

CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Stroke Rehabilitation Evidence Tables Management of the Upper Extremity following Stroke

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STROKE REHABILITATION Writing Group

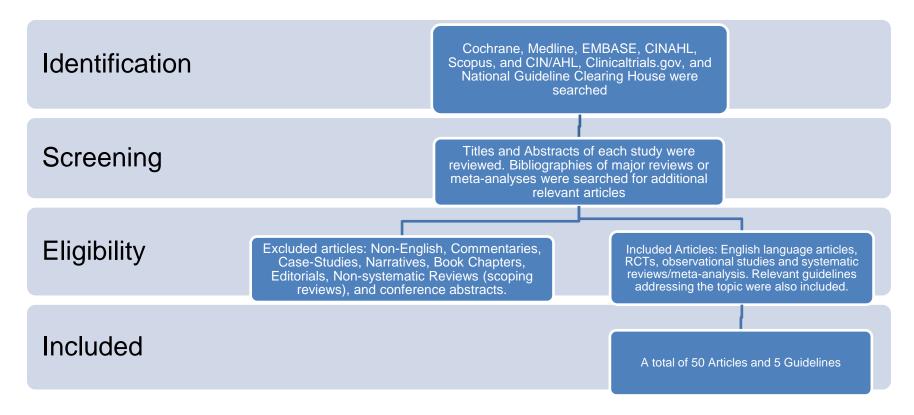
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Search Strategy



Cochrane, clinicaltrials.gov, Medline, EMBASE, CINAHL, Scopus were searched using the keywords: Stroke AND ("upper extremity" OR "upper limb" OR "hand" OR "arm") AND (rehabilitation OR therapy OR intervention). The same databases were searched to identify paediatric related evidence using additional keywords: (stroke OR CVD OR cerebrovascular disease) AND (rehabilitation OR intervention OR therapy) AND (paediatric OR paediatrics OR youth OR child OR children OR young) AND ("upper limb" OR "upper extremity" OR shoulder OR hand OR arm). Titles and abstract of each article were reviewed for relevance. Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, non-systematic review, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review. A total of 50 articles and 5 guidelines were included and were separated into separate categories designed to answer specific questions.

Published Guidelines

Guideline	Recommendations
Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with stroke: rehabilitation, prevention and management of complications, and discharge planning. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2010 Jun. 101 p.19	Upper-Limb Function-Summary of Recommendations (4.3.1) Consider constraint induced movement therapy; mental practice; electromechanical/robotic devices Not recommended repetitive task training/splinting; increased intensity of rehabilitation Insufficient evidence Electrostimulation; routine EMG biofeedback; virtual reality; bilateral training; approach to therapy
Management of Stroke Rehabilitation Working Group. VA/DoD clinical practice guideline for the management of stroke rehabilitation. Washington (DC): Veterans Health Administration, Department of Defense; 2010. p. 96	13.6 Recommendations 1. Recommend that UE functional recovery should consist of the practice of functional tasks, emphasizing progressive difficulty and repetition. 2. Recommend that treatment should be tailored to the individual patients considering the intervention that are most appropriate, engaging the patient, and are accessible and available. 3. Recommend Constraint-Induced Movement Therapy (CIMT) for individuals with at least 10 degrees of extension in two fingers, the thumb and the wrist. A 4. Recommend robot-assisted movement therapy as an adjunct to conventional therapy in patients with deficits in arm function to improve motor skill at the joints trained. B 5. Recommend bilateral practice to improve UE function. B 6. Recommend treatment with FES for patients who have impaired upper extremity muscle contraction, specifically with patients with elbow/wrist motor impairment. B 7. Recommend FES for patients who have shoulder subluxation. B 8. Consider FES and mental practice combined with repetitive and intense motor practice of functional tasks. B 9. Consider strengthening exercises in addition to functional task practice. C 10. Consider virtual reality as practice context. C 11. Insufficient evidence to recommend Mirror therapy. I 12. Do NOT use repetitive practice of movements in rehabilitation of upper extremity.
Clinical Guidelines for Stroke Management 2010. Melbourne (Australia): National Stroke Foundation; 2010 Sep. p. 87.	Upper-limb activity People with difficulty in their upper limb(s) should be given the opportunity to undertake as much tailored practice of upper limb activity (or components of such tasks) as possible. Interventions which can be used routinely include: Constraint-induced movement therapy in selected people; repetitive task-specific training; mechanical assisted training One or more of the following interventions can be used in addition to those listed above: Mental practice, EMG biofeedback in conjunction with conventional therapy, electrical stimulation, mirror therapy, bilateral training
Duncan PW, Zorowitz R, Bates B, Choi JY, Glasberg JJ, Graham GD, Katz RC, Lamberty K, Reker D. Management of adult stroke rehabilitation care: a clinical practice guideline. Stroke, 2005;36:e100-e143.	Recommend considering the use of CI therapy for a select group of patients—that is, patients with 20 degrees of wrist extension and 10 degrees of finger extension, who have no sensory and cognitive deficits. To date the only demonstrated benefit occurs in individuals who received 6 to 8 hours of daily training for at least 2 weeks. Recommend treatment with FES for patients who have demonstrated impaired muscle contraction, specifically with patients with ankle/knee/wrist motor impairment. There is insufficient evidence to recommend for or against using NDT in comparison to other treatment approaches for motor retraining after an acute stroke. The Working Group makes no recommendation for or against routine use of biofeedback for poststroke patients. The use

Guideline	Recommendations
	of biofeedback is left to the consideration of the individual provider.
Intercollegiate Stroke Working Party. National clinical guideline for stroke, 4th edition. London: Royal College of Physicians, 2012.	6.7.1 Recommendations A Patients who have some arm movement should be given every opportunity to practise activities within their capacity. B Constraint induced movement therapy (CIMT) should only be considered in people who have 20 degrees of active wrist extension and 10 degrees of active finger extension, and should only be started if the team has the necessary training and the patient is expected to participate fully and safely. C Bilateral arm training involving functional tasks and repetitive arm movement to improve dexterity and grip strength should be used in any patient with continuing limitation on arm function. 6.15.1 Recommendation A Robot-assisted movement therapy should only be used as an adjunct to conventional therapy when the goal is to reduce arm impairment or in the context of a clinical trial. 6.16.1 Recommendation B Repetitive task training for the upper limb, such as reaching, grasping and other functionally meaningful tasks, should be used to assist in rehabilitation of the arm post stroke
	6.17.1 Recommendation A People with stroke should be taught and encourage to use mental practice of an activity to improve arm function, as an adjunct to conventional therapy.

Summary of Therapeutic Upper-Extremity Interventions and Associated Strength of Evidence from Selected Guideline Documents

Intervention	CBPR 2013	SIGN 118 2010	NSF 2010	VA/DoD 2010	AHA/ASA 2005	RCP 2012
CIMT/mcIMT	Recommends mCIMT Recommends CIMT (late) [A] Not recommended (early) [A]	В	А	А	С	Recommended
Mental practice	Recommends [Early – A; Late – B]	D	В	Not included	Not included	Recommended
Mirror therapy	Recommends [A]	Not included	С	I	Not included	I
Bilateral arm training	Recommends	I	С	В	Not included	Recommended
Electrical stimulation	Recommends [Early – A; Late – A]	I	С	В	В	Not recommended (clinical trials only)
Task-specific training	Recommends [Early – A; Late – A]	A (not recommended)	В	Not recommended	Not included	Not Included
Robotic devices	Not included	A	В	В	Not included	Recommended (as adjunct therapy)
EMG biofeedback	Not recommended	I	Not included	С	No recommendation made	Not recommended (clinical trials only)
Virtual reality	Recommends [B]	I	Not included	С	Not included	Not Included
Therapy approaches	One approach not recommended over another	I	Not included	Not included	I	Not included
Splinting	Not included	B (not recommended)	Not included	Not included	Not included	Not recommended
Increased intensity (specific to UE)	Not included	B (not recommended)	Not included	Not included	Not included	Not included
Strengthening	Recommends	Not included	Not included	В	Not included	Recommended
GRASP	Recommends [Early – A; Late – C]	Not included	Not included	Not included	Not included	Not included

