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The impact of physical therapy on functional outcomes after stroke: what's the evidence?

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Objective: To determine the evidence for physical therapy interventions aimed at improving functional outcome after stroke.
Methods: MEDLINE, CINAHL, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, DARE, PEDro, EMBASE and DocOnline were searched for controlled studies. Physical therapy was divided into 10 intervention categories, which were analysed separately. If statistical pooling (weighted summary effect sizes) was not possible due to lack of comparability between interventions, patient characteristics and measures of outcome, a best-research synthesis was performed. This best-research synthesis was based on methodological quality (PEDro score).
Results: In total, 151 studies were included in this systematic review; 123 were randomized controlled trials (RCTs) and 28 controlled clinical trials (CCTs). Methodological quality of all RCTs had a median of 5 points on the 10-point PEDro scale (range 2–8 points). Based on high-quality RCTs strong evidence was found in favour of task-oriented exercise training to restore balance and gait, and for strengthening the lower paretic limb. Summary effect sizes (SES) for functional outcomes ranged from 0.13 (95% CI 0.03–0.23) for effects of high intensity of exercise training to 0.92 (95% CI 0.54–1.29) for improving symmetry when moving from sitting to standing. Strong evidence was also found for therapies that were focused on functional training of the upper limb such as constraint-induced movement therapy (SES 0.46; 95% CI 0.07–0.91), treadmill training with or without body weight support, respectively 0.70 (95% CI 0.29–1.10) and 1.09 (95% CI 0.56–1.61), aerobics (SES 0.39; 95% CI 0.05–0.74), external auditory rhythms during gait (SES 0.91; 95% CI 0.40–1.42) and neuromuscular stimulation for glenohumeral subluxation (SES 1.41; 95% CI 0.76–2.06). No or insufficient evidence in terms of functional outcome was found for: traditional neurological treatment approaches; exercises for the upper limb; biofeedback; functional and neuromuscular electrical stimulation aimed at improving dexterity or gait performance; orthotics and assistive

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devices; and physical therapy interventions for reducing hemiplegic shoulder pain and hand oedema.
Conclusions: This review showed small to large effect sizes for task-oriented exercise training, in particular when applied intensively and early after stroke onset. In almost all high-quality RCTs, effects were mainly restricted to tasks directly trained in the exercise programme.

Introduction

Systematic research has shown that organized multidisciplinary care and rehabilitation after stroke enhance patient survival and independence, as well as reducing the length of inpatient stay.[1–3] It remains unclear, however, why specialized stroke units are more effective than usual care. A number of components have been identified as contributing to the efficacious care delivered in such units. These include the comprehensive assessment of medical problems, impairments and disabilities; active physiological management; early mobilization and avoidance of bedrest; skilled nursing care; early setting of rehabilitation plans involving carers; and early assessment and planning for discharge needs.[1,4] Several of these factors are closely related to physical therapy which is often perceived as one of the key disciplines in organized stroke care.[5] In addition, a recent Cochrane review of 14 trials ($N = 1617$) showed that outpatient services, including physical therapy, may prevent deterioration in seven of 100 stroke patients residing in the community.[6] The main foci of physical therapy after stroke are to restore motor control in gait and gait-related activities and to improve upper limb function, as well as to learn to cope with existing deficits in activities of daily living (ADL) and to enhance participation in general. Besides using physical exercises, physical therapists often apply assistive devices for gait, and employ other equipment such as treadmills and electronic devices to support their treatments. In addition, advice and instructions are provided to the patient, family and other members of the stroke team regarding prevention of complications such as falls and shoulder pain. Today, the importance of evidence-based medicine as a guide for the clinical decision-making process is increasingly being recognized by physical therapists.[7,8] However, the efficacy of physical therapy interventions for stroke has not been summarized in a systematic review. The objective of the present systematic review was to establish the evidence of physical therapy interventions related to improving functional outcomes after stroke.

Material and methods

Literature search

A computerized literature search was conducted in MEDLINE, CINAHL, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, DARE, PEDro, EMBASE and DocOnline (Database of the Dutch Institute of Allied Health Care). Two researchers (RPSvP and JCFK) independently searched these electronic databases for relevant articles. The search strategy was built on cerebrovascular disease (patient type) and physical therapy interventions (treatment type). Randomized controlled trials (RCTs) as well as controlled clinical trials (CCTs) were included for review. Excluded were noncontrolled pre-experimental studies and controlled studies that investigated robotics or the effects of physical therapy in combination with acupuncture or drug therapies. Studies were collected up to January 2004. The following MeSH and keywords were used for the electronic databases: cerebrovascular disorders, cerebrovascular accident, stroke, hemiplegia, physical therapy, occupational therapy, exercise therapy, and rehabilitation. Bibliographies of review articles, narrative reviews and abstracts published in conference proceedings were also evaluated for relevant publications. In addition, citation tracking of all article references was conducted. Only articles written in English, German or Dutch were included for review. Inclusion of articles was based on agreement between the two independent reviewers. The full search strategy is available on request from the corresponding author.

Subsequently, the two reviewers independently determined from the title and the abstract if the papers satisfied the following criteria: population of adults (18 years or older) diagnosed with stroke and studies evaluating effectiveness of physical therapy interventions.

Intervention categories

For the present review, physical therapy was classified into 10 intervention categories to evaluate the effectiveness of: (1) traditional neurological treatment approaches; (2) programmes for training sensorimotor function or influencing muscle tone; (3) cardiovascular fitness and aerobic programmes; (4) methods for training mobility and mobility-related activities; (5) exercises for the upper limb; (6) biofeedback therapy for the upper and lower limb; (7) functional and neuromuscular electrical stimulation for both limbs; (8) orthotics and assistive devices for both limbs; (9) treatments for hemiplegic shoulder pain and hand oedema; and (10) intensity of exercise therapy.

This classification was based on the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization[9] and the *American Physical Therapy Association guide to physical therapist practice* (2nd edition).[10] A group of eight physical therapists and two reviewers (GK and RPSvP) reached consensus about the categories.

Methodological quality

The methodological quality of the RCTs was rated with the PEDro scale.[11] RCTs were scored by two independent reviewers (RPSvP and GK). Inter-rater reliabilities of individual items of the PEDro scale were calculated by Cohen's kappa. In case of disagreement, consensus was sought, but when disagreement persisted, a third independent reviewer (SWD) made the final decision. PEDro scores of 4 points or higher were classified as 'high quality', whereas studies with 3 points or lower were 'low quality'. PEDro scores were not used as inclusion/exclusion criteria, but rather as a basis for best-evidence synthesis and to discuss the strengths and weaknesses of studies.

Quantitative analysis

Analysis of the results was performed separately for each intervention and restricted to RCTs. When they were comparable in terms of interventions, patient characteristics and outcome measures, statistical pooling was performed. Randomized studies using a cross-over design were judged as an RCT by calculating effects before the point of cross-over. The data were reanalysed by pooling the individual effect sizes using fixed effect sizes.[12,13] Fixed effect sizes, g^u (Hedges' g), were calculated for each study by finding the difference between mean changes in the experimental group and in the control group and dividing by the average population standard deviation (SDi). To estimate SDi for g^u, baseline estimates and standard deviations of the control and experimental groups were pooled. The impact of sample size was addressed by estimating a weighting factor (w_i) for each study, and assigning larger effect-weights in studies with bigger samples. Subsequently, g^u values of individual studies were averaged, resulting in a weighted SES, whereas the weights of each study were combined to estimate the variance of the SES.[14] If significant between-study variation existed (statistical heterogeneity) a random effects model was applied.[15] Based on the classification of Cohen, effect sizes below 0.2 were classified as small, from 0.2 to 0.5 as medium and above 0.5 as large.[16]

Best-evidence synthesis

If pooling of studies was not possible due to differences in outcomes, intervention types, patient characteristics or lack of point estimates (means and medians) and/or measures of variability (e.g., standard deviations and confidence intervals) a best research synthesis was applied. For this purpose we used the criteria set out by Van Tulder *et al.*[17] based on the methodological quality score of the PEDro scale. Subsequently, studies were categorized into five levels of evidence: (1) strong evidence, (2) moderate evidence, (3) limited evidence, (4) indicative findings, (5) no or insufficient evidence (Appendix 1).[37]

Results

Literature search using multiple databases yielded 8024 citations on 29 January, 2004. After restricting these to the publication type 'clinical trial', 735 remained. Following the exclusion of: (1) pre-experimental studies and (2) controlled studies investigating the effects of physical therapy interventions that included people with nonstroke as a diagnosis or interventions with acupuncture, drugs or robotics, 204 relevant studies were selected by title and abstract. Twenty-two of these articles were systematic reviews,[13,18–38] and 20 were critical or narrative reviews.[39–58] Eleven of the remaining 162 studies had been published in more than one article.[59–80] A total of 151 publications (123 RCTs and 28 CCTs) that focused on the effectiveness of physical therapy interventions in people with stroke were included for further analysis. Cohen's κ, as an estimate of agreement between the two raters for methodological quality of the 123 RCTs, was 0.81.

