five rehab centre in the Netherlands;</li> <li>- Diagnosis of ABI: traumatic and stroke;</li> <li>- Setting 2012-2013</li> </ul>	<ul style="list-style-type: none"> <li>- Administration of the MOT-Q;</li> <li>- Visual analogue scale;</li> <li>- Self-awareness scale;</li> </ul>	<p>Outcomes:</p> <p>MOT-Q:</p> <ul style="list-style-type: none"> <li>- Scale was evaluated as feasible with good statistical properties; acceptable internal consistency; good internal consistency for total score;</li> <li>- Validity of the subscale requires further investigation,</li> </ul>	<p>Results:</p> <ul style="list-style-type: none"> <li>- Outpatient motivation was sign lower than that of the inpatients, this was interpreted as less rehab experience;</li> <li>- MOT-Q has good feasibility;</li> <li>- MOT-Q items correlated mostly with overall score, meaning that motivation was</li> </ul>	<p>++</p> <p>SIGN=high quality; Valid for research purposes, not quite practical for clinical rehab</p>

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
				<p>caution needed when interpreting subscores,</p> <ul style="list-style-type: none"> <li>- Predicted treatment motivation;</li> <li>- Scale able to predict lack of denial by inverse relation with self-awareness</li> </ul>	<p>measured by all items, a few items were found which appeared to be related to a different construct.</p> <ul style="list-style-type: none"> <li>- Lack of denial was not inversely related with self-awareness: means that this scale was associated somewhat.</li> <li>- It appeared that the measures used did not fit well, probably due to lack of denial and self-awareness not being on one dimension.</li> </ul>	
244	H. Boosman et al. (2016). Further validation of the Motivation for Traumatic Brain Injury Rehabilitation Questionnaire (MOT-Q) in patients with acquired brain injury. <i>Neuropsychological rehabilitation</i> , 26:1 87-102	<p>Questionnaire validation</p> <p>Inpatient and outpatient setting</p> <p>122 inpatients and 92 outpatients with acquired brain injury (ABI).</p>	None	To further validate the Motivation for Traumatic Brain Injury Rehabilitation Questionnaire (MOT-Q)	The MOT-Q showed adequate feasibility in terms of few items with missing responses. No floor/ceiling effects. Internal consistency was good.	N/A
245	S. Brockman et al. (2016). A Randomized, Placebo-Controlled, Double-Blind Efficacy Study of Nefiracetam to Treat Poststroke Apathy. <i>Journal of Stroke and Cerebrovascular</i>	<p>Setting: Australian Stroke Units</p> <p>Design: 12 week. Placebo controlled, double blinded randomised trial</p> <p>Subjects: Stroke survivors (age 40-90) at 8 weeks post ictus with apathy (on a screening tool) and no depression, dementia, aphasia</p> <p>Note 2514 screened and 13 randomised</p>	<p>Intervention: Nefiracetam 900mg (450mg bd) for 12/52 (n=6)</p> <p>Comparator: Placebo for 12/52 (n=7)</p>	<p>Primary: Apathy Scale score at 12 weeks (also collected at 4 and 8 weeks)</p> <p>Secondary: Clinical Global Impression Scale</p> <p>Stroke Impact Scale</p> <p>Functional Independence Measure</p>	<p>No change in Apathy Scale score</p> <p>Difference 1.2 (-14.8 to 17.2)</p> <p>No differences in any secondary measures</p>	<p>+</p> <p>No issues with design</p> <p>Substantially underpowered</p> <p>High drop out</p> <p>Limited generalisability</p>

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	<i>Diseases</i> , 25:5 1119-1127			Barthel Index EQ-5D PHQ-9 Neuropsych battery Caregiver Burden Scale Adverse events		
246	E. Douven et al. (2020). Imaging markers associated with the development of post-stroke depression and apathy: Results of the Cognition and Affect after Stroke - a Prospective Evaluation of Risks study. <i>European Stroke Journal</i> , 5:1 78-84	<ul style="list-style-type: none"> <li>- Design:</li> <li>- Research question: Are post-stroke apathy and depression related with generalised brain pathology, rather than the stroke lesion</li> <li>- Use of imaging markers</li> <li>- Longitudinal design</li> <li>- 250 participants</li> <li>- 3T MRI=n=188</li> <li>- Longitudinal study (1 year with multiple time measure points),</li> <li>- Almost complete data also at follow up</li> </ul>	<ul style="list-style-type: none"> <li>- Intervention</li> <li>- Measures used at several time points; pre-stroke variables were controlled for (e.g. pre-stroke depression, brain health);</li> </ul>	<ul style="list-style-type: none"> <li>- Result:</li> <li>- Predictive associations</li> <li>- Association between generalised atrophy and post-stroke apathy;</li> <li>- Lesser association between depression and stroke variables;</li> <li>- Pre stroke depression was controlled for as it was marginally correlated with post-stroke depression;</li> <li>- Controlled for small vessel disease which was also slightly correlated with post-stroke depression;</li> </ul>	<ul style="list-style-type: none"> <li>- outcome:</li> <li>- SIGN=high quality.