10. Upper Extremity Interventions

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Key Points

Initial degree of motor impairment is the best predictor of motor recovery following a stroke. Functional recovery goals are appropriate for those patients who are expected to achieve a greater amount of motor recovery in the arm and hand. Compensatory treatment goals should be pursued if there is an expected outcome of poor motor recovery.

Attempts to regain function in the affected upper extremity should be limited to those individuals already showing signs of some recovery.

Neurodevelopment techniques are not superior to other therapeutic approaches in treatment of the hemiparetic upper extremity.

It is uncertain whether enhanced therapy results in improved short-term upper extremity functioning.

It is uncertain whether repetitive task specific training techniques improve upper extremity function.

It is uncertain whether sensorimotor training results in improved upper extremity function.

It is uncertain whether mental practice results in improved motor and ADL functioning after stroke.

Hand splinting does not improve motor function or reduce contractures in the upper extremity.

Constraint-induced movement therapy is a beneficial treatment approach for those stroke patients with some active wrist and hand movement.

Sensorimotor training with robotic devices improves functional and motor outcomes of the shoulder and elbow, however, it does not improve functional and motor outcomes of the wrist and hand.

There is preliminary evidence that virtual reality therapy may improve motor outcomes post stroke.

*The Evidence-Based Review of Stroke Rehabilitation (**EBRSR**) reviews current practices in stroke rehabilitation.*

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Hand splints do not reduce spasticity nor prevent contracture.

Botulinum Toxin decreases spasticity and increases range of motion; however, these improvements do not necessarily result in better upper extremity function.

Botulinum Toxin in combination with electrical stimulation improves tone in the upper extremity.

More research is needed to determine the effectiveness of Nerve Blocks for spasticity.

Physical Therapy may not be effective for reducing spasticity in the upper extremity.

EMG/Biofeedback therapy is not superior to other forms of treatment in the treatment of the hemiparetic upper extremity.

Intermittent pneumatic compression is not an effective treatment for hand edema.

It is uncertain whether transcutaneous electrical nerve stimulation improves outcomes post-stroke

Functional Electrical Stimulation therapy improves hemiparetic upper extremity function.

Antidepressant drugs may improve short-term motor performance.

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10. Upper Extremity Interventions Post-Stroke

Impaired upper extremity function is a common and often devastating problem for stroke survivors. In the population-based Copenhagen Stroke Study (Nakayama et al. 1994), 32% of stroke patients had severe arm paresis at admission and 37% had mild paresis. In 64 out of 491 (13%) stroke survivors, the arm remained entirely non-functional despite comprehensive rehabilitation efforts. Regaining lost function in the upper extremities may be more difficult to achieve than return of normal function (ambulation) in the lower extremities (Hiraoka 2001). Similarly, Barreca et al. (2001) noted that, "*Rehabilitation of the hemiplegic upper limb remains difficult to achieve, with only 5% of stroke survivors who have complete paralysis regaining functional use of their impaired arm and hand (Dombovy 1993, Gowland 1982, Kwakkel et al. 2000). Limited rehabilitation resources, time constraints, and a lack of early motor recovery in the arm and hand tend to focus therapy on improving balance, gait and general mobility.*"

There is much discussion regarding which patients benefit the most from therapy. Nakayama et al. (1994) reported that in a sample of stroke patients with severe arm paresis, with little or no active movement on admission, that 14% of patients experienced complete motor recovery, while 30% achieved partial recovery (Hendricks et al. 2002). Similarly, Kwakkel et al. (2003) reported that 11.6% of patients had achieved complete functional recovery at 6 months, while 38% had some dexterity. Patients with anterior circulation infarcts, right hemispheric strokes, homonymous hemianopia, visual gaze deficits, visual inattention and paresis were associated with poor arm function. When Dominkus et al. (1990) assessed motor recovery in the upper extremity with the Motricity Index (Demeurisse et al. 1980), a patient with initial paresis was 4.58 times more likely to show motor recovery compared to a patient with initial paralysis. This finding has led to recommendations regarding which patients should receive more aggressive therapy (i.e. therapy aimed at strengthening and increasing range of motion), or to less aggressive therapy (i.e. therapy aimed at minimizing pain and contractures). Barreca et al. (2001) recommended that for patients with a poor prognosis for recovery, defined as a Chedoke McMaster score of less than stage 4, treatment should focus on minimizing contractures and pain in the involved upper extremity. However, there is evidence from a number of studies that treatment gains, albeit sometimes small, are observable in patients with severe initial impairment (Partridge et al. 2000, Lincoln et al. 1999, Sunderland et al. 1992, Kwakkel et al. 1999, Feys 1998). There is also evidence that motor rehabilitation of chronic stroke patients remains successful several months or years after the acute stroke (Hummelshein & Eickhof 1999, Kraft et al. 1992, Junkel et al. 1999). In terms of patients with less severe initial impairment (defined by a Chedoke McMaster score of stage 4 or greater), Barreca et al. (2001) have recommended that an aggressive restorative program geared towards regaining function in the affected upper extremity should be adopted.

Previous Reviews

Several previous reviews have focused on upper extremity therapies for stroke survivors. Two non-systematic reviews concluded that exercise therapy was beneficial and highlighted the importance of extensive practice (Duncan and Lai 1997, Richards and Pohl 1999), while a recent systematic review of 13 randomized controlled trials concluded that insufficient evidence was available to support the effectiveness of exercise therapies on arm function (van der Lee et al. 2001). However, these authors suggested that more intensive therapies might be beneficial.

Two reviews were able to pool their results quantitatively (Barreca et al. 2001, Hiraoka 2001). Barreca et al. (2001) reported that the pooled effect sizes associated with upper extremity treatments were: Z=4.87 for sensorimotor training (including 4 RCTs); Z=3.43 for EMG-electrical stimulation (including 3RCTs); and Z=4.44 for electrical stimulation (including 2 RCTs). Hiraoka (2001) included 14 RCTs evaluating upper extremity therapies and found an overall effect size (d) of 0.33, suggestive of a small to medium impact of therapy. Subgroup analyses suggested that there was no treatment effect of neurodevelopmental treatment compared with conventional physical therapy (d= -0.01); there was a medium effect of conventional physical therapy compared to no therapy (d=0.51) and a large effect of EMG biofeedback treatment compared to conventional physical therapy (d=0.85).

10.1 Consensus Panel Treatment and Recommendations

Barreca et al. (2001) provided consensus treatment recommendations for management of the post stroke arm and hand, based on a synthesis of best evidence. After reviewing the evidence the panel came to a consensus agreement that a hemiplegic upper extremity must be at least at a Chedoke-McMaster Stroke Impairment Inventory (CMSII) stage 4 before full rehabilitation efforts designed to restore function in the arm, are attempted. The panel concluded that attempts to rehabilitate the upper extremity of a person with a score less than a level 4 will not meet with success. A more palliative compensatory approach is recommended in such a case.

The stages of motor recovery assessed using the Chedoke McMaster Stroke Impairment Inventory, which is very similar to the Brunnstrom Recovery Stages, are described below.

Stages of Motor Recovery of the Chedoke McMaster Stroke Impairment Inventory (Gowland et al. 1993)

Stage	Characteristics
1	Flaccid paralysis is present. Phasic stretch reflexes are absent or hypoactive. Active movement cannot be elicited reflexively with a facilitory stimulus or volitionally.
2	Spasticity is present and is felt as a resistance to passive movement. No voluntary movement is present but a facilitatory stimulus will elicit the limb synergies reflexively. These limb synergies consist of stereotypical flexor and extensor movements.
3	Spasticity is marked. The synergistic movements can be elicited voluntarily but are not obligatory.
4	Spasticity decreases. Synergy patterns can be reversed if movement takes place in the

	weaker synergy first. Movement combining antagonistic synergies can be performed when the prime movers are the strong components of the synergy.
5	Spasticity wanes, but is evident with rapid movement and at the extremes of range. Synergy patterns can be revised even if the movement takes place in the strongest synergy first. Movements that utilize the weak components of both synergies acting as prime movers can be performed.
6	Coordination and patterns of movement can be near normal. Spasticity as demonstrated as resistance to passive movement is no longer present. Abnormal patterns of movement with faulty timing emerge when rapid or complex actions are requested.
7	Normal. A "normal" variety of rapid, age appropriate complex movement patterns are possible with normal timing, coordination, strength and endurance. There is no evidence of functional impairment compared to the normal side. There is a "normal" sensory-perceptual motor system.

2001 Consensus Panel Recommendations for Patients with Severe Impairment

"For the client with severe motor, sensory and functional deficits in the involved limb after stroke, the effectiveness literature indicates that additional treatment for the upper limb will not result in any significant neurological change. The evidence to date suggests that interventions may not lead to meaningful functional use of the affected limb at this stage of motor recovery."

1. Maintain a comfortable, pain-free, mobile arm and hand

- emphasize proper positioning, support while at rest and careful handling of the upper limb during functional activities.
- engage in classes overseen by professional rehabilitation clinicians in an institutional or community setting that teach the client and caregiver to perform self-range of motion exercises.
- avoid use of overhead pullies that appear to contribute to shoulder tissue injury
- use some means of external support for the upper limb in stages 1 or 2 during transfers and mobility
- place upper limb in a variety of positions that include placing arm and hand within the client's visual field.
- *Use some means of external support to protect the upper limb during wheelchair use."*

2. To maximize functional independence, stroke survivors with persistent motor and sensory deficits and their caregivers should be taught compensatory techniques and environmental adaptations that enable performance of important tasks and activities with the less affected arm and hand.

2001 Consensus Panel Recommendations for Patients with Moderate Impairment

"For clients with moderate impairments who demonstrate high motivation and potential for functional motor gains

1. Engage in repetitive and intense use of novel tasks that challenge the stroke survivor to acquire necessary motor skills to use the involved upper limb during functional tasks and activities.

2. Engage in motor-learning training including the use of imagery."

Conclusions Regarding Management of the Post Stroke Arm and Hand

There is consensus (Level 3) opinion that in severely impaired upper extremities (less than stage 4) the focus of treatment should be on palliation and compensation.

For those upper extremities with signs of some recovery (stage 4 or better) there is consensus (Level 3) opinion that attempts to restore function through therapy should be made.

Attempts to regain function in the affected upper extremity should be limited to those individuals already showing signs of some recovery.

10.2 Upper Extremity Interventions

A variety of treatment interventions to improve motor recovery in the upper extremity have been evaluated. They are presented in sections 10.2.1 to 10.2.9.

10.2.1 Neurodevelopmental Techniques

A variety of treatment approaches are in use currently. Arguably, the Bobath approach (a neurodevelopmental technique) is the most commonly used, although other methods, such as motor re-learning, orthopedic or mixed technique are also used.

The concepts of NDT emphasize that abnormal muscle patterns or muscle tone have to be inhibited, and that normal patterns should be used in order to facilitate functional and voluntary movements. There are a number of approaches that fall under the heading of neurodevelopmental techniques. These include the Bobath, Brunnstrom and Proprioceptive Neuromuscular Facilitation approaches. Therapy approaches aimed at the rehabilitation of the lower extremity are also discussed in Module 9.

Table 10.1 Neurodevelopmental Training (NDT) Approaches

Approach	Description
Bobath	Aims to reduce spasticity and synergies by using inhibitory postures and movements in order to facilitate normal autonomic responses that are involved in voluntary movement (Bobath 1990).
Brunnstrom's Movement Therapy	Emphasis on synergistic patterns of movement that develop during recovery from hemiplegia. Encourages the development of flexor and extensor synergies during early recovery, assuming that synergistic activation of the muscle will result in voluntary movement (Brunnstrom 1970).
Proprioceptive Neuromuscular Facilitation (PNF)	Emphasis on using the patient's stronger movement patterns for strengthening the weaker motions. PNF techniques use manual stimulation and verbal instructions to induce desired movement patterns and enhance motor function (Meyers 1995)

In their review of NDT vs. other treatment approaches, Barreca et al. (2003) included five RCTs (Basmajian et al. 1987, Dickstein et al. 1986, Gelber et al. 1995, Logigian et al. 1983, van der Lee et al. 1999) and concluded that NDT was not superior to other types of interventions. Van Peppen et al. (2004) recently conducted a systematic review of specific neurological treatment approaches and also concluded that compared to a Bobath approach, no one particular program was favoured over another with respect to improvement in functional outcomes (ADL), muscle strength or tone, dexterity, although motor relearning programs were associated with shorter lengths of hospital stays.

Paci (2003) conducted a review of 15 trials including six RCTs (Langhammer and Stanghelle 2000, van der Lee et al. 1999, Gelber et al. 1995, Partridge et al. 1990, Basmajian et al. 1987, Mulder et al. 1986), six non-randomized controlled trials and three case series to determine if neurodevelopmental treatment is an effective approach. They concluded that there is no evidence that supports neurodevelopmental treatment as being the superior type of treatment. We included eleven studies that evaluated the effect of neurodevelopmental techniques (NDT) (Logigian et al. 1983, Lord and Hall 1986, Dickstein et al. 1986, Basmajian et al. 1987, Wagenaar et al. 1990, Gelber et al. 1995, van der Lee et al. 1999, Langhammer and Stanghelle 2000, 2003, VanVliet et al. 2005, Platz et al. 2005, Hafsteinsdóttir et al. 2005). Eight of the eleven studies were RCTs. Another systematic review (Luke et al. 2004) which included the results from 8 trials (5 RCTs) came to similar conclusions.