Evidence Tables

Repetitive Task Training

<u>-</u>	<u> </u>				
Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Patten et al. 2013 USA Cross-over RCT	CA: ☑ Blinding: Assessor ☑ Patient ☑ ITT: 図	19 subjects in the chronic phase of stroke (12.96 months) with at least 10° of active wrist extension, 10° active thumb abduction, and 10° active extension of any two digits, three times within one minute.	Subjects were randomized into one of two groups: 1) functional task practice (FTP), or 2) HYBRID (combined FTP plus power training). Treatment was delivered in two, 4-wk blocks of twelve, 75min sessions interspersed with a 4wk washout period. Subjects then crossed over and received the other treatment protocol.	Primary Outcomes: Wolf Motor Function Test- Functional Abilities Scale (WMFT-FAS) Subjects were evaluated at baseline, following each block of therapy, following the washout period, and 6 months post-intervention.	Improvement in WMFT-FAS scores were significantly greater following HYBRID vs. FTP (p=0.049) regardless of the order of treatment. These improvements were retained 6-months post intervention (p=0.03).
Shimodozone et al. 2012 Japan RCT	CA: ☑ Blinding: Assessor ☑ Patient ☑ ITT: ☑	49 subjects in the sub- acute phase of stroke (experimental=6.4±2.1wk; control=7.4±3.0wk) having Brunnstrom proximal upper-limb stage ≥III.	Subjects were randomized to one of two groups: 1) repetitive facilitative exercise (RFE), or 2) controlconventional rehabilitation program. Both groups received 40 min sessions 5x/wk for 4 weeks of their allocated treatment. Both groups performed 30 min/day of dexterity-related training immediately after each treatment session. They also continued their participation in a standard inpatient rehabilitation program (e.g., physical therapy, mobility, speech).	Primary Outcomes: Action Research Arm Test (ARAT), Fugl-Meyer Assessment (FMA) Outcomes were assessed at baseline, and at week 2 and 4.	After 4 weeks of treatment, significantly larger improvements on the ARAT (p=0.009) and FMA (p=0.019) scores for the RFE group compared to the control group.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Han et al. 2012 China RCT	CA: ☑ Blinding: Assessor ☑ Patient 函 ITT: 函	32 subjects having impaired motor function of arm which was due to one or more of the following: weakness, sensory loss, ataxia, visuospatial impairment, on average, 40 days post stroke.	Subjects were randomized into one of three groups. All groups received arm training (5x/wk for 6 wks) including correct positioning and caring of the arm, passive, assisted and active movements, strength training, functional activities with varying intensities: 1) Group A-1 hr, 2) Group B-2 hr, or 3) Group C-3 hr.	Primary Outcomes: Fugl-Meyer Assessment (FMA), Action Research Arm Test (ARAT) Outcomes were assessed at baseline, two weeks, four weeks, and six weeks after treatment.	After two weeks, there were no significant between-group differences in FMA and ARAT scores (p>0.05). After four weeks of treatment, the improvements in FMA scores were more significant in group C than in groups A and B (p<0.05). There were no significant differences in FMA scores between groups A and B (p>0.05). The ARAT score improvement was more significant in group C than in group A (p<0.05). There were no significant differences in ARAT scores between groups A and B or groups B and C (p>0.05) After six weeks of treatment, the FMA and ARAT scores had increased significantly in each group (p<0.05 for all); FMA and ARAT scores improved more significantly in groups C and B than in group A (p<0.05). There were no significant differences in FMA and ARAT scores between groups B and C (p<0.05).
Langhorne et al. 2009 Systematic review and meta-analysis	N/A	8 RCTs specific to UE identified from a Cochrane review (French et al. 2007) from a total of 14 studies Subjects in these 6 studies were recruited in the first week following stroke up to 50 days; the remainder were recruited in the chronic phase of stroke	Comparison of task- specific training protocols +/- routine rehabilitation vs. control conditions that included other therapy approaches or a lower- limb therapy program. Treatment duration varied widely from a total of 20 to 63 hours provided over a 2 week to 11 week period.	MAS (upper arm and hand sections), Jebsen Taylor Hand Function Test, Upper Extremity Function Test, ARAT, Southern Motor Group Assessment, 10-hole Peg Test, RMA Scale, WMFT Outcomes were assessed before and after treatment. In 5 studies there were follow- up periods of 4, 6 and 9 months and 4 years.	Arm function: SMD=0.19, 95% CI -0.01 to 0.38, >0.05 (414 subjects) Hand function: SMD= 0.05, 95% CI (-0.18 to 0.29, p>0.05 (281 subjects) (Author recommends that task specific training should be used improve ADLs) Adverse events: No reporting

GRASP (Graded Repetitive Arm Supplementary Program)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Harris et al. 2009 Canada RCT	CA: ⊠ Blinding: Assessor ☑ ITT: ☑	103 subjects with infarct or hemorrhagic stroke recruited an average of 21 days following stroke	Comparison of a 4 week home-based, self-administered program designed to improve ADL skills through strengthening, ROM and gross/fine motor skills exercises vs. a non-therapeutic education control program	Primary Outcomes: Chedoke Arm & Hand Activity Inventory-9 (CAHAI) Secondary Outcomes: ARAT, MAL, hand grip strength, SF-12, pain, fatigue. Outcomes were assessed before and after treatment and at 3 months post treatment	At the end of the treatment period, subjects in the GRASP group had significantly higher CAHAI scores compared with the control group (32.6 to 46.7 vs. 32.7 to 40.1; mean change from baseline: 14.1 vs. 7.9, p<0.001. The improvement was maintained at 3 months (mean total score: 50.4 vs. 45.4, p=0.037). Completion rate was 60/103 (58%). At the end of the treatment period, subjects in the GRASP group had significantly higher ARAT and MAL scores and grip strength compared with the control group. ARAT: 31.1 to 42.8 vs. 31.0 to 38.0, p=0.025; grip strength (kg): 9.0 to 13.1 vs. 8.8 to 10.8, p=0.027; MAL (AOU): 2.0 to 3.3 vs. 1.9 to 2.8, p=0.023; MAL (QOU): 2.0 to 3.2 vs. 1.8 to 2.7, p=0.007. Completion rate: 60/103 (58%) Adverse events: pain n=15

