CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Rehabilitation, Recovery and Community Participation Following Stroke

Part Two: Delivery of Stroke Rehabilitation to Optimize Functional Recovery Evidence Tables

7th edition, Update 2025

Upper Extremity Function

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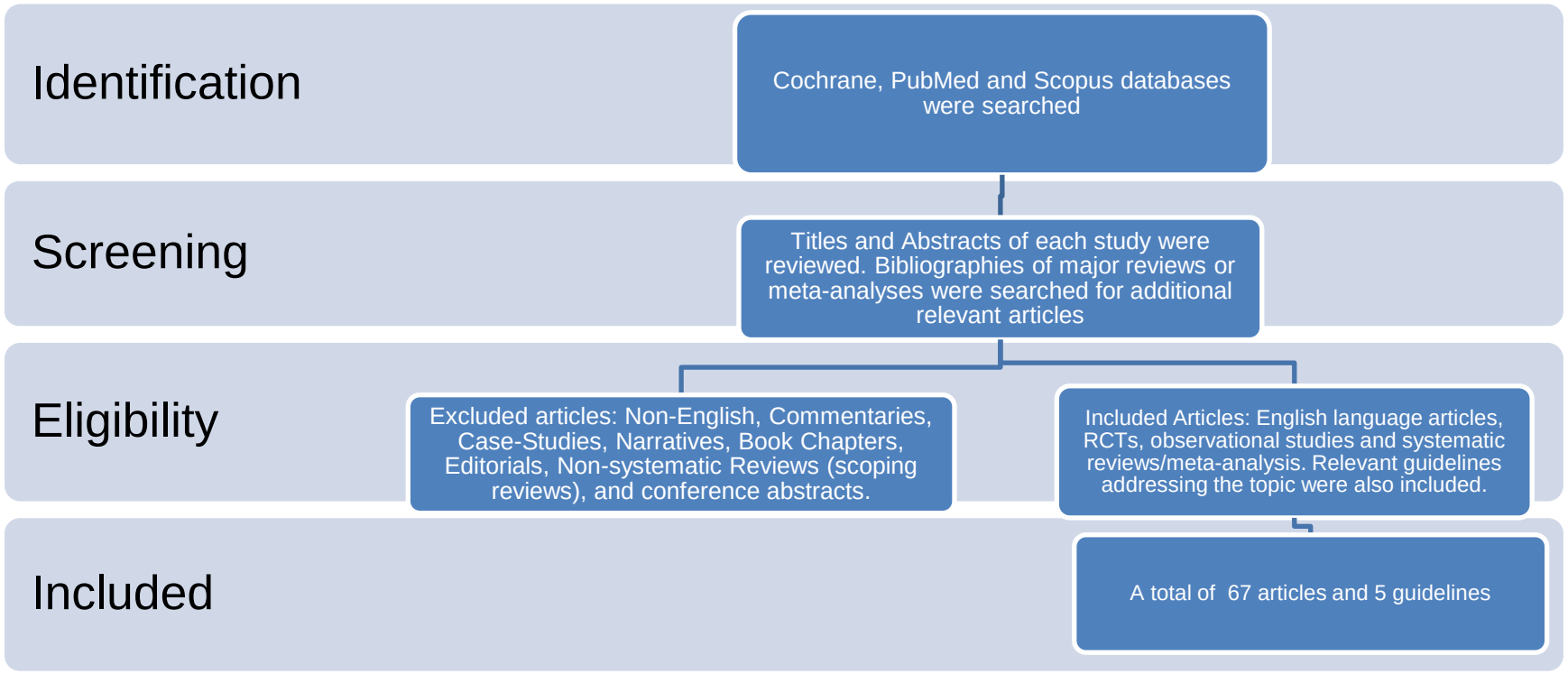
Search Strategy



Cochrane, PubMed and Scopus databases were searched using terms such as (Stroke OR cerebrovascular disease) AND (“upper extremity” OR “upper limb” OR “hand” OR “arm”) AND (rehabilitation OR therapy OR intervention). 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 67 articles and 5 guidelines were included and were separated into separate categories designed to answer specific questions.

Published Guidelines

Guideline	Recommendations
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; Version 5.0 – 2024. **Available at:** https://www.healthquality.va.gov/guidelines/Rehab/stroke/	We recommend task-specific practice (also known as task-oriented practice or repetitive task practice) to improve motor function, gait, posture, and activities of daily living. Strong (for) We suggest mirror therapy to improve motor outcomes and activities of daily living. Weak (for) There is insufficient evidence to recommend for or against constraint-induced movement therapy to improve upper extremity motor outcomes for individuals with some movement in the paretic limb. Neither for nor against There is insufficient evidence to recommend for or against motor imagery to improve motor function. Neither for nor against We suggest neuromuscular electrical stimulation to improve motor outcomes. Weak for There is insufficient evidence to recommend for or against robot-assisted therapy to improve upper or lower extremity motor outcomes. Neither for nor against There is insufficient evidence to recommend for or against the use of virtual reality/serious gaming to improve upper extremity motor outcomes, activities of daily living, or quality of life. Neither for nor against There is insufficient evidence to recommend for or against contralaterally controlled functional electrical stimulation to improve upper extremity motor outcomes and activities of daily living. Neither for nor against There is insufficient evidence to recommend for or against non invasive brain-computer interface to improve upper extremity motor outcomes and activities of daily living. Neither for nor against There is insufficient evidence to recommend for or against selective serotonin reuptake inhibitors to improve motor outcomes in patients with or without depression. Neither for nor against
National Clinical Guideline for Stroke for the UK and Ireland. London: Intercollegiate Stroke Working Party; 2023 May 4. **Available at:** www.strokeguideline.org**.** **(selected)**	People with some upper limb movement at any time after stroke should be offered repetitive task practice as the principal rehabilitation approach, in preference to other therapy approaches including Bobath. Practice should be characterised by a high number of repetitions of movements that are task-specific and functional, both within and outside of therapy sessions (self-directed). People with stroke who have at least 20 degrees of active wrist extension and 10 degrees of active finger extension in the affected hand should be considered for constraint induced movement therapy. People with wrist and finger weakness which limits function after stroke should be considered for functional electrical stimulation applied to the wrist and finger extensors, as an adjunct to conventional therapy. People with stroke may be considered for mirror therapy to improve arm function following stroke as an adjunct to usual therapy.

Guideline	Recommendations
	People with stroke who are able and motivated to participate in the mental practice of an activity should be offered training and encouraged to use it to improve arm function, as an adjunct to usual therapy
Clinical Guidelines for Stroke Management 2017/2022. Melbourne (Australia): National Stroke Foundation. Part 5: Rehabilitation	*New for 2022* Weak Recommendation Virtual reality and interactive games may be used to improve upper limb function. *2017* Strong Recommendation For stroke survivors with some active wrist and finger extension, intensive constraint-induced movement therapy (minimum 2 hours of active therapy per day for 2 weeks, plus restraint for at least 6 hours a day) should be provided to improve arm and hand use. Trunk restraint may also be incorporated into the active therapy sessions at any stage post-stroke. Weak Recommendation For stroke survivors with mild to severe arm weakness, mechanically assisted arm training (e.g. robotics) may be used to improve upper limb function. Strong Recommendation AGAINST Hand and wrist orthoses (splints) should not be used as part of routine practice as they have no effect on function, pain or range of movement. Weak Recommendation For stroke survivors with mild to moderate arm impairment, virtual reality and interactive games may be used to improve upper limb function. Virtual reality therapy should be provided for at least 15 hours total therapy time and is most effective when used in the first six months after stroke. Weak Recommendation For stroke survivors with mild to severe arm or hand weakness, electrical stimulation in conjunction with motor training may be used to improve upper limb function. Weak Recommendation For stroke survivors with mild to moderate weakness of their arm, mental practice in conjunction with active motor training may be used to improve arm function. Weak Recommendation For stroke survivors with mild to moderate weakness, complex regional pain syndrome and/or neglect, mirror therapy may be used as an adjunct to routine therapy to improve arm function after stroke. Weak Recommendation For stroke survivors with at least some voluntary movement of the arm and hand, repetitive task-specific training may be used to improve arm and hand function

Guideline	Recommendations
Zhang T, Zhao J, Li X, Bai Y, Wang B, Qu Y et al. **Chinese Stroke Association guidelines for clinical management of cerebrovascular disorders: executive summary and 2019 update of clinical management of stroke rehabilitation.** ***Stroke and Vascular Neurology* 2020: svn-2019-000321.** **(selected)**	8. Constraint-induced movement therapy is recommended to improve ADL (Grade I recommendation, Level A evidence). 9. Wii-based exercise therapy is reasonable to improve the motor function of the affected upper limb and ADL (Grade IIa recommendation, Level B evidence). 10. Transcranial direct current stimulation combined with virtual reality may be beneficial in improving patients' quality of life (Grade IIb recommendation, Level B evidence). 12. Vagus nerve stimulation paired with rehabilitation is acceptably safe and feasible. It is reasonable to improve upper limb motor function after chronic ischaemic stroke (Grade IIa recommendation, Level B evidence).
Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC et al; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research. **Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.** ***Stroke* 2016;47:e98–e169**	Functional tasks should be practiced; that is, task-specific training, in which the tasks are graded to challenge individual capabilities, practiced repeatedly, and progressed in difficulty on a frequent basis. Class I; LOE A All individuals with stroke should receive ADL training tailored to individual needs and eventual discharge setting. Class I; LOE A All individuals with stroke should receive IADL training tailored to individual needs and eventual discharge setting. Class I; LOE B CIMT or its modified version is reasonable to consider for eligible stroke survivors. Class IIa; LOE A Robotic therapy is reasonable to consider to deliver more intensive practice for individuals with moderate to severe upper limb paresis. Class IIa; LOE A NMES is reasonable to consider for individuals with minimal volitional movement within the first few months after stroke or for individuals with shoulder subluxation. Class IIa; LOE A Mental practice is reasonable to consider as an adjunct to upper extremity rehabilitation services. Class IIa; LOE A Strengthening exercises are reasonable to consider as an adjunct to functional task practice. Class IIa; LOE B Virtual reality is reasonable to consider as a method for delivering upper extremity movement practice. Class IIa; LOE B Somatosensory retraining to improve sensory discrimination may be considered for stroke survivors with somatosensory loss. Class IIb; LOE B Bilateral training paradigms may be useful for upper limb therapy. Class IIb; LOE A

Guideline	Recommendations
	Acupuncture is not recommended for the improvement of ADLs and upper extremity activity. Class III; LOE A

Evidence Tables

Systematic Review of Upper-Extremity Interventions

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Tenberg et al. 2023 **Germany** **Systematic review & Network meta-analysis (NMA)**	Overall risk of bias was assessed as high in 27% of trials, using the Cochrane risk of bias tool II (RoB II).	145 RCTs including 6,432 participants recovering from stroke, sustained within the previous 6 months. Mean age was 62 years, 41% were women. Mean time since stroke was 39 days.	Trials compared active exercise interventions intended for the affected upper limb as monotherapy or in combination with other treatments, provided for ≥2 weeks vs. an active or passive comparator. There were 45 different treatment categories, of which 41 were included in the NMA. Treatment categories included active electrical stimulation, active electrical stimulation + biofeedback, active mirror therapy, active mirror therapy + electrical stimulation, active mobilization, active non local therapy, active observation, active tDCS + biofeedback, active upper extremity therapy, bilateral training, bilateral training + biofeedback, bilateral training + electrical stimulation, biofeedback, boxing, CIMT + biofeedback, CIMT + mirror therapy, education, high CIMT, low CIMT, non local therapy (active + passive), passive mobilization, passive NMES, robotic, robotic + biofeedback, robotic + electrical stimulation, robotic + mobilization, robotic + task specific training, rTMS + biofeedback, sham, strength training, strength training + biofeedback, strength training +	**Primary outcome:** Motor function (e.g., Fugl-Meyer Assessment) **Secondary outcomes:** ADL and social participation	The mean intervention duration was 4.36 weeks, with mean follow-up period of 2.89 months. *i) Motor function (107 trials included)* 37 treatment classes were compared. 5 interventions were found to be superior to nonspecific/multimodal active upper limb therapy at the end of the intervention including: task-specific training + electrical stimulation (SMD=1.03, 95% CI 0.15-1.55; p score=0.11); high-intensity CIMT (SMD=0.86, 95% CI 0.40-1.32; p score=0.18); active observation (SMD=0.65, 95% CI 0.17-1.13; p score=0.28), strengthening (SMD=0.65, 95% CI 0.15-1.15; p score=0.28) and biofeedback (SMD=0.45, 95% CI 0.16-1.74; p score=0.39). Compared with each other, only task-specific therapy was found to be significantly better. 38 trials were included in the analysis of the primary outcome at follow-up. Two interventions were found to be superior to nonspecific/multimodal active upper limb therapy. Task specific therapy (SMD=0.74, 95% CI 0.08-1.40; p score=0.12) and biofeedback (SMD=0.63, 95% CI 0.00-1.27; p score=0.17) *ii) ADL (64 trials included)* 29 treatment classes were compared. Only active observation was found to be superior over nonspecific/ multimodal active upper limb therapy (SMD=0.48, 95%

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			mobilization, task-specific training, task-specific training + biofeedback, task-specific training + electrical stimulation, Task-specific training + strength training, tDCS + occupational, TENS, upper extremity therapy (active + passive) and virtual reality		CI 0.06-0.91; p score=0.14). 25 trials were included in the analysis at follow-up. 17 treatment classes were compared. The 3 interventions found to be superior over nonspecific/multimodal active upper limb therapy were: task-specific training + electrical stimulation (SMD=0.80, 95% CI 0.32-1.29; p score=0.06), low-intensity CIMT (SMD=0.28-1.30; p score=0.07) and robotic + task-specific training (SMD= 0.69, 95% CI 0.10-1.28; p score=0.11). *iii) Social participation (14 trials included)* 16 treatment classes were compared. No interventions were found to be superior to nonspecific/multimodal active upper limb therapy, while active mirror therapy and bilateral training were found to be inferior. No analyses at follow-up were possible.