Trials evaluating Neurodevelopmental techniques are summarized in Tables 10.2 and 10.3.

Table 10.2 Studies of Neurodevelopmental Techniques

Author/ Country/ PEDro score	Methods	Results
Logigian et al. 1983 USA 4 (RCT)	42 stroke patients were randomly assigned to receive either facilitated therapy or traditional techniques for remediation of motor loss in the affected upper extremity. Treatment duration was unclear.	No differences between the groups on any of the functional assessments (Barthel Index, manual muscle test). Unclear when the assessments were performed.
Lord and Hall 1986 USA No Score	39 patients 8-38 months post stroke from 2 different rehabilitation centers were identified retrospectively. One of the centers used neuromuscular re-education therapy (NRT) (n=20) and the other used a traditional functional retraining program (TFR) (n=19). A telephone questionnaire regarding current functional state was administered to patients/families.	There was no change in the overall reported self-care status between the groups. Of the 4 upper extremity functional skill levels (feeding, brushing hair, brushing teeth and upper extremity dressing), NRT patients showed slightly greater independence in feeding.
Dickstein et al. 1986 Israel 5 (RCT)	131 stroke patients were randomized to receive one of three treatments 1) conventional therapy (n=57), 2) Proprioceptive neuromuscular facilitation techniques (n=36) or 3) Bobath techniques (n=38), for 30-45 min/day x 5 days/week x 6 weeks.	No statistically significant differences between the groups were reported on any of the outcome measures (Barthel Index, muscle tone or active range of motion).
Basmajian et al. 1987 Canada	29 hemiparetic stroke patients were randomized to receive either integrated behavioural and physical	There were no differences between the groups on any of the outcome measures (Upper Extremity Function Test, finger

6 (RCT)	therapy (n=13) or physical therapy based on neuro-facilitated techniques (n=16), for45 min x 3 days/week x 5 weeks.	oscillation tests).
Wagenaar et al. 1990 Netherlands No Score	7 patients alternated between 2 therapy approaches 5-9 days post stroke: 1) Brunnstrom approach and 2) Neuro-developmental treatment (NDT). Therapies were provided for 30 min/session for 21 weeks. Starting order was randomized.	There were no differences in Action Research Arm test scores between the 2 groups.
Gelber et al. 1995 USA 5 (RCT)	20 patients with pure motor hemiparesis following a stroke within the previous month were randomized to neurodevelopmental technique (NDT) (Bobath) or traditional functional retraining (TRF) treatment approaches for the period of inpatient rehabilitation. FIM, Box & Block test and Nine Hole Peg Test were evaluated at admission, discharge, 6 and 12 months.	There were no significant differences between the groups at any of the testing intervals. Length of hospital stay was similar for both groups.
van der Lee et al. 1999 Netherlands 7 (RCT)	In an observer blind trial, 66 patients were randomized to receive either forced use therapy with immobilization of the unaffected arm combined with intensive treatment or to receive intensive bimanual training based on Neuro-Development Treatment.	Mean improvement on Action Research Arm test in patients with sensory disorder was significantly greater in that receiving force use rather than bimanual training. During treatment, force use patients also showed greater clinical significant improvement on Motor Activity Log than bimanual training patients.
Langhammer and Stanghelle 2000, 2003 8 (RCT)	61 first-ever stroke patients with hemiparesis were block randomized into 2 groups and stratified according to gender and hemiplegic site. Group 1 had physiotherapy according to the Motor Relearning Programme (MRP) and group 2 received physiotherapy according to the Bobath approach.	Patients in the MRP group had shorter hospital stays compared to the Bobath group. Both groups improved in motor function (Motor Assessment Scale and Sodring Motor Evaluation Scale), but the MRP group had significantly better gains than the Bobath group. No differences were seen between groups in the life quality test, use of assistive devices or accommodation after discharge from hospital. Follow-up 1 year and 4 years post stroke did not reveal any major influence of the two approaches on long-term function.
Van Vliet et al. 2005 UK 7 (RCT)	120 patients admitted to a stroke rehabilitation ward were randomized to two rehabilitation approaches Bobath based (BB) or movement science base (MSB). Rivermead Motor Assessment (RMA) and Motor Assessment Scale (MAS) scores were assessed at 1, 3 and 6 months.	There were no significant differences between the two groups. Scores on the subsections of both RAM and MAS associated with upper extremity function were similar.
Platz et al. 2005 Germany	62 patients with severe arm paresis having suffered from a stroke between 3 weeks and 6 months	There were no differences in the mean Fugl-Meyer, Action Research Arm or Ashworth scores between the groups at the end of the

8 (RCT)	previously were randomized to 3 different upper extremity regimens: i) no augmented therapy (n=20), ii) augmented therapy (Bobath) (n=21) or iii) augmented therapy (impairment –oriented training-BASIS training) (n=21). The treatments were provided for 4 weeks. Additional therapy was provided for 45 min x 5 days/week.	treatment period.
Hafsteinsdóttir et al. 2005 Netherlands No Score	A controlled, multi-site cluster trial. 225 patients in 6 hospitals received rehabilitation on units using the NDT (Bobath) approach and 101 patients on 6 wards received rehabilitation on units using a conventional (non-NDT) approach. The primary outcome was a poor outcome (Barthel Index scores < 12 or death) at one-year. Quality of life (QoL) was also assessed.	There were no differences in the proportion of patients experiencing a poor outcome between groups. The adjusted odds ratio associated with the NDT approach was 1.7 (95% CI: 0.8 to 3.5). There were no differences in median QoL scores between the groups at 12 months.
Hafsteinsdóttir et al. 2007 Netherlands No Score	Additional analyses from 2005 study. Health-related QoL (HRQoL) was measured using the SF-36; depression was measured with the Center of Epidemiological Studies Depression Scale and shoulder pain was measured with the Visual Analogue Scale at discharge, 6 and 12 months.	There were no differences between the groups on any of the outcomes assessed at either 6 or 12 months. The percentage of patients with depression at discharge, 6 months and 1 year were: Bobath: 55, 40 & 30%; Conventional rehab: 46, 45 and 43%. The percentages of patients with shoulder pain were: Bobath: 18, 22 and 20%, Conventional rehab: 22, 28 and 19%.
Platz et al. 2009 Germany 8 (RCT)	148 anterior circulation ischemic stroke patients were randomly assigned to receive 45 minutes of additional arm therapy daily over 3 to 4 weeks as either (a) passive therapy with inflatable splints or active arm motor therapy as either (b) individualized best conventional therapy (CONV) or (c) standardized impairment-oriented therapy (IOT), as Arm BASIS training for severe paresis or Arm Ability training for mild paresis. The main outcome measures, assessed at baseline, post treatment and 4 weeks were the Fugl-Meyer (FM) arm motor score (severely paretic arms) and the TEMPA time scores (mildly affected arms).	At the end of follow-up, there were no significant differences in FM scores among study groups (either groups: a vs. b/c or b vs. c). There was a significant interaction effect favouring the use of IOT therapy among subjects with mild paresis.
Langhammer and Stanghelle 2010 8 (RCT)	Additional analysis from 2000 study using the Movement Quality Model to examine differences in Motor Assessment Scores (MAS) and the Sodring Motor Evaluation Scale scores between groups at 3 weeks and 3	Among the hand and arm function items, scores on both the MAS and the SMES were significantly higher for patients in the Motor Relearning Program group compared with those in the Bobath group.

	months.	

Discussion

The results from two recent, high quality RCTs assessing similar treatment approaches and outcomes differed. Langhammer & Stanghelle (2000) reported improvements in upper extremity function and a shorter length of hospital stay associated with the motor relearning, while Van Vliet et al. (2005) did not report any significant difference between treatment approaches. Van Vliet et al. (2005) speculate that earlier, more intensive training provided in the L & S study as well as and higher (albeit non-statistically significant) baseline difference may have contributed to the differences. The content of the treatment programs within the two studies may also have differed. Platz et al. (2005) failed to demonstrate an effect of augmented arm therapy (in addition to regular rehabilitation) upon motor recovery, regardless of the treatment approach (BASIS arm training or Bobath) or following passive, conventional or impairment-oriented training (2010).

Hafsteinsdóttir et al. (2007) reported that the Bobath approach was not superior to that of non-NDT approach. There were no differences between the groups on any of the outcome measures assessed including FIM, quality of life, health- related quality of life, shoulder pain or depression at up to 12 months following stroke.

Table 10.3 Summary of RCTs Evaluating Neurodevelopmental Techniques

Author PEDro Score	n	Intervention	Main Outcome(s) Result
Platz et al. 2005 8 (RCT)	62	No augmented therapy vs. augmented therapy time (Bobath) vs. augmented therapy time (BASIS)	Fugl-Meyer arm motor score (-)
Platz et al. 2009 8 (RCT)	148	Passive therapy (with splints) vs. conventional therapy vs. impairment-oriented training (BASIS training for severe paresis or Arm Ability training for mild paresis)	Fugl-Meyer (-) TEMPA (-)
Langhammer and Stanghelle 2000, 2003, 2010 8 (RCT)	61	Motor Relearning Programme (MRP) vs. Bobath	Hospital stays (+ MRP) Motor Assessment Scale (+ MRP) (- at 1 and 4 yrs F/U) Sodring Motor Evaluation Scale (+ MRP) (- at 1 and 4 yrs F/U) Life Quality Test (-) Quality of Movement (+MRP)
Van Vliet et al. 2005 UK 7 (RCT)	120	Motor Relearning Programme (MRP) vs. Bobath	Rivermead Motor Assessment (-) Motor Assessment Scale (-)
van der Lee et al. 1999 7 (RCT)	66	NDT vs. Forced-use therapy	Action Research Arm test (+) Forced-use

Basmajian et al. 1987 6 (RCT)	29	Physical Therapy based on neuro-facilitated techniques vs. EMG	Upper Extremity Function Test (-) Finger Oscillation test (-)
Gelber et al. 1995 5 (RCT)	20	Bobath vs. Traditional techniques	FIM (-) Box & Block test (-) Nine Hole Peg test (-) LOS (-)
Dickstein et al. 1986 5 (RCT)	131	PNF vs. Bobath vs. Traditional techniques	Barthel Index (-) Muscle tone (-) Active range of motion (-)
Logigian et al. 1983 4 (RCT)	42	Facilitated therapy vs. traditional techniques	Barthel Index (-) Manual muscle test (-)

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Conclusions Regarding Neurodevelopmental Techniques

There is strong (Level 1a) evidence that neurodevelopmental techniques are not superior to other therapeutic approaches.

There is moderate (Level 1b) evidence from one "good" RCT that indicates that when compared to the Bobath treatment approach, Motor Relearning Programme may be associated with improvements in short-term motor functioning, shorter lengths of hospital stay and better movement quality.

Neurodevelopmental techniques are not superior or inferior compared with other therapeutic approaches in treatment of the hemiparetic upper extremity.

10.2.2 Therapy Approaches Used to Improve Dressing Performance

A variety of approaches can be used by occupational therapists to help patients to learn to dress independently following a stroke. While many therapists use a problem-solving approach to help with the rehabilitation of dressing tasks, a few other approaches have been evaluated. Some approaches have been developed to accommodate those with cognitive deficits.

Table 10.4 RCTs Treatment Approaches for the Rehabilitation of Dressing Activities

Author/ Country PEDro score	Methods	Results
Mew 2010 UK 5 (RCT)	5 patients with stroke onset <38 days were randomized to receive dressing practice based on either a Normal movement (Bobath)(n=3) approach or a functional approach (normal	At 8 weeks, 3 patients remained in the Normal movement group, but one patient in the Functional group had dropped out, precluding the use of inferential statistics. All patients improved in dressing independence

	movement therapy + compensatory strategies)(n=2) 3x/week for up to 8 weeks. The Nottingham Stroke Dressing Assessment (NSDA), the Rivermead Motor Assessment (RMA) and the Canadian Occupational Performance Measure (COPM) were assessed at baseline and 8 weeks.	over the treatment period.
Walker et al. 2012 UK 7 (RCT)	70 acute stroke patients with persistent dressing problems and accompanying cognitive difficulties at two weeks were randomized to a therapy program using a systematic neuropsychological approach, based on analysis of dressing problems and further cognitive testing, or to a control group who received conventional (functional) dressing practice. Patients in both groups received therapy 3x/week for 6 weeks. Outcome measures, assessed at baseline and 6 weeks included the Nottingham Stroke Dressing Assessment (NSDA), Line Cancellation test and 10-hole peg transfer test.	Patients in both groups improved over the treatment period, but there were no significant difference between groups. However, patients in the neuropsychological group showed a significantly greater improvement on a line cancellation test (mean change from baseline; 5.5 vs. -0.5, $p<0.05$).