Constraint-Induced Movement Therapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Nijland et al. 2011	N/A	5 RCTs (106 subjects who were recruited within 2 weeks of stroke onset)	Comparison of dose- match CIMT vs. control condition.	Fugl Meyer Assessment, Grooved Pegboard test (GPBT), MAL, ARAT, BI,	FMA: MD= 11.0; 95% CI 2.5 to 19.5, p=0.01 Results from 3 studies were included. (subgroup analysis indicated that LO CIMT was more
Netherlands			3 studies compared hi-	FIM, Wong-Baker Faces Scale, Geriatric Depression	effective).
Systematic review and			dose (HI) CIMT provided for 3 hours/day for 5-6	Scale	ARAT: MD=7.88, 95% CI 1.01 to 14.7, p=0.21 Results from 4 studies were included. (subgroup
meta-analysis			days/week for 2 weeks vs. control; 2 studies compared low-dose (LO)	Timing of outcome assessment not stated	analysis indicated that LO CIMT was more effective).
			CIMT provided for either		MAL (AOU): MD=1.15; 95% CI -0.33 to 2.62,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Sirtori et al.	N/A	19 RCTS (619 subjects)	½ hour/day 3 days/week for 10 weeks, or 2 hours/day, 5 days/week for 2 weeks vs. control; 1 study compared HI vs. LO CIMT vs. control. Constraints were worn for 5-6 hours/day or up to 90% of waking hours in all studies.	Primary Outcomes:	p=0.13. Results from 3 studies were included. (subgroup analysis indicated that LO CIMT was more effective). MAL (QOM): MD=1.11; 95% CI 0.81 to 1.41, p<0.001. Results from 3 studies were included. (subgroup analysis indicated that LO CIMT was more effective). GPBT: MD=0.05; 95% CI 0.02 to 0.09, p=0.004. Results from 2 studies were included. Disability post-intervention: SMD=0.36, 95% CI .06
2009 Italy Cochrane Review	TWA	Time since stroke was < 3 months in 5 trials, 3 to 9 months in 5 trials and > 9 months in 5 trials.	hours/day), modified CIMT (<3 hours therapy/day) and forced use vs. conventional rehabilitation or no additional rehabilitation	Disability: BI, FIM Secondary outcomes: WMFT, ARAT, Arm Motor Ability Test, Emory Function test, Assessment of motor and process skills, MAL, CMII, hand strength, Fugl Meyer Assessment, 9-Hole Peg Test, Grooved Pegboard Test, SIS	to 0.65, p= 0.018. Results from 6 studies included. Disability at three to six-month follow up: SMD= -0.07, 95% CI -0.53 to 0.40, p= 0.78. Results from 2 studies included. In subgroup analysis of time since stroke onset, effect sizes were estimable for 0 to 3 months (2 studies-SMD=0.18, 95% CI -0.31 to 0.67, p=0.47) and > 9 months (2 studies-SMD= 0.49, 95% CI -0.02 to 1.00, p=0.06). Arm Motor Function: SMD=0.72, 95% CI 0.32 to 1.12, p<0.0001. Results from 11 studies were included.
Singh et al. 2013 India RCT	CA: 图 Blinding: Assessor 图 Patient 图 ITT: 图	40 subjects having at least 10° of active extension of each metacarpophalengeal joints, inter-phalengeal joints of all the digits and 10° wrist extension of the affected limb, in the subacute phase of stroke (experimental=18.3±3.3 days; control= 19.6±3.9 days).	Subjects were randomized into one of two groups: 1) experimental - 2 hours of structured modified CIMT (m-CIMT) therapy 5x/wk for 2 wk plus use of a mitt to restrain affected arm 10h/day for 2 week, or 2) control - conventional rehabilitation timematched to experimental group.	Primary Outcomes: Wolf Motor Function Test (WMFT), Fugl-Meyer Assessment (FMA) Outcomes were assessed pre- and post-intervention.	For both groups, WMFT (p=0.003, p<0.001, respectively) and FMA (p<0.001 for both) scores improved significantly between baseline and post intervention. No between-group statistics were reported, although the difference in scores between pre and post were greater on both the WMFT and FMA for the experimental group compared to the control group.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Dromerick et al. 2009 USA VECTORS Trial	CA: ☑ Blinding: Assessor ☑ ITT:☑	52 subjects recruited within 28 days of admission to hospital with ischemic or hemorrhagic stroke and persistent hemiparesis.	Comparison of 2 weeks of standard CIMT (2 hours/day + constraint worn for 6 hours/day shaping exercises) vs. high-intensity CIMT (3 hours/day of shaping exercises + constraint worn for 90% of waking hours) vs. conventional occupational therapy	Primary Outcomes: ARAT Secondary outcomes: NIHSS, FIM, SIS, pain, Geriatric Depression Scale Assessments were conducted at baseline, 2 weeks and 3 months	At 3 months, subjects in the high-CIMT group had significantly lower mean total ARAT and SIS scores compared with subjects in the standard CIMT and control groups. ARAT (baseline to 3 months) Control: 19.7 ±3.7 to 45.3±3.7 Standard CIMT: 22.7±3.5 to 46.9±3.5 High CIMT: 25.4±3.9 to 38.0±3.8 (F=3.06, p=0.01) SIS (hand and arm) 3 months: Control: 72.2±6.4 Standard CIMT: 78.7±6.2 High CIMT: 55.0±6.6 (F=3.88, p=0.02) There were no differences among groups on FIM (upper extremity) scores at 3 months.
					Adverse events: not reported
Wolf et al. 2006 USA	CA: ☑ Blinding:	222 subjects with stroke onset of 3 to 9 months. (first-ever ischemic or	Comparison of CIMT vs. usual care.	Primary Outcomes: WMFT, MAL	203 subjects completed the treatment; data from 169 subjects were included in 12 month assessment.
	Assessor ☑	hemorrhagic stroke)	CIMT: 6 hours of shaping	Secondary Outcomes: FIM,	
EXCITE Trial	ITT:⊠	Patients were recruited	(task practice) each weekday + constraint	SIS	From baseline to 12 months, the CIMT group showed greater improvements than the control
RCT	(Primary analysis only)	who met criteria for either higher or lower motor function, High: at least 20° of wrist extension and at least 10° of active extension of each metacarpophalangeal and intraphalangeal joint of all digits. Low: 10° of active wrist extension, at least 10° of thumb	worn for a goal of 90% of waking hours (7 days/week), for 2 weeks Control group: usual care, which could range from no therapy to a formal structured therapy program.	Assessments were conducted at baseline, post-treatment and follow-up at 3, 8 and 12 months	group in both the WMFT Performance Time (19.3 to 9.3 seconds vs. 24.0 to 17.7 seconds, p<0.001) and in the MAL Amount of Use (1.21 to 2.13 vs. 1.15 to 1.65, p<.001) and MAL Quality of Movement (1.26 to 2.23 vs. 1.18 to 1.66, p<.001). In sub group analyses, there were no differences in any of the outcomes based on baseline hand function (hi vs. low) at 12 months. 35 serious adverse events were reported, none of which appeared to be related directly to the intervention.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		abduction/extension and at least 10° of extension in at least 2 additional digits			

Mental Practice

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Barclay-Goddard et al. 2011	N/A	6 RCTs (119 subjects with upper-extremity deficits)	Compared studies of MP + other treatment vs. other treatment	Primary Outcomes: Activity and activity limitations (Box & Block test, TEMPA, ARAT, MAS, Frenchay Arm Test,	SMD=1.37 (95% CI; 0.60 to 2.15, p<0.0001) Subgroup analysis based on stroke chronicity and dosage not possible due to small numbers.
Canada Cochrane Review		Mean chronicity of stroke for subjects was 3 weeks (1 study), 7 weeks (1 study) and > 6 months (4 studies)	Length of treatment ranged from 3 to 10 weeks	WMFT, components of BI)	No evidence of adverse events.
Timmermans et al. 2013	CA: 🗷 Blinding:	42 subjects who were 2- 6 weeks post stroke with elbow flexor strength	Subjects were randomized into one of two groups and trained	Primary Outcomes: Fugl-Meyer Assessment (FMA), Wolf Motor Function	There were no significant differences between groups over time on either the FMA or WMFT (p>0.05 for both).
Netherlands RCT	Assessor ☑ Patient 坚 ITT: ☑	Medical Research Council grades 1-3.	3x/day for 6 weeks: 1) conventional rehabilitation plus 10 min mental practice-based	Test (WMFT). Outcomes were assessed at baseline, post-intervention,	
			training (basic imagery principles, DVD viewing) for 10 min per session, or 2) usual therapy and additional bimanual upper extremity techniques based on neurodevelopmental principles for 10 min per session	and at 6- and 12-month follow-up.	
letswaart et al. 2011	CA: 🗷	121 subjects within 1-6 months of stroke onset	3 groups received treatment 3 days a week	Primary Outcomes: Action Research Arm test assessed	There were no differences among groups on any of the outcomes.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
UK RCT	Blinding: Assessor ☑ ITT:☑	with residual upper-limb weakness (ARAT score between 3 and 51)	for 45 min x 4 weeks. (total of 12 sessions) + an additional 8 structured independent, 30-minute audiotaped guided sessions. Motor imagery group (n=41), attention placebo control (n=39) and usual care control (n=41). Patients in the motor imagery group mentally rehearsed upper-limb movements while patients in the attention placebo group performed equally intensive non- motor mental rehearsal for same duration.	before treatment and at 5 weeks. Secondary outcomes: grip strength, hand function (manual dexterity performance speed measured in sec), BI, modified Functional Limitation Profile	Mean ARAT scores before/after treatment Motor Imagery training group: 25.6 ±18 to 31.5±20.7; Attention-placebo control: 26.2 ±17.8 to 32.9±20.8; Usual care group: 23.1 ±17.7 to 30.4±20.5 Mean BI scores before/after treatment Motor Imagery training group: 13.1 ±4.8 to 16.3±4.1; Attention-placebo control: 14.8 ±4.3 to 16.8±3.8; Usual care group: 12.3±5.4 to 14.9±4.8 Adverse events: No reporting
Riccio et al. 2010 Italy RCT	CA:⊠ Blinding: assessor ☑ ITT:⊠	36 hemiplegic subjects an average of 8 weeks post stroke onset with Motricity Index (UE) scores ≥30	Subjects in group A received 3 weeks of rehabilitation (3 hrs/day x 5 days/week) followed by 3 weeks of therapy + 60 minutes of mental practice (audio tape guided). Subjects in group B received the same treatment protocol but in reverse order (therapy + MP followed by therapy)	Primary Outcomes: Motricity Index (upper extremity) Secondary Outcomes: Arm Functional test (time), Arm functional test (Functional Ability Scale) Evaluations were conducted at baseline, and at 3 and 6 weeks.	At 3 weeks, subjects in group B had significantly higher scores on all outcomes Mean MI changes: 11.3 vs. 1.7, p<0.05; Mean AFT-FAS changes: 10.5 vs. 1.6, p<0.05; Mean AFT-T:-14.6 vs0.7, p<0.05. At 6 weeks, patients in group A had achieved similar gains; they had improved significantly from baseline on all outcomes assessed. There were no significant differences between groups at that point.