Repetitive task-specific training

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Systematic Reviews					
French et al. 2016 **UK** **Cochrane Review**	In 23 trials, risk of bias was assessed as low or unclear in 5/5 domains assessed using the Cochrane	33 RCTs including 1,853 participants with stroke, of which 11 measured arm function, 8 measured hand function and 6 measured sitting balance/reach. Mean ages ranged from 50 to 79 years. The percentage of men ranged from 43% to 70%.	Comparison of repetitive task training (RTT) protocols to various control conditions (attention control or usual care). Dosage ranged from <10hr to >40hr, with most trials providing 10-21hr. Duration of therapy ranged from 2	**Primary outcomes:** Action Research Arm Test, Frenchay Arm Test, Motor Assessment Scale, Wolf Motor Function Test, Southern Motor Group Assessment, Box & Block Test, 9/10-Hole	Following the intervention. RTT was associated with significant improvement in arm function (SMD=0.25, 95% CI 0.01 to 0.49; 11 trials, n=749: GRADE: low certainty), hand function (SMD=0.25, 95% CI 0.00 to 0.51; 8 trials, n=619; GRADE: low certainty) and sitting balance/reach (SMD=0.28, 95% CI 0.01-0.55, 6 trials, n=222).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	RoB tool		to 20 weeks, with most trials providing 2-4 weeks.	Peg Test, Functional Test of the Hemiparetic Upper Extremity, Stroke Impact Scale	At follow-up of ≤6 months, RTT was associated with significant improvement in upper limb function (SMD=0.92, 95% CI 0.58 to 1.26; 3 trials, n=1530, but not at 6-12 months (SMD=0.1, 95% CI 0.0 to 0.3, 6 trials, n=412).
Langhorne et al. 2009 **UK** **Systematic review & meta-analysis**	N/A	8 RCTs specific to upper limb were identified in a Cochrane review (French et al. 2007) from a total of 14 studies. Participants in 6 studies were recruited within the first week up to 50 days post stroke; the remainder were recruited in the chronic phase of stroke.	Comparison of task-specific training protocols (with or without routine rehabilitation) with control conditions (other therapy approaches or a lower-limb therapy program). Dosage ranged from a total of 20 to 63 hour. Duration ranged from 2 to 11weeks.	**Primary outcomes:** Motor Assessment Scale, Jebsen Taylor Hand Function Test, Upper Extremity Function Test, Action Research Arm Test, Southern Motor Group Assessment, 10-Hole Peg Test, Rivermead Motor Assessment, Wolf Motor Function Test 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, p>0.05 (414 participants) Hand function: SMD= 0.05, 95% CI (-0.18 to 0.29, p>0.05 (281 participants) Adverse events: No reporting (Authors recommended that task-specific training should be used improve ADLs)
Clinical Trials					
Lewthwaite et al. 2018; Winstein et al. 2016 **USA** **RCT *Interdisciplinary Comprehensive Arm Rehabilitation Evaluation***	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT ☑	361 patients with moderate upper extremity motor impairment following stroke duration <106 days with hemiparesis in the arm or hand, with some active finger extension movement, were recruited from 7 sites. Mean age was 60.7 years, 56% were men. Mean time since stroke was 46 days.	Patients were randomized to the Accelerated Skill Acquisition Program (ASAP), dose-equivalent usual and customary care (DEUCC) or monitoring only/usual care (UC) group. Patients in the ASAP group engaged in an impairment focused, task specific, intense, engaging, collaborative, and patient centered program with/without a constraint component for 30 hours (provided	**Primary outcome:** Mean change in log-transformed Wolf Motor Function Test time score (WMFT), from baseline to the end of the study (12 months) **Secondary outcome:** Mean change in WMFT score (sec),	The mean change from a baseline score of 2.2 sec on the ln WMFT was -0.8 in the ASAP group, -0.9 sec (baseline score of 2.0 sec) for the DEUCC group and -0.8 from a baseline of 2.1 sec in the UC group. There were no significant differences between groups in pair-wise analysis. The differences in raw scores ranged from 0.5 to 2 seconds. The mean change from a baseline score of 16.6 sec on the WMFT was -8.1 in the ASAP group, -8.7 sec (baseline score of 12.9 sec)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
(ICARE)			as 30, 1-hour sessions, 3x/week for 10 weeks). Patients in the DEUCC group received outpatient usual occupational therapy for the same intensity/duration as those in the ASAP group. Patients in the UC group received outpatient occupational therapy based on usual and customary practice without a specified dose.	and Stroke Impact Scale (SIS) hand sub-scale score from baseline to the end of the study (12 months)	for the DEUCC group and -7.5 from a baseline of 15.1 sec in the UC group. There were no significant differences between groups in pair-wise analysis. Patients in all groups improved ≥25 SIS hand subscale points from baseline to the end of treatment, with no significant differences between them. 304 patients (84%) completed the 12-month evaluation (87% in the ASAP, 88% in the DEUCC, and 79% in the UCC groups). 2/186 serious adverse events (hypertension and wrist fracture) were judged to be related to the intervention. *Additional outcome reporting (2018)* From baseline to the end of the study, there were significant improvements in mean FMA-UE scores within groups (from 41.7 to 51.6 [ASAP]; 41.5 to 53.4 [DEUCC]; and 41.6 to 53.7 [UC]), with no significant differences between groups. From baseline to the end of treatment, there was significantly greater improvement in mean SIS (hand) scores in the ASAP group, (scores at end of treatment: 70.3 vs. 65.3 and 62.2, p=0.020), but these differences were gone by the end of the study (ASAP 68.2; DEUCC 68.7 and UC 66.4).
Shimodozono et al. 2013 **Japan** **RCT**	CA: ☑ Blinding: Assessor ☑ Patient ☑ ITT: ☑	49 participants in the subacute phase of stroke (experimental=6.4±2.1wk; control=7.4±3.0wk) with Brunnstrom Proximal Upper-Limb stage ≥III.	Participants were randomized to receive repetitive facilitative exercise (RFE) or conventional rehabilitation. Both groups received 40min sessions 5x/wk for 4wk of their allocated treatment. Both groups performed 30min/d of dexterity-related training	**Primary Outcomes:** Action Research Arm Test (ARAT), Fugl-Meyer Assessment (FMA) Outcomes were assessed at baseline,	After 4 weeks of treatment, there were significantly greater improvements in 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
			immediately after each session. Both groups participated in a standard inpatient rehabilitation program. RFE involved 100 standardized movements of ≥5 joints of affected upper limb.	2wk, and 4wk.	

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: Patient ☒ Assessor ☑ ITT: ☑	103 patients, recruited from 4 acute facilities and then transferred to inpatient rehabilitation services following stroke with upper-limb impairment (Fugl-Meyer Upper Limb Motor Impairment Scale score of 10-57) and active scapular elevation (shoulder shrug) against gravity and palpatable wrist extension. Mean age was 69 years, 57% were men. Mean time since stroke was 20 days.	In addition to routine rehabilitation, patients were randomized to an experimental (GRASP) or an educational protocol (control) group. GRASP was a self-administered program including exercise books and kits, designed to improve ADL skills through exercises for strengthening, range of motion, and gross/fine motor skills. Participants were asked to complete the exercises 6 days/week for 60 minutes/day for 4 weeks. Persons in the control group received an education book with 4 modules with information on stroke recovery and general heath.	**Primary Outcomes:** Chedoke Arm & Hand Activity Inventory-9 (CAHAI) **Secondary Outcomes:** Action Research Arm Test (ARAT), Motor Activity Log (MAL), 12-Item Short Form Survey (SF-12), grip strength, pain, fatigue. Outcomes were assessed at baseline, 4wk, and 3mo follow-up.	At the end of the intervention, both groups showed improvement in mean CAHAI scores, but the GRASP group had significantly greater improvement (+14.1 vs. +7.9, p<0.001). This improvement was maintained at 3 months, with significantly higher scores in the GRASP group (50.4 vs. 45.4, p=0.037). At the end of the intervention, the GRASP group had significantly higher mean ARAT (+11.7 vs. +7.0, p=0.025), MAL scores (AOU: +1.3 vs. +0.9, p=0.023; QOU: +1.2 vs. +0.9, p=0.007) and grip strength (+4.1 vs +2.0, p=0.027). 9 participants withdrew from the study before postintervention testing (3 in the control group and 6 in the GRASP group). 28% of GRASP patients reported pain, mostly during the 2 weeks.

Constraint-Induced Movement Therapy (CIMT)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Gao et al. 2023 **China** **Systematic review & meta-regression**	Using the Cochrane RoB tool, 31 trials were at low risk of bias for randomization, 16 were at low risk for CA, 35 were at low risk for blinding outcome assessors, 28 trials were at low risk of attrition bias.	44 RCTs including 1,779 persons with upper-limb dysfunction following stroke. Mean age ranged from 46.4 to 71.9 years. Time since stroke was <30 days (n=9), 30 days to 6 months (n=6), and ≥6 months (n=24). In most trials the percentage of men was greater than women.	There were 4 categories of CIMT: CIMT1 (constraint for 90% of waking hours or at least 10 hours/day); CIMT2 (constraint for ≥ 6 hours to ≤10 hours/day) CIMT3 (constraint for ≥4 to ≤6 hours/day); CIMT4 (constraint for ≥ 1 hour to ≤4 hours/day). Trunk restraint was a cointervention in 6 trials. The most common control condition was conventional therapy. Other interventions included robot-assisted therapy, and bilateral arm therapy. The duration of the intervention ranged from 2 weeks to 6 months. The most common duration was 2 weeks (19 trials).	**Primary outcomes:** Motor function, ADL	*Motor function-FMA-UE* Compared with conventional therapy alone, CIMT3 combined with trunk restraint ranked as the most effective intervention (MD=11.25, 95% CI 0.70–21.81), followed by CIMT1 (MD=9.78, 95% CI 3.81–15.75), and CIMT4 (MD=8.53, 95% CI 1.15–15.91). Results from 24 trials and 911 participants. *Motor function-ARAT* Compared with conventional therapy alone, CIMT3 combined with trunk restraint ranked as the most effective intervention (MD=15.93, 95% CI 8.67–23.20), followed by CIMT3 alone (MD=10.94, 95% CI 5.63–16.25), and CIMT1 (MD=8.96, 95% CI2.28–15.63), and CIMT2 (MD=8.26, 95% CI 2.44–14.088). Results from 14 trials and 544 participants. *ADL-MAL-QOM* Compared with conventional therapy alone. CIMT3 combined with trunk restraint ranked as the most effective intervention (MD=1.49, 95% CI 0.84–2.15), followed by CIMT2 combined with conventional therapy (MD=0.98, 95% CI 0.38–1.58), CIMT3 alone (MD=0.96, 95% CI 0.47–1.45) and CIMT1 with conventional therapy (MD=0.87, 95% CI 0.17–1.58). Results from 30 trials and 1,190 participants. *ADL-MAL-AOU* Compared with conventional therapy alone. CIMT3 combined with trunk restraint ranked as the most effective intervention (MD=1.63, 95% CI 0.84–2.42). Results from 13 trials and 1,113 participants. *ADL-FIM* Although all interventions resulted in an increase in FIM score, there were no statistically significant improvements in ADL found. Results from 8 trials and 266 participants.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Liu et al. 2017 **China** **Systematic review & meta-analysis**	PEDro scores ranged from 5 to 8, with a median score of 6.5.	16 RCTs including 738 participants with upper limb impairment post stroke. Time from stroke onset was <3 months.	Trials compared CIMT to conventional therapy, without any additional therapies. Intensity ranged from 30min/d, 3d/wk to 6hr/d, 5d/wk, with most trials providing 2-3hr/d, 5d/wk. Duration ranged from 2wk to 10wk, with most trials providing 2wk.	**Primary outcomes:** Action Research Arm Test (ARAT), Wolf Motor Function Test (WMFT), Motor Activity Log (MAL), Fugl-Meyer Assessment (FMA), Modified Barthel Index (mBI) Outcomes were assessed before and after treatment, with 1-3mo follow-up in 6 trials and 3-6mo follow-up in 3 trials.	CIMT was associated with significant improvement in ARAT scores (WMD=8.35, 95% CI 1.98-14.71; 5 trials), MAL QOM (WMD=0.81, 95% CI 0.33-1.29, 4 trials), FMA (WMD=10.82, 95% CI 7.42-14.23; 13 trials) and mBI (SMD=10.71, 95%CI 4.42-16.97;6 trials). In subgroup analysis, low-intensity CIMT was found to have a greater effect than high-intensity CIMT on ARAT, FMA, and MAL. CIMT was not associated with significant improvement in WMFT or MAL AOU.
Kwakkel et al. 2016 **Netherlands** **RCT** ***EXPLICIT***	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☑	58 patients with upper-limb hemiparesis following first-ever stroke, with a baseline ARAT score of ≤53, but with a favourable prognosis (>10° finger extension). Mean age was approximately 61 years, 53% were men. Time since stroke was 9 days. (101 patients with unfavourable prognosis were also included in this trial and received EMG-NMS or usual care.)	Patients were randomized to receive usual care alone (control), provided by OT/PT for 30 minutes/day or modified CIMT (mCIMT), focused on improving task-specific use of the paretic arm and hand. Sessions were 60 minutes each (or 2, 30 minutes) provided 5 days/week for 3 weeks, with a restraint worn for 3 hours/day.	**Primary Outcomes:** Action Research Arm Test (ARAT), Wolf Motor Function Test (WMFT), Modified Erasmus Nottingham Sensory Assessment (mENSA), Frenchay Arm Test (FAT), Motricity Index (MI), Motor Activity Log (MAL), 9-Hole Peg Test (9HPT), Outcomes were assessed weekly for 5wk, and then at 8wk, 12wk, and 26wk.	Patients in the mCIMT had significantly greater improvement than usual care on ARAT at 5wk (β=1.757, p=0.011), 8wk (β=1.312, p=0.002), and 12wk (β=0.615, p=0.023), but not at 26wk (β=0.095, p=0.389). Patients in the mCIMT group had significantly greater improvement than usual care on SIS at 8wk (β=1.389, p=0.038). There were no significant differences between groups on WMFT, mENSA, FAT, MI, MAL, or 9HPT at 5wk, 8wk, 12wk, or 26wk.
Corbetta et al. 2015 **Italy**	Majority of studies had unclear risk of bias.	42 RCTs involving 1453 participants with residual motor power in paretic arm, potential for	Comparison of CIMT, mCIMT, or CIMT with adjunct to various control conditions (bilateral arm training, conventional therapy, no	**Primary outcomes:** Arm function, arm impairment, perceived function	CIMT was associated with significant improvement in arm function (SMD=0.34, 95% CI 0.12-0.55, 34 trials, n=858), arm impairment (SMD=0.82, 95% CI 0.31-1.34; 8 trials, n=372), perceived arm motor