Conclusions Regarding Dressing Approaches

There is moderate (Level 1b) evidence that both functional and neuropsychological approaches both help to improve dressing performance

10.2.2 Bilateral Arm Training

The use of bilateral training techniques with the upper limb following stroke has been advocated recently as new theories of neural plasticity have developed. Bilateral arm training is a technique whereby patients practice the same activities with both upper limbs simultaneously. Theoretically, the use of the intact limb helps to promote functional recovery of the impaired limb through facilitative coupling effects between the upper limbs. Practicing bilateral movements may allow the activation of the intact hemisphere to facilitate the activation of the damaged hemisphere through neural networks linked via the corpus callosum (Morris et al. 2008, Summers et al. 2007).

In a systematic review which included the results from 11 trials, Stewart et al. (2006) reported that bilateral movements alone or in combination with auxiliary sensory feedback are effective stroke rehabilitation protocols during the sub-acute and chronic phases of recovery. The overall effect size was relatively large, at 0.732. A second, more conservative analysis, excluding several studies, still produced a moderate effect size of 0.582. Another narrative review, (Latimer et al. 2010), which included the results from 9 studies (3 RCTs) in the chronic stage of stroke, also reported a benefit of bilateral training in recovery associated with motor function.

A recent Cochrane review on the subject (Coupar et al. 2010), which included the results from 18 RCTs, including 549 subjects, reported that there was no significant improvement in ADL function (standardized mean difference of 0.25, 95% CI: -0.14 to 0.63), functional movement of the arm (SMD-0.07, 95% CI -0.42 to 0.28) or hand, (SMD -0.04, 95% CU -0.50 to 0.42) compared with usual care following stroke (Coupar et al. 2010).

Cauraugh et al. (2010) conducted a meta-analysis, including the results from 25 studies, the majority of which were RCTs. The overall treatment effect was a standardized mean difference of 0.734, representing a large treatment effect. The effect size was influenced by the type of treatment (pure bilateral, BATRAC, coupled bilateral and EMG-triggered FES and active/passive movement using robotics). BATRAC and EMG-triggered FES studies were associated with the largest SMD.

Van Delden et al. (2012) evaluated the effectiveness of bilateral vs. unilateral upper-limb therapy and if it was affected by severity of paresis. The review included the results from 9 RCTs. Pooled analyses of 452 patients were conducted for the Fugl-Meyer Assessment, Action Research Arm test (ARAT), Motor Assessment Scale (MAS) and Motor Activity Log (MAL). Over all severity categories, unilateral training was superior when outcome was assessed using ARAT scores, but there were no differences in scores of patients in the severe and moderate groups. There were no significant differences in improvement between groups of either severe or moderate patients on MAS or FMA scores, suggesting both training approaches were effective. Improvements in MAL scores favoured patients in the unilateral training group, although only the mild subgroup was represented.

Table 10.5 RCTs Evaluating Bilateral Arm Training

Author/ Country PEDro score	Methods	Results
Cauraugh and Kim 2002 USA 5 (RCT)	25 chronic stroke patients with mild to moderate paresis were randomized to receive: 1) coupled protocol of EMG-triggered stimulation and bilateral movement (n=10); (2) EMG-triggered stimulation and unilateral movement (n=10); or (3) control (n=5). All participants completed 6 hours of rehabilitation during a 2-	Patients in the bilateral training group moved more blocks on the Box and Block test compared to the other two groups.

	week period according to group assignments. Motor capabilities of the wrist and fingers were evaluated.	
Luft et al. 2004 USA 7 (RCT)	21 chronic stroke patients with residual upper extremity weakness were randomized to receive bilateral arm training with rhythmic auditory cueing (BATRAC) or to the control condition of therapeutic exercises. (Same intervention as Whitall et al. 2002). Treatment sessions lasting 1 hour were provided 3x/week for 6 weeks. FMRI, motor function and electromyography assessments were made.	On fMRI there were significant changes in activation in portions of the cerebrum and cerebellum, for patients in the BATRAC group compared to control, although 3 BATRAC patients showed no fMRI changes. There were no differences in functional outcome between groups (Fugl-Meyer, shoulder strength, elbow strength, Wolf weight, and Wolf time of ADL).
Desrosiers et al. 2005 Canada 7 (RCT)	41 inpatients, 10-60 days post stroke were randomized to receive a training program focusing on symmetrical bilateral tasks consisting of 15-20, 45 minute sessions, based on motor learning based principles, in addition to routine rehabilitation or to routine rehabilitation, based on a neurodevelopmental approach. Outcome measures included: motor function (Fugl-Meyer upper extremity), grip strength, gross manual dexterity (Box & Block test), fine manual dexterity (Purdue Pegboard test), motor coordination (Finger-to-nose test), ADL (FIM)	Although both groups improved from baseline to end of treatment, there were no significant differences in outcomes between the groups.
Summers et al. 2007 Australia 5 (RCT)	12 chronic stroke patients were randomly assigned to one of two training protocols involving six daily practice sessions. Each session consisted of 50 trials of a dowel placement task performed either with both impaired and unimpaired arm moving synchronously (bilateral training group) or with only the impaired arm moving (unilateral training). Outcomes assessed before and after treatment included the Modified Motor Assessment Scale. Kinematic measurements of upper limb movements were made in four unilateral test trials performed prior to and following each practice session.	Individuals receiving bilateral training showed a reduction in movement time of the impaired limb and increased upper limb functional ability compared to individuals receiving unilateral training.
Morris et al. 2008 UK 7 (RCT)	106 acute stroke patients (2-4 weeks post stroke) were randomized to receive bilateral arm training (n=56) or unilateral arm training (n=50). The	While subjects in both groups improved over time, there were no significant differences in the change scores in short-term improvement (0-6 wk) on any measure. At follow-up, (0-18

	supervised training was provided for 20 min 5x/week x 6 weeks. The main outcome measure was the Action Research Arm Test (ARAT), which was assessed before/after treatment and at follow-up (18 weeks). Additional outcomes assessed included the Rivermead Motor Assessment upper-limb scale, Nine-Hole Peg Test (9HPT), the Modified Barthel Index, Hospital Anxiety and Depression Scale, and Nottingham Health Profile.	wk), the only significant between-group difference was a change in the 9HPT and ARAT pinch section, which was lower, indicating less recovery for the bilateral training group. Baseline severity significantly influenced improvement in all upper-limb outcomes, irrespective of the treatment group.
Stinear et al. 2008 New Zealand 6 (RCT)	32 patients with upper limb weakness at least 6 months after stroke were randomized to a 1-month intervention of self-directed motor practice with their affected upper limb (control group)(n=16) or to Active-Passive Bilateral Therapy (APBT)(n=16), using a device that mechanically couples the two hands, for 10-15 min prior to the same motor practice (manipulating wooden blocks). Upper extremity portion of the Fugl-Meyer (FM) score was assessed at baseline, post intervention and 1 month after the intervention.	Immediately after the intervention, motor function of the affected upper limb improved in both groups ($p < 0.005$). One month after the intervention, the APBT group had better upper limb motor function than control patients.
Cauraugh et al. 2009 USA 5 (RCT)	30 chronic stroke subjects were randomly assigned to one of three behavioral treatment groups and completed 6 hours of rehabilitation in 4 days: (1) coupled bilateral training with a load on the unimpaired hand, (2) coupled bilateral training with no load on the unimpaired hand, and (3) control (no stimulation assistance or load). Both bilateral groups received EMG-triggered electrical stimulation. The Box & Block test and reaction times were assessed before and after treatment.	From the pretest to the posttest, both the coupled bilateral no load and load groups moved more blocks and demonstrated more regularity in the sustained contraction task compared with the control group. Reaction times were faster across test sessions for the coupled bilateral load group.
Stoykov et al. 2009 USA 5 (RCT)	24 subjects with moderate impairment with stroke onset > 6 months participated in an 8-week training program. Subjects were randomized to a bilateral group (n = 12) in which they practiced bilateral symmetrical activities, or a unilateral group (n = 12) in which subjects performed the same activity with the affected arm only. The activities consisted of reaching-based tasks that were both rhythmic and discrete. The Motor Assessment Scale (MAS),	Subjects in both groups had significant improvements on the MSS and measures of strength. There were no differences between groups on the total MSS score or either of its 2 subscales (shoulder/elbow, wrist/hand). The bilateral group had significantly greater improvement on the Upper Arm Function scale (a subscale of the MAS-Upper Limb Items). There were no significant differences between groups on the 2 other subscales (advanced hand activities, hand movements and upper arm function).

	Motor Status Scale (MSS), and muscle strength were used as outcome measures. Assessments were administered at baseline and post training.	
Lin et al. 2009 a) Taiwan 7 (RCT)	60 patients > 6 months post stroke with a Brunnstrom stage II or greater in the proximal and distal part of the arm were randomized to one of 3 groups. Subjects received constraint-induced therapy (CIT), bilateral arm training (BAT), or a control intervention of less- specific but active therapy. Each group received intensive training for 2 hours/day, 5 days/week, for 3 weeks. Outcomes assessed included Fugl-Meyer Assessment (FMA), FIM, Motor Activity Log (MAL), and Stroke Impact Scale (SIS). The proximal and distal scores of FMA were used to examine separate upper limb (UL) elements of movement.	The CIT and BAT groups showed better performance in the overall and the distal part score of the FMA than the control group. The BAT group exhibited greater gains in the proximal part score of the FMA than the distributed CIT and control groups. Enhanced performance was found for the distributed CIT group in the MAL, the subtest of locomotion in the FIM, and certain domains of the SIS (e.g., ADL/IADL).
Lin et al. 2009 b) Taiwan 6 (RCT)	33 stroke patients, 6 to 67 months after onset of a first stroke and with a Brunnstrom stage II or greater in the proximal and distal part of the arm, were randomized to either a bilateral arm training (BAT) program concentrating on both upper extremities moving simultaneously in functional tasks by symmetric patterns or a control treatment for 2 hours on weekdays for 3 weeks. Outcome measures included the Fugl-Meyer Assessment (FMA) of motor-impairment severity and the Functional Independence Measure (FIM) and the Motor Activity Log (MAL) evaluating functional ability.	The BAT group showed a significantly greater improvement in the mean FMA than the control group (total score at end of treatment: 57.6 vs. 55.0, p=0.041) but not in the FIM (118 vs. 117, p=0.18) or MAL (amount of use subscale 1.34 vs. 1.61, p=0.12 quality of movement 1.56 vs. 1.86, p=0.17).
Wu et al. 2011 Taiwan 5 (RCT)	66 chronic stroke patients (mean of 16 months post onset) with mild to moderate motor impairment were randomized to a regimen of distributed constraint-induced movement therapy (dCIT), bilateral arm training (BAT), or routine therapy (control group)(CT). Each group received treatment for 2 h/d and 5 d/wk for 3 weeks. Assessments were conducted before and after the treatment period and included reaching kinematic variables in unilateral and bilateral tasks, the Wolf	The dCIT and BAT groups had smoother reaching trajectories in the unilateral and bilateral tasks than the CT group. The BAT group, but not the dCIT group, generated greater force at movement initiation than the CT group during the unilateral and bilateral tasks. MAL results suggested better performance in the amount and quality of use of the affected arm in the dCIT group compared with BAT and CT patients.

	Motor Function Test (WMFT), and the Motor Activity Log (MAL).	
Whitall et al. 2011 USA 7 (RCT)	111 adults with chronic upper extremity paresis were randomized to a program of 6 weeks (3x/week) of bilateral arm training with rhythmic auditory cueing (BATRAC) or dose-matched therapeutic exercises (DMTE). Primary outcomes were Fugl-Meyer UE Test (FM) and selected components of the Wolf Motor Function Test (WMFT)(time, weight, function) and were performed 6 weeks prior to and at baseline, after training, and 4 months later.	Patients in both groups experienced significant improvements in FM scores at the end of the treatment period; however, there were no significant differences between groups. The same result was found for all components of the WMFT, with the exception of the time component, whereby subjects in the DMTE did not improve over the treatment.
Ausenda & Carnovali (2011) Italy 4 (RCT)	20 subjects with chronic stroke were randomized to one of two groups. Patients in the bilateral group (n=10) performed the 9-Hole Peg Test (9HPT) 10 times a day, for three consecutive days, using both the paretic and unaffected hand. Patients in the control group (n=10) did not train the unaffected hand.	The mean time to complete the 9HPT decreased from 107 to 104 sec in patients' paretic hand. The mean time to perform the test among patients in the bilateral group decreased from 115 to 90 sec. $p<0.0001$. The results of between group comparisons were not reported.
Morris & Van Wijck 2012 UK 7 (RCT)	Additional reporting from Morris et al. 2008. Outcome assessments included Action Research Arm Test and Nine-Hole Peg Test (9HPT) of the ipsilateral arm.	The median change in ARAT scores for patients in both groups was 0 at 6 and 18 weeks. Patients in the bilateral training group moved a significantly greater number of pegs compared with the control group at 6 (0.06 vs. 0.02, $p=0.03$) but not 18 weeks (0.04 vs. 0.05, $p=.93$)
Brunner et al. 2012 Norway 7 (RCT)	30 patients 2-16 weeks post stroke were randomized to receive modified constraint-induced movement therapy with an emphasis on unimanual tasks, and to wear a restraining mitt on the unaffected hand for 4 hours a day for four weeks or bimanual task-related training. All patients trained with a therapist 4 hours a week for four weeks, followed by a 2-3 hours daily self-training program. Assessments were conducted before and after treatment and after three months. They included the Action Research Arm Test (ARAT), Nine-Hole Peg Test and Motor Activity Log.	Patients in both groups improved significantly over the treatment period and at follow-up, but there were no significant differences between groups on any of the outcomes. At 3 months, mean ARAT scores for patients in the mCIMT and bilateral training groups were 17.8 and 15.5, respectively.