For each intervention category the results of the studies that contributed to the meta-analysis or best-evidence synthesis are presented in Tables 1 and 2. The methodological quality of the RCTs is reported in Table 3.

Evidence related to the effects of the traditional neurological treatment approaches

Eight RCTs[67,81–87] and two CCTs[88,89] investigated the effects of using a specific neurological treatment approach. Numbers of patients, characteristics of the interventions, measures of outcome and observed effects are shown in Table 1. Different neurological treatment approaches including Bobath,[67,81–83,86,88] Brunnstrom,[85,87,89] Rood,[82,83] Johnstone,[84] Proprioceptive Neuromuscular Facilitation (PNF),[85,88] Motor Relearning Programme (MRP),[67] Ayres[82] or combinations of the above[89] were investigated. With exception of two RCTs[84,85] all studies evaluated the effects of Bobath in one of the treatment arms, whereas one study used two experimental groups.[86] Eight studies measured ADL with the Barthel Index (BI),[67,82,83,86,88] the Functional Independence Measure (FIM)[87] or other ADL scales[85,89] as an outcome, and four studies evaluated strength,[83,85] synergism[84] or muscle tone.[88] Three studies assessed the effects of a neurological approach on length of stay (LOS)[67,85,89] and compared the effects of MRP and Bobath,[67] PNF and Brunnstrom[85] or neuromuscular retraining techniques,[89] whereas one CCT compared an impairment orientated with a disability focused approach.[90]

The quality score of the RCTs ranged from 3[82,83] to 6.[67] Due to differences in both aims and outcomes, pooling of the studies was not possible. Best-evidence synthesis showed moderate evidence for a reduced LOS in favour of MRP or traditional care compared with an impairment-focused neuromuscular treatment approach such as Bobath.[67,89,90] No evidence was found for applying a specific neurological treatment programmes in terms of muscle strength,[83,85] synergism,[84] muscle tone,[88] walking ability,[88] dexterity[67,81,87] or ADL.[67,82,83,85–89]

Programmes for training sensorimotor function or influencing muscle tone

'Sensory motor training' was defined as exercises for improving motor performance, strength, power and endurance,[10(S72)] as well as sensory integrity (proprioception, pallaesthesia, stereognosis and topognosis).[10(S90)]

Strengthening paretic muscles

Six RCTs[91–96] and two CCTs[97,98] investigated eccentric[98] and concentric strengthening exercises for the lower[91–94,96–98] and upper limbs.[92,97] Treatment sessions ranged from 30[96] to 90[95] min per day, and were applied 2[91] to 5[95] times a week for 2[95] to 6[93,94] weeks (Table 1). Methodological quality ranged from 4[91,93] to 7.[94] A meta-analysis was possible for three RCTs[91,92,94] that assessed self-selected comfortable walking speed. A homogeneous nonsignificant SES was found in favour of strengthening muscles of the paretic lower limb on gait speed (Table 2). By weighting the quality of the studies, a best-evidence synthesis showed strong evidence for the value of increasing the muscle strength of the lower limb in terms of maximal voluntary efforts,[92] mass motion (on an Elgin-table)[93] or maximal isokinetic strength (on a Kin-Com).[94] Limited evidence was found for increasing walking endurance[91,92] and gait performance (average torque of muscle groups of paretic and nonparetic leg).[94,98] No evidence was found for strengthening exercises to improve hand grip force,[92,97] to support strengthening muscles for climbing stairs,[94] transferring,[92] establishing symmetry of weight distribution between hemiplegic and nonhemiplegic sides,[98] dexterity[92,97] or for physical and mental health.[94]

Table 1 Physical therapy intervention categories

Intervention categories	Type of intervention	*N*	Start study: time post-stroke (Ranges between studies given only)	Intensity of intervention Mean (range)	Results	Methodological quality (PEDro) of RCTs (Ranges between studies given only)	References
1) Traditional neurological treatment approaches	Traditional neurological treatment approaches	RCTs: 369 CCTs: 170	– 1 w–4.8 y	30–90 min/day 3–5 × a week during 2–8 weeks	Moderate evidence found for reducing LOS in favour of control groups. No evidence found for improving muscle strength, synergism, muscle tone, walking ability, dexterity or ADL	3–6 points	8 RCTs[67,81–87] 2 CCTs[88,89]
2) Programmes for training sensorimotor function or influencing muscle tone	Strengthening paretic muscles	RCTs: 294 CCTs: 47	– 3 mo–4 y	30–90 min/day 2–5 × a week during 2–6 weeks	Strong evidence found for improving muscle strength of lower extremity in favour of experimental groups. Limited evidence found for improving gait performance or walking endurance. No evidence found for improving hand-grip force, dexterity, symmetry of weight distribution, transferring, gait speed, stair-walking or physical and mental health	4–7 points	6 RC Ts[91–96] 2 CCTs[97,98]
	Training sensory integrity	CCT: 39	6.2 y	20–45 min/day 3–5 × a week during 4–6 weeks	Indicative findings found for improving somatosensory perception	4 points	1 CCT[99]
	Influencing muscle tone and stiffness	RCTs: 245 CCT: 8	< 11 w–6.7 y	5–60 min/day 2–5 × a week during 3–12 weeks	Strong evidence found for reducing muscle tone in favour of TENS. Limited evidence found for AROM in favour of slow stretch techniques. Insufficient evidence found for improving PROM in favour of TENS and casts or splints	2–7 points	9 RCTs[71,84,100–106] 1 CCT[107]
3) Cardiovascular fitness and aerobic programmes	Training endurance	RCTs: 154 CCT: 9	> 30d– > 6 mo	30–90 min/day 3–5 × a week during 8–10 weeks	Strong evidence found for maximal workload, gait speed or walking distance in favour of experimental groups. Limited evidence found for aerobic capacity. No evidence found for synergism, basic ADL or instrumental ADL	4–7 points	3 RCTs[109–111] 1 CCT[112]

Table 1 (*Continued*)

Intervention categories	Type of intervention	*N*	Start study: time post-stroke (Ranges between studies given only)	Intensity of intervention Mean (range)	Results	Methodological quality (PEDro) of RCTs (Ranges between studies given only)	References
	Training aerobics	RCTs: 197	10 d–8 y	60–90 min/day 3–10 × a week during 4–12 weeks	Strong evidence found for aerobic capacity and muscle strength of the lower extremity in favour of the experimental groups. No evidence found for synergism, walking endurance and gait speed	3–7 points	5 RCTs[80,113–116]
4) Methods for training mobility and mobility-related activities	Training sitting balance	RCTs: 108	2 w–6.3 y	30–120 min/day 5 × a week during 2–4 weeks	Strong evidence found for weight distribution between paretic and nonparetic side in favour of experimental groups	5–7 points	4 RCTs[86,117–119]
	Training transfers from sit-to-stand and *vice versa*	RCTs: 156	38 d–6.3 y	15–30 min/day 5–15 × a week during 2–6 weeks	Strong evidence found for symmetry between both legs during sit-to-stand and stand-to-sit or time needed to stand up or sit-down in favour of experimental group. Limited evidence found for reducing the occurrence of falls	5–7 points	5 RCTs[61,113,117,119,120]
	Training standing balance	RCTs: 212 CCT: 42	33 d–18 mo	15–60 min/day 3–10 × a week during 2–8 weeks	Strong evidence found for for reducing postural sway or increasing symmetry of weight distribution during stance in favour of experimental groups. No evidence found for balance measured with the Berg Balance Scale, whereas negative effects found for timed up-and-go	4–6 points	8 RCTs[121–127,129] 1 CCT[128]
	Body weight supported treadmill training	RCTs: 268 CCT: 43	17 d–26 mo	20–45 min/day 3–5 × a week during 2–11 weeks	Strong evidence found for improving walking endurance in favour of BWSTT. No evidence found for improving postural control, walking ability or comfortable gait speed	4–7 points	5 RCTs[77,130–133] 2 CCT[134,135]