Bilateral Arm Training

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Van Delden et al. 2012 Netherlands Systematic Review and meta- analysis	N/A	9 RCTs (452 subjects) 8 included trials included chronic stroke subjects, 1 included acute (<30 days) 4 studies included subjects with mild hemiparesis, 2 with moderate hemiparesis, and 3 studies included patients with mild, moderate and severe hemiparesis.	Compared studies of unilateral arm training with bilateral arm training (motor task performed simultaneously with both limbs). Studies using robot assistance, electrical stimulation, mirror therapy or virtual reality were excluded. Interventions were provided from 20 minutes to 6 hours/day, 3 to 6 days/week for 1 to 8 weeks	Impairment: Fugl Meyer, Motor Status Score Activity: ARAT, WMFT	Impairment: SMD=0.06; 95% CI -0.20 to 0.33, p=0.65 Activity: SMD=0.20; 95% CI 0.0 to 0.4, p=0.05 Adverse events: No reporting
Coupar et al. 2010 UK Cochrane Review	N/A	18 RCTs (549 subjects) 14 RCTS (421 subjects) were included in pooled analysis 12 trials included subjects with chronic stroke, 4 trials included subjects with stroke onset <3 months, one trial included both acute and chronic stroke subjects. Time since stroke was not reported in 1 trial.	Comparisons of bilateral training vs. placebo/no intervention, bilateral training vs. usual care, bilateral training vs. specific intervention or programs 7 trials used adjunctive treatments (electrical stimulation, robotic devices, auditory cueing) Intervention period ranged from a single session up to 30 sessions over a 6-week period.	Primary outcomes ADL: BI, Rivermead ADL, Rivermead Motor Ability Scale, Rankin Scale, FIM, Katz ADL, Rehabilitation Action Profile Functional movement: ARAT, Motor Assessment Scale, Frenchay Arm Test, WMFT, Upper-Extremity Function Test, Box & Block Test, TEMPA, Chedoke Arm and Hand Activity Inventory Secondary outcomes Extended ADL: Nottingham EADL, Rivermead EADL, Frenchay Activity Index Motor impairment: Fugl Meyer Assessment, Rivermead Motor Assessment, Motor Club Assessment	Bilateral training versus usual care ADL (FIM): SMD= 0.25; 95% CI -0.14 to 0.63, p=0.21 Results from 3 studies were included. Functional movement (Arm function): SMD= -0.07; 95% CI -0.42 to 0.28, p=0.68. Results from 4 studies were included Extended ADL: SMD=0.1; 95% CI -0.47 to 0.77, p=0.63. Results from 1 study included Motor impairment: SMD= 0.43; 95% CI 0.06 to 0.81, p=0.023. Results from 4 trials included Bilateral training versus other upper limb intervention ADL: SMD=-0.25; 95% CI -0.57 to 0.08, p=0.14. Results from 3 trials included Functional movement (arm function): SMD= -0.20; 95% CI 0.49 to 0.09, p=0.18. Results from 6 studies included EADL: SMD= -0.65, 95% CI -1.29 to -0.01, p=0.04.5 Results from 1 study included Motor Impairment: SMD= -0.25; 95% CI -0.55 to 0.0, p=0.099. Results from 4 studies included

Mirror Therapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Thieme et al. 2013 Germany Cochrane Review	N/A	14 studies (567 subjects) Studies included subjects with acute/subacute and chronic stroke.	Comparison of mirror therapy vs. no treatment, usual/standard practice or other any other control treatment Treatment duration of 30- 45 minutes, 3-5 days/week for 3-6 weeks	Primary outcome Motor function: Fugl Meyer Assessment, ARAT WMFT (functional ability), Motor Assessment Scale, Brunnstrom Secondary outcome: ADL: FIM, BI, pain and visuospatial neglect	Motor function at end of treatment: SMD=0.61; 95% CI 0.22 to 1.0, p= 0.00220. Results from 11 studies were included. Motor function at 6 month follow-up: SMD=1.09; 95% CI 1.09 to 1.87, p= 0.0068. Results from 4 studies included ADL at end of treatment: SMD=0.33; 95% CI 0.05 to 0.60, p= 0.020. Results from 4 studies included. One study reported assessment of adverse events
Ezendam et al. 2009 Netherlands Systematic review (narrative)	N/A	15 studies including 5 that were stroke specific. Sample sizes of included trials: n=1, n=2, n=9, n=16, n=36 3 studies included chronic stroke subject, 2 included subacute and chronic	Comparison of mirror therapy vs. control condition during object manipulation tasks, in addition to conventional rehabilitation therapies. Treatment duration of up to 1 to 5 hours/day for 4 to 5 weeks.	27 outcomes assessed across 5 stroke studies including: ROM, speed and accuracy of reaching tasks, grip strength, shoulder flexion/abduction/external rotation, functional reach, timed tasks, CMSA, spasticity, Brunnstrom, FIM, ARAT	All studies reported improvements in arm and hand function over the study period, which was maintained at follow-up. Subjects were followed in 3 studies for differing periods (4, 10 and 12 weeks). Treatment was not associated with improvement in spasticity. Adverse events: No reporting
Radajewska et al. 2013 Poland RCT	CA: 図 Blinding: Assessor 図 ITT: 図	60 right-handed participants, a mean of 9.25 weeks post first ever stroke.	Patients were randomized to mirror therapy (n=30) or a control group (n=30). Within each group, patients were divided into left- versus right-arm paresis subgroups. Both groups received standard rehabilitation. The treatment group received 15 minute sessions of mirror therapy 2x/day, 5d/wk for 3 wk.	Primary Outcomes: Functional Index 'Repty', Frenchay Arm Test, and Motor Status Score Outcomes were assessed at baseline, post intervention and at 3-week follow-up.	When evaluating the left-handed subgroups, those in the mirror therapy group showed a greater improvement on the Frenchay Arm test than those in the control group (p=0.035) but no significant differences were shown on the other measures (p>0.05 for all). No significant between-group differences were noted for the right handed subgroups (p>0.05 for all).
Wu et al. 2013 Taiwan RCT	CA:☑ Blinding: Assessor ☑	44 community dwelling individuals, within 2 years post stroke, meeting the following criteria: first-ever	Patients were stratified based on FMA-UE scores 26-40 or 40-66. Patients then received either mirror therapy or	Primary Outcomes: FMA-UE Secondary Outcomes: Revised Nottingham	The mirror therapy group showed significantly greater improvement compared to the control group on FMA-UE (p=0.009). No significant between-group differences were found for the Motor Activity Log (p>0.05) and ABILHAND

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	ITT: ⊠	unilateral stroke, Fugl Meyer Assessment Upper Extremity (FMA- UE) score of 26-56, and Modified Ashworth Score of <3.	traditional therapy (control group). Treatment was 1.5 hrs/d, 5d/wk, for 4 weeks. Specifically, the treatment group had 1hr mirror therapy and 0.5hr task-oriented practice.	Sensory Assessment (rNSA), Motor Activity Log, and ABILHAND questionnaire.	(p>0.05).
Thieme et al. 2012 Germany RCT	CA:☑ Blinding: assessor ☑ ITT:☑	60 subjects with severe paresis within 3 months of stroke onset	Comparison of individual motor therapy vs. group mirror therapy vs. control condition with restricted view of the affected arm during inpatient rehabilitation In all 3 groups, patients received a maximum of 30 minutes/day of mirror/control therapy. 20 sessions over 5 weeks in addition to regular therapies.	Primary Outcomes: Fugl Meyer Assessment, (arm section) ARAT Secondary outcomes: BI, SIS, Ashworth Scale, Star Cancellation Test Outcomes were assessed before and after treatment	Subjects in all groups improved over the treatment period, but there were no significant differences between groups on any of the outcomes assessed except MAS (finger) and the SCT, both favouring greater improvement in the individual mirror therapy group (median Δ 1 vs. 0 vs. 0, p<0.05; Δ mean 20 vs. 4.4 vs2.3, p<0.01). Drop outs: individual mirror therapy- 3, group mirror therapy- 5, control therapy-4.