The results from the RCTs presented above are summarized in Table 10.6. The majority of trials were conducted on patients in the chronic stage of stroke, at least 6 months post onset, although several included patients receiving inpatient rehabilitation shortly after stroke onset.

The study conducted by Ausenda & Carnovali (2011) was described as using bilateral hand training; however, in this trial the tasks were executed by the paretic hand and the unaffected hand sequentially. In the other trials, the tasks were performed by the affected and unaffected upper limb in tandem. In several trials, the treatment contrasts included CIMT as the unilateral control group.

Table 10.6 Summary of Studies Evaluating Bilateral Arm Training

Author/ PEDro Score	n	Intervention	Main Outcome(s) Result
Morris et al. 2008 7 (RCT)	106	Bilateral vs. unilateral training	ARAT (-)
Whitall et al. 2011 7 (RCT)	111	Bilateral vs. unilateral training	Fugl Meyer (-)
Brunner et al. 2012 7 (RCT)	30	Bilateral training vs. mCIMT	ARAT (-)
Desrosiers et al. 2005 7 (RCT)	41	Symmetrical bilateral tasks vs. conventional therapy	Fugl Meyer (-) Grip strength (-)
Luft et al. 2004 7 (RCT)	21	Bilateral arm training + rhythmic auditory cueing vs. Therapeutic exercises.	Fugl-Meyer (-)
Lin et al. 2009b 6 (RCT)	33	Bilateral vs. unilateral training	Fugl-Meyer (+) FIM (-) Motor Assessment Log (-)
Stinear et al. 2008 6 (RCT)	32	Active-Passive Bilateral Therapy vs. self-directed motor practice	(Fugl-Meyer (+) Grip strength (-)
Wu et al. 2011 5	66	dCIT vs. BT vs. control	Force generation, (+BAT) Movement smoothness (+ BAT)
Stoykov et al. 2009 5 (RCT)	21	Bilateral vs. unilateral training	Motor Assessment Scale (-) Motor Status Scale (-)
Summer s et al. 2007 5 (RCT)	12	Unilateral vs. bilateral training	Modified Motor Assessment Scale (+)
Cauraugh and Kim 2002 5 (RCT)	25	Electrical stimulation + bilateral training vs. Electrical stimulation + unilateral training vs. control	Box & Block test (+ bilateral group)

Conclusions Regarding Bilateral Arm Training

There is conflicting (Level 4) evidence that bilateral arm training is superior to unilateral training.

10.2.3 Additional/Enhanced Upper Extremity Therapy

In this section we included studies that examined the effects of providing additional or enhanced upper extremity therapy, usually compared to conventional therapy. The results are found in Table 10.7 and 10.8.

Table 10.7 RCTs Evaluating Additional/Enhanced Upper Extremity Therapies

Author/ Country PEDro score	Methods	Results
Trombly et al. 1986 USA 4 (RCT)	20 patients randomly assigned to receive 1 of 4 treatment conditions: (1) resisted grasp therapy; (2) resisted extension therapy; (3) ballistic extension therapy; or (4) therapy that did not involve affected hand for 20 sessions or until patient was discharged.	No significant differences were noted between any of the groups on any of the outcome measures.
Sunderland et al. 1992 UK 6 (RCT)	132 stroke patients were randomized to receive enhanced therapy (ET) (n=67) or conventional therapy (CT) (n=65). ET consisted of Bobath exercises, EMG biofeedback computer games and goal setting, for 10 weeks. Patients were divided into mild and severe sub-groups.	Repeated measures analysis of Extended Motricity Index scores showed that patients in the ET group had improved arm function within the first month. Median Motor club assessment and nine-hole peg test scores were higher for patients with mild strokes in the ET group at six months.
Sunderland et al. 1994 UK 6 (RCT)	One-year follow-up of 97 patients from 1992 study.	No significant differences between enhanced therapy and conventional therapy sub-groups on any of the measures at follow-up.
Butefisch et al. 1995 Germany 3 (RCT)	27 hemiparetic stroke patients, 3-19 weeks post stroke were assigned to an enhanced non-specific therapy (n=12) or to enhanced specific therapy + TENS (n=15). Both groups received conventional OT/PT. 2 phase, multiple baseline study.	Grip strength, peak force of isometric hand extensions and peak acceleration of isotonic hand extensions, significantly improved during training, for both groups. No between treatment group statistics were reported.
Dickstein et al. 1997 Israel 3 (RCT)	Randomized controlled trial of 15 patients who received 8 repeated movement exercises for 19-21 days as compared to controls who performed conventional physiotherapy.	There were similar improvements in Barthel Index and Fugl-Meyer scores between the two groups.
Kwakkel et al. 1999 Netherlands 8 (RCT)	101 patients were randomized 14 days following stroke to receive one of 3 therapies: 1) arm training, 2) leg training or 3) basic rehabilitation only. Leg and arm treatments were applied for 30 min 5 days/week x 20 weeks. All patients received basic rehabilitation.	At week 26, significant differences in median Action Research arm (ARA) scores between the three groups were observed. Median Barthel Index and ARA scores of patients in both arm and leg training groups were significantly higher when compared to the control group.
Lincoln et al. 1999 UK 7 (RCT)	A single blind trial of 282 patients randomized to receive either routine physiotherapy, or additional physiotherapy (10 hrs over 5 weeks) from a qualified therapist or a physiotherapy assistant.	No significant differences between the groups on any of the outcome measures (Rivermead Motor Assessment Arm Scale, Action Research Arm test or Barthel Index) were observed post intervention, at 3 or 6 month follow-up.
Platz et al.	A single blind trial of 60 patients	All patients who received ATT demonstrated a

2001 Germany 7 (RCT)	randomized to one of three groups: Group 1 received Arm Ability Training (ATT) with knowledge of their results. Group 2 received ATT without knowledge of their results and Group 3 did not receive ATT.	significantly greater mean improvement in time needed to perform all TEMPA tasks.
Bourbonnais et al. 2002 Canada 5 (RCT)	25 chronic stroke patients with hemiplegia were randomized to an upper-limb (UL) or lower-limb motor re-education program. 13 patients with UL weakness received 3 weeks of force-feedback program 3 times a week. Patients in the LE group served as the control. Upper limb performance was evaluated at 8 weeks using the TEMPA, finger to nose test and the Fugl-Meyer.	With the exception of the handgrip force, strength measurements of the treated limb increased after completion of the treatment. The outcome measurements of the upper limb of the subjects included in the upper paretic limb were not significantly different after treatment from those measured in the lower paretic limb.
Rodgers et al. 2003 United Kingdom 7 (RCT)	123 patients with stroke causing upper limb impairment within the previous 10 days were randomized to either an experimental group or into a control group. The experimental group received stroke unit care plus enhanced upper limb therapy from both a physiotherapist and an occupational therapist commencing within 10 days of stroke and available up to 30 minutes/day, five days/week for 6 weeks. The control group received stroke unit care.	There was no significant difference between groups on any outcome measure (Action Research Arm Test, Motricity Index, Frenchay Arm Test, upper limb pain, Barthel ADL, Nottingham E-ADL) at 3 and 6 months after stroke. There was no significant difference in service costs between groups.
Duncan et al. 2003 USA 8 (RCT)	A multi-centre, single-blind clinical trial of 92 subjects randomized to receive either a structured therapist supervised home program of 36 90-minute sessions over 12- 14 weeks, or to the usual care group with services assigned by their physician and home visits every 2 weeks for health education, vital signs and a test of oxygen saturation.	While gains were made in balance, gait and endurance, no significant gains were made in upper extremity function.
Pang et al. 2006 Canada 7 (RCT)	63 chronic stroke patients (≥50 years) were randomly assigned into an upper-extremity exercise program or a lower-extremity program for 3 1-hour sessions/week for 19 weeks. Each therapy session had 9-12 participants and consisted of physiotherapy, an exercise instructor and an occupational therapist. Main Outcome measures included: The Wolf Motor Function Test (WMFT), Motor Activity Log (MAL), the hand-held dynamometry (grip strength)	There was significant improvement made for the upper-extremity exercise group compared to the lower-extremity group for the WMFT and the Fugl-Meyer Assessment. Patients who benefited most from the exercise program where those with moderate arm deficits.

	and the Fugl-Meyer Assessment (FMA).	
Harris et al. 2009 Canada 8 (RCT)	103 patients admitted for inpatient rehabilitation participated in a 4-week program of upper extremity therapy. Patients were randomized to either a graded repetitive upper limb supplementary program (GRASP group, n=53) or the control group (education protocol, n=50). The primary outcome measure was the Chedoke Arm and Hand Activity Inventory (CAHAI). Assessment was conducted before and after treatment and at 5 months post stroke. Secondary measures were used to evaluate grip strength and paretic upper limb use outside of therapy time.	Subjects in the GRASP group showed greater improvement in upper limb function (CAHAI) compared to the control group (mean change score: 14.1 vs. 7.9, $p<0.001$). The GRASP group maintained this significant gain at 5 months poststroke. Significant differences were also found in favor of the GRASP protocol for grip strength and paretic upper limb use.
Ross et al. 2009 Australia 8 (RCT)	39 subjects adults with hand impairment following chronic stroke (90% stroke) or traumatic brain injury (10%) were randomized to an experimental group (n = 20) and received an additional one-hour session of task-specific motor training for the hand 5x/week over a six-week period. The control group (n = 19) received standard care which consisted of 10 minutes of hand therapy three times a week. Both groups continued to receive therapy directed at the shoulder and elbow. The primary outcomes were the Action Research Arm and Summed Manual Muscle Tests measured at the beginning and end of the six-week period.	The mean and (standard deviation) Action Research Arm Test values for experimental participants improved from the beginning to the end of study from 10 points (15) to 21 points (23) and the equivalent values for the Summed Manual Muscle Test improved from 35% (33) to 49% (35). There were similar improvements in control participants. There were no significant between-group differences for either outcome.
Donaldson et al. 2009 UK 6 (RCT)	30 subjects with upper limb weakness and within 3 months of anterior circulation infarction were randomized to receive conventional physical therapy (CPT), CPT + CPT, and CPT + functional strength training (FST). The intervention lasted for 6 weeks (24 hours in total). Primary outcome measure was the Action Research Arm Test (ARAT), assessed before/after treatment and at 12 weeks.	Attrition rate was 6.7% at the end of treatment and 40% at follow-up. Median (interquartile range) increases in ARAT scores were 11.5 (21.0) for CPT; 8.0 (13.3) for CPT + CPT; and 19.5 (22.0) for CPT + FST. The results were not statistically significant, although subjects in the CPT + FST group achieved the clinically important improvement of 5.7 points.

Discussion

A variety of treatments were delivered and outcomes assessed, under the rubric of enhanced therapy, making general conclusions difficult to draw. Additionally, most of the interventions were non-specific in nature. Rodgers et al. (2003) reported no benefit of therapy associated with any of the outcomes assessed (Figure 10.1).