</li> <li>- generalised degenerative and vascular brain pathology appears to predict apathy, but not so much depression;</li> <li>- description of brain pathology in association with post-stroke depression and apathy identified, but not caused by the stroke as well as the overlap of anhedonia in both psychol. Conditions;</li> <li>- therefore, global or cumulative brain pathology was thought more important than presence of location of a specific stroke lesion/location</li> </ul>	<ul style="list-style-type: none"> <li>- implication:</li> <li>- the study outcomes appear important for post-stroke diagnostics; it highlights the need for attention to premorbid brain health; also its important to help with the differential diagnosis of depression or apathy. This seems useful as depression appears to be over diagnosed after stroke and apathy appears to be less understood.</li> </ul>
247	E. Douven et al. (2018). Baseline Vascular Cognitive Impairment Predicts the Course of Apathetic Symptoms After Stroke: The CASPER Study. <i>American Journal of</i>	Context of study suitably outlined. Predictive cohort study Study aims clearly outlined (i.e., exploration of VCI, PSD and PSA, over a 12-month period Time since stroke of cohorts unclear- acute phase but how early on, post stroke?	No intervention observational study over different time points (within 12 months)	VCI was found to significantly link to PSA, with levels of PSA increasing over time Type of cognitive impairment implied as predictive of level of PSA over time i.e., worse PSA levels in the face of	PSA at greater risk of development over the course of recovery i.e., '9-15 months' & more strongly linked to MCI than PSD existence – hence indicating the need for MCI to be identified early in the post stroke journey	+ acceptable (Lack of definition of how soon after a stroke, cohorts were assessed and included in the study is a limitation, raising the possibility of a range of 'time since stroke' differences

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	<i>Geriatric Psychiatry</i> , 26:3 291-300			impaired info processing or executive abilities (or with multiple impairments) PSD not found to be a predictor of PSA (over time)- no association over time found	general themes raised ring true clinically i.e., that PSA is commonly associated with cognitive impairment post stroke and not readily explainable by depression relationships. Although PSA (with an organic basis) can be misunderstood as depression related	influencing cohort experience and raising a confounding factor in conclusions) Small sample sizes in some cognitive sub domain groups (stated by authors as a limiting factor)
248	C. F. Fitzsimons et al. (2020). Stroke survivors' perceptions of their sedentary behaviours three months after stroke. <i>Disability and rehabilitation</i> , : Jan-13	Study aim: The aim of this study was to undertake the first step in the intervention design process by undertaking a behavioural diagnosis of SB in the early post stroke phase, guided by COM-B and more broadly informed by the ICF. Qualitative study; Anonymised transcripts were analysed using the Framework Method, which is a matrix based seven stage method providing a systematic, comprehensive and transparent approach to analysing qualitative data 31 stroke survivor interviews (16 male/ 15 female)/ 3 months after stroke Independently mobile stroke survivors were purposively sampled on the basis of gender and recruited from Royal Infirmary, Edinburgh The interview topic guide was informed by COM-B Semi-structured interviews were conducted, at three months post	N/A	<ul style="list-style-type: none"> <li>· Hospital Anxiety and Depression scale</li> <li>· Fatigue Assessment Scale (FAS)</li> <li>· Physical Activity Scale for the Elderly (PASE)</li> <li>· Barthel Index of Activities of Daily Living</li> <li>· Simplified Modified Rankin Scale</li> <li>· a Visual Analogue Scale to determine the percentage of the day spent sedentary.</li> </ul>	Our qualitative findings provide an essential point of reference for the development of robust SB interventions in the early phase after a stroke. The most salient factors that future SB interventions should consider related to: > influence of physical tiredness and fatigue > pain/discomfort acting as both a motivator and inhibitor > environmental barriers to participation in physical, domestic and leisure activities > importance of social interaction > fear of falling; > enjoyment of SB/lack of intention to move > importance of valued physical, domestic and leisure activities > the habitual nature of SB.	The study followed the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist for reporting qualitative research. No sign checklist for Qualitative studies? This was a high-quality qualitative study

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		stroke, in participant's own homes, audio-recorded on a digital device and transcribed verbatim.				