Strength Training

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Harris & Eng 2010	N/A	13 RCTs (517 subjects)	Comparison of programs	Grip strength	Grip strength: SMD=0.95, 95% CI 0.05 to 1.85,
		Subjects in 9 studies	that included a	Upper limb function (Motor	p=0.04. Results from 5 studies included
Canada		were recruited an	component of	Assessment Scale, TEMPA,	ADL: SMD=0.26, 95% CI -0.10 to 0.63, p=0.16.
		average of < 20 weeks	strengthening or	Rivermead Motor	Results from 5 studies included
Systematic		following stroke onset, 4	resistance training	Assessment, Purdue Peg	Limb function: SMD=0.21, 95% CI 0.03 to 0.39,
review and meta-		studies recruited	(excluding robotic	Board, WMFT, Box & Block	p=0.03. Results from 11 studies included.
analysis		subjects in the chronic	devices, electrical	test, ARAT, Functional Test	Subgroup analysis: subacute phase (8 trials)
		stage of stroke	stimulation, CIMT) vs. a	of the UE)	SMD=0.27, 95% CI 0.06 to 0.48, p=0.01; chronic
			control condition, which	ADL (SF-36 Physical	phase (4 trials) SMD=0.32, 95% CI 0.02 to 0.63,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			could be an active (non- strengthening) program, usual care or no therapy. Average treatment duration was 1 hour, 2- 3x/week for 4 weeks.	Function Subscale, FIM, BI)	p=0.04 Adverse events: 6 studies reported none; no reporting in remaining trials
Dispa et al. 2013	CA: 🗷	10 Subjects (6months post-stroke) having the	Subjects were randomized into two	Primary outcomes: Two- way repeated measure	RM-ANOVA comparison between t ₀ and t ₁ results did not show any significant difference.
Belgium	Blinding: Assessor ☑	ability to lift and hold an object of 250 g between	groups: 1) started with the bilateral movement	analysis of variance (RM- ANOVA)	Results of the paretic hand at t1, t2, and t3 did not detect any difference between the bilateral and
Crossover RCT	Patient ⊠	the thumb and the index finger for a few seconds.	therapy, 2) started with the unilateral movement therapy. Therapy sessions occurred for 1hr 3x/wk for 4wk followed by another 4wk of the opposite treatment.	Outcomes were assessed at inclusion (t ₀), baseline (t ₁), 4 weeks (t ₂), and 8 weeks (t ₃).	unilateral movement therapies (p>0.144 in all instances). A highly significant difference between both hands was detected for digital dexterity (p<0.001). The temporal grip-lift parameters tended to take longer; however, only the loading phase showed a significant difference between both hands (p=0.048). The grip-lift dynamics showed no significant difference between the paretic and the nonparetic hand (p>0.507 in all instances)

Interventions for Sensory Impairment

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Doyle et al. 2010	N/A	13 RCTs (467 subjects) with disturbance in	Types of interventions evaluated included:	36 measures of sensory impairment	All 26 pooled analyses included the results of a single trial.
USA		sensory function	sensory retraining		5g.5 ts
		following stroke.	programs (n=5), electrical	13 measures of UE function	Fugl Meyer upper limb (n=18) MD=-6.0, 95% CI -
Cochrane Review			stimulation (n=2),		16.6 to 4.6
		Subjects in 3 studies	inflatable splints (n=2),		
		were recruited and	thermal stimulation (n=1),		Fugl Meyer wrist/hand (n=18) MD=-0.12, 95% CI -
		average of within 1	rTMS (n=1), intermittent		9.06, 8.82
		month of stroke; subjects	pneumatic compression		
		in 5 studies were	(n=1), tensive		ARAT (n=100) MD=12.9, 95% CI 5.7 to 20.2
		recruited within 6 months	mobilizations (n=1)		

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		of stroke and subjects in 2 studies were recruited in the chronic phase of stroke. Stroke chronicity of subjects was not stated in 3 trials.			% of subjects achieving a >10% improvement in Brunnstrom Fugl Meyer at 12 months (n=100) OR=6.05, 95% CI 2.0 to 18.3 Adverse events: No reporting
Laufer & Elboim-Gabyzon 2011 Israel Systematic review (Narrative)	N/A	15 RCTs or quasi RCTs. Treatment was applied to the UE in 7 studies. Subjects in 5 of the studies included subjects in the chronic phase of stroke; in 2 studies subjects were recruited < 60 days post stroke.	Examination of the effectiveness of TENS on motor recovery Surface electrodes were placed over the median nerve at the wrist in all studies of UE. The ulnar, and radial nerves were also stimulated in 2 studies. Pulse duration ranged from 0.125 to 1 ms. Intensity of stimulation: just below sensory threshold, mild to strong paresthesias Treatment durations were a single 2 hour session (n=5), 2x 2hour sessions (n=1) and 2 hours, 3x/week for 1 month (n=1) Subjects in the control group received sham stimulation, minimal perception, subsensory, or subparathesia levels of TENS	Pinch strength, Jensen-Taylor Hand Function Test (JTHF), FIM, ARAT, tapping frequency Outcomes were assessed before and after treatment only in 4 studies with follow-up at 24 hours (n=1), 30 days (n=1), 2 & 3 months (n=1)	No inferential statistics reported. The pinch strength of subjects in the TENS group was significantly greater than those in the control condition in 2/3 studies. JTHF test scores were higher in TENS group compared with control condition in 4/4 studies. In the single study that assessed ARAT, there was no difference in scores between the study groups. Adverse events: No reporting

Electrical Stimulation

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations				
NMES									
Meilink et al. 2008 Netherlands Systematic review and meta-analysis	N/A	8 RCTs (157 subjects) Subjects in 6 of the studies were recruited in the chronic phase.	Examination of the effectiveness of surface EMG-NMES on motor recovery Treatment: 35-100 Hz, 5-60 mA, average treatment parameter-1 sec ramp up, 5 sec stimulation, 1 sec ramp down, 25 sec rest Duration 2-3 x/day for 30 min, 3-4 days/week for 2-8 weeks Control condition was either no treatment or conventional therapy Treatment contrasts also included EMG-NMES vs. cyclical NMES	ARAT, Fugl Meyer Assessment (UE), Block & Box test, reaction time. No indication of timing of outcome assessment.	FMA (UE): SMD=0.10, 95% CI -0.43 to 0.64, p=0.35. Results from 3 studies included. Box & Block test: SMD=0.37, 95% CI -0.27 to 1.01, p=0.13. Results from 3 studies included. ARAT; SMD=0.0, 95% CI -0.56 to 0.57, p=0.5. Results from 2 studies included Reaction time: SMD=0.41, 95% CI -0.20 to 1.03, p=ns. Results from 2 studies included Adverse events: No reporting				
Boyaci et al. 2013 Turkey RCT	CA: ☑ Blinding: Assessor ☑ Patient ☑ ITT: ☑	31 hemiplegic subjects >4 wk post stroke with the ability to voluntarily extend the wrist.	Participants were randomized into three groups; 1) EMG triggered neuromuscular electrical stimulation (active NMES), 2) passive NMES, and 3) sham stimulation. Treatments occurred for 45 min/day, 5x/wk for 3 wk.	Primary Outcomes: UE motor subscore of Fugl-Meyer Motor Assessment (FMA), self-care of FIM, Motor Activity Log (MAL), modified Ashworth Scale, measurement of joint extension at wrist and metacarpophalangeal (MCP) Outcomes were assessed pre- and post-intervention.	Significant improvements were noted in the UE FMA, MAL, self-care FIM, wrist extension, and grip strength among the active NMES and passive NMES treatments (p<0.05 for all); these improvements were significantly better in the active and passive NMES groups compared with the control group at the end of treatment (p<0.05 for both). There were no significant differences for any parameters between active NMES group and the passive NMES group.				
De Jong et al. 2013	CA:	46 subjects 2-8 weeks post stroke, and a score	Subjects were randomized into one of	Primary Outcomes: Passive ROM	There were no significant group effects or time-by- group interactions on any of the passive range of				