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Cochrane Review	Publication bias and small study effects were potential issues.	recovery, and limited pain/spasticity. Participants were recruited in the acute phase of stroke in 13 trials, the subacute phase in 6 trials, and the chronic phase in 5 trials. The remaining trials had a wide range or were unclear in terms of onset.	treatment) for upper limb. Restraint ranged from 2-6hr/d, with most trials providing 6hr/d. Practice ranged from 5-45hr/wk, with most trials providing 10-25hr/wk. Duration ranged from 2-10wk, with most trials providing 2wk.	(Motor Activity Log), dexterity, disability, quality of life (Stroke Impact Scale), assessed at the end of treatment	function, quality (MAL QOM: MD=0.68, 95% CI 0.47-0.88; 29 trials, n=891), perceived arm motor function (MAL AOU: MD=0.79, 95% CI 0.50-1.08, 28 trials, n=851) and dexterity (SMD=0.42, 95% CI 0.04-0.79, 7 trials, n=113 participants). CIMT was not associated with significant improvement in disability, assessed post intervention of at 3/6-month follow-up, or quality of life. In subgroup analysis, there were no significant effects of stroke onset, amount of practice, or region of restraint.
Dromerick et al. 2009 **USA** ***Very Early Constraint-Induced Movement during Stroke Rehabilitation (VECTORS) Trial***	CA: ☒ Blinding: Assessor ☑ ITT:☒	52 patients recruited within 28 days of admission to hospital with ischemic or hemorrhagic stroke and persistent hemiparesis.	Patients were randomized to receive 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 Outcome:** ARAT **Secondary outcomes:** NIHSS, FIM, SIS, pain, Geriatric Depression Scale Assessments were conducted at baseline, 2 weeks and 3 months	At 3 months, patients in the high-CIMT group had significantly lower mean total ARAT and SIS scores compared with participants 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, 2008 **USA** **RCT**	CA: ☒ Blinding: Assessor ☑ Patient ☒	222 patients with first-ever ischemic or hemorrhagic stroke of onset 3 to 9 months prior, recruited from 7 sites. Patients were	Patients were randomized to a CIMT or usual care group. CIMT patients received 6 hours of shaping (task practice) each weekday + constraint worn for a goal of 90% of waking hours (7	**Primary Outcomes:** WMFT, MAL **Secondary Outcomes:** FIM, SIS	203 participants completed the treatment (99 in the CIMT group and 105 in the UC group. Data from 169 patients were included in 12-month assessment. From baseline to 12 months, the improvement in

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Extremity Constraint-Induced Movement Therapy Evaluation (EXCITE) Trial	ITT: ☑ (primary outcome only)	recruited who met criteria for either higher or lower motor function, High functioning patients had at least 20º of wrist extension and at least 10º of active extension of each metacarpophalangeal and intraphalangeal joint of all digits. Low functioning patients had 10º of active wrist extension, at least 10º of thumb abduction/extension and at least 10º of extension in at least 2 additional digits. Mean age was 62 years, 64% were men. Mean time since stroke was 182 days.	days/week), for 2 weeks. The control group received usual care, which could range from no therapy to a formal structured therapy program.	Assessments were conducted at baseline, posttreatment and follow-up at 3, 8 and 12 months	CIMT group WMFT Performance Time was significantly better (19.3 to 9.3 seconds vs. 24.0 to 17.7 seconds, p<0.001) and in the MAL AOU (1.21 to 2.13 vs. 1.15 to 1.65, p<.001) and MAL QOM (1.26 to 2.23 vs. 1.18 to 1.66, p<.001). In subgroup 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. *24 months post intervention* Data from 68 patients in the CIMT group were available. From 12 to 24 months, there was no significant decline in mean WMFT time scores or mean scores of the MAL (AOU and QOM) After treatment during the next 12 months, the primary outcome measures of WMFT and MAL continued to improve. SIS scores were significant post intervention and were maintained at follow up assessment.

Mental Practice

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Barclay-Goddard et al. 2020 **Canada** **Cochrane Review**	Risk of bias was identified in 50% and 25% of trials for randomization and concealed allocation, respectively. Risk of bias was high for blinding of participants and personnel. Risk of bias was low for selective reporting.	25 RCTs including 676 adult participants with upper limb dysfunction following stroke. 424 participants were men, 220 were women, and 32 were not reported. Chronicity of stroke was ≥6 months (n=12), <6 months (n=10) or not stated (n=3)	Comparisons of mental practice + other treatment vs. conventional therapy (n=21), mental practice vs. conventional therapy (n=4). Treatment was provided for a total of >360 minutes in 15 trials and ≤360 minutes in 10 trials.	**Primary outcome:** Activity and activity limitation **Secondary outcomes:** Impairment, measures of ADL, health related QoL (HR QoL)	*Mental practice + other treatment vs. other treatment (± placebo)* Mental practice was associated with a significant improvement in measures of upper limb activity and impairment (SMD=0.66, 95% CI 0.39-0.94 and SMD=0.59, 95% CI 0.3-0.87, respectively). Data from 15 trials (397 participants) were included for both outcomes. GRADE: moderate certainty of evidence Mental practice was not associated with significant improvement in performance of ADL (SMD=0.08, 95% CI -0.24 to 0.39; data from 4 trials, 157 participants). GRADE: low certainty of evidence. There were no trials that assessed HR QoL *Mental practice vs. conventional treatment* Mental practice was not associated with significant improvement in measures of impairment (SMD=0.34, 95% CI -0.33 to 1.00; data from 3 trials, 50 participants). GRADE: low certainty of evidence. There were no trials that reported on any of the other outcomes of interest. Neither chronicity of stroke nor intensity of therapy appeared to be significant effect size moderators for the primary outcome.
Guerra et al. 2017 **Brazil** **Systematic review & meta-analysis**	Using an 11-point Cochrane RoB tool, scores ranged from 2-9.	20 RCTs involving 606 participants with upper limb impairment. Stroke onset was <1mo in 3 trials, <3mo in 5 trials, >3mo in 2 trials, <6mo in 2 trials, >6mo in	Comparison of MP + other treatment (physiotherapy, occupational therapy, physical practice) vs other treatment. Duration of sessions ranged from 10 to 60 minutes, with most trials delivering 30	**Primary outcomes:** ADL performance and motor function Outcomes were assessed before and after treatment	Including the results from 11 trials, MP was associated with significant improvement in the primary outcome (SMD=0.36, 95% CI 0.16-0.55). But the effect was lost when the analysis was restricted to trials of higher methodological quality (score >6): SMD=0.17, 95% CI -0.07 to 0.40.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		1 trial, <12mo in 1 trial, and >12mo in 6 trials.	minutes. Number of sessions ranged from 10 to 30, with most trials delivering 12 sessions.		

Bilateral Arm Training (BAT)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Gnanaprakasam et al. 2023 **India** **Systematic review & meta-analysis**	Using the Cochrane RoB tool, performance bias (blinding of participants and assessors) and lack of CA, were the domains associated with the highest risk of bias, across all trials.	13 RCTs including persons with first-ever stroke with upper-limb paresis. Mean ages ranged from 48.7 to 78.8 years. One trial included patients with acute stroke, 4 trials with subacute stroke and 8 trials with chronic stroke.	Trials compared task-based BAT (described as a method that entails repetitive practice of goal-oriented functional movements using both, more and less affected arm to complete the task) vs. a comparator typically, conventional rehabilitation (including CIMT), or unilateral arm training. Trials that used movement-based BAT, robotic-assisted arm training, arm cycling, and bilateral arm training with rhythmic auditory cueing were excluded. Sessions lasted from 20 minutes to 2 hours, and were provided 4-5 days/week for 3-12 weeks.	**Primary outcomes:** Impairment (FMA-UE), activity (ARAT, WMFT, MAL, Box & Block test [BBT], modified BI [mBI], FIM, and participation (Stroke Impact Scale [SIS]) In most trials, assessments were conducted before and after treatment.	*Bilateral arm training vs control group (both unimanual + conventional)* BAT was associated with significantly higher mean FMA-UE scores (SMD=0.62, 95% CI 0.12-1.12, 9 trials). BAT was not associated with significantly higher mean ARAT scores (SMD=0.35, 95% CI -0.31 to 1.00, 4 trials), MAL-AOU scores (SMD=0.09, 95% CI -0.56 to 0.74, 8 trials or mean MAL-QOM (SMD=-0.10, 95% CI -0.77 to 0.58, 8 trials). BAT was not associated with significantly higher mean BBT, mBI, FIM or SIS scores, although the results were based on 1-2 trials. *Bilateral arm training vs unimanual group* BAT was not associated with significantly higher mean FMA-UE, ARAT, MAL-AOU, or BBT scores, but was associated with significantly higher mean MAL-QOM scores (SMD=-0.64, 95% CI -1.08 to -0.20, 3 trials). *Bilateral arm training vs conventional group* BAT was associated with significantly higher mean FMA-UE scores (SMD=0.84, 95% CI 0.32-1.36, 7 trials), reductions in WMFT-TIME (SMD= -0.72, 95% CI -1.43 to -0.01), and BBT (SMD=0.52, 95% CI 0.04- 1.00).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Chen et al. 2022 **China** **Systematic review & meta-analysis**	PEDro scores ranged from 5-8.	25 RCTs, including 1,103 participants with upper limb impairment post stroke. Mean age ranged from 48.4 to 74.3 years. The percentage of men ranged from 40 to 94.1%. Time since stroke was acute (n=10, subacute (n=8) and chronic (n=16). Severity of upper limb paresis was mild (n=14, moderate (n=9) and severe (n=2)	Trials compared BAT vs. control conditions. Four categories of BAT trials were included: (1) bilateral functional task training (BFTT) (n = 10), (2) bilateral robot-assisted training (BRAT) (n = 9), (3) mirror therapy (MT) (n= 2), and (4) bilateral training with rhythmic auditory cueing (BATRAC) (n = 4). The control conditions included conventional therapy (CT) (n = 21) and unilateral arm training (UAT) (n = 10), including CIMT and robotic assisted therapy and dose-matched unilateral functional task training (UFTT)(n=2). Higher dose therapy was defined as ≥7 hrs/wk or total treatment hours ≥ 30. Lower dose therapy was defined as <7 hr/wk, or total treatment hours <30 hr. Treatment was provided 3-5days/week for 30-90 minutes for 3-8 weeks.	**Primary outcomes:** Fugl-Meyer Assessment of Upper Extremity (FMA-UE), Action Research Arm Test (ARAT), Box and Block Test (BBT) Wolf Motor Function Test (WMFT-time), Motor Activity Log (MAL)	*BAT vs Conventional Therapy* Overall, BAT was associated with significant improvement in total FMA-UE scores (MD= 3.94, 95% CI 1.73-6.15), 19 trials). The effect was significant in the chronic stage of stroke (MD = 4.59, 95% CI 2.00- 7.19) but not the subacute (MD=−0.74, 95% CI−5.94 to 4.46). The greatest benefit of BAT was found in patients with mild paresis, in the chronic stage of stroke (MD = 6.71, 95% CI [3.47- 9.94). Of the 4 types of BAT, only patients in the BFTT group demonstrated significantly greater gains in FMA-UL scores (MD=7.84, 95% CI 4.37-11.30, 6 trials). The benefit of BAT was significantly greater when BAT was delivered at high doses (MD=6.52, 95% CI: 3.48-9.57 vs. low dose: MD=0.82, 95% CI −2.42 to 4.06). BAT was not associated with significant improvement in ARAT, BBT, WMFT (time) of MAL. *BAT vs. unilateral arm training* Overall, BAT was not associated with significant improvement in FMA-UE scores (MD = −0.90, 95% CI −5.17 to 3.38, 6 trials)
Meng et al. 2018 **China** **RCT**	CA:☑ Blinding: Patient ☒ Assessor ☑ ITT: ☒	128 patients with acute stroke occurring less than 48 hours previously with hemiparesis, and impaired upper extremity function. Mean age was 57 years, 51% were men.	Patients were randomized to receive hand-arm bimanual intensive training (HABIT) or convention rehabilitation program (CRP) for 2 weeks (total of 20 hours).	**Primary Outcome:** Fugl-Meyer Motor Assessment (FMA) UE, Action Research Arm Test (ARAT) **Secondary Outcome:** Central motor	There was significantly greater improvement in mean FMA scores from baseline to end of treatment in the HABIT group (33.3 to 51.7 vs. 32.9 to 43.5, p<0.001). There was significantly greater improvement in mean ARAT scores from baseline to end of treatment in the HABIT group (30.3 to 34.5 vs. 31.5 to 33.3, p=0.022).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				conduction time (CMCT), motor-evoked potential amplitude (AMP)	There was significantly greater improvement in mean AMP (mV) in the HABIT group (0.63 to 1.4 vs. 0.63 to 0.96, p<.001). There was significant improvement in mean CMCT (sec) within each group over the 2 weeks, but no significant differences between groups.
Van Delden et al. 2012 **Netherlands** **Systematic review & meta-analysis**	PEDro scores ranged from 5 to 8.	9 RCTs including 452 participants with acute (n=1) and chronic (n=8) stroke. Mean age ranged from 51 to 68 years, 59% were men. Hemiparesis was mild in 4 trials, moderate in 2 trials, and mild to severe in 3 trials.	Trials compared unilateral arm training to bilateral arm training (BAT), defined as motor task performed simultaneously with both limbs. Studies using robot assistance, electrical stimulation, mirror therapy, or virtual reality were excluded. Interventions were provided as 20 minutes to 6 hours sessions, 3-6 days/week for 1-8 weeks.	**Primary outcomes:** Function (ARAT, WMFT), impairment (FMA-UE, Motor Status Scale, performance (Motor Assessment Scale) and perceived performance (MAL)	BAT was associated with significantly higher scores on tests of function (SMD=0.20, 95%CI 0.0–0.4), and MAL (AOU: SMD=0.42, 95% CI 0.09-0.76 and QOM: SMD=0.45, 95% CI 0.12-0.78). BAT was not associated with significantly higher scores on tests of impairment or performance.
Coupar et al. 2010 **UK** **Cochrane Review**	Majority of studies were of poor or uncertain quality.	18 RCTs with 549 participants (14 RCTS with 421 participants were included in pooled analysis). Stroke onset was acute/subacute in 4 trials, chronic in 12 trials, mixed in 1 trial, and not reported in 1 trial.	Trials compared bilateral arm training (BAT) training to usual care or other intervention. 7 trials used adjunctive treatments (electrical stimulation, robotic devices, auditory cueing). Intervention period ranged from 1 to 30 sessions over 6 weeks.	**Primary Outcomes** ADL performance, functional movement of the upper limb **Secondary Outcomes** EADL performance, measures/scales of upper limb impairment, muscle strength, and muscle tone	*Bilateral training vs usual care (4 trials)* BAT was not associated with significantly higher scores for any of the primary or secondary outcomes. *Bilateral training vs other intervention (11 trials)* BAT was not associated with significantly higher scores for any of the primary or secondary outcomes, except one. Using the results from a single trial, EADL scores were significantly higher in the BAT group (SMD= -0.65, 95% CI -1.29 to -0.01, p=0.04).