	Treadmill training without body weight support	RCTs: 163	10 d–(> 6 mo)	5–60 min/day 3–5 × a week during 3–6 weeks	Strong evidence found for improving walking ability in favour of treadmill training without body weight support. No evidence found for imcreasing comfortable gait speed	5–8 points	5 RCTs[80,136–139]
	External auditory rhythms	RCTs: 80	16 d–32 mo	20–30 min/day 2–10 × a week during 3–12 weeks	Strong evidence found for improving stride length and comfortable gait speed in favour of external auditory rhythms	3–6 points	3 RCTs[140–142]
	Limb loading	RCT: 24	> 6 mo	10 min/day 7 days a week during 6 weeks	No evidence found in favour of limb loading for improving lance control or gait speed	7 points	1 RCT[143]
	Wheelchair self-propelling	RCT: 40 CCT: 18	RCT: 16 d CCT:?	RCT: during 8 weeks CCT:?	No evidence found for influencing muscle tone or improving ADL	3–7 points	1 RCT[144] 1 CCT[145]
5) Exercises for the upper limb	Exercising the paretic arm	RCTs: 971	7 d–4.8 y	30–90 min/day 3–5 × a week during 5–20 weeks	Insufficient evidence found for improving dexterity or ADL in favour of the experimental groups No evidence found for muscle strength and synergism	3–7 points	11 RCTs[65,69,73,82,83,87,110,146-149]
	Constraint-induced movement therapy	RCTs: 134	6 d–4.8 y	2–10 h immobilization per day; 1–6 h training/day per day 3–7 × a week during 2–10 weeks	Strong evidence found for dexterity of the paretic arm in favour of CIMT. No evidence found for the amount of (paretic) arm use or ADL	4–7 points	6 RCTs[150–155]
	Bilateral arm training	RCT: 7 CCT: 27	8.4 w–6.5 y	15–20 min/day 3–10 × a week during 2–6 weeks	Indicative findings found for improving grip strength or dexterity of the paretic arm in favour of bilateral arm training-programmes	3 points	1 RCT[156] 1 CCT[97]
	Mirror therapy	RCTs: 25	10 mo–4.8 y	15–30 min/day 2–6 × a week during 5–8 weeks	Limited evidence found for improving dexterity of the paretic arm in favour of mirror therapy	4–5 points	2 RCTs[146,157]
6) Biofeedback therapy	Biofeedback to the paretic lower limb	RCTs: 262 CCTs: 92	36 d–33.6 mo	20–60 min/day 2–5 × a week during 2–12 weeks	No evidence found for improving active ROM ankle or comfortable gait speed in favour of biofeedback therapy	2–6 points	12 RCTs[140,158–168] 4 CCTs[169–172]
	Biofeedback to the paretic upper limb	RCTs: 247 CCTs: 60	7 w–3.1 y	20–60 min/day 2–5 × a week during 1–10 weeks	Insufficient evidence found for improving dexterity in favour of biofeedback therapy. No evidence found for improving muscle strength and or active ROM	2–7 points	10 RCTs[81,163,173–180] 3 CCTs[181-183]

Table 1 (*Continued*)

Intervention categories	Type of intervention	*N*	Start study: time post-stroke (Ranges between studies given only)	Intensity of intervention Mean (range)	Results	Methodological quality (PEDro) of RCTs (Ranges between studies given only)	References
7) Functional electrical stimulation and neuromuscular stimulation	Effects of FES on the lower limb	RCTs: 176	26 d–4.5 y	20–60 min/day 3–5 × a week during 4–6 weeks	Limited evidence found for improving muscle strength, physiological cost index or walking ability in favour of FES. No evidence found for improving synergism of lower extremity, gait speed or ADL	4–6 points	5 RCTs[162,184–187]
	NMS of the paretic forearm without EMG-triggering	RCTs: 154	16 d–3 mo	30–90 min/day 1–3 × a week during 3–8 weeks	Limited evidence found for improving muscle strength of the extensors of the paretic forearm or dexterity. The evidence for dexterity was restricted only for patients with voluntary movement control of extension of wrist and fingers. No evidence found for dexterity in patient without voluntary movement control. Indicative findings found for improving active ROM in favour of the experimental groups	3–7 points	4 RCTs[188–191]
	NMS of the paretic forearm with EMG-triggering	RCTs: 81 CCT: 22	18 d–3.5 y	30–90 min/day 3–5 × a week during 2–12 weeks	Insufficient evidence found for improving muscle strength or dexterity of the paretic arm. No evidence found for improving synergism in favour of the experimental groups	3–5 points	4 RCTs[192–195] 1 CCT[196]
	NMS for glenohumeral subluxation and hemiplegic shoulder pain	RCTs: 161 CCTs: 144	2 d–430 d	30 min/day tot 6–7 h/day resp. 4 tot 1 × a day during 4–8 weeks	Strong evidence found for increasing passive ROM (lateral rotation of paretic shoulder) and reduction of caudal subluxation in favour of NMS. Insufficient evidence found for reducing hemiplegic shoulder pain	4–7 points	4 RCTs[63,75,197,198] 2 CCTs[199,200]

8) Applying orthotics and assistive devices for the lower and upper extremities	Appliying ankle foot orthosis	RCT: 60	3 mo–3 y	1 d–3 mo	No evidence found for improving gait speed in favour of applying an AFO	7 points	1 RCT[59]
	Slings, supportive devices and strapping techniques for reducing GHS and HSP	RCT: 98 CCTs: 22	15 d–8 mo	Daily during 6–12 weeks	No evidence found for reducing glenohumeral subluxation or decreasing hemiplegic shoulder pain to support the effectiveness of hemi-slings or strapping techniques	7 points	1 RCT[202] 2 CCTs[201,203]
9) Treatment of hemiplegic shoulder pain and hand oedema	Exercises for the hemiplegic shoulder	RCTs: 98 CCTs: 76	15 d–8.2 mo	15– 30 min/day 3–5 × a week during 4 w–3 mo	No evidence found for decreasing hemiplegic shoulder pain or improving active ROM	4–5 points	2 RCTs: [204,205] 2 CCTs: [206,207]
	Treatment of hand oedema	RCT: 37	RCT: 3.7 w	2 x 2 hours/day during 4 weeks	No evidence found for intermittend pneumatic compression for reducing hand volume	7 points	1 RCT[208]
10) Intensity of exercise therapy	Intensity of exercise therapy	RCTs: 2686 CCTs : 813	7d–4.7 y	132–6816 min	Strong evidence found for improving comfortable gait speed, basic ADL and instrumental ADLin favour of augmented exercise therapy. No evidence found for improving dexterity of the paretic arm	4–8 points	20 RCTs[65,69,73,80,85,147–149,209–220] 3 CCTs[221–223]

ADL, activities of daily living; AFO, ankle-foot orthosis; AROM, active range of motion; BWSTT, body weight supported treadmill training; CCT, controlled clinical trial; CIMT, constraint-induced movement therapy; EMG, electromyography; FES, functional electrical stimulation; GHS, glenohumeral subluxation; HSP, hemiplegic shoulder pain; LOS, length of stay; N = number of patients involved; NMS, neuromuscular stimulation; PEDro, Physiotherapy Evidence Database; RCT, randomized controlled trial; PROM, passive range of motion; ROM, range of motion; TENS, transcutaneous electrical stimulation.