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Netherlands RCT	Blinding: Assessor: ☑ ITT: ☑	of 1-3 on the recovery stages of the Bruunstrom based on the severity of paralysis or severe paresis of the arm.	two groups. Both groups received conventional rehabilitation in accordance with Dutch guidelines. Subjects in the experimental group received arm stretch positioning (60 hr) plus NMES (51 hr) whereas the control group received sham stretching treatment and lowintensity TENS (51 hr).	Outcomes were assessed at baseline, mid-treatment, at the end of the treatment period (8 weeks) and at follow-up (20 weeks).	arm motions.
FES					
Kim et al. 2014 Korea RCT	CA: 🗷 Blinding: Assessor 🗹 Patient 🗹 ITT: 🗵	23 participants <6 mo post-stroke with hemiparesis of upper limb.	Participants were randomized into one of two groups. Both groups were given conventional rehabilitation therapy for 60 min/day, 5 days/wk for 4 wk. For 30 minutes/day, 5 days/wk for 4 wk, the experimental group also received FES with mirror therapy (MT+) while the control group received FES without mirror therapy (MT-).	Primary Outcomes: Fugl-Meyer (FMA) Assessment, Brunnstrom's motor recovery stage (BMRS), Manual Function Test (MFT), Box and Block Test (BBT) Outcomes were assessed pre- and post-intervention.	FMA scores for shoulders, lower arms, wrists, hands and upper limb coordination increased significantly in both groups (p<0.05). Both groups demonstrated a significant improvement in BMRS scores post intervention (p<0.05), but with hand recovery in the experimental group showing significantly greater increases than the control group (p<0.05). Both groups improved MFT scores significantly in shoulder and hand function (p<0.05); the experimental group showed a more significant improvement in hand function than the control group (p<0.05). BBT demonstrated significant improvement in both groups (p<0.05).
Langhorne et al. 2009 UK Systematic review and meta-analysis	N/A	10 trials (126 subjects) specific to UE identified from a Cochrane review (Pomeroy et al. 2009) from 24 studies that examined electrostimulation for promoting recovery of movement or functional ability after stroke + an	Comparison of single channel, multi-channel, patterned multichannel stimulators, EMG-triggered FES, TENS +/-conventional therapy vs. control condition (no stimulation, sham stimulation)	Box & Block test, Fugl Meyer Assessment (UE), MAL, Jebsen-Taylor Hand Function test, MAS, Upper Extremity Function test, ARAT, 9-Hole Peg Test Outcomes were assessed before and after treatment. In a single trial additional	Arm Function: SMD=0.47, 95% CI -0.03 to 0.97, p=ns. (227 subjects) Hand function: SMD=0.12, 95% CI -0.34 to 0.59, p=ns (71 subjects) Adverse events: No reporting (authors recommends that FES of the arm or leg should not be used on a routine basis)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		additional 5 RCTs were identified Subjects in 8 studies were recruited during the chronic phase of stroke, subjects in 7 studies were recruited during the acute or subacute phase.	Frequency of intervention ranged from one to 5x/week for a duration of up to 5 months. Details of the specific magnitudes of the stimulation and treatment protocols are difficult to summarize.	assessments were conducted at 4, 8 and 12 weeks post intervention.	
Page et al. 2012 USA RCT	CA:☑ Blinding: assessor ☑ ITT:☑	32 subjects with chronic stroke with no active extension in the affected wrist	Comparison of 30, 60, or 120-minute sessions of repetitive task-specific practice (RTP) + FES using the Bioness device every weekday for 8 weeks vs. a control group that participated in a 30-minute per weekday home exercise program.	Primary Outcomes: Fugl Meyer Assessment (UE) Secondary outcomes: Arm Motor Ability test, Box & Block Test, ARAT Outcomes were assessed one week before and one week after intervention	No overall test of group x time interaction reported for any of the outcomes. FMA change score from baseline to post intervention: Control group (n=7): 1.2±3.0 , p=0.23 30 min group (n=9): 1.9 ±1.6, p=0.30 60 min group (n=8): 1.3±2.2, p=0.22 120 min group (n=8): 4.1±2.9, p=0.0007 Adverse events: No reporting
tDCS	·				
Khedr et al. 2013 Egypt RCT	CA: ☑ Blinding: Assessor ☑ Patient ☑ ITT: ☑	40 subjects with ischemic stroke resulting in acute hemiparesis, mean time since onset of stroke 12.9 days.	Subjects were randomized into one of three groups: 1) anodal tDCS over affected hemisphere, 2) cathode tDCS over unaffected hemisphere, or 3) sham stimulation. Treatment lasted 25 min for 6 consecutive days over the motor cortex hand area.	Primary Outcomes: Orgogozo's MCA scale (OMCASS), Barthel Index (BI), Friedman test. Outcomes were assessed at pre-, post-, 1, 2, and 3 months post treatment.	There was a significant time x group (real vs. sham) effect on the OMCASS (p=0.005) and BI (p=0.006). A significant time x group effect for anodal vs. sham was noted on OMCASS (p<0.001), BI (p=0.002) and marginally significant effect for cathodal vs. sham OMCASS (p=0.033) and BI (p=0.017). A significant improvement of strength was noticed in all groups post-treatment on the Friedman Test (p<0.0001). A greater improvement was found in the combined group than in the sham group for shoulder abduction, foot dorsiflexion, and hip flexion (p=0.005).
Lee et al. 2014 Korea	CA: 国 Blinding:	59 subjects <1 mo post- stroke with impaired unilateral UE motor	Subjects were randomized into one of three groups: 1) Group	Primary Outcomes: Manual Muscle Test (MMT), Manual Function Test	Changes in scores on the MFT and FMS were significantly different between the three groups (p=0.021, p=0.03 respectively).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
RCT	Assessor 🗹 Patient 🗷 ITT: 🗷	function.	A-cathodal tDCS, 2) Group B-virtual reality (VR), or 3) Group C- tDCS plus VR. In addition to their specified group treatments, all participants received standard therapy. In total, 15 treatments were received over a 3-wk period.	(MFT), Fugl-Meyer Assessment (FMA), Box and Block Test (BBT), Korean-Modified Barthel Index (K-MBI). Outcomes were assessed at pre- and post-treatment.	Improvement in Group C was significantly greater compared to Group A and B on MFT (Group C vs. Group A, p=0.016; Group C vs. Group B, p<0.01). Group B also had a significantly greater improvement in MFT score compared to Group A (p<0.01). FMS score improvement was significantly greater in Group C than Group A (p=0.013) and Group B (p<0.01). Further, Group A was significantly improved compared to Group B (p=0.035). In all three groups, significant increases were noted in the MMT (shoulder) and K-MBI. Only Group C showed a significant increase on the Box and Block Test (p-values were not provided).
Wu et al. 2013	CA: 🗷	90 subjects, 2-12 mo post-stroke with upper	Subjects were randomized into one of	Primary Outcomes: Fugl-Meyer Assessment	Post-intervention, compared to the sham group, the tDCS group showing greater improvements on FMA
RCT	Blinding: Assessor ☑ Patient ☑ ITT: ☑	extremity spasticity.	two groups: 1) tDCS to the primary sensorimotor cortex of the affected hemisphere with cathodal stimulation, or 2) sham stimulation to the same area. Stimulation sessions lasted 20 minutes/day, 5 days/week, for 4 wk. Both groups also received physiotherapy for two 30 min sessions per day, for 4 wk.	(FMA) of motor recovery, Barthel Index (BI) Secondary Outcomes: Modified Ashworth Scale (MAS) Outcomes were assessed pre-, post-treatment and follow up.	(p<0.001), and BI (p<0.05). At the four week follow up, the tDCS showed significantly greater improvement on FMA (p<0.001) and BI (p<0.01) than the sham group.
rTMS	1				
Le et al. 2014 China Systematic Review and Meta-Analysis	N/A	8 RCTs (273 subjects, >18 yr) published in English between 1990 and 2012 that examined the effect of rTMS on hand function and plasticity of the motor cortex; time since stroke	The frequency of rTMS ranged from 1 Hz to 25 Hz. Stimulation sites of low-frequency rTMS were primary motor cortex and premotor cortex whereas high-frequency rTMS	Primary Outcomes: Finger dexterity, hand function	Finger coordination and hand function (at 3Hz) demonstrated a significant standard mean difference of 0.58 (p=0.01) and -0.82 (p=0.007), respectfully. No improvement was demonstrated for hand function at 10Hz (p=0.34) compared to control groups.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		onset ranged from 5 days to 10.7 years.	occurred at M1. Seven studies examined rTMS compared to a control and in the remaining study it was compared to constraint induced movement therapy. Treatments duration ranged from 1 day to 10 days, with a frequency of 0.4-1 sec to 25 min.		
Ji et al. 2014 Korea RCT	CA: ☑ Blinding: Assessor ☑ Patient ☑ ITT: ☑	35 subjects with upper limb hemiparesis, mean time since onset of stroke 8.9mo.	Subjects were randomized into one of three groups: 1) combined mirror therapy plus rTMS (MT+rTMS), 2) mirror therapy alone (MT), or 3) sham stimulation. All participants received physical therapy 30 min/day, 5 times/wk, for 6 wk.	Primary Outcomes: Fugl-Meyer Assessment (FMA), Box and Block Test (BBT). Outcomes were assessed at pre- and post-treatment.	FMA and BBT scores of all groups significantly improved following treatment (p<0.05). Scores were significantly better for MT+rTMS compared to MT (p<0.05) and sham (p<0.05) groups.
Wang et al. 2014 China RCT	CA: ☑ Blinding Assessor: ☑ ITT: ☑	48 subjects 2-6 post stroke with a grade of 3 or more on the distal Medical Research Council Scale (MRC).	Subjects were randomized into one of three groups: 1) Group A received rTMS (10 sessions, 1 Hz) over the unaffected hemisphere and then intermittent theta burst stimulation (iTBS) over the affected area (3 sessions, 50Hz), 2) Group B received had the same protocol as Group A but in the reverse order, 3) Group C received sham stimulation in the same order as Group A. Treatment lasted 4 wk. All subjects also	Primary Outcomes: MRC proximal and distal, Fugl-Meyer Assessment (FMA), Wolf Motor Functioning Test (WMFT) Outcomes were assessed at baseline, post intervention, and at 3 month follow-up.	Group A showed the largest improvement out of the three experimental groups. Group A demonstrated various improvements: MRC (proximal) from 2.6±1.5 to 3.9±1.0 (p<0.01), MRC (distal from 2.3±1.6 to 3.4±1.4 (p<0.05), FMA from 26.2±21.6 to 36.6±24.0 (p<0.001), and WMFT from 30.4±14.5 to 40.3±29.1 (p<0.001). Group B demonstrated less improvement on motor skills than Group A with MRC (proximal) of 2.6±1.3 to 3.8±1.5 (p<0.01), MRC (distal) of 2.4±1.3 to 3.7±1.3, FMA of 28.4±24.1 to 34.7±28.3 (p<0.01), and WMFT of 30.9±15.7 to 36.5±23.5 (p<0.05). FMA was particularly improved in Group A but not in other groups. Group C in comparison to the other groups showed the least improvement.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			received physiotherapy for one hour (task orientation).		
Kim et al. 2014	CA: ☑	31 subjects post stroke with a score <2 on the	Subjects were randomly assigned to either rTMS	Primary Outcomes: Motor Function Test (MFT)	There was a significant improvement in MFT at 4 weeks in the rTMS group (13.20±5.00 to
Korea	Blinding: Assessor ☑	Modified Ashworth Scale, and a score	(10 sec, 10 Hz), or rTMS with sessions lasting 10	Outcomes were assessed	22.20±2.86, p<0.05). The sham rTMS also demonstrated an improvement in MFT but to a
RCT	ІТТ: ☑	higher than fair on the Manual Muscle test.	min, 5x/wk for 4 wk. Subjects also received 30 min of task orientation training (maneuvering of objects along with increasing the number of repetitions and difficulty).	at baseline and 4 wk follow- up.	smaller degree at 4 weeks (14.20±2.82 to 16.90±2.13, p<0.05). Improvements in the rTMS group were significantly greater compared to the sham rTMS group (p<0.05).
TENS					
Au-Yeung et al. 2014	CA: ☑ Blinding:	73 subjects ≤ 46 hr post- stroke, demonstrating moderate to severe arm	Subjects were randomized into one of three groups: 1) Group	Primary Outcomes: Hand grip, pinch strength, Action Research Arm Test	The TENS group improved significantly more than the control group in hand grip (p=0.015) and pinch strength (p=0.007) compared to controls beginning
China	Assessor ☑ Patient ☑	weakness, contralateral to the lesion.	1-TENS, 2) Group 2- sham stimulation, or 3)	(ARAT)	at week 4; improvements were maintained at follow up (p≤ 0.006). No significant differences were found
RCT	ΙΤΤ: ☑		Group 3-standard rehabilitation. Groups 1 and 2 also received standard rehabilitation therapy. Electrical Stimulation Treatment was received fir 60 min/day, 5 days/wk, for 4 wk.	Outcomes were assessed at pre-, 4, 12, and 24 wk post-treatment.	between the sham stimulation group and the control group for hand grip or pinch strength. There were no significant differences in ARAT scores between groups (p>0.05 for all).