Mirror Therapy (MT)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Antoniotti et al. 2019 **Italy** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☒	40 patients with upper-limb impairment following first-ever stroke, occurring within the previous 4 weeks. Mean age was 69 years, 74% were men. Mean time since stroke was 23 days.	Patients were randomized to receive MT or sham treatment, 30 min/day, 5x/ week, for 6 weeks, in addition to conventional rehabilitation therapy.	**Primary outcome:** FMA-UE **Secondary outcomes:** ARAT, FIM Outcomes were assessed before and after treatment	There was significant improvement in mean FMA-UE scores in both groups over the study period with no significant difference between groups (intervention group 28.5 to 38.3 vs. control group 30.9 to 40.6). There was significant improvement in mean ARAT scores in both groups over the study period with no significant difference between groups (intervention group 23.5 to 30.0 vs. control group 25.1 to 31.9). There was significant improvement in mean FIM scores in both groups over the study period with no significant difference between groups (intervention group 72.9 to 99.4 vs. control group 71.0 to 100.3). There were 4 dropouts in the intervention group vs. 1 in the control group.
Yang et al. 2018 **China** **Systematic review & network meta-analysis**	PEDro scores ranged from 5 to 8. Critical Appraisal Skills Program Scale scores ranged from 10-15 (out of 16)	37 RCTs (42 analysis) including 1,685 participants recovering from stroke. Baseline demographics were not reported.	29 trials compared MT vs. conventional therapy (CT), 7 trials compared MT + electrical stimulation vs. conventional therapy and one trial compared MT + mesh glove (MG) stimulation vs. conventional therapy.	**Primary outcomes:** Fugl–Meyer Assessment (FMA), FIM, modified Ashworth Scale (MAS) **Secondary outcomes:** Brunnstrom stage score, Action Research Arm Test (ARAT), Box & Block test (BBT), modified Barthel Index (mBI), Motor Activity Log (MAL) and pain (VAS)	*Pairwise analysis* Overall, MT was associated with significantly greater improvement in FMA scores compared with conventional therapy (SMD=0.73, 95% CI 0.50-0.97; 32 trials). GRADE: moderate Overall, MT was associated with significantly greater improvement in FIM scores compared with conventional therapy (SMD=0.60, 95% CI 0.36-0.84; 10 trials). GRADE: high MT was not associated with significantly greater improvement in mAS scores (SMD= -0.13, 95% CI -0.30 to 0.05; 11 trials). GRADE: high MT was associated with significantly greater improvement in Brunnstrom scores (SMD=0.97, 95% CI 0.74-1.20; 7 trials). GRADE: high

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					MT was associated with significantly greater improvement in ARAT scores (SMD=1.90, 95% CI 0.45-3.34; 7 trials). GRADE: moderate MT was associated with significantly greater improvement in BBT scores (SMD=0.53, 95% CI 0.23 to 0.83; 10 trials). GRADE: high MT was associated with significantly greater improvement in MBI scores (SMD=1.32, 95% CI 0.57 to 2.08; 10 trials). GRADE: moderate MT was not associated with significantly greater improvement in MAL scores (SMD=0.36, 95% CI -0.14 to0.86; 5 trials). GRADE: moderate MT was associated with significantly greater improvement in pain scores (SMD=-1.73, 95% CI -2.63 to -0.82; 4 trials). GRADE: moderate *Network Meta-analysis* MT + electrical stimulation + conventional therapy provided for ≤ 4 weeks was more effective than conventional therapy only for improving FMA scores (SMD=0.38, 95% CI 0.22–0.55). No combinations of MT +/- electrical stimulation, or other therapies were better than conventional therapy for improving mAS scores. MT + conventional therapy provided for ≤ 4 weeks was more effective than conventional therapy + sham therapy for improving mBI scores (SMD=1.00, 95% CI 0.36–1.64).
Thieme et al. 2018 **Germany** **Cochrane review**	Risk of bias was generally low across 4 domains (randomization, CA, incomplete outcome data	62 RCTs including 1,982 participants with upper and lower-limb impairment following stroke. Mean age was 59 years, 60% were men. 29 trials included participants in the acute or	Trials compared mirror therapy vs. no-treatment, usual or standard practice, or any other control treatment. 10 trials examined mirror	**Primary outcomes:** Upper limb and hand motor function, lower-limb motor function and global motor function: **Secondary Outcomes:**	Results were available for the upper-limb subgroup for a single outcome. Mirror therapy was associated with significantly better upper-limb motor function compared with the control group at the end of the intervention (SMD=0.46, 95% CI 0.23-0.69, 31 trials,

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	and blinded assessors)	subacute phase after stroke (within 6 months) and 21 trials included participants in the chronic phase (>6 months).	therapy for the lower extremity and 52 trials examined the upper extremity. Mirror therapy was provided 3-7x/week, as 15–60-minute sessions for 2 to 8 weeks. (On average, 5x/week, for 30 minutes for 4 weeks).	Upper and lower-limb impairment, ADL, pain and visuospatialneglect	n=1,048).
Zeng et al. 2017 **China** **Systematic review & meta-analysis**	Using the Cochrane RoB tool, selection bias was low; performance bias (blinding of participants) was high; detection bias, attrition bias and reporting bias were all low.	11 RCTs including 347 participants with upper-limb impairment following stroke. Mean age ranged from 45 to 64.9 years. Stroke onset was acute/subacute in 4 studies and chronic in 7 studies.	Trials compared mirror therapy (MT) +/- conventional therapy (CT) vs. CT alone. Therapy in the MT group was provided 5 days/week, with 20–90-minute sessions, with most trials providing 30 minutes. Durations of therapy ranged from 3-8 weeks (average of 4). Therapy in the control group was provided 5 days/week.	**Primary outcome:** Motor function (FMA-UE)	Mirror therapy was associated with significantly better motor function, compared with the control condition (SMD=0.51, 95%CI 0.29-0.73, p<0.00001).
Arya et al. 2015 **India** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	33 patients aged < 60 years, with single unilateral stroke of duration >24 weeks, with upper limb paresis (Brunnstrom recovery stage of arm ≥2). Mean age was 45 years, 76% were men. Mean time since stroke was 12.5 months.	Patients were randomized to a MT or a control group that received conventional occupational therapy. Therapy was provided for 45 min/day, 5x/ week, for 8 weeks.	**Primary Outcomes:** Brunnstrom Recovery Stage, FMA-UE Outcomes were assessed before and after treatment	There was significantly greater improvement in mean FMA-UE scores in the MT group. Improvement in the wrist/hand subscore was significantly higher with no significant differences between groups in the upper arm component. After intervention, the experimental group exhibited a 12% increase in the number of participants at stage 5 both for BRS-A and BRS-H compared with 0% in the control group.
Timmermans et al. 2013 **The Netherlands** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑	42 participants, recruited from rehabilitation departments with upper-limb paresis following stroke with onset 2-6 weeks previously. Mean	Participants were randomized 1:1 to receive mirror therapy (MT) + regular therapy (to be practiced 3x/day for 10 minutes) or usual care (control) for the	**Primary Outcomes:** Fugl-Meyer Assessment (FMA)-UE, Wolf Motor Function Test (WMFT), Frenchay Arm Test (FAT), BI,	There was significant improvement from baseline to 6 and 12 months in mean BI scores within groups, with no significant between group differences. There was no significant improvement from

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	ITT: ☑	age was 59 years, 62% were men. Mean time since stroke was approximately 34 days.	same amount of time. The study duration was 6 weeks.	Frenchay Activity Index (FAI) Outcomes were assessed before and after treatment, and at 6- and 12-month follow-up.	baseline to end of treatment and 6 months in mean FAI scores within or between groups. There was significant improvement in FMA-UE scores from baseline to end of treatment and at 12 months in both groups with no significant differences between groups. Both groups showed significant improvements on WMFT after treatment (time, functional ability subscale, grip strength and lifting), but there were no significant differences between groups except for the lifting subcomponent, whereby patients in the MT group scored higher. There was significant improvement in FAT scores in both groups from baseline to 12 months. Only patients in the MT group showed significant improvement on FAT after treatment, and at 12-month follow-up, but there was no significant difference within the control group. There were 3 dropouts in the MT group and 7 in the control group.

Strength Training

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Hunter et al. 2018 **United Kingdom** **RCT** ***FAST-INdiCATE Trial***	CA ☑ Blinding Patient ☒ Assessor ☑ ITT: ☑	288 participants who had sustained a stroke in the anterior cerebral circulation territory within the previous 2-60 days, with some voluntary muscle contraction in the paretic upper limb and without full dexterity. Mean age was 72 years, 64.6% were men.59% of patients were recruited within 30 days of stroke onset.	Patients were randomized to receive functional strength training (FST) or movement performance therapy (MPT) in addition to conventional rehabilitation. Treatment was provided 60 minutes/day, 5 days/week for 6 weeks.	**Primary Outcome:** Action Research Arm Test (ARAT) **Secondary measures** Wolf Motor Function Test (WMFT) Outcomes were assessed at 6 weeks and 6 months.	There was significant improvement in mean ARAT scores at 6 weeks within each group with no significant differences between groups (FST: 24.4 to 34.1 vs. MPT: 26.5 to 34.4, p=0.29). There was no significant difference between groups in mean ARAT scores or mean change scores from baseline. There were no significant differences between groups in mean WMFT scores, or mean change scores at 6 weeks or 6 months. Baseline neuro measures could not predict therapy response and were not correlated with regained upper extremity function. Adverse events were experienced by 129 participants, serious events by 41 participants.
Harris & Eng 2010 **Canada** **Systematic review & meta-analysis**	PEDro scores ranged from 2 to 8.	13 RCTs including 517 participants recovering from stroke. Mean age ranged from 46 to 74 years. Stroke onset was acute/subacute in 9 trials and chronic in 4 trials.	Trials compared programs that included strength or resistance training (excluding robotic devices, electrical stimulation, CIMT) vs. various control conditions (active program, usual care, or no therapy). Treatment was provided on average for 60 minutes/day, 2-3 days/week for 4 weeks.	**Primary outcomes:** Motor function, ADL and grip strength Outcomes were assessed before and after treatment.	Strength training was associated with significantly better motor function scores (SMD=0.21, 95% CI 0.03 to 0.39, 11 trials), and grip strength (SMD=0.95, 95% CI 0.05 to 1.85, 5 trials), but not performance of ADLs (SMD=0.26, 95% CI -0.10 to 0.63,5 trials). *Subgroup analyses* Effect sizes were similar for the outcome of motor function, in trials that included participants in the subacute and chronic stages of stroke (SMD=0.27 and SMD=0.32). Effect size was larger for motor outcome in trials that included participants with moderate motor impairment (SMD=0.45, 95% CI 0.05 to 0.84), compared with persons with mild impairment (SMD=0.26, 95% CI 0.08 to 0.61).