Table 2 Quantitative analysis of RCTs

Intervention categories	Type of intervention	Pooling possible for:	References	Measurements	*N* (pooling)	Type effects model[a]	SES (95% CI)	Calculated mean change (direction effect)
Programmes for training sensorimotor function or influencing muscle tone	Strengthening paretic muscles	a. Comfortable gait speed	a: [91,92,94]	a: 4MW, 10MW	a: 84	a: fixed	a: 0.32 (−0.18–0.81)	a: –
	Influencing muscle tone and stiffness (TENS)	a: Muscle tone	a: [71,105]	a: MAS, AS	a: 104	a: fixed	a: 0.44 (0.04–0.83)*	a: 11% ↑
Cardiovascular fitness and aerobic programmes	Training endurance	a: Synergism b: Gait speed	a: [109,110] b: [110,111]	a: BFM b: 10MW	a: 62 b: 112	a: random b: fixed	a: −0.56 (−0.64–1.76) b: 0.65 (0.27–1.04)*	a: – b: 0.08 m/s ↑
	Training aerobics	a: Synergism b: Muscle strength c: Aerobic capacity d: Walking endurance e: Gait speed	a: [80,114] b: [114–116] c: [114,115] d: [113,114] e: [80,113,114,116]	a: BFM-leg b: Cybex II, leg press c: peak VO_2 d: 6min walk e: 4MW, 10MW, 22MW	a: 117 b: 148 c: 135 d: 109 e: 139	a: fixed b: random c: fixed d: fixed e: fixed	a: 0.28 (−0.08–0.65) b: 0.99 (0.49–1.50) c: 0.39 (0.05–0.74) * d: 0.27 (−0.11–0.65) e: 0.25 (−0.08–0.59)	a: – b: – c: 11 % ↑ d: – e: –
Methods for training mobility and mobility-related activities	Training sit-to-stand transfers and vice versa	a: Postural symmetry sit-to-stand b: Postural symmetry stand-to-sit c: Time needed to stand-up d: Time needed to sit-down	a: [61,113,117,120] b: [61,120] c: [61,120] d: [61,120]	a: RBWD, VFD LR, PV GRF b: RBWD, VFD LR c: time (seconds) d: time (seconds)	a: 128 b: 96 c: 84 d: 84	a: fixed b: fixed c: fixed d: random	a: 0.92 (0.54–1.29)* b: 0.92 (0.50–1.35)* c: 0.74 (0.30–1.19)* d: 0.68 (0.23–1.13)*	a: 15% ↑ b: 18% ↑ c: 9% ↑ d: 8% ↑
	Training standing balance	a: Postural sway/ symmetry b: Balance c: Timed Up & Go	a: [121–125] b: [124,126,127] c: [124,126,127]	a: postural sway/symmetry b: BBS c: TUG	a: 126 b: 59 c: 59	a: fixed b: fixed c: random	a: 0.50 (0.14–0.87)* b: −0.16 (− 0.68–0.35) c: −0.72 (−1.28–(−0.17))*	a: 5% ↑ b: – c: −15 s ↓
	Body weight supported treadmill training	a: Balance b: Walking endurance c: Walking ability d: Comfortable gait speed	a: [77,131] b: [77,130,133] c: [131,133] d: [77,130–133]	a: BBS b: 5 min walk, MDUF c: FAC d: 5MW, 10MW, 2 min walk	a: 145 b: 148 c: 79 d: 220	a: fixed b: fixed c: fixed d: fixed	a: 0.27 (−0.07–0.61) b: 0.70 (0.29–1.10)* c: 0.33 (−0.09–0.76) d: 0.10 (−0.17–0.37)	a: – b: 31% ↑ c: – d: –

	Treadmill training without body weight support	a: Walking ability b: Gait speed	a: [136,138] a: [80,136–138]	a: FAC b: 10MW	a: 65 b: 102	a: fixed b: random	a: 1.09 (0.56–1.61)* b: 0.58 (–0.45–1.62)	a: 17% ↑ b: –
	External auditory rhythms	a: Stride length b: Gait speed	a: [140,142] b: [140–142]	a: gait analysis b: 10MW, 30 sec walk	a: 43 b: 67	a: fixed b: fixed	a: 0.68 (0.06–1.30) b: 0.91 (0.40–1.42)	a: 0.18 m ↑ a: 0.22 m/s ↑
Exercises for the upper limb	Constraint-induced movement therapy (CIMT)	a: Dexterity b: Amount of use (paretic arm)	a: [150–152,154,155] b: [154,155]	a: ARAT, AMAT b: MAL	a: 104 b: 71	a: fixed b: fixed	a: 0.46 (0.07–0.85)* b: 0.23 (– 0.24–0.70)	a: 13.5% ↑ b: –
Biofeedback therapy	Biofeedback to the lower limb	a: Active ROM b: Comfortable gait speed	a: [140,158,159,166] b: [140,159,161,162,164–166]	a: ROM, AROM b: Gait analysis, 6MW, 15MW	a: 66 b: 98	a: fixed b: fixed	a: 0.41 (– 0.10–0.91) b: 0.35 (– 0.04–0.73)	a: – b: –
Functional electrical stimulation (FES) and neuromuscular stimulation (NMS)	FES for lower limb	a: Synergism b: Gait speed	a: [184,186] b: [184,185]	a: BFM b: 10MW, 20MW	a: 58 a: 52	a: fixed b: random	a: 0.01 (–0.51–0.53) a: 0.73 (–0.93–2.40)	a: – b: –
	NMS with EMG triggering	a: Synergism	a: [193,194]	a: BFM	a: 44	a: fixed	a: –0.06 (– 0.76–0.63)	a: –
	NMS for glenohumeral subluxation and hemiplegic shoulder pain	a: Reduction subluxation b: Passive ROM (lateral rotation)	a: [63,75,197,198] b: [63,198]	a: X-rays b: PROM	a: 161 b: 66	a: random b: fixed	a: 1.41 (0.76–2.06)* b: 0.55 (0.05–1.04)*	a: 5 mm ↑ b: 13° lat.rot. ↑
Intensity of exercise therapy		a: ADL b: Gait speed c: Dexterity d: Instrumental ADL	a: [65,69,73,80,85,147–149,209–220] b: [65,80,210,214,215,218] c: [65,69,147,149,218] d: [65,69,149,210,212,213,216,218,219]	a: BI, FIM b: 10MW c: ARAT d: NEADL	a: 2686 b: 576 c: 676 d: 1570	a: random b: fixed c: fixed d: fixed	a: 0.13 (0.03–0.23)* b: 0.19 (0.01–0.36)* c: 0.03 (–0.13–0.19) d: 0.23 (0.13–0.33)*	a: 4.5% ↑ b: 0.07 m/s ↑ c: – d: 5% ↑

*Statistical significant summary effect size (SES): $p < 0.05$.
[a]In case of a random effects model, no sensitivity analysis took place.
AMAT, Arm Motor Activity Test; ARAT, Action Research Arm Test; AROM, active range of motion; AS, Ashworth Scale; BBS, Berg Balance Scale; BFM, Brunnstrom Fugl-Meyer Assessment; BI, Barthel Index; FAC, Functional Ambulation Categories; FIM, Functional Independence Measure; MAL, Motor Activity Log; MAS, Modified Ashworth Scale; MDUF, maximal distance until fatigue; MW, Metre Walk; N, number of patients; NEADL, Nottingham Extended ADL; PROM, passive range of motion; PV GRF, peak vertical ground reaction force through affected foot; RBWD, ratio body weight distribution; RCT, randomized controlled trial; ROM, range of motion; TUG, timed up & go-test; VFD LR, vertical force difference between left+right.