EMG-Biofeedback

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Langhorne et al. 2009 UK Systematic review and meta-analysis	N/A	4 trials (126 subjects) specific to upper extremity identified from a Cochrane review (Woodford & Price 2009) from 13 studies that examined EMG biofeedback for the recovery of motor function after stroke Subjects in these 4 studies were recruited an average of 2-8 weeks (n=1),4 months (n=2)	Treatment contrasts: Exercise program plus EMG-BFB or exercise plus placebo EMG-BFB 20-minute sessions 5 times a week for 4 weeks Physiotherapy alone vs. physiotherapy plus EMG-BFB 45-minute sessions 3 times a week for 5 weeks Physiotherapy alone vs.	Upper Extremity Function Test, ARAT Outcomes were assessed before and after treatment. 12 week follow-up in one study.	Arm function: SMD=0.41, 95% CI 0.05 to 0.77, p<0.05 (Author recommends that biofeedback should not be used on a routine basis) Adverse events: No reporting
		and 19 months (n=1) following stroke	physiotherapy plus EMG-BFB for 12 weeks 20 sessions of EMG-BFB plus physiotherapy or physiotherapy alone		

Virtual Reality

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Laver et al. 2011	N/A	19 RCTs (565 subjects),	Comparison of upper	Primary Outcomes	Arm function (composite measure)
Australia		of which 8 examined upper-limb training. Subjects with mild to	limb training programs using virtual reality or control condition (therapy	Upper limb function & activity (Motor Assessment Scale, ARAT, Wolf Motor	SMD=0.53, 95% CI 0.25 to 0.81, p= <0.0001. Results from 7 studies (205 subjects) included
Cochrane		moderate upper-limb	only).	Function Test)	Arm Function (Fugl Meyer): MD=4.43, 95% CI 1.98
Systematic		impairment were			to 6.88, p<0.0001. Results from 5 studies (171
Review		recruited.	In 2 studies commercially	Arm function (9-Hole Peg	subjects) included.
			available devices were	test, Box & Block test)	
		3 and 5 trials,	used (Playstation		Hand function: MD=3.55 95% CI -0.20 to 7.3,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		respectively, recruited subjects an average of < 6 months and > 6 months following stroke onset.	EyeToy, Nintendo Wii). In the remaining studies, custom software was designed for use with a personal computer. Total dose of therapy varied from 6 to >21 hours of therapy over 3 to 7 weeks.	Outcomes were assessed before and after treatment in all studies	p=0.063. Results from 2 studies (44 subjects) included. In sub group analysis, based on time since stroke onset, treatment provided in both the acute and chronic phase of stroke was effective (Upper limb function SMD=0.76, p=0.01 and 0.46, p<0.0001). Adverse events: No adverse events were reported in 5 studies. Dizziness was reported by 2 subjects in the intervention group in one study. Pain was reported by 3 subjects in the intervention group (compared with 2 subjects in the control group) in 1 study.
Saposnik et al. 2011 Canada Systematic review and meta- analysis	N/A	12 studies (5 RCTs) of which 4 recruited subjects in the acute or sub acute phase of stroke and 8 recruited subjects in the chronic phase.	Comparison of VR programs vs. conventional therapy. 8 studies used non-immersive systems. Treatment was provided for 1 hour each weekday in most studies, for 4-6 weeks.	Primary Outcomes: Fugl-Meyer Assessment Secondary Outcomes: Wolf Motor Function test (WMFT), Box & Block test, Jensen-Taylor Hand Function Test Timing of outcome assessment was not stated- assumed to have been done before and after treatment.	Improvement in Motor impairment: OR= 4.89, 95% CI 1.31 to 18.29, p<0.05. Results from 5 RCTs included. Improvement in Box & Block test: OR=0.49, 95% CI 0.091 to 2.65, p=ns. Results from 2 RCTs included. Improvement in WMFT (manual function): OR=1.012, 95% CI 0.28 to 5.90, p=ns. Results from 3 RCTs included. Adverse events: No reporting
RCT Italy	CA: 図 Blind Assessor: 図 ITT: ☑	44 subjects within one year of a first-ever stroke	Subjects were randomized into one of two groups: 1) reinforced feedback in virtual environment (RFVE) 1hr/day plus traditional rehabilitation (TR), or 2) TR only. Training occurred for 2 hr/day, 5x/wk, for 4 wk.	Primary Outcomes: Fugl-Meyer Upper Extremity Scale (F-M UE), Functional Independence Measure (FIM) Outcomes were assessed at baseline and at 4 wk follow- up.	F-M UE scores significantly increased in only the RFVE group (p<0.001) but not the TR group (p<0.053). FIM was significantly increased in both the RFVE (p<0.001) and TR groups (p<0.006).
Lee et al. 2014 Korea RCT	CA: ☑ Blinding: Assessor ☑ Patient ☑	59 subjects <1 mo post- stroke with impaired unilateral UE motor function.	Subjects were randomized into one of three groups: 1) Group Acathodal tDCS, 2) Group B-virtual reality (VR), or	Primary Outcomes: Manual Muscle Test (MMT), Manual Function Test (MFT), Fugl-Meyer Assessment (FMA), Box and	Changes in scores on the MFT and FMS were significantly different between the three groups (p=0.021, p=0.03 respectively). Improvement in Group C was significantly greater