Interventions for Sensory Impairment

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
de Diego et al. 2013 **Spain** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☒	21 participants with severe motor and sensory impairment following stroke with onset >6 months, who were receiving conventional rehabilitation at a rehabilitation centre. Mean age was 61 years. Mean time since stroke was approximately 55 months.	Participants were randomized to an experimental group (EG) or a control group (CG). The EG received 16 sessions of the protocol of 1 hour at the center during 8 weeks, 2 sessions per week, and 1 daily session of 30 minutes of functional activity training at home. Sessions included 30 minutes of sensory stimulation of the hand, 15 minutes of isolated activity and 15 minutes of ADL training. Constraint - induced movement therapy was used in the sessions. The CG received conventional rehabilitation of the upper limb as 2 sessions per week.	**Primary outcomes:** Fugl Meyer Assessment (FMA)-UE, Motor Activity Log (MAL) and Stroke Impact Scale-16 (SIS-16) scores, and sensory tests (discrimination of motion, discrimination of filament and discrimination of object consistency) Outcomes were assessed before and after treatment.	There was significant improvement in mean FMA scores within groups over the study period with no significant differences between groups. There was no significant improvement in mean MAL (AOU) scores within either group, but there was significant improvement in mean MAL (QOM) scores in the EG but not the CG. There was significant improvement in mean SIS-16 scores in the EG but not the CG. There was significant improvement in all the measures of sensory tests in the EG, but not the CG.
Carey et al. 2011 **Australia** **RCT** ***Study of the Effectiveness of Neurorehabilitation on Sensation (SENSe)***	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☒	50 participants with impaired texture discrimination, limb position sense, and/or tactile object recognition, following stroke, with duration of onset >6 weeks. Mean age was 61 years, 74% were men. Median time since stroke was 48 weeks. Median baseline NIHSS score was 48.	Patients were randomized 1:1 to receive somatosensory discrimination training or repeated exposure to sensory stimuli during 10, 60-minute sessions, 3x/week (total of 10 hours).	**Primary outcome:** Change in a composite standardized somatosensory deficit (SSD) Outcomes were assessed after treatment and at 6weeks and 6 months.	Following the intervention, there was significantly greater improvement in the primary outcome in the active intervention group (19.1 vs. 8.0 SSD, mean change=11.1, 95% CI 3.0 to 19.2). These benefits were maintained at 6 weeks and 6 months.
Doyle et al. 2010 **USA** **Cochrane Review**	In 4 trials, risk of bias was high in ≥1 domain. Risk of bias	13 RCTs including 467 participants with disturbance in sensory function following stroke. Mean age ranged from	Types of interventions evaluated included: sensory retraining programs (n=3), electrical stimulation (n=2), inflatable splints (n=2), thermal	**Primary outcome:** Sensation (13 measures) **Secondary outcome:**	No pooled analyses were conducted. A single trial of electrical stimulation + exercise vs. exercise only, found no difference between groups in kinesthesia and position sense of wrist and

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	was low or unclear in the remaining trials.	22 to 87 years. Time since stroke was <1 month (3 trials); within 6 months (5 trials); and ≥6 months (2 trials). Time since stroke was not reported in 3 trials.	stimulation (n=1), rTMS (n=1), intermittent pneumatic compression (n=1), tensive mobilizations (n=1)	Upper limb functional use, activity limitations, and participation	fingers. A single trial using an inflatable pressure splinting intervention vs. no splinting found a significant reduction in pain in the splinting group. A single trial of thermal stimulation (heating alternating with cooling) + standard therapy vs. standard therapy, reported a greater rate of recovery of sensation in the experimental group. Thermal stimulation was associated with significant improvement in arm function. Mirror therapy was associated with significant improvement in light touch, pain (hot) and pressure pain. Intermittent pneumatic compression of the hemiplegic upper limb was associated with significantly higher overall Nottingham Sensory Assessment scores. Mirror therapy and neuromuscular electrical stimulation were associated with better performance on measures of upper arm function.

Neuromuscular Electrical Stimulation (NMES)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Monte-Silva et al. 2019 **Brazil** **Systematic review & meta-analysis**	Median PEDro score was 6 (range 3-8)	24 RCTs including 751 participants with upper-limb impairment following stroke. Mean age ranged from 43 to 71 years. 7 trials included persons with acute or subacute stroke and 17 included those with chronic stroke.	Trials compared EMG-NMES vs a control group, which could include cyclic NMES, sham NMES, unilateral or bilateral hand training, self-exercise of wrist extension, or occupational/physical therapy. Sessions were 20-90 minutes each, provided 2-5x/week for 3-20 weeks.	**Primary Outcomes:** Measures using the ICF classification system including body structures and function, activity and participation. Outcomes were assessed before and after treatment, with 9 studies including follow-up ranging from 5 weeks to 1 year.	*Body Structure and Function* Domain Total: EMG-Overall, NMES was associated with significantly greater improvement (SMD=0.47, 95% CI 0.21 to 0.72, 24 trials). The benefit was greater in the chronic stage (SMD=0.52, 95% CI 0.22 to 0.81) vs. acute (SMD=0.36, 95% CI –0.13 to 0.86). There was no benefit of treatment at follow-up (SMD=.22, 95% CI −0.12 to 0.55, 7 trials). *Activity limitations* Overall, NMES was not associated with significantly greater improvement (SMD=0.20, 95% CI –0.3 to 0.42, 24 trials), nor in either in acute or subacute stroke (SMD=0, 95% CI-0.28 to 0.28) or in chronic stroke (SMD=0.29, 95% CI –0.02 to 0.60). There was no benefit of treatment at follow-up (SMD=0.05, 95% CI −0.17 to 0.0.28, 8 trials). *Participation* Overall, NMES was not associated with significantly greater improvement (SMD=0.44, 95% CI –0.08 to 0.96, 7 trials), nor in either acute or subacute (SMD=0.32, 95% CI –0.55 to 1.19) or in chronic stroke (SMD=0.63, 95% CI 0.08 to 1.17).
Kwakkel et al. 2016 **Netherland** **RCT** ***EXplaining PLastICITy after stroke (EXPLICIT) trial***	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☑	101 patients with upper-limb paresis and an unfavourable prognosis (no voluntary finger extension), <14 days after first-ever ischemic stroke. Mean age was 59 years, 64% were men.	Patients were randomized to receive 2, 30-minute sessions/day of EMG-NMES on finger extensors for 3 weeks or usual care (passive range-of-motion exercises and facilitation of voluntary movements, provided for 30 minutes/working day for 3 weeks).	**Primary Outcomes:** Action Research Arm Test (ARAT). **Secondary Outcomes:** Fugl Meyer Assessment (FMA-UE), Wolf Motor Function Test (WMFT), Motricity Index for the Upper Extremity (MI-UE), Erasmus modification of the Nottingham	There were no significant differences between groups on any of the outcomes, assessed at any time point.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				Sensory Assessment of the Upper Extremity (EmNSA-UE), Nine Hole Peg Test (NHPT), Frenchay Arm Test (FAT), Motor Activity Log-Quality of movement (MAL-QOL), Motor Activity Log-Amount of Use (MAL-AOU), Hand Domain of the Stroke Impact Scale (SIS-Hand). Outcomes were assessed at baseline and at 5, 8, 12, and 26wk post-treatment.	
Meilink et al. 2008 **Netherlands** **Systematic review & meta-analysis**	PEDro scores ranged from 2-6.	8 RCTs including 157 participants with stroke. Mean age ranged from 55 to 69 years. Mean time since stroke was >12 months in 7 trials and < 90 days in one trial.	Trials compared surface EMG-NMES vs. conventional therapy or no therapy. on motor recovery (n=), EMG-NMES vs. cyclical NMES (n=1) and conventional electrostimulation vs. EMG-triggered feedback combined with movement imagery (n=1). NMES was applied as 35-100 Hz, 5-60 mA, average treatment parameter-1 sec ramp up, 5 sec stimulation, 1 sec ramp down, 25 sec rest. Treatment was provided 2-3 x/day for 30 min, 3-4 days/week for 2-8 weeks.	**Primary Outcomes:** ARAT, Fugl Meyer Assessment (UE), Block & Box test, reaction time. No indication of timing of outcome assessment.	NMES was not associated with significantly higher FMA-UE scores (SMD=0.10, 95% CI -0.43 to 0.64, 3 trials), Box & Block test (SMD=0.37, 95% CI -0.27 to 1.01, 3 trials), ARAT scores (SMD=0.0, 95% CI -0.56 to 0.57, 2 trials) or reaction time (SMD=0.41, 95% CI -0.20 to 1.03, 2 trials).

Functional Electrical Stimulation (FES)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Khan et al. 2023 **Mexico** **Systematic review**	Most of the RCTs were rated as low risk of bias using the Cochrane RoB tool. 7 of the observational studies were of good quality and 4 were of 4 quality using the NIH Quality Assessment tool	25 studies (9 RCTs) including patients recovering from stroke with upper-limb impairment.	Studies examined the benefit of different types of FES systems, including manually controlled FES, brain-computer interface (BCI)-controlled FES, and electromyography (EMG)-controlled FES.	**Primary outcome:** FMA, ARAT	**Manually Controlled FES:** Mean improvement in FMA scores was 5.6 points (95% CI 3.77 to 7.5; P < 0.001). **BCI-Controlled FES:** Mean improvement in FMA scores was 5.37 points (95% CI 4.2 to 6.6; P < 0.001). **EMG-Controlled FES:** Mean improvement in FMA scores was 14.14 points (95% CI 11.72 to 16.6; P < 0.001); ARAT scores improved by 11.9 points (95% CI 8.8 to 14.9; P < 0.001).
Eraifej et al. 2017 **UK** **Systematic review & meta-analysis**	Using the Cochrane RoB tools, risk of bias was low or unclear in all 7 domains across all trials, except for blinding of participants, in which risk of bias was high. The authors considered 9 trials to be at low risk of bias, one to	20 RCTs including participants > 18 years with haemorrhagic or ischaemic stroke. Mean age was 60 years. Mean time since stroke was <2 months (n=5), 1-3 years (n=5), and >3 years (n=6).	Trials compared upper limb transcutaneous FES applied to the peripheral nervous system, defined as (a) applied to the skin externally and (b) during voluntary movement in addition to standard post-stroke rehabilitative therapy vs. a control group received standard care. FES ranged 20–50 Hz, peak current ≤ 70 mA and duration of stimulation from 3 to 10 s. Muscles stimulated included deltoid, triceps and the wrist and finger extensors/flexors. Treatment duration ranged from 2 weeks to 3 months.	**Primary outcome:** Activities of daily living **Secondary outcomes:** Performance on non-ADL tasks	FES was not associated with significant improvement in ADL performance (SMD=0.64, 95% CI -0.02-1.30, 8 trials). In subgroup analysis, persons who received FES within the first 2 months of stroke did benefit from treatment (SMD=1.24, 95% CI 0.46, 2.03, 5 trials). FES was associated with significant improvement in Fugl-Meyer Assessment scores (MD=6.72, 95% CI 1.76-11.68, 7 trials), but not on the Box & Block test (MD=5.37, 95% CI -0.06-10.75, 3 trials).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	be at high risk and in the remaining trails the risk of bias was unclear.				
Vafadar et al. 2015 **Canada** **Systematic review & meta-analysis**	PEDro scores ranged from 3 to 8.	10 trials (9 RCTs and 1 quasi-RCT) including persons recovering from stroke. Mean age ranged from 53 to 75.5 years. 9 studies evaluated UE motor function, of which only 6 applied FES during the early stages of stroke recovery (<6 months).	Trials compared FES + conventional therapy vs. conventional with OT/PT. Frequency of the intervention ranged from 1x/d to 5x/d and lasted from 4 to 6 weeks.	**Primary Outcomes:** Motor Assessment Scale, Fugl Meyer Assessment, Action Research Arm Test, Frenchay Arm Test, Motricity Index, Brunnstrom stages, Assessment time point of outcomes was not indicated.	FES was not associated with a significantly improved motor function when applied within 6 months of stroke (SMD=0.36, 95% CI -0.27 to 0.99, 5 trials, n=295).

Non-Invasive Brain Stimulation

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Non-invasive brain stimulation (all forms)					
Ahmed et al. 2022 **Belgium** **Systematic review & network meta-analysis**	Using the Cochrane RoB tool, most trials were at low or unclear risk of bias across the 6 domains assessed. The domain with the highest	87 RCTs including 3,750 participants in the acute/subacute (<6 months) or chronic (>6 months) stage of ischemic and/or hemorrhagic stroke	Trials compared non-invasive brain stimulation (NIBS) modalities including tDCS (bihemispheric, anodal and cathodal), repetitive transcranial magnetic stimulation (rTMS; low and high frequency), theta-burst stimulation (TBS; intermittent and continuous), and transcutaneous vagus nerve stimulation (taVNS) +/- physical rehabilitation vs.	**Primary outcome:** Performance of ADL, motor function	*Motor function* There were 79 trials (103 arms). Of these, 1,917 patients received the real NiBS, and 1,205 patients received sham NiBS as a comparator intervention (67 studies), and 166 patients received physical rehabilitation as the comparator intervention. All NiBS protocols except continuous TBS and cathodal tDCS were significantly better than sham stimulation or physical rehabilitation with SMDs ranging from 0.42-1.20 (sham stimulation) and 0.68 to 1.48 (physical rehabilitation). The most effective treatment was taVNS.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	percentage of trials at high risk of bias was intention-to-treat (35%)		sham stimulation or active physical rehabilitation.		In pair-wise comparisons of NIBS vs. sham, taVNS had the highest efficacy (SMD=1.20, 95% CI 0.46 to 1.95). Anodal tDCS was more effective than cathodal tDCS and HF rTMS was better than LF rTMS. *ADL performance* There were 46 trials (58 arms). Of these, 1,074 patients received the real NiBS, while 728 patients received sham NiBS as a comparator intervention, and 83 patients received physical rehabilitation as the comparator intervention. taVNS, anodal tDCS, HF-rTMS, and LF-rTMS interventions were superior to sham stimulation, with SMDs ranging from 0.52-1.00 and 0.74-1.21 for physical rehabilitation. In pair-wise comparisons of NIBS vs. sham, anodal tDCS, HFrTMS and LF rTMS were significantly better, with SMDs of 0.65, 0.55 and 0.52, respectively. In subgroup analysis, taVNS, anodal tDCS, HF-rTMS, and LF-rTMS were more efficacious than sham stimulation for improving upper limb motor function (SMD range 0.53-1.63), and performance in ADLs (SMD range 0.56-0.95) in acute/sub-acute stroke. iTBS, anodal, and dual tDCS were more efficacious than sham stimulation for improving upper limb motor function in chronic stroke (SMD range 0.39-1.16).
tDCS					
Elsner et al. 2020 **Germany** **Cochrane review**	Risk of bias was assessed as low or unclear in all	67 RCTs including 1,729 participants with stroke. Mean age ranged from 43 to 75 years. The percentage of men	Trials compared active anodal or cathodal tDCS vs. sham treatment or an active treatment comparator (physical therapy,	**Primary outcome:** ADL performance **Secondary outcome:** Upper limb function	tDCS was associated with significant improvement in ADL performance, measured after the intervention, compared with placebo or passive control interventions (SMD=0.28, 95% CI 0.13 to 0.44, 19 trials, n=686). GRADE: moderate. At