248	C. F. Fitzsimons et al. (2020). Stroke survivors' perceptions of their sedentary behaviours three months after stroke. <i>Disability and Rehabilitation</i> , : Jan-13	Setting: acute stroke unit/unclear Edinburgh Royal Infirmary, Scotland, UK Design: qualitative study (aiming to inform behaviour-change intervention design but not an intervention itself aimed at improving outcomes) Sample: 31 independently mobile stroke survivors	n/a Six weeks after stroke, participants were sent a questionnaire booklet (containing HADS, Fatigue Assessment Scale, Physical Activity Scale for the Elderly, Barthel Index of Activities of Daily Living, Simplified Modified Rankin Scale, Visual Analogue Scale to determine % of the day spent sedentary). Interviews held with stroke survivors 3 months post stroke in their own homes.	Quant tools not used as outcome measures, simply to describe the sample. Interviews held 3 months post stroke. Topic guide focussed on perceptions of own behaviour and sedentary behaviour (e.g. questions about how long spent sitting, how stroke has influenced this and how would feel is asked to sit less, motivation for reducing sedentary behaviour as well as ideas for what could help with this in the future)	Themes related to: <ul style="list-style-type: none"> <li>· Behaviour – where participants spoke about their leisure and day to day activities</li> <li>· Capability – where participants spoke about their sense of physical capability and impact of stroke (particularly fatigue), and psychological capability (particularly mood, anxiety and knowledge of the importance of reducing sedentary behaviour)</li> <li>· Opportunity – where participants talked about opportunities in their lives for being more active/reducing sedentary behaviour</li> <li>· Social support</li> <li>· Professional support</li> <li>· Motivation</li> </ul> Overall: qualitative findings provide an essential point of reference for the development of robust SB interventions in the early phase after a stroke, that will inevitably complement the broad goals of rehabilitation	<b>N/A</b> Qualitative study - not applicable to SIGN checklist

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
					during that phase, by also encouraging participation and skill development in a wide range of physical, domestic and leisure activities. The study identified barriers and facilitators to involving people in interventions in the future: The most salient factors that future SB interventions should consider related to the influence of physical tiredness and fatigue on SB; pain/discomfort acting as both a motivator and inhibitor to these activities; environmental barriers to participation in physical, domestic and leisure activities; the importance of social interaction; fear of falling; enjoyment of SB/lack of intention to move; the importance of valued physical, domestic and leisure activities; and the habitual nature of SB.	
249	A. M. Goldfine et al. (2016). Quantifying poststroke apathy with actimeters. <i>Journal of Neuropsychiatry and Clinical Neurosciences</i> , 28:3 199-204	Acute rehabilitation hospital USA Correlational study 57 patients with ischemic or haemorrhagic stroke. Exclusions: bilateral upper extremity arm weakness, individuals who they could not diagnose apathy severity (including those taking sedating or antipsychotic medication, hyperarousal from infection or	n/a not an intervention study. Aim of study was to investigate whether apathy severity and amount of movement during 9am and 5pm were correlated. All participants wore actimeter on the wrist of an upper extremity with intact strength	Apathy Inventory-Clinician Version (AI-C) Montgomery-Asberg Depression Rating Scale (MADRS) Fugl-Meyer motor scale Acceleration values from actimeter	Apathy severity inversely correlated with total movement per hour ( $r=-.49$ , $p<.001$ ). Multiple linear regression accounting for age and stroke severity, movement time remained significantly inversely correlated with AI-C. $R^2=.34$ .	<b>N/A</b>

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		sleep disturbance, active psychiatric disease other than depression). Apathetic patients: Median 8 days post stroke (IQR 4), median age 73 (IQR 8.5). Non apathetic patients: Median 6 days post stroke (IQR 2), median age 77.5 (IQR 14).	(Fugl-Meyer score of 66). Data collected for at least 36 hours. Data analysed from the day and the second night.		No significant correlation between MADRS and total movement time (p=.17). Apathy severity correlated with change in FIM score from admission to discharge (r=-0.44, p<.001).	