Table 3 Methodological quality analysis of the RCTs based on the PEDro scale

Intervention categories	*N*	Item on PEDro scale: 1* Eligibility criteria	2 Random allocation	3 Concealed allocation	4 Similarity baseline	5 Blinding patients	6 Blinding therapists	7 Blinding assessors	8 Outcome > 85% patients	9 Intention-to-treat	10 Between-group comparisons	11 PM and MV	Median/mean (range)
1) (Traditional) neurological treatment approaches	8	67,81–83, 86,87	67,81–87	–	67,81, 84–86	–	–	67,81,82,86	67,84,87	–	67,81–87	67,81, 83–85,87	4 / 3.8 (3–6)
2) Programmes for training sensorimotor function or influencing muscle tone	15	92–94,96, 100–102, 104–106	71,84, 91–96, 100–106	92–94,96, 100,102	71,84, 91–94,96, 100,101, 104	–	–	94–96,100, 104–106	84,92,94–96-96,101,105, 106	100,102,106	71,84,91–94, 100,101,103,105	71,84,91, 92,94,96, 100,101, 104–106	4 / 4.7 (2–7)
3) Cardiovascular fitness and aerobic programmes	8	80,110,111, 113–116	80,109–111, 113–116	110,111,113, 114	80, 109–111, 113–115	–	–	80,114	110,111, 114,115	110,114	80,109–111,113 111,113–116	80, 109–111, 113,115, 116	5 / 5.3 (3–7)
4) Methods for training mobility and mobility-related activities	29	61,77,80, 86,113, 117–121, 123,124, 126,127, 129–133, 136–139, 141–144	61,77,80,86, 113,117–124,126,127, 129–133, 136–144	113,117,124, 129,131,139, 142,143	61,77,80, 86,113, 117–120, 122–124, 126,127, 129–133, 136–139, 141–144	–	–	77,80,86,117–120,123, 129,131–133,136–140,143,144	61,117,118, 120–123, 127, 129–131, 136–139, 142–144	137,139,144	61,77,80,86,113, 117–124,126, 127,129–133, 136–143	61,77, 80,113, 117–124, 126,127, 131,133, 136–139, 142–144	5 / 5.3 (3–8)
5) Exercises for the upper limb	19	65,69,73, 82,83, 87,110, 147–155, 157	65,69,73,82, 83,87,110, 146–157	65,69,110, 149,155	65,69, 73,110, 146–154, 156,157	–	–	65,69,73,82, 146–148, 150–155, 157	65,73,87, 110,147, 149–157	110,151,152, 155	65,69,73,82, 83,87,110, 147–150,154, 155,157	65,69,73, 83,87,11-0, 146,147, 149,155	5 / 5.0 (3–7)
6) Biofeedback therapy for the lower and upper limb	21	81, 160–165, 167,168, 173–175, 179	81,140, 158–168, 173–180	162,168,175	81, 162–164, 167,168, 173, 175–177	–	–	81,140, 159,160, 163–165, 173,175, 178,179	158–160, 163,164, 173,175, 176,178, 179	–	81,140, 159–164, 166–168, 173–177, 179,180	81,158, 159, 161–164, 166–168, 173,175, 176,179, 180	4 / 4.2 (2–7)
7) Functional electrical and neuromuscular stimulation	17	75,162, 184–187, 189, 191–194, 197,198	63,75,162, 184–195, 197,198	162,184,185, 191,195	63,162,184, 186,187, 189,191, 193,194, 197,198	–	–	75,186,188, 189,191,193, 198	184,185, 189–192, 194,195, 198	185,198	63,75,162,184–187,189–195, 197,198	63,75,16-2, 184–191, 193–195, 197,198	5 / 4.9 (3–7)
8) Applying orthotics and assistive devices for the lower and upper extremity	2	59,202	59,202	59,202	59,202	–	–	59,202	59	202	59,202	59,202	7 / 7 (7–7)

9) Treatment of hemiplegic shoulder pain and hand oedema	3	204,205, 208	204,205,208	208	204,205, 208	–	–	204,205,208	208	–	204,205,208	204,205, 208	5 / 5.6 (5–7)
10) Intensity of exercise therapy	20	65,69, 73,80, 147–149, 210–220	65,69,73,80, 85,147–149, 209–220	65,69, 149,209, 211–216, 219,220	65,69,73, 80,85, 147–149, 209,210, 212–217, 219,220	–	–	65,69,73,80, 147,148,210, 212–216, 218,219	65,73,147, 149,210, 211, 213–215, 217–219	212, 215–219	65,69,73,80,85, 147–149,209 149,209–220	65,69,73, 80,85, 147,149, 209–219	6 / 5.9 (4–8)
Total (RCTs)	142	116	142	46	108	0	0	83	81	21	127	111	–
Total without doubles of RCTs	123	100	123	39	93	0	0	72	74	19	109	97	5 / 5.1 (2–8)

*PEDro-item 1 evaluates the external validity and is not included in the sumscore of the PEDro. Sumscore of the PEDro is based on the items 2–11.
N, Number of RCTs; PEDro, Physiotherapy Evidence Database; PM and MV, point measures and measures of variability; RCTs, randomized controlled trials.

Training sensory integrity

In one CCT[99] the effectiveness of sensory re-education of arm and hand was investigated of the paretic limb. Training was provided for 45 min, three times a week for six weeks (Table 1). Cutaneous stimulation contained tasks such as identificating letters, discriminating objects and localizing body parts on the hemiplegic side. While significant effects were reported for somatosensory perception, evaluation of treatment effects for functional outcomes was lacking. Based on one CCT,[99] there were indicative findings that sensory training may improve somatosensory perception.

Influencing muscle tone and stiffness

In nine RCTs[71,84,100–106] and one CCT[107] the effects of different interventions for the treatment of spasticity of the paretic limbs were investigated by applying: an inflatable pressure splint[84]; reflex inhibiting positioning[100,108]; spastic muscle stretchings[101]; inhibitory casts or thermoplastic splints to the upper limbs[102,103,107]; and transcutaneous electrical nerve stimulation (TENS)[71,104–106] (Table 1). The quality scores of these RCTs ranged from 2[103] to 7.[100]

Due to differences in outcomes and treatment modalities, pooling of the studies was only possible for TENS, and showed a significant homogeneous SES for reducing muscle tone according to a (modified) Ashworth Scale[71,105] (Table 2). In addition, best-evidence synthesis showed limited evidence for slow stretch techniques in improving active ROM.[101] Insufficient evidence was found for TENS[71,104] and inhibitory casts or thermoplastic splints[102,103,107] in improving passive ROM. No evidence was found that stretching techniques, splinting or TENS improved functional outcome.

Cardiovascular fitness and aerobic programmes

Aerobic capacity and physical endurance were defined as the ability to perform work or participate in activity over time using the body's oxygen uptake, delivery and energy release mechanisms.[10(S48)]

Three RCTs[109–111] and one CCT[112] investigated the effects of cardiovascular fitness training after stroke. They studied the use of a home-based exercise programme[110] incorporating a leg cycle ergometer[109,111] or muscle strengthening[110], in terms of synergism,[109,110] aerobic capacity,[109] gait speed,[110,111] walking endurance[110,111] and instrumental ADL.[110,111]

Treatment sessions ranged from 30[109] to 90[110] min and were applied 3[109,110] to 5[111] times a week for 8[110,111] to 10[109] weeks (Table 1). The quality of the RCTs ranged from 4[109] to 7.[110,111] Due to differences in measurements, pooling was only possible for the Fugl-Meyer (FM) motor scores and gait speed. It showed a statistically significant homogeneous SES for gait speed[110,111] and a nonsignificant heterogeneous SES for FM motor score[109,110] (Table 2). Best-evidence synthesis demonstrated strong evidence for maximal workload[109,111] and walking distance,[110,111] whereas limited evidence was found for aerobic capacity (VO_2, Ve and VCO_2).[109] No evidence was found for basic[110] or instrumental[110,111] ADL.

Five RCTs[80,113–116] investigated the effects of interventions combining muscle strengthening and endurance training. Outcomes were reported for lower limb strength,[114–116] synergism of the lower extremity,[80,114] balance,[80,114] aerobic capacity,[114,115] endurance,[113,114] rising from sitting to standing,[113] gait speed,[80,113,114,116] dexterity[114] and ADL.[80] Training sessions ranged from 60[113,115] to 90[114,116] min per day, and were applied 3[113–116] to 10 times a week for 4[113] to 12[114,115] weeks (Table 1). Methodological quality ranged from 3[113,115,116] to 7[114] points.