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	9 domains, using the RoB tool.	ranged from 25 to 100%. Persons in the acute, subacute and chronic stages of stroke were included.	occupational therapy, mirror therapy or virtual reality).	(Other outcomes, not of focus, assessed lower limb function, cognition, muscle strength and safety)	follow-up, the benefit of tDCS remained (SMD=0.31, 95% CI 0.01 to 0.62; 6 trials, n=269). GRADE: moderate In subgroup analysis of stroke chronicity, tDCS was not associated with improvement in ADL in weeks 1-4 post stroke (SMD=0.26, 95% CI -0.01 to 0.53, 5 trials), or 6 months of later (SMD=0.14, 95% CI -0.15 to 0.42, 9 trials), but was associated with improvement 1-6 months post stroke (SMD=0.34, 95% CI 0.09 to 0.59, 5 trials). tDCS was not associated with significant improvement in upper-limb function measured after the intervention, compared with placebo or passive control interventions (SMD=0.17, 95% CI -0.05 to 0.38; 24 trials, n=792). GRADE: moderate, without a benefit at follow-up (SMD=0.0, 95% CI -0.39 to 0.39; 5 trials, n=211). GRADE: moderate tDCS was associated with significant improvement in ADL performance, measured after the intervention, compared with an active intervention control (Barthel Index MD=6.59, 95% CI 1.26 to 11.9, 3 trials, n=121). GRADE: low tDCS was associated with significant improvement in upper-limb function measured after the intervention, compared with an active intervention control (SMD=0.84, 95% CI 0.2 to 1.48; 5 trials, n=124). GRADE: low
Chhatbar et al. 2016 **USA** **Systematic review and meta-analysis**	N/A	8 RCTs (213 participants) investigating the role of tDCS (≥5 sessions) in post stroke recovery of upper limb.	Comparisons were conducted between active and sham tDCS stimulation groups.	**Primary Outcomes:** Fugl Meyer Assessment (FMA-UE). Hedges' *g* effect sizes were calculated, and evaluated based on the criteria: <0.2 = mild ~0.5 = moderate	**Hodge's g effect sizes:** tDCS (n=8): SMD=0.61, 95% CI 0.08 to 1.13, I^2=71%, p=0.02. [moderate effect size] Anodal tDCS (n=3): SMD=0.21, 95% CI -0.72 to 1.14, I^2=71%, p=0.65. Cathodal tDCS (n=4): SMD=0.43, 95% CI -0.23 to 1.08, I^2=45%, p=0.2.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				>0.8 = strong	Bihemispheric tDCS (n=3): SMD=1.30, 95% CI -0.14 to 2.75, I^2=81%, p=0.08. Acute stroke (n=6): SMD=0.18, 95% CI -0.30 to 0.66, I^2=51%, p=0.47. Chronic stroke (n=4): SMD=1.23, 95% CI 0.20 to 2.25, I^2=71%, p=0.02. [strong effect size] **Meta-analysis:** tDCS (n=7): SMD=-0.06, 95% CI -0.31 to 0.20, I^2=0%, p=0.65. Anodal tDCS (n=2): SMD=-0.18, 95% CI -0.63 to 0.27, I^2=0%, p=0.43. Cathodal tDCS (n=4): SMD=0.03, 95% CI -0.37 to 0.42, I^2=0%, p=0.9. Bihemispheric tDCS (n=3): SMD=-0.05, 95% CI-0.59 to 0.49, I^2=0%, p=0.85. Acute stroke (n=5): SMD=-0.08, 95% CI -0.38 to 0.23, I^2=0%, p=0.62. Chronic stroke (n=4): SMD=-0.02, 95% CI -0.49 to 0.46, I^2=0%, p=0.65.
rTMS					
Edwards et al. 2023 **USA** **RCT** ***Electric Field Navigated 1hz Rtms for Post-stroke Motor Recovery Trial E-FIT*** ***(extension of the***	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☑	60 patients recruited from 12 outpatient rehabilitation centres, with a unilateral ischemic stroke occurring within 3 to 12 months of enrollment, and with a Chedoke assessment stage of 3-6 for both arm and hand. Mean age was 58.5 years, 70% were men. 55% of patients were recruited	Patients were randomized to receive active rTMZ (1 Hz) over the noninjured motor cortex (n=31) or sham stimulation (n=29, different sham coil than that used in NICHE), prior to each of 18 therapy sessions, lasting 60 minutes, and delivered over 6 weeks.	**Primary outcome:** A 5-point change in the FMA-UE (considered clinically meaningful) at 6 months following end of treatment. **Secondary outcomes:** FMA-UE, Action Research Arm Test (ARAT), NIHSS, EQ-5D	*Combined data from NICHE and E-FIT* The combined mean odds of achieving the primary outcome were not significantly higher in the active rTMS group (posterior mean OR=0.94, 96% credible interval of 0.61–4.80). *E-FIT* The percentage of patients in the active rTMS group who achieved the primary outcome was 60% vs. 50% in the sham group (OR=1.49, 95% CI 0.53 to 4.22). There was significant within group improvement in

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
NICHE trial)		from 6-12 months post stroke			mean scores for all the secondary outcomes at 6 months, with no significant differences between groups. There were 10 serious adverse events in 9 patients (4 in the active rMTS group and 6 [5 patients] in the sham group.
Chen et al. 2022 **China** **Systematic review & meta-analysis**	Mean PEDro score was 8.4.	45 RCTs including 2,064 participants with stroke. Mean age ranged from 50.5 to 75 years. Time since stroke was acute in 12 trials, subacute in 14 trials, and chronic in 19 trials.	Trials compared rTMS +/- an additional intervention vs. a control group that received sham rTMS or no rTMS. High frequency rTMS (20 Hz) was used on the affected side in 2 trials. Medium frequency rTMS (3-10 Hz) was used on the affected side in 18 trials. Low frequency (1 Hz) was used on the unaffected side in 31 trials, rTMS was applied bilaterally in 9 trials. The number of sessions ranged from 5 to 40.	**Primary outcome:** FMA-UE **Secondary outcomes:** Box & block test (BBT), 9-hole peg test, and Purdue pegboard test	Overall, rTMS was associated with significantly greater improvement in upper arm function, assessed using the FMA-UE (SMD=1.12, 95% CI 0.56-1.68, 17 trials). The benefit persisted up to 5 months following the intervention. Overall, rTMS was associated with significantly greater improvement in hand function (SMD=0.38, 95% CI 0.19 to 0.58, 17 trials). The benefit was greatest in the subacute and chronic stage (SMD= 0.69, 95% CI 0.22 to 1.16 and SMD=0.38, 95% CI 0.07 to 0.69, respectively), with no significant improvement in the acute stage (SMD=0.27, 95% CI −0.02 to 0.56).
Tang et al. 2022 **China** **Systematic review & meta-analysis**	Mean PEDro scores ranged from 6-10.	15 RCTs including 449 participants with upper-limb motor impairment following stroke. Mean age ranged from 49 to 71 years, 67% were men. Time since stroke was < one month (n=6), 1-3 months (n=3) and >3 months (n=6).	Trials compared high-frequency (3-10 Hz) rTMS (HF-rTMS, n=11) or intermittent theta-burst stimulation (iTBS, n=4) applied over the ipsilateral motor cortex vs. sham stimulation (n=13) or conventional rehabilitation (n=2). In most trials, 10 sessions were provided.	**Primary outcomes:** Upper limb motor function (FMA-UE), hand strength and dexterity	The FMA-UE score was significantly higher in the experimental group (MD=5.88, 95% CI 3.32 to 8.43, 11 trials, n=181). The benefit was significant when treatment was delivered <3 months after stroke. Hand strength was significantly greater in the experimental group (SMD=0.53, 95% CI 0.04 to 1.01). Hand dexterity was significantly better in the experimental group (SMD=0.76, 95% CI 0.39 to 1.41).
Harvey et al. 2018 **USA** ***Navigated***	CA: ☒ Blinding: Patient ☑ Assessor ☑	199 patients, recruited from 12 outpatient rehabilitation centres, with a unilateral ischemic or hemorrhagic stroke	Patients were randomized to receive active rTMZ (1 Hz) over the noninjured motor cortex (n=132) or sham stimulation (n=67), prior to	**Primary outcome:** A 5-point change in the FMA-UE (considered clinically meaningful) at 6 months following end	Six-month data were available for 113 patients in the active rTMS group and for 60 in the sham group. There was significant improvement in mean scores

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Inhibitory rTMS to Contralesional Hemisphere (NICHE) Trial	ITT: ☑	occurring within 3 to 12 months of enrollment, and with a Chedoke assessment stage of 3-6 for both arm and hand. Mean age was 58.7 tears, 65.3% were men. 71% of patients were recruited from 6-12 months post stroke.	each of 18 therapy sessions, lasting 60 minutes, and delivered over 6 weeks.	of treatment. **Secondary outcomes:** Action Research Arm Test (ARAT) and Wolf Motor Function Test (WMFT) testing hand speed and dexterity.	for all outcomes in both groups at 6 months. At 6-month follow-up, 67% (95% CI, 58%–75%) of patients in the active group had achieved the primary outcome compared with 65% (95% CI, 52%–76%) in the sham group (p=0.76). At 6 months, there was also no difference between experimental and sham groups in the mean change from baseline in ARAT (5.0 vs. 5.0, p=0.80) or WMF -9.0 vs. -10.6, p=0.55).
Li et al. 2016 **China** **RCT**	CA: ☒ Blinding: Patient ☑ Assessor ☒ ITT: ☒	127 participants with upper-limb dysfunction following stroke. Mean age was approximately 56 years, 68.5% were men. Mean time since stroke was <2 months.	Participants were randomized 1:1:1 to receive either low frequency rTMS (1Hz), over the contralateral hemisphere primary motor cortex (MI), high frequency rTMS (10Hz) over the ipsilateral M1, or sham stimulation daily for 20min, 5d/wk for 2wk.	**Primary Outcomes:** Fugl-Meyer Assessment (FMA-UE), Wolf Motor Function Test (WMFT). Outcomes were assessed at baseline and post-intervention.	There was significant improvement in mean FMA-UE scores in all groups, although improvement was significantly greater in the LF-rTMS and HF-rTMS groups compared to the sham stimulation group. There was significant improvement in mean WMFT scores in all groups, with no significant among them. There were 9 losses in the LF-rTMS group, 7 in the HF-rTMS group and 9 in the sham group.