Figure 10.1 Median Outcome Measures at 6-months: Enhanced Upper Limb Rehabilitation vs. Control

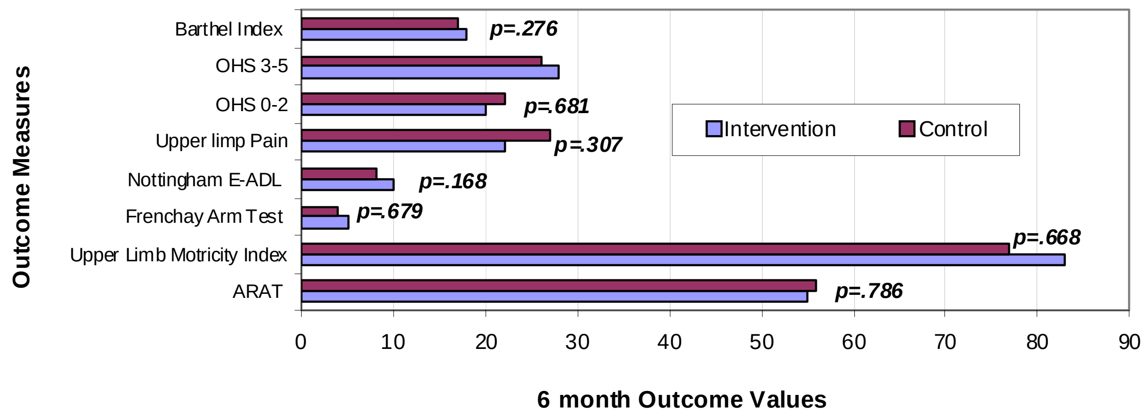


Table 10.8 Summary of Studies Evaluating Enhanced/Additional Therapies

Author/ PEDro Score	n	Intervention	Main Outcome(s) Result
Kwakkel et al. 1999 8 (RCT)	101	Arm training vs. leg training vs. basic rehab	Barthel Index (+) Action Research Arm Test (+)
Ross et al. 2009 8 (RCT)	39	Additional task-specific motor training vs. standard care	Action Research Arm Test (-) Summed Manual Muscle Tests (-)
Harris et al. 2009 8 (RCT)	103	Upper extremity task-specific therapy vs. education	Chedoke Arm and Hand Activity Inventory (+)
Duncan et al. 2003 USA 8 (RCT)	92	Supervised home program vs. usual care	Fugl-Meyer Score (-) Grip Strength (-) Functional Reach (-) Wolf Motor Function Test (-)
Lincoln et al 1999 7 (RCT)	282	Routine physiotherapy vs. additional physiotherapy	Rivermead Motor Assessment (arm) (-) Action Research Arm Test (-) Barthel Index (-)
Pang et al. 2006 7 (RCT)	63	Arm training vs. leg training	Fugl-Meyer Score (+) Wolf Motor Function Test (+)
Platz et al. 2001 7 (RCT)	74	Arm ability training vs. routine therapy	Tests of upper extremity function (+)
Rodgers et al. 2003 7 (RCT)	123	Stroke unit care + enhanced upper limb rehab vs. conventional stroke unit care	Action Research Arm Test (-) Motricity Index (-) Frenchay Arm Test (-) Upper limb pain (-) Barthel ADL (-) Nottingham E-ADL (-)
Donaldson et al. 2009	30	Conventional physical therapy (CPT) vs. CPT [2] vs. functional	Action Research Arm Test (-)

6 (RCT)		strength training + CPT	
Sunderland et al. 1992, 1994 6 (RCT)	132	Enhanced therapy vs. conventional therapy	Extended Motricity Index (+ first month) Motor Club Assessment (+ mild strokes/6 months) 9-hole Peg Test (+ mild strokes/6 months) (- at 1 year for all outcomes)
Dickstein et al. 1997 3 (RCT)	27	Repeated movement therapy vs. conventional therapy	Barthel Index (-) Fugl-Meyer scores (-) Frenchay tests (-)

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Conclusions Regarding Enhanced/Additional Therapies

There is conflicting (Level 4) evidence that enhanced therapies improve short-term upper extremity function. There is evidence that results may not be long lasting.

It is uncertain whether enhanced therapy results in improved short-term upper extremity functioning.

10.2.4 Strength Training

A small group of studies were identified that evaluated treatments directed at increasing strength in the upper extremity as opposed to function. A much larger pool of studies has been published on strength training in the lower extremity.

Harris & Eng (2010) conducted a systematic review and meta-analysis of strength training on upper-limb strength, function and ADL performance following stroke. They identified 14 studies in total. Six studies (306 subjects) evaluated the effect on grip strength. There was a significant effect associated with training (standardized mean difference=0.95, 95% CI 0.05 to 1.85, p=0.04). Two trials assessed other measures of strength with conflicting results.

We identified 5 studies that evaluated strength training and that assessed measures of strength.

Table 10.9 RCTs Evaluating Strength Training in the Upper Extremity

Author/ Country PEDro score	Methods	Results
Trombly et al. 1986 USA 4 (RCT)	20 patients randomly assigned to receive 1 of 4 treatment conditions to help improve improve finger extension function: (1) resisted grasp therapy; (2) resisted extension therapy; (3) ballistic extension therapy; or (4) therapy that did not involve affected hand for 20 sessions or until patient was discharged.	Significantly more subjects assigned to ballistic or resisted extension conditions improved in their ability to rapidly reverse movement over the course of treatment as opposed to those assigned to resisted grasp or control conditions; however, there were no significant differences were noted between any of the groups on any of the outcome measures.
Butefisch et	27 hemiparetic stroke patients, 3-19	Grip strength, peak force of isometric hand

al. 1995 Germany 3 (RCT)	weeks post stroke were assigned to an enhanced non-specific therapy (n=12) or to enhanced specific therapy + TENS (n=15). Both groups received conventional OT/PT. 2 phase, multiple baseline study.	extensions and peak acceleration of isotonic hand extensions, significantly improved during training, for both groups. No between treatment group statistics were reported.
Bourbonnais et al. 2002 Canada 5 (RCT)	25 chronic stroke patients with hemiplegia were randomized to an upper-limb (UL) or lower-limb motor re-education program. 13 patients with UL weakness received 3 weeks of force-feedback program 3 times a week. Patients in the LE group served as the control. Upper limb performance was evaluated at 8 weeks using the TEMPA, finger to nose test and the Fugl-Meyer.	With the exception of the handgrip force, strength measurements of the treated limb increased after completion of the treatment. The outcome measurements of the upper limb of the subjects included in the upper paretic limb were not significantly different after treatment from those measured in the lower paretic limb.
Carr & Jones 2003 USA 2 (RCT)	40 subjects with chronic stroke were randomly assigned to two groups, an aerobic training only (ATO) group and an aerobic and strength training (A&ST) group. Both groups were required to exercise aerobically for 20 minutes for 3 days a week at a moderate intensity for 16 weeks. The A&ST group also completed a series of eight strength-training activities. Outcomes were assessed before and after treatment.	The ATO group increased a mean of 3.2 ft-lbs during peak shoulder extension compared with an increase of 3.8 ft-lbs in the A&ST group. Arm flexion increased by 0.07 ft-lbs in the ATO group and by 3.7 ft-lbs in the A&ST group.

Conclusions Regarding Strength Training of the Upper Extremity

There is strong (Level 1a) evidence that strength training increases grip strength following stroke.

10.2.5 Repetitive/Task- Specific Training Techniques

Schmidt and Wrisberg (1999) note that it is well established that task-specific practice is required for motor learning to occur. According to Classen et al. (1998) focal transcranial magnetic stimulation and functional magnetic resonance imaging have shown that task-specific training, in comparison to traditional stroke rehabilitation, yields long-lasting cortical reorganization specific to the corresponding areas being used. More specifically, Karni et al. (1995), using functional magnetic resonance imaging, and Classen et al. (1998), using transcranial magnetic stimulation, both reported a slowly evolving, long-term, experience-dependent reorganization of the adult primary motor cortex following daily practice of task-specific motor activities. Also of interest is that task-specific sessions i.e. thumb and hand movements, for as short as 15 minutes are also effective in inducing lasting cortical representational changes (Classen et al. 1998, Butefisch et al. 1995). According to Page (2003) intensity alone does not account for the differences between traditional stroke and task-specific rehabilitation. For example, Galea et al. (2001) reported that stroke patients who underwent a 3-week long program that consisted of 45-minute task-specific, upper limb training showed improvements in measures of motor function, dexterity, and increased use of the more affected upper limbs. According to Page (2003), other, task-specific, low-intensity regimens designed to improve use and function of the affected limb have also reported significant improvements (Smith et al. 1999, Whitall et al. 2000, Winstein and Rose 2001).

Barreca et al. (2003) reviewed 2 studies (Butefisch et al. 1995, Dickstein et al. 1997) of repetitive training, including repeated practice of elbow, wrist and finger flexion and extension, and concluded that there was a positive treatment effect.

A recent Cochrane review authored by Thomas et al. (2007) evaluated the effect of task-specific training, on both upper and lower-extremity function. Trials were included if one of the intervention arms included "an active motor sequence [that] was performed repetitively within a single training session, and where the practice was aimed towards a clear functional goal." Eight and five RCTs respectively were identified that assessed arm and hand function and their results pooled. Task-specific training was not associated with improvement in either hand or arm function. The standardized mean differences were small (0.17 and 0.16) and not statistically significant.

More recently, Timmermans et al. (2010) conducted a review that examined the effectiveness of task-oriented training following stroke. 15 components were identified to characterize task-oriented training. They included exercises that were: functional, directed towards a clear goal, repeated frequently, performed in a context-specific environment, and followed by feedback. Sixteen studies representing 528 patients were included. From 3 to 11 training components were reported within the included studies. The components associated with largest effect sizes were "distributed practice" and "feedback". There was no correlation between the number of task-oriented training components used in a study and the treatment effect size. "Random practice" and "use of clear functional goals" were associated with the largest follow-up effect sizes.

Our review included several additional studies. The results are summarized in Tables 10.10 and 10.11.

Table 10.10 Studies Evaluating Repetitive, Task- Specific Training Techniques

Author/ Country PEDro Score	Methods	Results
Cauraugh & Kim 2003 USA 6 (RCT)	34 patients were randomly assigned to 1 of 3 treatment groups: blocked practice (same movement is performed repetitively on successive trials) + active neuromuscular stimulation, random practice (different movements on successive trials) + active stimulation, or no active stimulation assistance control group. Subjects completed training for 90 minutes/day, 2 days/week for 2 weeks. A session consisted of 3 sets of 30 successful active neuromuscular trials with 3 movements	At follow-up, the number of blocks moved (Box and Block Test) and reaction time improved significantly for both the blocked and random practice groups in comparison to the control group. No differences were found between the block and random practice groups.

	executed 10 times/set.	
Blennerhassett & Dite 2004 Australia 9 (RCT)	30 stroke patients were randomized to either an Upper Limb or Mobility Group. All subjects received their usual rehabilitation and an additional session of task-related practice using a circuit class form for 4 weeks. Outcome measures were assessed pre-and post-treatment and at six months and included three items of the Jebsen Taylor Hand Function Test (JTHFT), two arm items of the Motor Assessment Scale (MAS), and three mobility measures, the Timed Up and Go Test (TUGT), Step Test, and Six Minute Walk Test (6MWT).	Only the Upper Limb Group made a significant improvement on the JTHFT and MAS upper arm items. The JTHFT dexterity scores in the Upper Limb Group were significantly faster than the Mobility Group.
Thielman et al. 2004 USA 4 (RCT)	12 patients matched using the Motor Assessment Scale (MAS) were randomized to receive 12 sessions (4 weeks) of home-based unrestrained trunk training, while sitting unrestrained in a chair, using one of two treatments. i) Task-related training (TRT) involved asking patients to grasp objects, which differed in size, shape and weight. ii) Progressive resistive exercises (PRE) involved whole-arm pulling against resistive therapeutic tubing in planes and distances similar to that in TRT. Pre- and post-test kinematic analysis of arm movements MAS and Rivermead Motor Assessment scores were collected.	For data analysis, patients were divided into high and low functioning subgroups based on the results from pretests. Kinematic analysis of arm trajectories revealed that hand paths of low-level subjects straightened significantly after TRT, but not PRE. After training, high-level PRE subjects used less trunk motion, while reaching for an ipsilateral target, while high-level TRT group patients showed no change in truck movement after training.
Winstein et al. 2004 Canada 6 (RCT)	64 patients with recent stroke admitted for inpatient rehabilitation were randomized into 1 of 3 intervention groups: Standard care (SC), functional task practice (FT), and strength training (ST). The FT and ST groups received 20 additional hours of upper-extremity therapy beyond standard care distributed over a 4- to 6-week period. The main outcome measures assessed before and after treatment included Fugl-Meyer (FM) Assessment, isometric torque, and Functional Test of the Hemiparetic Upper Extremity (FTHUE).	Compared with SC participants, those in the FT and ST groups had significantly greater increases in FM scores (P=.04) and isometric torque (P=.02) post treatment. Treatment benefit was primarily in the less severe participants. Similar results were found for the FTHEU and isometric torque. During the long term, at 9 months, the less severe FT group continued to make gains in isometric muscle torque, significantly exceeding those of the ST group (P<.05).
Higgins et al. 2006 Canada 8 (RCT)	47 chronic stroke patients were randomized to receive a 6-week program (3 sessions/week x 90 min) of arm training (treatment condition) or to leg training (control condition). Arm interventions were tailored to each subject's' perceived need for improvement in various tasks of ADL. Evaluations performed at baseline and study end included the Box & Block test, the nine-hole peg test, TEMPA, grip strength, STREAM, Barthel Index, OARS-IADL, SF-36,	There were no statistically significant changes in any of the outcome measures between groups.