Pooling was possible for muscle strength, synergism, aerobic capacity, walking endurance and gait speed. A homogeneous statistically significant SES was calculated for aerobic capacity[114,115] and a heterogeneous statistically significant SES for muscle strength of the lower extremity.[114–116] No statistically significant homogeneous SESs were found for synergism in the lower extremity,[80,114] walking endurance[113,114] or gait speed[80,113,114,116] (Table 2).

Methods for training mobility and mobility-related activities

Training mobility and mobility-related activities was divided into three subcategories: balance, gait and wheelchair propulsion.

Training balance and postural control

Fourteen RCTs and one CCT studied the effects of balance training on improving sitting balance (four RCTs[86,117–119]), rising from sitting to standing (five RCTs[61,113,117,119,120]), and standing balance with visual feedback (seven RCTs[121–127] and one CCT[128]) or perceptual feedback (one RCT).[129] Treatment sessions ranged from 15[61] to 120[118] min per day, 3[123,127] to 15 times a week[61] for 2[86,117,121,129] to 8[124,126] weeks (Table 1). The goals of these interventions were to reduce postural sway,[121–127,129] to increase the symmetry of weight distribution between paretic and nonparetic sides[61,86,113,117–120,122–124] and to reduce number of falls.[120] Outcomes of these studies were evaluated in terms of weight distribution between paretic and nonparetic side, while sitting[86,117–119] or standing up,[61,113,117,120] the time to rise from the sitting to standing position[61,120] the Timed Up & Go,[124,126,127] postural sway/symmetry[121–125,129] and gait speed.[128] The methodological quality ranged from 4[121,126] to 7[117] points.

Pooling was possible for those studies that aimed to improve transfers and standing balance. Statistically significant homogeneous SESs were found for postural symmetry of rising from sitting to standing,[61,113,117,120] sitting down from standing,[61,120] and time needed to rise,[61,120] whereas training standing balance resulted in a significant reduction in postural sway and an increase in the symmetry of weight distribution between paretic and nonparetic sides[121–125] (Table 2). A significant heterogeneous SES was found for time needed to sit in making transfers,[61,120] whereas the Timed Up & Go test showed a heterogeneous significant negative SES for those patients who had received training for standing balance.[124,126,127] Moreover no significant effects were found in those studies[124,126,127] that measured control of balance by the Berg Balance Scale (Table 2).

The best-evidence synthesis for evaluating effects of training sitting balance showed strong evidence that this intervention improves the ability to reach forward with the arm when in a seated position[86,117–119]; limited evidence was observed for reducing the occurrence of falls in programmes aimed at improving transfers.

Treadmill training

Treadmill training was applied (1) with body weight support and (2) without body weight support. Five RCTs[77,130–133] and two CCTs[134,135] investigated the effects of body weighted supported treadmill training (BWSTT) on recovery of balance,[77,131,134] gait,[77,130–134] and walking endurance.[77,130,133] Amount of body weight support ranged from 0%[77] to more than 40%[134] and was applied 3[132,134] to 5[130,131,133] times a week for 20[77,132,133] to 45[130] min per day for 2[134] to 11[131] weeks (Table 1). The methodological quality ranged from 4[130,133] to 7[131] points.

Meta-analysis demonstrated large effect sizes for walking endurance,[77,130,133] whereas no significant effect sizes were found for postural control as measured by the Berg Balance Scale,[77,131] walking ability[131,133] or gait speed[77,130–133] (Table 2).

Five RCTs[80,136–139] with methodological quality ranging from 5[80] to 8[139] points investigated the effects of treadmill training without body weight support. Treatment sessions lasted from 5 min[136] to 1 h[137] per day, and were applied 3[137–139] to 5[80,80] times a week for 3[136] to 6[80] weeks (Table 1). The RCTs showed significant homogeneous SES for walking ability,[136,138] whereas a heterogeneous nonsignificant SES was found for gait speed[80,136–138] (Table 2).

External auditory rhythms (EAR)

Three RCTs[140–142] investigated the effects of EAR on tempero-spatial parameters of gait including stride length, cadence, symmetry of gait and gait speed.[140–142] Training sessions ranged from 20[142] to 30[141] min per day, occurred 2[140] to 10[141] times a week for 3[142] to 12[140] weeks (Table 1). The methodological quality varied from 3[140,141] to 6[142] points on the PEDro scale. Pooling these studies showed a homogeneous significant SES for stride length[140,142] and gait speed[140–142] (Table 2).

Limb loading

One RCT[143] investigated the effects of exercise training with weighted garments to improve balance and gait (Table 1). Home training with weighted garments was compared with a training programme without garments. The study showed no statistically significant effects, and thus, no evidence to support limb loading in terms of balance or gait speed.

Wheelchair propulsion

One RCT[144] and one CCT[145] investigated the effects of self-propelling a wheelchair on muscle tone,[144] control in accuracy of wheelchair driving[145] and ADL.[144] Best-evidence synthesis of the studies showed no evidence that wheelchair propulsion with only the nonhemiplegic hand and foot resulted in better ADL, or that it influenced spasticity (Table 1).

Exercises for the upper limb

Effectiveness of exercising the paretic arm

Eleven RCTs[65,69,73,82,83,87,110,146–149] studied the effects of exercise therapy aimed at improving function of the paretic arm. Exercise training included the use of specific neurological treatment approaches or task-oriented training programmes. Therapy time ranged from 30[147] to 90[110,149] min per day, 3[110] to 5[65,82,147,149] days a week for 5[69] to 20[65] weeks (Table 1). Outcomes were evaluated in terms of muscle strength,[73,83,149] synergism,[110,147] dexterity[65,69,73,87,147,149] or ADL.[65,69,73,82,83,87,110,147–149] In some studies the specific exercise programme was added to a conventional treatment programme.[65,69,73,147–149] Methodological quality ranged from 3[82,83] to 7[65,110] points. Due to differences in outcomes, study pooling was not possible. Further, best-evidence synthesis showed insufficient evidence for the use of exercise programmes aimed at enhancing dexterity of the paretic arm or improving ADL. No evidence was found for improving muscle strength or synergism from exercise programmes for the paretic arm.

Constraint-induced movement therapy (CIMT)

Six RCTs[150–155] investigated the effects of CIMT on motor performance,[151,152,155] dexterity of the paretic arm[150–155] and ADL.[150,155] The nonparetic arm was constrained for 5[151,152] to 10[153] h per day over a 2[150,154,155] to 10[151,152] week period. In addition, exercise training was provided for 1[151,152] to 6[153–155] h a day from 3 times a week[151,152] to every weekday[153] (Table 1). Quality of the RCTs ranged from 4[153] to 7[155] points on the PEDro scale.

The meta-analysis using dexterity measured with the Arm Motor Activity Test (AMAT) or Action Research Arm Test (ARAT) as an outcome showed a statistically significant SES[150–152,154,155] in support of CIMT. No significant effects were found for the Motor Activity Log that evaluates the amount of use in daily living[154,155] (Table 2). Best-evidence synthesis showed no differential effects due to CIMT for ADL as measured by Barthel Index,[150] Rehabilitation Activities Profile (RAP)[155] or the Functional Independence Measure.[150]

Bilateral arm training

One RCT[156] and one CCT[97] investigated the effects of high repetitive bilateral cyclic training of the upper limb. Outcomes were muscle strength and dexterity[97,156] (Table 1). Due to relatively poor methodological quality as well as differences in outcomes, pooling was not possible. Best-evidence synthesis showed indicative findings in favour of bilateral arm training on grip strength[97] and dexterity of the paretic arm.[97]

Mirror therapy

Using subjects with stroke, two RCTs[146,157] investigated the effects of mirror therapy on active ROM,[146] muscle tone[157] and dexterity as assessed with the ARAT.[157] Patients were asked to move the nonparetic arm while looking in a mirror that gave the impression that the paretic limb was moving. Therapy sessions ranged from 15[146] to 30[157] min per day, 2[157] to 6[146] times a week for 5[157] to 8[146] weeks (Table 1). Based on studies of moderate quality (scores of 4[146] to 5[157] points), a best-evidence synthesis suggested limited support for improving dexterity through the use of mirror therapy.