Virtual Reality

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Chen et al. 2022 **Hong Kong** **Systematic review & meta-analysis**	2 trials each were at high risk of bias for random sequence generation and incomplete reporting (attrition bias).	43 RCTs, including 1,893 participants with upper-limb dysfunction following stroke. Mean age was 60 years, 61% were men. Time since stroke was ≤6 months (22 trials) and >6 months (20 trials).	Trials compared VR-supported exercise therapy alone vs. no therapy (n=2); VR-supported exercise therapy alone compared with conventional therapy (CT, n=13) and VR-supported exercise therapy + CT vs. CT (n=28). In 16 RCT's, commercial games were used and in 27 RCT's, programs designed for rehabilitation were used. Treatment was provided >3X/week in most trials as 20-45 minutes sessions (n=23) or >45 to ≤75 minutes sessions (n=16). Duration of therapy was 2 weeks to 1 month (n=31) and >1 to ≤2 months (n=10).	**Primary Outcome:** Impairment: Fugl Meyer Assessment (FMA-UE) **Secondary Outcomes:** Activity limitations: FIM, BI, Box & Block Test (BBT), (ARAT), Wolf Motor Function Test (WMFT); Participation outcomes: Stroke Impact Scale (SIS), Motor Activity Log (MAL)	*Impairment* VR was associated with significantly higher FMA-UE scores (SMD=0.45, 95% CI 0.21 to 0.68, 28 trials). Effect size was decreased when one outlier was removed (SMD=0.35, 95% CI 0.19-0.50). The effect was significantly greater in trials that provided therapy for >15 hours (SMD=0.92, 95% CI 0.35 to 1.49) vs. ≤15 hours (SMD= −0.10, 95% CI −0.35 to 0.15). *Activity Limitation* VR was associated with significantly higher FIM scores (SMD=0.23, 95% CI 0.06-0.40, 13 trials, but not BI scores (SMD=0.20, 95% CI −0.16 to 0.55, 11 trials). VR was not associated with significantly higher BBT, ARAT WMFT (total score or time) scores. *Participation* VR was not associated with significantly higher SIS or MAL scores.
Laver et al. 2017 **Australia** **Cochrane Review**	N/A	72 RCTs including 2,470 participants of which 22 RCTs (1,038 participants evaluated upper limb motor function and activity. Mean ages ranged from 46 to 75 years.Time since stroke was <3 months in 13 trials, >6 months in 31 trials	Trials compared upper limb training programs using virtual reality (VR) +/- conventional therapy or conventional therapy only. 22 RCTs used commercially available gaming consoles: 1 RCT used Playstation EyeToy, 15 RCTs used Nintendo Wii, 4 RCTs used Microsoft Kinect, 2 RCTs used mixed gaming consoles, 8 RCTs, used GestureTek IREK, 1 RCT used Armeo, 1 RCT used CAREN and 1 RCT used Lokomat. Dosage of therapy varied: 22	**Primary Outcomes:** Measures of arm and hand function and activity Outcomes were assessed before and after treatment in all studies.	*Virtual reality vs. conventional therapy* VR was not associated with significantly better arm function (SMD=0.07, 95% CI -0.05 to 0.20, 22 trials, n=1,038) post intervention GRADE: low, or after 3-month follow-up (SMD=0.11, 95% CI -0.10 to 0.32, 9 trials, n=366). VR was associated with significantly higher FMA-UE scores (MD=2.85, 95% CI 1.06 to 4.65, 16 trials, n=599), but not grip strength (SMD=-0.02, 95% CI -0.27 to 0.22; 6 trials, n=266) or subjective assessment of amount of Use (SMD=-0.11, 95% CI -0.42 to 0.21; 5 trials, n=161). Time since onset of stroke, severity of impairment, and the type of device (commercial or customized) were not significant effect modifiers.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			RCTs delivered 6-10hr, 26 RCTs delivered 11-20hr, 7 RCTs delivered >21hr, or a combination of high intensity and low intensity.		*Virtual reality + conventional therapy vs. conventional therapy* VR was associated with significantly better arm function (SMD=0.49, 95% CI 0.21 to 0.77, 10 trials, n=210). GRADE: low Adverse events: 23 studies reported data. 19 RCTs reported no significant adverse events. Reported adverse events included transient dizziness and headache (2 RCT), pain cause by treatment (2 RCT), and hypertonicity (1 RCT).
Adie et al. 2017 **UK** **RCT**	CA: ☑ Blinding: Assessor ☑ Patients ☑ ITT: ☑	240 participants, recruited from 10 centres with arm weakness recruited within 6 months of stroke onset. Mean age was 67.3 years, 56% were men. Mean time since stroke was 57.3 days.	Participants were randomized to an experimental group which received VR based therapy, or to the control group and received tailored arm exercises. Both groups were instructed to exercise for up to 45 min/d for 6wk in a seated position at home.	**Primary Outcomes:** Action Research Arm Test (ARAT) at 6 weeks. **Secondary Outcomes:** Action Research Arm Test (ARAT) at 6 months, Canadian Occupational Performance Measure (COPM), Stroke Impact Scale (SIS), Modified Rankin Scale (MRS), EQ-5D. Outcomes were assessed at baseline, after the intervention, and at 6mo.	There was no significant difference between groups in mean ARAT scores at 6 weeks (MD= −1.7, 95% CI −3.9 to 0.5) or at 6 months (MD= −0.4, 95% CI −3.2 to 2.4). There were no significant differences between groups on any of the other outcomes. The study was completed by 209 participants (87.1%).
Brunner et al. 2017 **Denmark** **RCT** ***The Virtual Reality Training***	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	120 participants recruited from 5 rehabilitation institutions with upper extremity motor impairment within 12 weeks of stroke onset. Mean age was 62 years, 64% were men. Mean	Participants were randomized to receive virtual reality training using the YouGrabber system or dose-matched conventional training. Therapy was provided during a minimum of 16 sessions (60 min/session) over 4 weeks.	**Primary Outcome:** Action Research Arm Test (ARAT). **Secondary Outcome:** Box and Blocks Test (BBT), FIM, ABILHAND and Patient Global	There were no significant between-group differences on any of the outcomes at either 4 weeks or 3 months.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
for Upper Extremity in Subacute Stroke (VIRTUES) trial		time since stroke was 35 days.		Impression of Change Outcomes were assessed at baseline, after the intervention, and at 3-month follow-up.	
Saposnik et al. 2016 **Canada** **RCT** ***EVEREST trial***	CA: ☑ Blinding: Patients ☒ Assessor ☑ ITT: ☑	141 participants recruited from 14 inpatient stroke rehabilitation units from 4 countries with upper limb motor dysfunction (≥3 Chedoke McMaster scale) following first ever stroke with onset within the previous 3 months. 48% of patients were aged 56-69 years, 67% were men. Mean time since stroke was <30 days.	Participants were randomized 1:1 to receive a programme of structured, task-oriented, upper extremity sessions (10 sessions, 60 min each) of either non-immersive VR using the Nintendo Wii gaming system (VRWii) or simple recreational activities (playing cards, bingo, Jenga, or ball game) as add-on therapies to conventional rehabilitation for 2 weeks.	**Primary Outcomes:** Wolf Motor Function Test (WMFT) **Secondary Outcomes:** Box and Blocks Test (BBT), Stroke Impact Scale (SIS), Barthel Index (BI), FIM, Modified Rankin Scale (mRS), grip strength. Outcomes were assessed at baseline, after the intervention and at 4wk post intervention.	There was no significant difference between groups at the end of the intervention on the WMFT performance time (adjusted between-group mean difference estimate: 4·1 sec, 95% CI –14·4 to 22·6) or 4-weeks post-intervention (–14·2 sec, 95% CI –52·0 to 23·7). There were no significant differences in mean change scores between groups on any of the secondary outcomes at the end of the intervention, or 4 week-follow-up, with one exception. The mean change in BBT score was significantly higher in the recreation group. 59 patients in the VR Wii group completed the intervention vs. 62 in the recreational therapy group.

Functional Dynamic Orthoses

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Wong et al. 2022 **Norway** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	30 patients recruited following admission to a neurorehabilitation ward for first-ever stroke, with partial finger movement (defined as ≥ 10° of active finger flexion). The mean age was older in the experimental group (63 vs. 56 years), 77% were men. Mean time since stroke was 52 days. Mean baseline BI scores were 65 in the experimental group and 67 in the control group	All participants received 4 weeks (60 min per day, 5 days a week) of unilateral task-oriented training. Patients were randomized 1:1 to wear adynamic hand orthosis (Saeboglove®) during half of the training time (30 min per day) or not to wear the device (control group). In general, each session was divided into 10 min of gross motor training, 10 min of fine motor training, 10 min of strength training, and 30 min of activities of daily living training.	**Primary Outcome:** Action Research Arm Test (ARAT) **Secondary Outcomes:** 9-hole Peg Test, Fugl-Meyer Assessment for upper extremity, grip strength, modified Ashworth Scale, BI and EuroQol-5D Assessments were conducted before and after treatment	At the end of the intervention, there was no significant difference in mean ARAT change score between groups (from 19 to 32 in the experimental group vs. 23 to 35 in the control group; mean difference in change= 4, 95% CI –5 to 13, p=0.39 There were no significant differences between groups on any of the secondary outcomes.
Alexander et al. 2021 **UK** **Systematic review & meta-analysis**	The risk of bias was generally considered to be high.	4 RCTs including 56 persons with upper limb impairment following stroke. Mean age was 54 years, 69% were men. Mean time post-stroke was 38.9 months.	Trials compared a non-robotic dynamic hand orthosis (DHO) rehabilitation program with the goal of improving repetitive, functional practice and upper limb functional recovery) vs. usual care, placebo or no care. SaeboFlex ™ was used in 3 trials and a customized 3-Dimensional DHO was used in the 4th. Study durations were 4, 6 and 8 weeks.	**Primary outcomes:** Functional movement of the upper limb and ADL performance **Secondary outcomes:** Instrumental ADL, motor impairment, adverse events	DHOs were associated with significant improvement in ARAT scores (MD= 6.23 points, 95% CI 0.28 to 12.19; 2 trials included) and Box and Block Test (MD=2.99, 95% CI 0.39 to 5.60; 4 trials included). DHO's were not associated with significant improvements in SIS self-reported arm ability (MD=9.75, 95% CI −3.38 to 22.89; 2 trials included) or SIS recovery domain (MD= −5.77, 95% CI −26.70 to 15.17; 2 trials included). There was no significant improvement in motor function associated with DHOs, assessed using FMA-UE and grip strength. The authors state there is currently insufficient evidence to recommend the implementation of such devices into clinical practice.
Lannin et al. 2016 **Australia**	CA: ☑ Blinding:	9 patients admitted to an acute inpatient rehabilitation ward	Patients were randomized to receive standard multidisciplinary rehabilitation	**Primary outcomes:** Feasibility of applying the device, compliance	All therapists in the intervention group were willing to take the extra time needed to apply the device. All patients in the intervention group were

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RCT	Patient ☒ Assessor ☑ ITT: ☒	following first-ever stroke with upper-limb hemiplegia (<6 on item 6 or 7 of the Motor Assessment Scale for stroke). Mean age was 58 years, 78% were men. Mean time since stroke was 3 months.	that targeted task specific motor training of the affected UL + an 8-week programme using the Saebo-Flex™ device, which was worn for at least one, 45-minute one-on-one session daily, 5 days/week (intervention group, n=5), or to a waitlist control group, which received standard rehabilitation only (n=4).	using the device **Secondary outcomes:** Motor Assessment Scale-UL items, Box and Block Test, hand grip strength, Stroke Impact Scale (SIS), range of motion (ROM) Outcomes were assessed at baseline and post intervention	compliant with the therapy. There were no adverse events. There were no significant differences between groups on any of the secondary outcomes.

Trunk Restraint

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Zhang et al. 2020 **China** **Systematic review & meta-analysis**	PEDro scores ranged from 4-8. 7 trials were of good quality and 3, of fair quality.	10 RCTs including 255 patients with upper-limb impairment following stroke. Mean age ranged from 47 to 69 years, 65% were men. 3 trials included patients in the subacute stage of stroke and 7, in the chronic stage.	Trials compared trunk restraint used within task-oriented training vs. task-oriented training alone. The duration of treatment ranged from 2-10 weeks, and the frequency of intervention varied from 2-5 sessions per week. The length of each session ranged from 45 minutes to 6 hours per day.	**Primary Outcome:** Motor Activity Log (MAL) **Secondary outcomes:** Fugl-Meyer Assessment Upper Limb (FMA-UL), Action Research Arm Test (ARAT), Wolf Motor Function and measures of ADL	Trunk restraint was associated with significant improvement in MAL-amount of use and MAL-quality of use (MD=0.34, 95% CI 0.20-0.47 and MD=0.34, 95% CI 0.18-0.50, respectively). The benefit was greatest for patients in the subacute stage of stroke. Trunk restraint was associated with significant improvement in FMA-UL (MD=0.68, 95% CI 0.39-0.98) and ARAT (MD=4.3, 95% CI 2.33-6.27). The benefits were greatest for patients in the subacute stage of stroke. Trunk restraint was associated with significant improvement in ADL performance (SMD=0.98, 95% CI 0.07 -1.89). The benefits were greatest for patients in the subacute stage of stroke. The Wolf Motor Function was assessed in only 2 small trials.

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Greisberger et al. 2016 **Austria** **Systematic review**	PEDro scores ranged from 4-7.	8 RCTs that included 229 persons with chronic hemiparesis following stroke (> 6 months). Mean age ranged from 47 to 69 years, 72% were men. Mean time since stroke ranged from 13.7 months to 4 years.	Trials compared reach-to-grasp training with trunk restraint (TR) vs. any other training. Cointerventions included modified CIMT. In most trials, 12-15 sessions were provided.	**Primary outcome:** Measures of body function/ structure and activity and participation In most trials assessments were conducted before and after	No pooled analyses were conducted. Outcome measures used to assess body structure and function included trunk displacement (assessed in 4 trials), elbow extension (assessed in 2 trials), shoulder flexion (assessed in 2 trials), Reaching Performance Scale (assessed in 1 trial), FMA-UE (2 trials). In 5 trials there was significantly greater improvement in at least one of the outcomes compared with the control group. Outcome measures used to assess activity/participation included TEMPA (assessed in 1 trial), ARAT (assessed in 1 trial), SIS (hand function, assessed in 1 trial), MAL AOU (assessed in 2 trials), MAL QOM (assessed in 2 trials). Persons in the trunk training group improved more in 3 trials at post-test. Long-term effects were found in one trial after 4 weeks.

Trunk Training

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Thijs et al. 2023 **Belgium** **Cochrane review**	Most (≥50%) of the included trials were at high or unclear risk of bias for all domains assessed (random sequence generation, CA, blinding of patients,	68 RCTs including 2,585 participants recovering from stroke. Mean age was 60 years (range 44-76 years). In 16 trials, stroke occurred from one week to 3 months previously; in 8 trials, stroke occurred within 3-6 post stroke. In 29 trials, stroke had occurred >6 months previously. Details of stroke timing were not provided in 15	Trunk training interventions assessed included core-stability training (isometric strengthening of the trunk muscles, n=18 trials) electrical stimulation that targeted ≥ 1 core trunk muscles (n=7 trials), selective-trunk training aimed at improving selective movements of the upper and lower part of the trunk (n=15 trials), sitting-reaching therapy (n=6 trials), 10° steady-tilted platform (n=2 trials) and weight-shift training	**Primary outcomes:** Arm-hand activity, trunk function, and ADL	*Trunk training vs. non dose-matched therapy* Trunk training was associated with a significant improvement in arm-hand activity (SMD=0.84, 95% CI 0.09 to 1.59; 1 trial included. GRADE: very low certainty), trunk function (SMD=1.49, 95% CI 1.26 to 1.71; 14 trials included. GRADE: very low certainty) and ADL performance (SMD=0.96, 95% CI 0.69 to 1.24; 5 trials included. GRADE: very low certainty). *Trunk training vs. dose-matched therapy* Trunk training was not associated with a significant improvement in arm-hand activity (SMD=0.17, 95% CI -0.21 to 0.56; 3 trials included. GRADE: very

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	incomplete outcome data and selective reporting).	trials.	(n=4 trials). The median duration of therapy was 4 weeks, providing a median of 600 minutes of total training. The intensity of training ranged from 30 minutes to 2,700 minutes (45 hours). Trials were classified as dose-dependent (n=44) or non dose dependent (n=20), based on the amount of therapy provided in the control arms. Therapy provided in the control groups was diverse.		low certainty) or improvement in performance in ADL (SMD= -0.10, 95% CI -0.17 to 0.37; 9 trials included. GRADE: very low certainty). Trunk training was associated with significant significant improvement in trunk function (SMD=1.03, 95% CI 0.91 to 1.16; 36 trials included. GRADE: very low certainty).