	Geriatric Depression Scale	
McDonnell et al. 2007 Australia 7 (RCT)	20 sub acute hemiparetic stroke patients were randomized to receive a course of task-specific training with or without afferent stimulation. All patients received 9 sessions of physiotherapy training over 3 weeks. Prior to each training session, electrical stimulation of the motor point of 2 hand muscles was given in the stimulation group, whereas the control group received sham stimulation. Changes in dexterity were assessed using a grip-lift task, and standard measures of upper-limb function including the Action Research Arm test (ARAT) and the Fugl-Meyer (FM) Assessment were made before and following the intervention.	Patients in both groups improved on mean ARAT and FM scores although the differences were not statistically significant. Of the 20 patients, only 14 could perform the grip-lift task, which is an objective measure of dexterity. Patients in the stimulation group exhibited significantly greater improvements in this task than the control group.
Boyd et al. 2010 Canada 5 (RCT)	18 subjects with chronic stroke were randomized into either a task-specific group or a general arm use group. Five sessions were completed within 2-weeks. All patients completed a serial targeting task during an fMRI scan on day 1 and were re-tested (retention) on session 5. Three intervention sessions were performed on days 2-4 in which patients in the task-specific group performed serial targeting practice, while patients in the general arm use group underwent training sessions of increased but non-task specific use of the hemiparetic arm. Both groups performed a repeated sequence of responses that may be learned, and random sequences of movement, which cannot be learned. Mean reaction time (RT) and movement time (MT) were calculated. RT was the time from target highlight to the beginning of the subject's response. MT was movement onset to target hit. A change score for was calculated for RT and MT.	The task-specific group made greater gains in RT and MT compared with the control group on both the random and repeated sequences of testing.
Arya et al. 2012 India 9 (RCT)	103 patients with a Brunnstrom stage of 2 for arm recovery, an average of 12 weeks following stroke, were randomized to receive a 4 week course of either task-specific training or standard training using the Bobath neurodevelopmental technique. Patients in both groups received 1 hr of therapy 5x/week. Outcomes were assessed before and after treatment and at 8 weeks follow-up and included Fugl-Meyer assessment (FMA), Action Research Arm Test (ARAT), Graded Wolf Motor Function Test (GWMFT), and Motor Activity Log (MAL).	Ninety-five participants completed the 8-week follow-up. Patients in the task-specific group achieved significantly greater gains compared to patients in the control group, at both the end of treatment and at follow-up on FMA, ARAT, GWMFT, and MAL.

Many of the treatments reviewed were non-specific in nature, not well described and were evaluated on patients at different stages of neurological recovery. Sample sizes were generally small. Furthermore, the interventions varied across studies severely limiting comparability. Often, multiple outcomes were assessed, some of which demonstrated a benefit, while others did not; typically there were improvement on impairment level outcomes, which did not transfer to functional improvements (disability level). The conclusions that we draw pertain only to the basket of interventions that were assessed, and cannot be generalized to any specific treatment within the broader group.

Table 10.11 RCTs of Repetitive Task- Specific Techniques for the Upper Extremity

Author PEDro Score	n	Intervention	Main Outcome(s) Result
Blennerhassett & Dite 2004 9 (RCT)	30	Upper or lower extremity task-related practice -1 hour a day x 5 days x 4 weeks	Jebsen Taylor Hand Function Test (+) Motor Assessment Scale (+)
Arya et al. 2012 9 (RCT)	103	task-specific training or standard training using the Bobath approach	Fugl-Meyer (+) ARAT (+)
Higgins et al. 2006 8 (RCT)	47	Upper or lower extremity task-related practice: 90 min x 3 sessions/week x 6 weeks	Box & Block test (-)
McDonnell et al. 2007 7 (RCT)	20	Task-specific training with or without afferent stimulation	Fugl-Meyer (-) ARAT (-) Dexterity (+)
Cauraugh & Kim al. 2003 6 (RCT)	34	Blocked practice + active stimulation vs. random practice + active stimulation vs. no active stimulation assistance (control)	Box and Block Test (+) Reaction time (+)
Winstein et al. 2004 6 (RCT)	64	Standard care (SC) vs. functional task practice (FT) vs. strength training (ST)	Fugl-Meyer (+ FT/ST vs. SC) Functional Test of the Hemiparetic Upper Extremity (+ FT/ST vs. SC)
Boyd et al. 2010 5 (RCT)	18	Task-specific training vs. general arm training	Changes in reaction and movement time (+)
Thielman et al. 2004 4 (RCT)	12	Task-related training vs. Progressive resistive exercises	Kinematic analysis of arm movements (+/-) MAS (-) Rivermead Motor Assessment (-)

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Conclusions Regarding Repetitive Task Specific Techniques

There is strong (Level 1a) evidence that repetitive task specific training techniques improve measures of upper extremity function.

Repetitive task-specific training may improve upper extremity function.

10.2.6 Trunk Restraint

Reaching movements made with the affected arm in hemiparetic patients are often accompanied by compensatory trunk or shoulder girdle movements, which extend the reach of the arm (Michaelson et al. 2001). Restriction of compensatory trunk movements may encourage recovery of "normal" reaching patterns in the hemiparetic arm when reaching for objects placed within arm's length (Michaelson et al. 2004). Several trials have evaluated the effectiveness of trunk restraint combined with task-specific training to improve the movement quality of reaching tasks.

Table 10.12 Studies Evaluating Trunk Restraint

Author/ Country PEDro Score	Methods	Results
Michaelsen & Levin 2004 Canada 5 (RCT)	28 chronic, hemiparetic stroke patients were randomized to a trunk restraint group with practiced reach-to-grasp movement tasks or to un restrained group, with verbal instruction not to move trunk. Training consisted of 60 trials. Kinematics of reaching and grasping an object placed within arm's length were recorded before, immediately after and 24 hours after training.	The trunk restraint group used more elbow extension, less anterior trunk displacement, and had better interjoint coordination than the control group after training, and range of motion was maintained 24 hours later in only the trunk restraint group. Significant between group differences for changes in trunk displacement (mm) and elbow extension.
Michaelsen el al. 2006 Canada 7 (RCT)	30 chronic stroke patients with hemiparesis were randomized into a Trunk-restraint (TR) or non-restraint group. Patients received 3 1-hour sessions per week with object-related reach-to-grasp training supervised by a therapist for 5 weeks. Outcome measures included: motor function (Upper Extremity Performance Test), effectiveness for improving arm impairment (Fugl-Meyer Arm Section) and Isometric force and manual dexterity (Box and Blocks Test).	The TR training group experienced larger decreases in impairment (Fugl-Meyer Arm Section; $p<0.035$) and greater gains in function (Upper Extremity Performance Test; $p<0.05$) compared with non-restraint at follow-up. Both groups showed significant improvements for elbow strength ($p<0.002$), Box and Blocks Test ($p<0.01$), peak velocity ($p<0.002$), trajectory smoothness ($p<0.001$) and straightness ($p<0.01$).
Woodbury et al. 2009 USA 5 (RCT)	11 chronic stroke patients with baseline Fugl-Meyer Assessment (FMA) scores 26 to 54 were randomized to 2 constraint-therapy intervention groups. All participants wore a mitt on the unaffected hand for 90% of waking hours over 14 days and participated in 10 days/6 hours/day of supervised progressive task practice. During supervised sessions, one group trained with a trunk restraint (preventing anterior trunk motion) and one group did not. Outcome measures included FMA, Wolf Motor Function Test (WMFT) Motor Assessment Log (MAL) Amount of Use (AOU) and Quality of Movement (QOM), kinematics of unrestrained targeted reaching and tests of functional arm ability assessed before and after treatment.	Mean FMA scores improved from 38 to 49 in the trunk restraint group and from 42 to 46 in the control group. WMFT scores improved from 9.41 to 5.16 in the trunk restraint group and from 9.35 to 6.16 in the control group. Post training, the trunk-restraint group demonstrated significantly straighter reach trajectories and less trunk displacement. The trunk-restraint group achieved significantly greater gains in shoulder flexion and elbow extension
Thielman 2010 USA	16 subjects with moderately-severe impairment of hand function with scores of 20 to 44 on the	Subjects in both groups demonstrated significant

4 (RCT)	Upper-Arm subsection of the Fugl-Meyer (FM) Scale were randomly assigned to either the Sensor (n=8) or the Stabilizer group (n=8). Subjects in the Stabilizer group were restrained by a chair harness while sitting in a chair while subjects in the Sensor group received auditory feedback to ensure their backs touched the chair. A faded feedback protocol was used for subjects in both groups to decrease reliance on the feedback or restraint. Subjects in both groups participated in 12 task-related training sessions (2-3 x/wk, 40-45 min each). Outcomes were assessed before and after training. The primary outcome was the Reaching Performance Scale (RPS). FM Scale scores, active range of motion, grip strength, Wolf Motor Function Test (WMFT) and Motor Activity Log (MAL) were also assessed.	improvement over time on: RPS (near & far sub scores) FMA, and WMFT. Subjects in the Sensor group performed significantly better than those on the RPS (near sub score), but not the far sub score.
Wu et al. 2012a) Taiwan 5 (RCT)	57 subjects with stroke onset of 6 to 55 months were randomized to one of 3 groups and received dose-matched therapy of 2 hours/day x5 days/week x 3 weeks. Groups were distributed constraint-induced therapy + trunk restraint (dCIT-TR), distributed constraint-induced therapy (dCIT), or control therapy based on neurodevelopmental principles. Assessments were conducted before and after treatment and included the Action Research Arm Test (ARAT), Motor Activity Log (MAL), Frenchay Activities Index (FAI), and Stroke Impact Scale (SIS).	Subjects in the dCIT-TR and dCIT groups exhibited higher overall scores on the ARAT, FAI, and hand function domain of the SIS and higher MAL (QOM) scores than participants in the control group.
Wu et al. 2012b) Taiwan 5 (RCT)	45 subjects, an average of 15.5 months post stroke onset, were randomized to 3 groups as per the protocol of Wu et al. 2012a). Outcome measures included movement kinematics, Fugl-Meyer Assessment (FMA) and the Motor Activity Log (MAL).	The dCIT + TR group showed better preplanned grasping movement and less trunk motion at the early phase of the reach-to-grasp movements than the dCIT or control groups. Compared with the controls, the dCIT + TR subjects demonstrated greater gains in FM scores (total and distal subsection) The dCIT + TR and dCIT participants demonstrated significantly greater functional use of the affected arm.

The trials examining interventions to improve reaching tasks evaluated trunk restraint +task-specific therapy, trunk restraint combined with constraint-induced movement therapy and trunk restraint with sensory feedback. In the two studies that compared trunk restraint with simply no restraint, subjects in the TR group performed significantly better on at least one of the outcomes assessed. In the two studies included 2 active treatment groups, patients in the trunk restrain +CIMT group or the CIMT group fared better than patients in the therapy group.

Table 10.13 RCTs Examining Truck Restraint to Improve Reaching

Author PEDro Score	n	Intervention	Main Outcome(s) Result
Michaelsen el al. 2006 7 (RCT)	30	1 hr sessions 3x /wk x 5 wks with object-related reach-to-grasp training for Trunk-restraint vs. non-restraint	Upper Extremity Performance Test (+) Fugl-Meyer Arm Section (+) Box and Blocks Test (-)
Wu et al. 2012 5 (RCT)		CIMT + trunk restraint (1) vs. CIMT (2) vs. control (3)	Kinematics (+1 & 2 vs. 3) ARAT (+1 & 2 vs. 3) Fugl-Meyer (+1 & 2 vs. 3)
Woodbury et al. 2009 5 (RCT)	11	CIMT + trunk restraint vs. CIMT	Fugl-Meyer (-) Wolf Motor Function test (-) Kinematic analyses of reaching (+)
Michaelsen & Levin 2004 5 (RCT)	28	Trunk restraint group vs. no restraint	Trunk displacement (+) Performance outcome measures (-)
Thielman 2010 4 (RCT)	16	Trunk restraint vs. sensory feedback	Reaching Performance Scale Near (+) Sensory group Far (-)

Conclusions Regarding Interventions designed to Improve Reaching

There is conflicting (Level 4) evidence that specialized programs improve reaching.

10.2.7 Sensorimotor Training and Somatosensory Stimulation

Somatosensory deficit is common following stroke. Connell et al. (2008) reported that among 70 patients with first-ever stroke, 7-53% had impaired tactile sensations, 31-89% impaired stereognosis, and 34-64% impaired proprioception. Sensorimotor impairment is associated with slower recovery following stroke; therefore, therapies to increase sensory stimulation may help to improve motor performance. Stimulation can be applied using a variety of methods including electroacupuncture, repetitive passive movement therapy, thermal stimulation, robotic devices and TENS.

Barreca et al. (2003) included four studies in their review of sensorimotor training for the upper extremity (Feys et al. 1998, Jongbloed et al. 1989, Volpe et al. 1999, 2000). The authors concluded that stroke survivors who obtained sensorimotor stimulation showed more improvement at the end of the treatment phase compared to the control group. This improvement was still seen at follow-up 12 months later.

A review of sensory-motor training by Steultjens et al. (2003) included three RCTs (Feys et al. 1998, Jongbloed et al. 1989, Kwakkel et al. 1999), one case control trial (Turton and Fraser 1990), and one noncontrolled trial (Whitall et al. 2000). The authors concluded that sensorimotor training was not effective for improving ADLs, extended ADLs, social participation, or arm and hand function.