Biofeedback therapy

Biofeedback to the paretic lower limb

Twelve RCTs[140,158–168] and four CCTs[169–172] investigated the effects of biofeedback including EMG feedback[158–160,162–167] and positional feedback.[140,161] Biofeedback was aimed at improving knee flexion,[165] knee extension,[167] ankle dorsiflexion[158,159,162,163,166] or ankle plantar flexion[140] or reducing hyperextension of the knee[168] of the paretic leg during gait. In six RCTs[158,159,161,164,165,167,168] biofeedback was applied in adjunct to basic exercises, whereas in five studies the control group received a specific neurological treatment approach,[159,161,164,166,167] gait training,[158] placebo biofeedback[160] or no treatment at all.[140] The intensity of biofeedback training ranged from 20[163] to 60[164] min per day, 2[140,161] to 5 times a week[163,164,167,168] for 2[163] to 12[140] weeks (Table 1). The quality of the RCTs ranged from 2[165] to 6[162–164,168] points. Pooling of studies was only possible for two outcomes. Homogeneous nonsignificant SESs were found for active ROM of the paretic ankle[140,158,159,166] and gait speed[140,159,161,162,164–166] (Table 2).

Biofeedback to the paretic upper limb

Ten RCTs[81,163,173–180] and three CCTs[181–183] studied the effects of EMG feedback on motor control and dexterity of the paretic upper limb. In 3 of 10 studies EMG feedback was applied as an adjunct to a basic exercise programme[173,175,177] and compared with a neurological treatment approach,[81,173,176–178,181] placebo EMG[163,175,180] or no treatment.[182] In terms of intensity, biofeedback was given for 30[179] to 60[177,178,181] min per day, 2[176,178] to 5 times a week[163,179] for between one week[179] and six months[182] (Table 1). Study quality ranged from 2[174] to 7 points.[175] Due to different aims and outcomes across the studies, pooling of data was not possible. Most of the RCTs showed no statistically significant effects. Best-evidence synthesis showed no evidence to support the use of biofeedback for improving strength[177] or increasing active ROM,[163,176,177,179] whereas there was insufficient evidence to determine its effect on dexterity of the paretic upper limb.[173,175]

Functional electrical stimulation (FES) and neuromuscular stimulation (NMS)

Effects of FES on the lower limb

Five RCTs[162,184–187] investigated the effects of FES on muscle strength,[187] synergism,[184,186] Physiological Cost Index (PCI),[185] walking ability,[186] gait speed[162,184,185] and ADL[186] in stroke patients. A nonsignificant homogeneous SES was found for studies investigating synergism of the lower limb measured with the Fugl-Meyer Motor Assessment,[184,186] whereas a nonsignificant heterogeneous SES was observed for gait speed[184,185] (Table 2). Based on best-evidence syntheses, limited evidence was found in support of FES for muscle strengthening,[187] PCI[185] and walking ability.[186] No evidence was found for ADL as measured with the Barthel Index.

Neuromuscular stimulation of the paretic forearm, with and without EMG triggering

Four RCTs[188–191] investigated the effects of NMS without EMG triggering on active ROM of the wrist and dexterity in stroke patients. NMS of the extensors of the wrist and fingers of the paretic forearm was applied 30[188] to 90[191] min per day during 3[189] to 8[191] weeks. Outcome was evaluated in terms of muscle strength of the wrist extensors,[188,191] synergism,[189] active ROM,[188] dexterity[191] or ADL[189,191] (Table 1). Methodological quality ranged from 3[188] to 7.[191] Pooling was not possible due to differences in outcomes and in the parameters of NMS that were used. Best-evidence synthesis showed indicative findings in favour of NMS for active ROM[188] and limited evidence for muscle strength[188,191] and dexterity.[191] However, the evidence for dexterity was restricted to only those patients with some voluntary control of wrist and finger extension at baseline of the study.[191]

Four RCTs[192–195] and one CCT[196] studied the effects of NMS with EMG triggering for improvement of finger and hand extension in stroke patients. In two trials only patients with some voluntary wrist extension[192] or strength in the forearm extensors[193] were included. Stimulation ranged from 30[193,194] to 90[195] min per day, 2[195] to 5[193,194,196] times a week for 2[192,195] to 12[194,196] weeks (Table 1). Outcome was evaluated on the basis of strength of forearm extensors[192] and flexors,[196] synergism,[192–194,196] dexterity[192,194,195] and ADL.[193] Methodological quality of the studies ranged from 3[192] to 5[193–195] PEDro points.

Pooling individual RCTs for synergism showed a nonsignificant homogeneous SES[193,194] (Table 2). Insufficient evidence was found for EMG-triggered NMS for muscle strength[192,196] and dexterity.[192,194]

Neuromuscular stimulation for glenohumeral subluxation (GHS) and hemiplegic shoulder pain (HSP)

Four RCTs[63,75,197,198] and two CCTs[199,200] investigated the effects of NMS on the subluxated hemiplegic shoulder. NMS was restricted to the supraspinatus and dorsal deltoid muscles of the paretic shoulder. Treatment sessions ranged from 30 min[198,200] to 6 hours a day[63,75,197], 5[75,197,200] to 7[63,198] days a week for 4[198] to 6[63,75,197,200] weeks (Table 1). Study quality ranged from 4[63,75,197] to 7[198] points. Meta-analysis of the RCTs showed a heterogeneous, statistically significant SES for reduction in caudal subluxation,[63,75,197,198] and a homogeneous statistically significant SES for the increase in lateral passive ROM[63,198] (Table 2). The best-evidence synthesis showed insufficient evidence for effects of NMS on reducing HSP.

Applying orthotics and assistive devices for the lower and upper extremities

Assistive, supportive and adaptive devices for the lower limb were defined as equipment used to aid patients in ambulation. Assistive and supportive devices included crutches, canes, walkers, electric neuromuscular devices, static and dynamic (knee) ankle-foot orthosis (AFO), whereas adaptive devices included environmental controls and seating systems.[10(S54)] Orthotic, assistive and supportive devices for the upper limb included braces, casts, slings, splints and supportive taping, neuromuscular stimulation and kinetic and EMG feedback equipment.[10(S76)]

Applying ankle-foot orthoses (AFOs)

One RCT[59] investigated the effects of an AFO on walking ability and gait speed.[59] Best-evidence synthesis based on one high-quality RCT[59] showed no evidence for increased gait speed when an AFO was provided after stroke (Table 1).

Slings, supportive devices and strapping for reducing glenohumeral subluxation

Several techniques aimed at reducing GHS and thereby decreasing hemiplegic shoulder pain have been studied. One CCT[201] investigated the effectiveness of using a hemi-sling. In addition, one RCT[202] and one CCT[203] investigated the impact of supportive taping for the hemiplegic shoulder (strapping). The quality of the RCT[202] was 7 points (Table 1). Undertaken because of lack of comparability between studies, a best-evidence synthesis revealed no evidence for reducing a glenohumeral subluxation or decreasing hemiplegic shoulder pain to support the effectiveness of hemi-slings and strapping techniques.

Treatment of hemiplegic shoulder pain and hand oedema

Effectiveness of exercises for the hemiplegic shoulder

Two RCTs[204,205] and two CCTs[206,207] studied the effects of an exercise programme for a painful hemiplegic shoulder. Comparisons were made with ultrasound,[204] cryotherapy,[205] nonsteroid anti-inflammatory drugs[207] or pulley exercises for the paretic shoulder.[206] The exercise programmes were given for 15–30 min per day, 3[204,207] to 5[206] times a week for four weeks[204,205] to three months[207] (Table 1).[206] The quality of the studies ranged from 4[206] to 5[204] points.[205] Best-evidence synthesis showed no positive effects of exercising the hemiplegic shoulder in terms of decreasing shoulder pain[204–207] or improving active ROM.[204–207]

Treatment of hand oedema

One RCT[208] studied the effects of Intermittent Pneumatic Compression (IPC)[208] on oedema of the paretic hand. IPC was offered for 2 h two times per work day for four weeks.[208] Best-evidence synthesis showed no evidence for IPC in terms of reduction of oedema of the paretic hand (Table 1).