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	ITT: 🗵		3) Group C- tDCS plus VR. In addition to their specified group treatments, all participants received standard therapy. In total, 15 treatments were received over a 3-wk period.	Block Test (BBT), Korean-Modified Barthel Index (K-MBI). Outcomes were assessed at pre- and post-treatment.	compared to Group A and B on MFT (Group C vs. Group A, p=0.016; Group C vs. Group B, p<0.01). Group B also had a significantly greater improvement in MFT score compared to Group A (p<0.01). FMS score improvement was significantly greater in Group C than Group A (p=0.013) and Group B (p<0.01). Further, Group A was significantly improved compared to Group B (p=0.035). In all three groups, significant increases were noted in the MMT (shoulder) and K-MBI. Only Group C showed a significant increase on the Box and Block Test (p-values were not provided).
Sin et al. 2013	CA: 🗷	40 hemiplegic participants >6mo post-	Participants were randomized into one of	Primary Outcomes: Fugl- Meyer Assessment	In both groups FMA motor function scores and BBT gross manual dexterity scores increased
Korea RCT	Blinding: Assessor ☑ Patients ☒ ITT: ☒	participants >6mo post- stroke with active range of motion of the shoulder, elbow, wrist, and fingers of more than 10 degrees	two groups: 1) virtual reality (VR) training using the Xbox Kinect for 30 min followed by standard occupational therapy for 30 min, or 2) standard occupational therapy alone. Therapy was	(FMA), Active Range of Motion (AROM) of upper extremity, Box and Block Test (BBT). Outcomes were assessed at pre- and post-intervention.	significantly (p<0.05). Between the two groups, FMA and BBT scores differed significantly (p<0.05), with the VR group experiencing a greater improvement. Significant improvements were seen in the AROM of flexion, extension and abduction of the shoulder; flexion of the elbow; and flexion and extension of the wrist. Significant differences between the two groups were noted at follow up for
Turolla et al. 2013	N/A	376 post-stroke patients	3x/wk for 6 wks. Participants were	Primary Outcomes:	the shoulder and flexion of the elbow (p<0.05). A significant improvement in the FM-UE scores
Italy Prospective Controlled Trial		with hemiparesis, and a Motor Arm sub-score between 1 and 3 on the Italian version of the National Institute of Health Stroke Scale (It-NIHSS).	assigned to one of two of groups: 1) upper limb conventional (ULC) rehabilitation, or 2) reinforced feedback in the virtual environment (RFVE) group. Participants received 40 sessions of therapy 5x/wk for 4 wks.	Fugl-Meyer Upper Extremity (FM-UE), Functional Independence Measure (FIM) Outcomes were assessed at pre- and post-intervention.	were noted for both groups following treatment, a 4% increase in the ULC group (p<0.001), and a 10% increase in the RFVE group (p<0.001); FIM scores were significantly higher among the RFVE group compared to the ULC group post-treatment (p=0.007). An analyses based on Stroke to Rehabilitation Interval (SRI) sub-groups on the FM-UE scores showed significant improvements for the RFVE group compared to the ULC group on all three sub-groups (p<0.001).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Yin et al.	Blinding:	23 post-stroke patients	Participants were	Primary Outcome:	All participants improved in FMA scores (mean
2014	Assessor 🗷	with Fugl-Meyer	randomized to one of two	Fugl-Meyer Assessment	change (SD) = 11.65 (8.56), p<0.001). These
Cingonoro	Patients ☑	Assessment for the	groups: 1) 30 minutes of	(FMA)	effects were sustained at one month after
Singapore	ITT: 🗷	upper extremity (FMA) score of below 62 and	non-immersive virtual reality training for nine	Outcomes were assessed at	intervention (mean (SD) change from baseline = 18.67 (13.26), p<0.001).
RCT	11 1. <u>E</u>	Mini Mental State Examination (MMSE) 11 score of above 20.	weekdays within two weeks (five days a week) and conventional therapy, or 2) only	baseline, post intervention and 1-month post intervention. Participants' feedback and adverse	All other outcome measures showed similar patterns. There were no significant differences in improvement between both groups.
			conventional therapy.	effects were recorded	Majority of the participants found VR training useful and enjoyable, with no serious adverse effects reported.

Neurophysiological Approaches

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Luke et al. 2004 Australia Systematic review and meta- analysis	N/A	8 studies (5 RCTs) including samples sizes that ranged from 7 to 131 subjects Time since stroke onset was less than 1 month in 3 studies, varied from 6 weeks to 9 years in 3 studies and was not stated in 2 studies.	Compared a pure Bobath program with a control program (no active control, Motor relearning program, PNF, Brunnstrom, functional retraining). Treatment programs were provided for 30 to 45 minutes 3 to 5 days per week for 3 to 20 weeks.	Impairment outcomes: muscle tone, finger oscillation test, VAS (shoulder pain), grip strength, isometric hand extension Activity outcomes: Upper Extremity Function Test (UEFT), ARAT, BI, Rivermead Motor Assessment, Sodring Motor Evaluation Scale (SMES)Box & Block test, 9- Hole Peg test, Motor Assessment Scale (MAS)	Impairment Tone: SMD=0.46, 95% CI 0.01 to 0.91, p<0.05. Results from 1 study included. Finger Oscillation test: SMD= -0.02, 95% CI (-0.75 to 0.71, p>n/s. Results from 1 study included. Activity UEFT: SMD=0.17, 95% CI -0.56 to 0.90, p=n/s. Results from 1 study included. MAS: SMD=-0.29, 95% CI -0.80 to 0.21, p =n/s. Results from 1 study included. SMES: SMD= -0.32, 95% CI -0.83 to 0.19, p=n/s. Results from 1 study included. Adverse events: No reporting
				Outcomes were assessed before and after treatment. 12 week follow-up in one	

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Van Vliet et al. 2005 UK RCT	CA: ☑ Blinding: assessor ☑ ITT:☑	120 patients admitted for stroke rehabilitation within 2 weeks of event. Inclusion criteria: able to tolerate at least ½ hour to complete the physical tasks required for initial evaluation	Comparison of Bobath based treatment (n=60) vs. motor relearning approach (n=60) Treatment was outpatient based and provided for as long as needed. No details regarding the content of the treatment programs are provided. Therapy was based on written guidelines consisting of theoretical concepts and clinical objectives.	Primary Outcomes: Rivermead Motor Assessment (RMA), Motor Assessment Scale (MAS) Secondary Outcomes: 10-Hole Peg Test, 6 m walk test, MAS, BI, Extended Activities of Daily Living, Nottingham Sensory Assessment Outcomes were assessed at 1, 3 and 6 months after randomization	There were no significant differences between groups on any of the outcome measures at any assessment points. Data from 45 patients in the Bobath group and 42 patients in the Motor relearning group were available for analysis Median RMA (gross function) at baseline and 6 months: Bobath 2 to 8 vs. Motor relearning 1 to 8, p=0.61 Median RMA (arm) at baseline and 6 months: Bobath 4 to 10 vs. Motor relearning 4 to 8, p=0.64 Median MAS (Advance hand activities): at baseline and 6 months: Bobath 0 to 6 vs. Motor relearning 0 to 2, p=0.23 Median MAS (Upper arm): at baseline and 6 months: Bobath 3 to 5 vs. Motor relearning 3 to 4, p=0.53 Adverse events: No reporting
Langhammer & Stanghelle 2000 Norway RCT	CA: ☑ Blinding: assessor ☑ ITT:函	61 patients with first- ever stroke admitted acutely to hospital	Comparison of inpatient physiotherapy programs based on either the Bobath (n=28) or Motor Relearning approach (n=33). Treatment sessions in both groups were provided for 40 minutes, 5 days a week during hospitalization In addition, patients in both groups were treated by a comprehensive, multidisciplinary team. When possible, treatment continued following discharge (home or outpatient)	Primary Outcomes: Motor Assessment Scale (MAS) Secondary outcomes: Sødring Motor Evaluation Scale (SMES), BI, Nottingham Health Profile Outcomes were assessed 3 days after admission to hospital, two weeks later and at 3 months post stroke.	Data from 24 patients in the Bobath group and 29 patients in the Motor relearning group were available for analysis. Subjects in both groups improved over the study period, but subjects in the Motor relearning group experienced greater improvement. Mean MAS scores at baseline and 3 months: 24 to 37 vs. 19 to 33, p=0.016; Mean SMES (part 2 sum scores): 47 to 65 vs. 39 to 58, p=0.018. Mean hospital LOS was significantly shorter for patients in the Motor relearning group (21 vs. 38 days, p=0.008). There were no significant differences between groups from baseline to 3 months for: SMES (part 1 or 3 sum scores) Or BI scores.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Adverse events: No reporting

Glossary

RCT= Randomized Controlled Trial N/A = Not Applicable CA = Concealed Allocation

ITT = Intention to treat

FES = Functional Electrical Stimulation

NMES = Neuromuscular Electrical Stimulation

rTMS = repetitive Transcranial Magnetic Stimulation
rTDS = repetitive Transcranial Direct Stimulation
ROM = Range of Motion
OR = Odds Ratio

SMD = Standardized Mean Difference

tDCS = transcranial direct current stimulation

CI = Confidence Interval

IQR = Interquartile Range

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