250	M. J. Hollocks et al. (2015). Differential relationships between apathy and depression with white matter microstructural changes and functional outcomes. <i>Brain</i> , 138:12 3803-3815	Setting - N=118 with small vessel disease, mean age 68.9, 65% male, - N=398 healthy contr., mean age 64.3, 53% male,	Interventions - Cognitive tests, - Apathy measures, - Depression measures; - Quality of life measures, DT Imaging - Analysis used structural equation statistical modelling;	Outcome - SMD patients had higher Depression and apathy scores than control; - SVD patients either reported both apathy and depression or either condition in isolation - Cognitive performance was isolated from psychological characteristics;	Results: - Apathy and depression is increased in SMD patients; - Study confirmed that white matter microstructural changes in small vessel disease predict apathy and - Small vessel disease is not directly related with depression - Apathy could be isolated from depression; or if it co-existed in patients (less frequently noted in one patient) could be identified as separate and co-existing symptoms; - apathy (not depression) relates to cortical/subcortical networks associated with emotion regulation, reward- and goal-directed behaviour; the identified networks help to explain the difference	++ SIGN = high quality



Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
					<p>between apathy and depression</p> <ul style="list-style-type: none"> <li>- apathy relates to distinct white matter changes in associated cortical/sub-cortical regions</li> <li>- depression does not relate to white matter changes</li> </ul>	
251	M. Lin et al. (2019). Comparison of Motor Relearning Program versus Bobath Approach for Prevention of Poststroke Apathy: A Randomized Controlled Trial. <i>Journal of Stroke and Cerebrovascular Diseases</i> , 28:3 655-664	<p>Setting: Stroke unit/acute rehab of the Department of Neurology at Ji'an Central People's Hospital in China</p> <p>Design: RCT</p> <p>Sample: N=488 (Group A (motor learning programme group) n=245, Group B (Bobath group) n=243)</p> <p>New, first time ischaemic stroke within 7 days of onset, aged 18+</p> <p>Exclusion criteria: cognitive impairment that precludes scale completion, diagnosis of terminal illness or Parkinson's, apathy diagnosis pre stroke, history of schizophrenia, anxiety, depression or mental illness, thrombolysis, unable to consent.</p> <p>Baseline characteristics of the subjects are age mean 65.1 (SD 10.9); 47.1% female; AES-C mean 24.9 (SD 4.7); National Institutes of Health Stroke Scale mean 3.9 (SD 3.8); Barthel Index mean 87.9 (SD 8.7); Mini-Mental State Examination mean 23.3 (SD 4.5); Hamilton Depression Scale</p>	<p>Group A: motor relearning programme</p> <p>Group B: Bobath</p> <p>No description of these (external reference to a manual)</p> <p>Patients received physio 5 days per week for four weeks.</p> <p>Daily sessions were min of 40 mins duration. Patients in both groups received the "same comprehensive multidisciplinary treatment for stroke patients."</p>	<p>Outcomes assessed at:</p> <ol style="list-style-type: none"> <li>1. Baseline (n=488)</li> <li>2. One month post stroke (n=463)</li> <li>3. 3 months post stroke (n=332)</li> <li>4. 6 months post stroke (n=251)</li> <li>5. 9 months post stroke (n=194)</li> <li>6. 12 months post stroke (151)</li> </ol> <p>Apathy as measured by Apathy Evaluation Scale-Clinical</p>	<p>The AES-C scores of participants in both groups declined gradually from M1 to M12. Worse scores observed in the Bobath Group at M3 than M1.</p> <p>Motor Learning Programme group (Group A) participants had significantly less apathy severity compared with Bobath participants at each timepoint.</p>	<p>- Study report doesn't seem very clear and there are a number of uncertainties about whether people with or without apathy were recruited at baseline and throughout (contradictory information between the abstract and body of the text), had to spend a lot of time working out the drop out rates (which seem high) and doesn't seem to be information about a power calculation that allows for a proportion of sample dropping out. It's not clear if the figures reported in Figure 2 are 'new' recruits or people who continued after baseline in the groups (again ambiguous wording in the paper leads to questioning this). The figures of the outcomes are difficult to interpret. ? relevance since participants were excluded if offered thrombolysis too. Exclusion criteria fairly strict</p>

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		mean 17.5 (SD 6.6); and Hamilton Anxiety Scale mean 14.4 (SD 6.2).				and limits representativeness of sample?