In a more recent review, including the results of 14 RCTs (Schabrun & Hiller 2009), the authors distinguished between passive forms of sensory retraining through electrical stimulation (TENS) and active forms, primarily through specific exercises. The included trials assessed the outcomes of function, sensation and prorioception in both the upper and lower extremity. Only 2 of the included trials assessed sensation in the upper extremity. The results were ambiguous.

A recent Cochrane review (Doyle et al. 2010) included the results from 13 studies (467 participants) examining a variety of treatments for sensory impairment following stroke and concluded that there was insufficient high-quality evidence available to recommend the use of any of them. Treatments with preliminary evidence of benefit include mirror therapy, thermal stimulation and intermittent pneumatic compression.

The results of studies evaluating sensorimotor stimulation treatments are summarized in Tables 10.14 and 10.15. Sensorimotor training involving TENS is included in a separate section.

Table 10.14 Studies Evaluating Sensorimotor Training or Somatosensory Stimulation

Author, Year Country PEDro score	Methods	Results
Jongbloed et al. 1989 Canada 5 (RCT)	90 stroke patients were randomized to receive either sensorimotor stimulation by an OT (40 min/day x5 days/week x 8 weeks) (n=43) or functional therapeutic approach (n=47). Mean of 40 days post stroke to admission to study	No significant differences between the two groups on the three outcome measures (Barthel Index, meal preparation and 8 subsets of the Sensorimotor Integration test).
Feys et al. 1998 Belgium 6 (RCT)	Single blind multi-centre trial of 100 patients randomized to either a treatment or control group. 2-5 weeks after stroke onset, patients in the treatment group received additional sensorimotor treatment for 30 minutes, 5 days a week for 6 weeks while patients in the control group received a placebo treatment.	There were no differences in Fugl-Meyer scores between the groups at 6 wks. Patients in the experimental group scored significantly higher at 6 month and 12 month follow-up. No significant differences between the groups in Arm Research Action or Barthel Index scores. Patients in both groups improved significantly over time in FM, ARA and BI scores.
Cambier et al. 2003 Belgium 7 (RCT)	23 patients were enrolled in a multi-centre randomized controlled preliminary trial that compared the application of intermittent pneumatic compression with a passive treatment strategy. All patients received NDT therapy. The experimental group received an additional 30 min of sensorimotor stimulation therapy 5 days/wk, for 4 wks, while the control group received sham short-wave therapy for the same amount of time.	While both groups demonstrated significant improvements in Nottingham Sensory Assessment scores from baseline to the end of the study, patients in the treatment group scored significantly higher than the control group. Patients in the experimental group also showed significantly higher scores on the Fugl-Meyer Assessment.
Byl et al. 2003 USA 6 (RCT)	21 subjects who were 6 months to 7 yrs post stroke and able to walk 100 feet with or without a cane; partially open and close the hand; and	Subjects with right-sided hemiparesis improved significantly more than those with a left hemiparesis in terms of functional independence ($p<0.002$), sensory

	partially elevate the shoulder and elbow against gravity. Eligible patients were then randomly assigned to Group A (sensory training 4 wks, motor training 4 wks) or Group B (motor training 4 wks, sensory training 4 wks). 18 patients completed the study.	discrimination ($p<0.05$), and gait speed $p<0.05$). Across both groups, more than 20% ($P < 0.01$) improvement was measured in functional independence and UE function (fine motor, sensory discrimination, and musculoskeletal performance).
Chen et al. 2005 Taiwan 7 (RCT)	46 acute stroke patients were randomly assigned to standard rehabilitation treatment or standard treatment plus thermal stimulation (TS) for 30 minutes daily for 6 weeks. Outcome measures included: Brunnstrom staging, modified motor assessment scale, grasping strength, angles of wrist extension and flexion, sensation by monofilament, and muscle tone by modified Ashworth scale. Assessments were performed weekly to evaluate sensory and motor functional outcomes.	29 patients completed the study. The performance of Brunnstrom stage and wrist extension and sensation were improved significantly after TS intervention. Recovery rates of 6 measures after TS were significantly higher than those of the control, except for grasping.
Hummel et al. 2005 Germany 6 (RCT)	Crossover trial whereby 6 chronic stroke patients received 1 session of non-invasive, painless cortical stimulation by transcranial direct current stimulation (tDCS) and one sham session. Outcome was assessed by the Jebsen-Taylor Hand Function test (JTT).	Five patients completed the two treatment sessions. Following treatment there was significant improvement in the paretic limb that received tDCS, but not in the sham treated arm.
Mann et al. 2005 UK 5 (RCT)	22 patients between 1 and 12 months post stroke were randomized to receive NMES of the elbow, wrist and finger for 30 min a day, 2x/day for 12 weeks or passive extension exercises. Outcomes were assessed before, midway and after treatment and at 24 weeks and included the ARAT for motor function and static 2-point discrimination for sensation.	At the end of 12 and 24 weeks, there was a significant difference in ARAT scores between groups, favouring the NMES group, although there were no differences in sensation assessments between groups.
Sawaki et al. 2006 Switzerland 5 (RCT)	7 chronic stroke patients participated in 3 training sessions, randomly ordered and separated by at least 24 hrs between treatments. Use-dependent plasticity was tested after 2 hrs of stimulation of: i) the ulnar, median and radial nerves of the paretic hand; ii) tibial, superficial peroneal and sural nerves in the paretic leg, and iii) no stimulation. Movement threshold, amplitude of motor-evoked potential and training kinematics were analyzed.	Use-dependent plasticity was more prominent with arm stimulation (increased by 22.8%) than with idle time (increased by 2.9%) or leg stimulation (increased by 6.4%).

Sullivan & Hederman 2007 USA No Score	10 subjects with onset of stroke between 2 and 6 years previously participated in an 8-week, individualized, home program of neuromuscular and sensory amplitude electrical stimulation. All subjects engaged in stimulation-assisted task-specific exercises for 15 minutes, 2 -3 times daily. Participants with sensory deficits received an additional 15 minutes of sensory amplitude stimulation twice daily. The following outcomes were assessed before and after treatment: The Action Research Arm Test (ARAT), the Stroke Rehabilitation Assessment of Movement (STREAM) (to examine movement quality) and the Modified Ashworth Assessment of Spasticity (MAS). The Nottingham Stereogennosis Assessment (NSA) was used to examine sensation.	6 subjects demonstrated a statistically significant improvement on the ARAT, 5 on STREAM and 4 demonstrated a 10% or greater improvement in spasticity (MAS). Two subjects demonstrated significant improvement on all three outcome measures. Nine subjects demonstrated sensory deficits at baseline. Among the 6 subjects who were tested at the end of the intervention, 4 demonstrated improvements in NSA scores.
Byl et al 2008 USA 6 (RCT)	45 subjects, an average of 2.3 years post stroke participated in a 6-8 week learning-based sensorimotor training (LBSMT) program of varied dosage: group I (n = 18; 1x/week, 1.5 hours/visit); group II (n = 19, 3x/week, 0.75 hours/visit); and group III (n = 8; 4x/week, 3 hours/visit). All subjects reinforced their training with home-based practice. The primary outcome measures, assessed before and after treatment, were functional independence, strength, sensory discrimination, and fine motor skills.	Subjects in group III achieved greater gains than subjects in either groups I or II on all 4 primary outcome variables. Across all individual subjects, significant gains were measured on the 4 dependent variables (improvement ranging from 9.0% to 38.9%).
Hesse et al. 2008 Germany 7 (RCT)	8 sub-acute stroke patients were randomized to receive additional therapy with the Finger Trainer (a device for repeating controlled passive movements of paralyzed fingers) for 20 min every work day for four weeks, or the same duration of bimanual group therapy, in addition to their usual rehabilitation. Assessments conducted before and after treatment included the Fugl Meyer (FM) Assessment, the Box and Block test and Modified Ashworth scores.	The mean initial/final FM scores for the treatment and control group were 11.3/26.5 vs. 10.5/18.5. Only 1 subject (experimental group) was able to move any blocks following treatment. Median Modified Ashworth score increased from 0/5 to 2/5 in the control group, but not in the treatment group, 0 to 0. Only one patient, in the treatment group, regained function of the affected hand.
Barker et al. 2008 Australia	42 stroke survivors with severe and chronic paresis were randomized to receive: i) Sensorimotor Active	There was a significant treatment effect associated with both of the SMART arm groups, but not for the control group. Median

8 (RCT)	Rehabilitation Training (SMART) Arm (n=10) with electromyography-triggered electrical stimulation; ii) SMART Arm alone (n=13) or iii) no intervention (control)(n=10). Training consisted of 12 1-hour sessions over 4 weeks. The primary outcome measure was "upper arm function," item 6 of the Motor Assessment Scale (MAS). Secondary outcome measures included impairment measures; triceps muscle strength, reaching force, modified Ashworth scale; and activity measures: reaching distance and Motor Assessment Scale. Assessments were administered before (0 weeks) and after training (4 weeks) and at 2 months follow-up (12 weeks).	scores on item 6 of the MAS improved from: 0 to 2 (SMART arm + stim); 1 to 3 (SMART arm with no stim) and remained at 1 over the intervention period among subjects in the control group.
Volpe et al. 2008 USA 5 (RCT)	21 chronic stroke patients were randomized to receive a course of intensive upper-extremity treatment that was provided by either a therapist or a robotic device (InMotion[2]). Treatment consisted of 1 hr sessions, 3x/week for 6 weeks. Primary outcome was the Fugl-Meyer (FM) score for shoulder/elbow. Secondary outcomes were the FM wrist/hand and the Motor Power Scale for Shoulder/elbow. Assessments were conducted monthly for 3 months.	Patients in both groups demonstrated improvement over time, which was maintained at 3 months; however, there were no significant between group differences on either the primary or secondary outcomes.
Wu et al. 2010 Taiwan 6 (RCT)	23 participants with stroke onset of 3 months to 3 years were randomly assigned to either the experimental group or the control group in an outpatient setting. In addition to regular rehabilitation programs, the experimental group received thermal stimulation (TS)(n=12) with alternating hot/cold application for 30 minutes per day (3 days/week for 8 weeks); the control group (n=11) received the same TS protocol on lower extremity. The UE subscale of the Stroke Rehabilitation Assessment of Movement (STREAM) and the Action Research Arm Test (ARAT) were primary outcome measures and were assessed at baseline, after TS, and at 1-month follow-up.	After treatment, participants in the TS group had significantly higher UE-STREAM (10.0 vs. 8.0, $p<0.002$) and ARAT scores (25.3 vs. 16.7, $p<0.009$) compared to those in the control group.
Stein et al. 2010	30 community-dwelling stroke survivors with residual hemiparesis	The average stroke onset interval was 6 years. There were no significant differences between

USA 10 (RCT)	were screened for residual motor ability using a functional task, and those who functioned below this level were excluded. Subjects were stratified by baseline upper extremity Fugl-Meyer (FM) (more impaired [28-35] and less impaired [36-55]) and were randomized to one of two groups: treatment (stochastic resonance stimulation, which included a combination of subthreshold electrical stimulation and vibration) plus exercise, or a control (sham stimulation plus exercise. There were 12 therapy sessions given over a 4-week period, each lasting 1 hour. The outcomes were assessed at baseline, after treatment and at 1-month post treatment. They included FM, Motor Activity Log (MAL), action research arm test (ARAT), Wolf Motor Function test (WMFT), Stroke Impact Scale and Reaching Performance Scale (RPS)	the groups on any of the outcomes assessed.
Carey et al. 2011 Australia 8 (RCT)	50 subjects with impaired texture discrimination, limb position sense, and/or tactile object recognition with stroke onset of >6 weeks were randomized to receive somatosensory discrimination training (n = 25) or non-specific repeated exposure to sensory stimuli (n = 25) in 10, 60-minute sessions. The primary outcome was change in a composite standardized somatosensory deficit (SSD) index following intervention at 6 weeks and 6 months post training.	Patients in the somatosensory training group achieved significantly greater improvement in sensory capacity following sensory discrimination training that was maintained at 6 weeks and 6 months.
Hunter et al. 2011 UK 7 (RCT)	76 patients with severe upper limb impairment, within 3 months of stroke were randomized to receive conventional rehabilitation but no extra therapy (group 1), or conventional therapy plus 1 of 3 daily doses of Mobilization and Tactile Stimulation (MTS), up to 30 (group 2), 60 (group 3), or 120 (group 4) minutes for 14 days. MTS was delivered using a standardized schedule of techniques (e.g., sensory input, active-assisted movement). The primary outcome was the Motricity Index (MI) and secondary outcome was the Action Research Arm Test (ARAT) assessed on day 16.	MI and ARAT scores improved in patients randomized to all 4 groups, but there were no significant difference in mean scores among groups. However, patients in the 30 min, 60 min and 120 min MTS groups received only 77%, 62% and 55% of the scheduled amount of therapy.
Caliandro et	49 patients with chronic stroke were	There was significant improvement in WMFT

al. 2012 Italy 7 (RCT)	randomized to receive a 3-day course of repetitive focal muscle vibration (rMV) or a sham treatment to the upper arm. The vibration frequency for those receiving the active treatment was 100 Hz. A single treatment consisted of 3x10 minute vibration applications, separated by 1 min. All patients received rehabilitation for 1 hr/day, 3X/week. The primary endpoint was an improvement of more than .37 points on the Functional Ability Scale of the Wolf Motor Function Test (WMFT FAS). The Modified Ashworth Scale and the visual analog scale were the secondary outcome measures. All measures were administered before the treatment, at 1 week and at 1 month after the treatment.	FAS score over time for patients in the rMV group, but not for patients in the control group. At one month, the treatment was successful for 7 (33%) of 21 patients recruited in the rMV group and for 2 (13%) of 15 patients recruited in the control group, although the difference was not statistically significant. (Success was defined as patients exceeding the MDC_{90} threshold, or the smallest change in a single subject that reflects true change, rather than measurement error).