Intensity of exercise therapy

Intensity of exercise therapy was defined as the additional time spent (in minutes) in exercise training when the experimental group was compared with the control group. Twenty RCTs[65,69,73,80,85,147–149,209–220] and three CCTs[221–223] investigated the effect of augmented exercise therapy on functional outcomes (Table 1). In RCTs, the contrast in therapy time spent between the intervention and control groups ranged from 132[215] to 6816 min.[209] Outcomes were evaluated in terms of comfortable walking speed,[65,80,210,214,215,218] dexterity,[65,69,147,149,218] ADL[65,69,73,80,85,147–149,209–220] and instrumental ADL.[69,149,210,212,213,216,218,219] The quality of the RCTs ranged from 4[85,148] to 8.[215,219] Pooling the RCTs for differences in treatment contrast showed statistical significant SESs for ADL,[65,69,73,80,85,147–149,209–220] comfortable walking speed[65,80,210,214,215,218] and instrumental ADL.[65,69,149,210,212,213,216,218,219] A homogeneous nonsignificant SES was found for dexterity[65,69,147,149,218] (Table 2). (See ref. 224 for an up-to-date review.)

The methodological quality for all 123 RCTs is presented in Table 3. The median score of these studies was 5 points (mean 5.1; range 2–8 points on a scale from 0 to 10 points). Only 39 RCTs mentioned a concealed allocation, whereas just 19 RCTs described an intention-to-treat analysis. In none of the studies was blinding possible for patient or therapist, and only 72 of the 123 RCTs had blinded the observer (Table 3).

Discussion

Evidence for physical therapy interventions

The present review showed small but statistically significant SESs supporting the intensity of exercise training. This represented a mean improvement of 5% on ADL. Significant medium-sized SESs were found for aerobic training, TENS and constraint-induced movement therapy. Large SESs were found for training sit-to-stand transfers, applying neuromuscular stimulation for glenohumeral subluxation, external auditory rhythms during gait and treadmill training with and without body weight support. The small to large effect sizes in high-quality RCTs represent a mean improvement favouring the experimental group ranging from 5% for intensity of exercise therapy to 31% for BWSTT on walking endurance. The clinical meaning of effects in favour of physical therapy is difficult to judge. The present findings however, support the use of physical therapy to improve performance as well as the capacity to perform regular daily activities after stroke, in particular when studies started early after stroke.[224] It should be noted that all the effective studies were characterized by focused exercise programmes within which the functional tasks were directly trained. In several studies task-oriented exercise training was intensified by offering a gait programme on a treadmill,[30] by constraining the nonparetic arm for several hours per day[225] or by offering patients a progressive series of different workstations aimed at improving strength and endurance in a functional way.[114] In contrast, impairment focused programmes such as muscle strengthening, muscular re-education with support of biofeedback,[21] neuromuscular[22] or transcutaneous[105] nerve stimulation showed significant improvement in range of motion, muscle power and reduction in muscle tone; however these changes failed to generalize to the activities themselves. Interestingly, a similar trend was found for studies designed to improve cardiovascular fitness by a cycle ergometer.[27] Despite significant improvements in workload in the high-quality RCTs,[27] general fitness failed to change. Strong evidence was found that neuromuscular stimulation aimed at reducing the amount of glenohumeral subluxation had no positive impact on hemiplegic shoulder pain.

It was also noted that significant outcomes were most frequently found for those variables measured by continuous parameters defined at interval or ratio levels, such as gait speed,[77] walking distance,[110] postural sway and symmetry in weight bearing between hemiplegic and nonhemiplegic side.[61] Although these findings are perceived as important for functional activities,[226] their real impact on performance of gait-related activities needs further clarification in future research.

The present review revealed no evidence in terms of functional outcomes to support the use of neurological treatment approaches, compared with usual care regimes. To the contrary, there was moderate evidence that patients receiving conventional functional treatment regimens needed less time to achieve their functional goals[88] or had a shorter length of stay compared with those provided with specific neurological treatment approaches, such as Bobath.[67,85,89] This discovery is in agreement with the criticism that these traditional approaches are too impairment focused.[33,47,49] In addition, several treatment approaches have been criticized for having a weak theoretical framework[49,227,228] that is in conflict with recent theories of motor control.[229,230] For the development of more effective exercise strategies, a better theoretical understanding of the underlying mechanisms of disordered movement co-ordination in terms of perception and action is needed.[49] Moreover, best-evidence synthesis showed no support for providing orthotics, such as AFOs to the lower limb,[59] or for decreasing hand oedema.[208] Neither was evidence found for providing walking aids, perhaps due to the lack of

Clinical messages

- There is strong evidence that patients benefit from exercise programmes in which functional tasks are directly and intensively trained.
- Impairment-focused programmes such as biofeedback, neuromuscular or transcutaneous nerve stimulation, cardiovascular fitness training and muscle strengthening, fail to generalize to functional improvements.
- The rational for different treatment approaches is still weak and needs a better understanding of the 'nature' of coordination deficits in functional tasks after stroke.

controlled studies. Insufficient evidence was found for interventions designed to reduce hemiplegic shoulder pain[204,205] or to correct the spastic hand.[24]

Limitations of this study

The present review has a number of shortcomings in terms of the studies investigating the diversity of treatments used in physical therapy. First, most studies exhibited methodological flaws such as lack of randomization, or intention-to-treat analyses and the use of unblinded observers. A negative trend was found between the unbiased effect sizes of the selected RCTs and the methodological quality based on the PEDro scale ($r = -0.19$; $p = 0.08$). This finding suggests that bias due to the previously mentioned problems as well as the disregard for systematic dropouts tends to overestimate observed effects. On a more positive note, there was a significant association between year of publication and PEDro score ($r = 0.42$; $p < 0.01$) suggesting an increased awareness by researchers to aim for high-quality studies that will provide an unbiased assessment of the effectiveness of physical therapy. Another major problem in most RCTs was the small numbers of patients involved, and with that, the low statistical power to reveal statistically significant effects. Due to the diversity of selected outcomes and interventions, pooling of RCTs was limited in the present review. In contrast, there are few RCTs aimed at investigating the effects of physical therapy interventions on stair climbing, use of walking aids or instructions for fall prevention in the literature. These shortcomings emphasize both the need for more high-quality RCTs and for a consensus about using the same core set of measures in stroke rehabilitation studies in the future.

Due to lack of comparability of many interventions, and the small number of high-quality RCTs, a qualitative best-evidence synthesis was often used in the present study to analyse the results. Although this approach may be criticized as being based on arbitrary criteria, it seems justified when pooling is not appropriate or severely hampered.[37]

Finally, in the present review only studies written in English, Dutch or German were included. The classification of 'physical therapy' into 10 different intervention categories was an arbitrary choice to deal with the heterogeneity of study objectives in the field.

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Appendix 1 – Best-evidence synthesis

Strong evidence	Provided by statistically significant findings in outcome measures in • at least two high-quality RCTs, with PEDro scores of at least 4 points[a]
Moderate evidence	Provided by statistically significant findings in outcome measures in • at least one high-quality RCT <u>and</u> • at least one low-quality RCT ($\leq$3 points on PEDro) <u>or</u> one high-quality CCT[a]
Limited evidence	Provided by statistically significant findings in outcome measures in • at least one high-quality RCT <u>or</u> • at least two high-quality CCTs[a] (in the absence of high-quality RCTs)
Indicative findings	Provided by statistically significant findings in outcome measures in at least • one high-quality CCT <u>or</u> low-quality RCTs[a] (in the absence of high-quality RCTs), <u>or</u> • two studies of a non-experimental nature with sufficient quality (in absence of RCTs and CCTs)[a]
No or insufficient evidence	• In the case that results of eligible studies do not meet the criteria for one of the above stated levels of evidence, <u>or</u> • in the case of conflicting (statistically significant positive and statistically significant negative) results among RCTs and CCTs, <u>or</u> • in the case of no eligible studies

[a]If the number of studies that show evidence is $<50\%$ of the total number of studies found within the same category of methodological quality and study design (RCT, CCT or non-experimental studies), no evidence will be classified.