251	M. Lin et al. (2019). Comparison of Motor Relearning Program versus Bobath Approach for Prevention of Poststroke Apathy: A Randomized Controlled Trial. <i>Journal of Stroke and Cerebrovascular Diseases</i> , 28:3 655-664	<p>Setting: Acute Stroke Unit</p> <p>Methods: A randomized controlled study of acute stroke patients.</p> <p>Unclear if participants did or did not have apathy at recruitment point (Reported differently in abstract and study design section).</p> <p>Abstract: Four hundred and eighty-eight patients <u>without evidence</u> of apathy or depression at the initial visit were consecutively recruited,</p> <p>Study design: To be eligible for the trial, the <u>patients had to be identified as having post stroke apathy</u> at the recruitment point (baseline or 1, 3, 6, 9, or 12 months later).</p> <p>258 males and 230 females.</p> <p>Patients were block randomized into 2 groups</p> <p>A) Motor relearning programme or B) Bobath.</p> <p>Exclusion criteria: (1) inability to complete the scale evaluation due to communication or cognitive disorders; (3) administered thrombolysis therapy;</p> <p>Comment: Stroke patients without any motor control problem may have been included?? Motor Relearning</p>	<p>Group A (n = 245) Motor Relearning Program</p> <p>Group B (n = 243) Bobath</p> <p>Participants included in study were given physiotherapy 5 days weekly/min 40 mins duration for a period of 4 weeks.</p> <p>Besides physiotherapy, the patients received the same comprehensive, multidisciplinary treatment for stroke patients.</p>	<ul style="list-style-type: none"> <li>· Apathy Evaluation Scale-Clinical,</li> <li>· National Institutes of Health Stroke Scale scores</li> <li>· Barthel Index</li> <li>· Mini-Mental State Examination,</li> <li>· Hamilton Depression Scale</li> <li>· Hamilton Anxiety Scale</li> </ul> <p>scores upon admission.</p> <p>Baseline scores on admission and at 1-, 3-, 6-, 9-, and 12-month follow-up after stroke</p>	<p>Participants in both groups had similar levels of apathy symptoms at study admission.</p> <p>Apathy scores of participants in both groups decline gradually from month 1 to month 12.</p> <p>Motor Learning Program participants had significantly less apathy severity compared with Bobath participants</p> <p>At each time point 1-, 3-, 6-, 9-, and 12- Participants given Bobath approach were more likely to develop post stroke apathy than patients given Motor Relearning Program over 12 months.</p> <p>Conclusions: Physiotherapy treatment in acute stroke rehabilitation using Motor Relearning program was significantly more effective in preventing of new onset of apathy following stroke compared with Bobath approach.</p>	<p>-</p> <p>Low quality RCT; Poorly reported Blinding: 2 physiotherapy treatments could not be Blinded; treatment allocation known by the therapists who treated the patients and the ward secretary who was in charge of randomization.</p> <p>No (untreated) control group.</p> <p>Power of the study not reported</p> <p>The study had a relatively small sample size, Study carried out on one site Figure 1,2 and 3 not easy to understand/ interpret % dropouts not reported</p>

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		programme designed specifically to improve motor control/function.				