Pharmacotherapy and Functional Recovery

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Mead et al. 2024 **UK** **Systematic review & patient-level meta-analysis**	All trials were at low risk of bias.	3 RCTs (AFFINITY, EFFECTs and FOCUS) that included 5907 patients with stroke. Mean age was 69.9 years, 63% were men. 94% were independent prior to stroke. Baseline median NIHSS score was 5.	Participants in all trials were randomized 1:1 to receive 20 mg fluoxetine daily or placebo for 6 months.	**Primary outcome:** mRS score at 6 months **Secondary outcomes:** mRS scores at 12 months, Stroke Impact Scale sub scores	99% of patients were enrolled as inpatients a mean of 6.6 days after stroke. At 6 months, the distribution of mRS scores did not differ significantly between groups (common OR=0·96, 95% CI 0.87 to 1.05). GRADE: high quality. Neither was the distribution of scores significantly different between groups at 12 months (common OR=0.98, 95% CI 0.89 to 1.07). There were no significant differences between groups in SIS subscores (motor, physical function). Fluoxetine was associated with a significantly increased frequency of seizures (2.64% vs. 1.8%, p=0.03), falls with injury (6.26% vs 4.51%, p=0·03), and fractures (3.15% vs 1.39%,

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					p=0.01). The frequency of new onset depression was significantly lower in the fluoxetine group. (10.05% vs 13.42%, p<0.0001).
Legg et al. 2021 **UK** **Cochrane review**	Pooled analyses were conducted using data from 6 trials, assessed as being at low risk of bias across all domains.	76 RCTs including 13,029 participants who had suffered a stroke within the previous 12 months. In 37 trials, depression was an inclusion criterion. The mean age ranged from 51 to 75.6 years with most studies recruiting participants in their 60s. Men outnumbered women in most trials.	Trials compared SSRIs vs. placebo. Agents included fluoxetine (n=38), sertraline (n=8), paroxetine (n=13), citalopram (n=9), escitalopram (n=5), citalopram or fluoxetine (n=2) and sertraline or fluoxetine (n=1). Time since stroke was 0-90 days (n=44), 3-6 months (n=4), 6-9 months (n=2) and in the remaining trials, time since stroke was not reported. Data on doses and duration of treatment are not summarized.	**Primary outcome:** Disability scores at the end of treatment, independence (mRS 0-2) at the end of treatment. **Secondary outcomes:** Neurological deficit, depression, death, adverse events	There was no difference between groups in measures of disability (SMD=0.0, 95% CI -0.5 to 0.5, 5 trials, n=5,436; GRADE: high). SSRIs were not associated with a higher chance of being independent (RR=0.98, 95% CI 0.93 to 1.03, 5 trials, n=5,926; GRADE: high). SSRIs were associated with significantly lower depression scale scores (SMD=-0.14, 95% CI -0.19 to -0.08, 4 trials, n=5,356; GRADE: high). SSRIs were not associated with a significantly higher risk of death (RR=1.01, 95% CI 0.82 to 1.24, 6 trials, n=6,080; GRADE: moderate) SSRIs were associated with significantly higher risk of seizures (RR=1.4, 95% CI 1.00 to 1.98, 6 trials, n=6,090; GRADE: moderate) and bone fractures (RR=2.35, 95% CI 1.62 to 3.41, 6 trials, n=6,080; GRADE: high).
EFFECTS Trial Collaboration 2020, Lundström et al. 2021, Tay et al. 2023 **Sweden** **RCT** ***The Efficacy oF Fluoxetine—a randomisEd Controlled Trial in Stroke***	CA: ☒ Blinding: Patient ☑ Therapist ☑ Assessor ☑ ITT: ☑	1,500 participants recruited from 35 hospitals in Sweden with a recent acute stroke in the previous 2–15 days and at least one persisting focal neurological deficit. Mean age was 71 years, 62% were men. 96.5% were independent pre stroke. Median NIHSS score was 3. At baseline, no patients had ongoing depression.	Participants were randomized 1:1 to receive 20 mg fluoxetine daily or placebo for 6 months.	**Primary outcome:** mRS scores at 6 months **Secondary outcomes:** 6-month survival, depression (new diagnosis-not reported how assessed), cognition (MoCA) NIHSS score **Safety outcomes:** New stroke, SIS scores,	The median duration of treatment was 180 days. 1,338 (89%) patients took the study medication for at least 150 days. The distribution of mRS scores at 6 months was similar between groups (common OR=0·94, 95% CI 0·78–1·13). There were no significant differences between the groups in median SIS domain scores except for memory, in which the placebo group had significantly higher scores (92.6 vs. 89.3, p=0.0064) and mood and emotional control, in

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
(EFFECTS) trial				acute coronary events, upper gastrointestinal hemorrhage, new bone fractures, epileptic seizures, hyponatraemia, all assessed at 6 months	which the scores were higher in the fluoxetine group (80.6 vs. 76.4, p=0.0002). There were 25 (3%) deaths in the duloxetine group vs. 23 (3%) in the placebo group (p=0.66). New onset depression was diagnosed less frequently in the fluoxetine group (7% vs. 11%, p=0.015). There were no other significant differences between groups in any of the other secondary outcomes. Hyponatremia was more common in the fluoxetine group (11 [1%] 1 [<1%], p=0.0038), as were fractured bones (28 [4%] 11 [2%], p=0.0058). There were no other significant differences between groups in any of the other safety outcomes. *12-month outcomes* The distribution of mRS scores at 12 months was similar between groups (adjusted common OR=0.92, 95% CI 0.76–1.10). There were no significant differences between groups on any of the SIS domains, including mood and emotional control except for memory, in which the placebo group had significantly higher scores (93 vs. 89, p=0.0021) and communication, in which the scores were higher in the placebo group (96 vs. 93, p=0.024). Except for death (5 in each group), 12-month safety data were not reported. *Depression outcomes (Tay 2023)* Montgomery–Åsberg Depression Rating Scale (MADRS) was administered at baseline and 6 months. There was no significant difference between

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					groups in mean total MADRS scores or depression subscores between groups at 6 months. Apathy subscores increased significantly in both groups from baseline, with significantly greater increases in scores in the fluoxetine group.
AFFINITY Trial Collaboration 2020, Hankey et al. 2021, Almeida et al.2021 **Australia** **RCT** ***Assessment oF FluoxetINe In sTroke recovery (AFFINITY)***	CA: ☒ Blinding: Patient ☑ Therapist ☑ Assessor ☑ ITT: ☑	1,280 participants recruited from 43 hospitals in 3 countries (Australia, New Zealand, Vietnam) with a recent acute stroke in the previous 2–15 days and with an mRS score of ≥1. Mean age was 63 years, 63% were men. Median NIHSS score was 6. At baseline, 32 patients were identified with depression, of whom 10 were taking a non-SSRI medication.	Participants were randomized 1:1 to receive 20 mg fluoxetine daily or placebo for 6 months.	**Primary outcome:** mRS scores at 6 months. **Secondary outcomes:** 6-month survival, depression (change in PHQ-9 score from baseline and PHQ-9 score ≥15), cognition (Telephone Interview for Cognitive Status [TICS] score), Stroke Impact Scale scores (SIS), health related quality of life (EQ-5D-5L), new diagnosis of depression requiring treatment with antidepressants, and trial medication adherence and cessation.	The mean duration of the trial was 167 days. 108 persons in the fluoxetine group had discontinued the medication vs. 100 in the placebo group. The distribution of mRS scores at 6 months was similar between groups (common OR=0·94, 95% CI 0·76–1·15). There were no significant differences in proportions between groups when mRS scores were dichotomized (0–2 vs 3–6). There were no significant differences between groups in the proportions of persons with new onset depression, those starting on an antidepressant medication, or those with PHQ-9 scores ≥15. The median TICS score was 24 in both groups. Median SIS scores were similar in all domains except mood and emotional control, in which the scores were higher (better) in the fluoxetine group (80.6 vs. 77.8, p=0.0028). The median HQ-5D-L scores in each group were not significantly different (0.81 vs. 0.78). There were 15 deaths in each group. The frequencies of epileptic seizures, falls with injuries and bone fractures were all significantly higher in the fluoxetine group (2-3% vs. ≤1%). *12-month outcomes*

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					The distribution of mRS scores at 12 months was similar between groups (common OR=0·93, 95% CI 0·76–1·14). There was no significant difference in the frequency of epileptic seizures (1.71% vs. 1.25%, p=0.65), falls with injury (4.21% vs. 2.35%, p=0.08) or new bone fractures (3.58% vs. 1.72%, p=0.054). *Depression outcomes (Almeida et al.2021)* At 26 weeks, the proportion of participants with PHQ-9 scores ≥9 was not significantly different between the groups (20.2% [fluoxetine] vs. 21.1% [placebo]). The proportion with any depression outcome including antidepressant use or nonpharmacologic treatment was not significantly different between groups (24.0% vs. 25.4%). A significantly lower proportion of participants in the fluoxetine group reported a clinician had diagnosed them with depression (4.3% vs. 7.0%). Among persons with PHQ-9 scores of <9 at baseline, there were no significant differences between groups for any of the depression outcomes.
Mead et al. 2020 **UK** **Systematic review &meta-analysis**	4 trials were assessed as having a low risk of bias	13 RCTs (n=4,145) including persons with/without a mood disorder at randomization who were treated with fluoxetine within the first year of stroke. This review was an extension of the 2012 Cochrane review, and includes the results of the	Trials compared any dose of fluoxetine, any mode of delivery, given for any duration vs. placebo or usual care. No co-treatments were permitted. Doses were 20 mg (n=12), 30 mg (n=1). Duration of therapy was single dose (n=1), 1 month (n=1) 2 months (n=2), 3 months	**Primary outcomes:** Independence (mRS 0-2) and disability **Secondary outcomes:** independence and disability at the end of follow-up. Neurological score, depression, anxiety, cognition, death, motor scores, adverse events (at the	There was no difference in the proportion of patients who were independent at the end of treatment (36·6% fluoxetine vs 36·7% control; RR= 1·00, 95% CI 0·91 to 1.09, p=0·99, s trials included). There was no significant difference between groups in measures of disability (SMD 0.05, 95% CI -0.02 to 0.12, p=0.15, 7 trials included). Fluoxetine was associated with better neurological scores (SMD -0.28, 95% CI -0.42 to

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		FOCUS trial	(n=8), and 6 months (n=1)	end of treatment and/or at the end of follow-up)	-0.14 p=<0.001, n=8 trials), better depression scores (SMD -0.16, 95% CI -0.23 to -0.09, p<0.0001, n=6 trials), fewer diagnoses of depression (RR=0.77, 95% CI 0.65 to 0.90, p=0.001, n=2 trials), but more seizures (3.9% vs 2.6%, RR 1.49, 95% CI 1.05 to 2.11, p=0.03, n=7 trials)
Dennis et al. 2019 **UK** **RCT** ***Fluoxetine Or Control Under Supervision (FOCUS) trial***	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☒	3,127 patients recruited from 103 hospitals, ≥18 years with a clinical diagnosis of stroke, who were enrolled between 2 days and 15 days post onset. Mean age was 71 years, 61% were men. Patients with current or recent (within the last month) depression, treated with an SSRI, were excluded.	Patients were randomized 1:1 to receive 20 mg fluoxetine or placebo orally once daily for 6 months.	**Primary outcome:** (ordinal) mRS scores at 6 months **Secondary outcomes:** Survival at 6 and 12 months, mRS scores at functional status at 12 Stroke Impact Scale scores at 12 months, Mental Health Inventory (MHI-5), the Vitality subscale of SF3 and the EuroQoL-5 Dimensions-5 Levels (EQ5D-5L)	There was no significant difference between groups in the distribution of mRS scores (common OR= 0·951, 95% CI 0·839–1·079, p=0·439), nor was there a significant difference in proportions when mRS scores were dichotomized (0–2 vs. 3–6). There were no significant differences between groups based on all subgroup analyses. A lower percentage of patients in the fluoxetine group were likely to be diagnosed with new depression (13·4% vs. 17.2%; difference in proportions of 3·78%, 95% CI 1·26–6·30, p=0·0033). Median MHI-5 scores were significantly higher in the fluoxetine group (76 vs. 72, p=0·0100). There were no significant differences in any other secondary outcomes. The risk of bone fractures was significantly higher in the fluoxetine group 2·88% vs.1·47%, p=0·0070), as were the number of epileptic seizures (3.8% vs. 3.5%, p=0.03). *12-month outcomes* The distribution of mRS scores between groups was not significantly different, nor was there a significant difference in proportions when mRS scores were dichotomized (0–2 vs. 3–6). There were no significant differences between groups in survival, median SIS scores, MHI-5, EQ5D-5L, or new onset depression.

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Chollet et al. 2011 **France** **RCT** ***Fluoxetine for motor recovery after acute ischaemic stroke (FLAME)***	CA: ☑ Blinding: Patient ☑ Therapist ☑ Assessor ☑ ITT: ☒	118 patients aged 18-85 years, free from clinical depression and not taking any anti-depressant medication enrolled within 5 to 10 days of stroke with Fugl-Meyer Motor Scale (FMMS) scores of <55. Mean age was 65 years, 61% were men.	A mean of 9 days after stroke, participants were randomized 1:1, 5-10 days post-stroke to receive fluoxetine (20 mg/day) or placebo for 90 days. All participants received physiotherapy and standard inpatient stroke care during the study period.	**Primary outcome:** FMMS scores at day 90. **Secondary outcomes:** NIHSS, modified Rankin Scale, and the Montgomery Asberg Depression Ration Scale at 90 days.	At the end of the 90-day treatment period, participants who received fluoxetine demonstrated significantly greater mean improvement on the FMMS, controlling for centre, age, history of stroke, and baseline FMMS (9.8 points, 95% CI 3.4-16.1, p=0.003). Participants who received fluoxetine also demonstrated significantly greater mean improvement on the FMMS upper sub scale scores (9.7 points, 95% CI 3.6-15.9, p=0.02), and the lower sub scale (3.3 points, 95% CI 0.8-5.7, p=0.01). Two serious adverse events occurred in the fluoxetine group (hyponatraemia and partial seizure). Transient digestive disorders (nausea, diarrhea, and abdominal pain) were more common in the active treatment group (25% vs. 11%). There were 2 dropouts in the fluoxetine group and 3 in the placebo group.

Abbreviations

ARAT: Action Research Arm Test	CA: Concealed Allocation	CI: Confidence Interval
FAI: Frenchay Activities Index	FES: Functional Electrical Stimulation	FMA: Fugl Meyer Assessment
ITT: Intention to treat	Motor Activity Log AOU: MAL Amount of Use	MAL QOM: Quality of Movement;
N/A: Not Applicable	NMES: Neuromuscular Electrical Stimulation	OR: Odds Ratio
RCT: Randomized Controlled Trial	RoB: Risk of bias	ROM: Range of Motion
rTDS: Repetitive Transcranial Direct Stimulation	SMD: Standardized Mean Difference	tDCS: transcranial direct current stimulation

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