252	N. Sasaki et al. (2017). The efficacy of high-frequency repetitive transcranial magnetic stimulation for improving apathy in chronic stroke patients. <i>European Neurology</i> , 78:445-93 28-32	Pilot RCT; Quasi Randomised based on date of entry to study; Chronic Stroke >1 year, Supratentorial ICH without cerebral cortex invasion or subcortical MCA infarction.	Repetitive transcranial magnetic stimulation (rTMS) [n=13] vs Sham [n=6]; 5 sessions over 5 consecutive days	Primary Outcome – Apathy Scale; assessed immediately prior to rTMS/ Sham and immediately after last application of rTMS/ Sham. Secondary Outcome – Quick Inventory of Depressive Symptomatology; assessed immediately prior to rTMS/ Sham and immediately after last application of rTMS/ Sham.	Primary Outcome – Apathy Scale score had significantly improved in the rTMS group (from 15.9 ± 6.3 to 9.3 ± 6.0; p < 0.05) Secondary Outcome – Quick Inventory of Depressive Symptomatology score had significantly improved in the rTMS group (from 17.0 ± 6.7 to 9.9 ± 6.0; p < 0.05) A pilot study, not powered to detect clinically significant changes between groups.	<b>N/A</b> Pilot/ Feasibility Study Clear risk of multiple biases e.g. selection bias
252	N. Sasaki et al. (2017). The efficacy of high-frequency repetitive transcranial magnetic stimulation for improving apathy in chronic stroke patients. <i>European Neurology</i> , 78:445-93 28-32	13 consecutive outpatients. Inclusion criteria: more than one year post stroke, clinical diagnosis of supratentorial intracerebral haemorrhage without invasion into the cerebral cortex or cerebral subcortical infarction in the territory of the MCA, aged 40-85 years, no surgical management, no disturbance of consciousness, no apparent aphasia, no serious complications Recruited in Japan Randomised controlled trial rTMS (n=7): mean age at admission 66.1 (SD 11.2), 71% male	Randomly assigned to rTMS or sham stimulation “on the basis of the date of their entry into this study”. Intervention or control scheduled to receive 5 sessions over 5 consecutive days as outpatients. rTMS: intensity 80% of the resting motor threshold. 20 mins (2,000 pulses per session). Sham stimulation: with pseudo coil that	Apathy Scale (AS) Quick Inventory of Depressive Symptomatology (QIDS) Completed by OT (blind to allocation) before first application and immediately after the last application.	Groups comparable at baseline on AS and QIDS AS score significantly improved in the rTMS group (p<.05) but not in the sham group. Degree of change on AS score significantly greater in the rTMS group than sham group. QIDS score significantly improved in the rTMS group (p<.05) but not in the sham group. Degree of change on QIDS non significantly greater in rTMS than sham group.	<b>SIGN -</b> Low quality. Not clear on randomisation and allocation concealment.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		Sham (n=6): mean age at admission 62.8 (SD 10.1), 100% male Time between admission and intervention mean 4.7 years (SD 4.3).	was not connected to the stimulator. Received recorded sounds of 10Hz from speaker for 20 mins.			
253	E. R. Skidmore et al. (2015). Strategy Training During Inpatient Rehabilitation May Prevent Apathy Symptoms After Acute Stroke. <i>PM and R</i> , 7:6 562-570	- Secondary analysis of randomized controlled trial - 30 Acute inpatient rehab setting - Acute stroke patients with cognitive impairment	-patients were randomized into a 15 subject treatment group and a 15 subjects active listening group -trainers blinded to group assignments - Apathy training: based on goal strategy training - Listening: reflections on rehab experiences	- Apathy Evaluation Scale was used - time 1 admission - time 2 at 3 months - time 3 at 6 months	- treatment group/Apathy goal strategy training showed large difference to control group at 3month (p=.013); and moderate to large at 6month (p=.073)	++ SIGN = high quality - As there are limited options for effective treatments in acute stroke rehab. This is an interventions which would be highly acceptable by clinical rehab teams and from a pragmatic point easily implementable. The outcomes are promising and increased goal activation would clinically optimise patients overall rehab participation and their outcomes Psychiatric rather than neurological/neuroscientific definition of apathy was used. This may have played a role for the choice of the most valid intervention method: i.e. was the goal strategy training too much focussed on 'insight' rather than basal ganglia/brain stem functioning?
253	E. R. Skidmore et al. (2015). Strategy Training During	Acute inpatient rehabilitation Secondary analysis of randomized controlled trial.	Strategy training (one session/day, 5 days per week, in addition	Apathy Evaluation Scale at study admission, 3 and 6 months	A significant group by time interaction (F2,28 =3.61, p =.040) indicated that changes	- Low quality

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	Inpatient Rehabilitation May Prevent Apathy Symptoms After Acute Stroke. <i>PM and R</i> , 7:6 562-570	N=30 Participants with acute stroke who exhibited cognitive impairments and were admitted for inpatient rehabilitation	to usual inpatient rehabilitation		in apathy symptom levels differed between groups over time. The magnitude of group differences in change scores was large ( $d=-0.99$ , $t_{28}=-2.64$ , $p=.013$ ) at month 3, and moderate to large at month 6 ( $d= -0.70$ , $t_{28}=-1.86$ , $p=.073$ )	Small numbers – only a pilot study No power calculation