Discussion

There was a broad range of interventions provided, which complicated the process of formulating conclusions. Among the RCTs, sensorimotor stimulation treatment included thermal stimulation (Chen et al. 2005, Wu et al. 2010), intermittent pneumatic compression (Cambier et al. 2003), splinting (Feys et al. 1998), cortical stimulation (Hummel et al. 2005), repetitive muscle vibration and sensory training programs (Byl et al. 2003, 2009, Carey et al. 2011, Hunter et al. 2011, Jongbloed et al. 1989), which in one case was delivered by a robotic device (Volpe et al. 2008).

The interventions were evaluated in the acute (Chen et al. 2005), subacute (Feys et al. 1998, Cambier et al. 2003, Jongbloed et al. 1989, Hesse et al. 2008, Carey et al. 2011, Hunter et al. 2011) and chronic (Byl et al. 2003, 2009, Caliandro et al. 2012) stages of stroke.

One small feasibility trial evaluated the potential benefit of stochastic resonance stimulation among a group of community-dwelling stroke survivors, using a prototype device (Stein et al. 2010). Unfortunately, the treatment did not prove to be effective.

Table 10.15 Summary of Results From RCTs Evaluating Sensorimotor Training or Stimulation

Author/ PEDro Score	n	Intervention	Main Outcome(s) Result
Stein et al. 2010 10	30	Stochastic resonance stimulation	Fugl-Meyer Assessment (-) Motor Activity Log (-) Action Research Arm Test (-)
Carey et al. 2011 8 (RCT)	50	somatosensory discrimination training vs. sham training program	composite standardized somatosensory deficit (+)
Barker et al. 2008	42	Non-robot training device	MAS (+)

8 (RCT)		with stimulation vs. device only vs. control	
Caliandro et al. 2012 7 (RCT)	49	Focal muscle vibration	Wolf Motor Function Test (+)
Hunter et al. 2011 7 (RCT)	76	Mobilization and Tactile Stimulation (3 dose levels) vs. conventional therapy	Motricity Index (-) Action Research Arm test (-)
Cambier et al. 2003 7 (RCT)	23	Intermittent pneumatic compression vs. sham short-wave therapy	Nottingham Sensory Assessment (+) Fugl-Meyer Assessment (+) Ashworth Scale (-) Visual Analogue Scale (-)
Chen et al. 2005 7 (RCT)	46	Thermal stimulation	Brunnstrom (+) MMAS (-) Grasping (-) Sensation (+)
Wu et al. 2010 6 (RCT)	23	Thermal stimulation vs. no stimulation	UE-STREAM (+) ARAT (+)
Byl et al. 2008 USA 6 (RCT)	45	Leaning-based sensorimotor training (3 intensity levels)	Functional independence, strength, sensory discrimination, fine motor skills (+ for highest intensity group compared with other 2)
Hummel et al. 2005 6 (RCT)	5	cortical stimulation vs. sham stimulation	Jebsen-Taylor Hand Function test (+)
Feys et al. 1998 6 (RCT)	100	Sensorimotor stimulation vs. control	Fugl-Myer Assessment (+ at 6 and 12 months) Action Research Arm test (-) Barthel Index (-)
Jongbloed et al. 1989 5 (RCT)	90	Functional approach vs. sensorimotor integrative approach	Barthel Index (-) 8 subsets of the Sensorimotor Integration test (-)
Volpe et al. 2008 5 (RCT)	21	Sensorimotor arm training delivered by a therapist vs. robotic device	2 subsections of the FM Assessment (-)

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Conclusions Regarding Sensorimotor Training

There is conflicting (Level 4) evidence that sensorimotor treatments improve upper extremity function.

It is uncertain whether sensorimotor training results in improved upper extremity functioning.

10.2.8 Mental Practice

The use of mental imagery or mental practice as a means to enhance performance following stroke was adapted from the field of sports psychology were the technique has been shown to improve athletic performance, when used as an adjunct to standard training methods. The technique, as the name suggests, involves rehearsing a specific task or series of tasks, mentally. A series of small trials have adapted and evaluated the effects of mental practice as a treatment following stroke. The ability of the treatment to improve motor function or ADL performance is the outcome most frequently assessed in these studies. The most plausible mechanism to explain the success of the technique is that stored motor plans for executing movements can be accessed and reinforced during mental practice (Page et al. 2001). Mental practice can be used to supplement conventional therapy and can be used at any stage of recovery.

A systematic review (Braun et al. 2006) included the results from 10 studies, three of which were RCTs. Sample sizes ranged from 1 to 46. The patient characteristics, interventions and outcomes assessed of the included studies were sufficiently heterogeneous to preclude pooled analysis. The authors were unable to draw conclusions based on the available evidence and suggested more research is needed.

Zimmerman-Schlatter et al. (2008) also assessed the efficacy of motor imagery in recovery post stroke. Theses authors included the results from only 4 RCTs (Liu et al. 2004, Page et al. 2001, 2006 2007) in which the duration and frequency of treatment lasted from 10 minutes to one-hour a day, with 3 to 5 sessions per week for 3 to 6 weeks. Mean time of stroke onset ranged from several days to several years. Three of these studies reported improvements in the mean Action Research Arm Test and Fugl-Meyer scores. Two of these studies also found higher mean change scores than the minimally clinically relevant difference in the ARAT and FM scores. These authors concluded that although there was evidence of benefit of treatment, larger and more rigorous studies are required to confirm these findings.

More recently, Nilsen et al. (2010) conducted a systematic review on the use of mental practice as a treatment for motor recovery, including the results from 15 studies, 4 of which were classified as Level 1 (i.e. RCTs). Although the authors concluded that there was evidence that mental practice was effective, especially when combined with upper-extremity therapy, they also discussed the problems in summarizing the results of heterogeneous trials. Studies varied with respect to treatment protocols, patient characteristics, eligibility criteria, dosing, methods used to achieve mental practice (audiotapes, written instruction, pictures) the chronicity of stroke, outcomes assessed. The authors cautioned that additional research be conducted before specific recommendations regarding treatment can be made.

A Cochrane review on the subject (Barclay-Goddard et al. 2011), restricted to RCTs (n=6) concluded that there was limited evidence that mental practice in addition to other rehabilitation therapies was effective compared with the same therapies without mental practice. There were significant treatment effects for the outcomes associated with both impairment and disability.

A meta-analysis (Cha et al. 2012) included the results from 5 RCTs and assessed the additional benefit of mental practice combined with functional task training. The outcomes assessed in the individual studies included the Fugl-Meyer Assessment, the Action Research Arm test and the Barthel index. The estimated treatment effect size when the studies were pooled was 0.51 (95% CI 0.27 to 0.750, indicating a moderate effect.

The details of all studies from this review with a sample size greater than 2 are summarized in table 10.16.

Table 10.16 Studies Evaluating the Use of Mental Practice Following Stroke

Author/ Country PEDro Score	Methods	Results
Page et al. 2000 USA 4 (RCT)	16 chronic stroke patients were randomized to receive OT + imagery training (IT) (n=8) or to OT (n=8) and received a ½ hr session 3 x /week for 4 weeks as outpatients. Patients in the imagery group received a tape-recorded guided mental imagery session which lasted for 20 min. Patients in the control group listened to tape-recorded message on general stoke information. Therapy was provided on an outpatient basis.	Patients receiving IT demonstrated significantly greater improvement in Fugl-Meyer scores over the treatment period, compared with controls. The associated effect size was 1.39.
Page et al. 2001 USA 5 (RCT)	13 stroke patients (stroke onset 4 weeks to 1 year) with stable motor deficits were randomized to receive either OT +imagery training (IT)(n=8) or OT (n=5) and received one-hour sessions 3x/week for 6 weeks. Therapy sessions focused equally on upper and lower extremities. Therapy was provided on an outpatient basis.	No inferential statistics were reported. Patients in the IT group had greater improvements in mean Fugl-Meyer and Action Research Arm tests, compared with patients in the control group (FM changes: + 13.8 vs. + 2.9; ARA changes: 16.4 vs. + 0.7).
Dijkerman et al. 2004 UK No Score	20 chronic stroke patients performed a reach and grab task on a daily basis for 4 weeks. Additionally, 10 patients performed the task mentally (group 1). Five patients practiced a visual imagery task, recalling a set of pictures (group 2) and 5 patients did not practice any mental imagery (group 3).	Groups 2 and 3 were pooled for statistical analysis. At the end of 4 weeks, there were no statistically significant differences between groups on: BI scores, Hospital Anxiety and Depression scale, or Recovery of Locus Control. While there was a significant difference in the mean scores of Functional Limitations Profile, this was due to deterioration within the control group and not to improvements among patients in the treatment group. There was significant between group improvement only on the performance of the practiced motor reaching task.
Liu et al. 2004 Hong Kong 7 (RCT)	46 acute stroke patients were randomized to receive either 15 sessions (1hr/day x 3 weeks) of either a mental imagery program or functional training designed to improve performance of ADLs.	At the end of weeks 2 and 3, patients in the mental imagery group had higher scores on the ADL tasks and at one-month follow-up. There were no significant differences in mean FM or CTT between groups.

	During the 3 weeks, patients were trained to perform 3 sets (5 items each) of daily tasks. Patients also received 1-hour of PT daily. The ability to perform tasks was assessed on a 7-point Likert scale, where the higher values were associated with increasing independence. Fugl-Meyer (FM) and Colour Trails Test (CTT) were also assessed at the end of treatment	
Page et al. 2005 USA 6 (RCT)	11 chronic stroke patients received 30 minute therapy sessions twice a week for 6 weeks. Patients were randomized to an intervention consisting of either mental practice of ADL activities or to sessions which focused on relaxation techniques. Outcome measures included the Motor Activity Log and Action Research Arm tests.	Patients in the mental practice group had a greater mean change score of ARA test results (10.7 vs. 4.6, p=0.004). Patients in the MP group also increased the amount of use in their affected upper limb and the quality of the movements improved to a greater degree.
Ertelt et al. 2007 Germany 5 (RCT)	15 chronic stroke patients with moderate motor deficits of the upper extremity were randomly assigned to receive either action observation therapy (treatment) or traditional therapy (control). The treatment group underwent 18 consecutive daily sessions lasting 90 min each, in which patients watched 6 min videos of sequences of arm and hand movements and then performed the movements for 6 mins following the video. The control group received the same therapy however they watched a video with geometric shapes. Outcome measures included Frenchay Arm Test (FAT), the Wolf Motor Function Test (WMFT) and the Stroke Impact Scale (SIS).	Patients in the treatment group showed significantly greater improvements from pre-test to post-test on FAT, WMFT and SIS at post-treatment (4 weeks) compared to patients in the control group. The improvements were sustained at 8 weeks following the intervention.
Muller et al. 2007 Germany 4 (RCT)	17 patients, an average of 29 days following stroke were randomized to one of 3 groups: conventional therapy (n=5), motor practice (n=6) or mental practice (n=6). All patients participated in 30 minute sessions, 5 days a week for 4 weeks. Patients in the MP group initially watched a videotape of a hand in the desired pattern and then mentally rehearsed the hand sequence. Outcomes included	Patients in the motor and mental practice groups fared better on individual components of the Jebsen hand function test and in pinch grip compared with patients in the conventional group.

	pinch and grip strength, the Jebsen hand function test and the BI.	
Page et al. 2007 USA 6 (RCT)	32 chronic stroke patients were randomly assigned to receive 30-min mental practice (MP) sessions (n=16) or a sham intervention consisting of 30 min of relaxation exercises (n=16), 2 days/wk for 6 weeks and were preceded by 30 min of standard therapy. Outcomes included the upper-extremity portion of the Fugl-Meyer Assessment (FM) and the Action Research Arm test (ARA).	The MP group improved significantly on the FM compared to the control group (+ 6.7 vs. + 1.0, p<0.0001) and the ARA (+ 7.8 vs.+ 0.44, p< 0.001).
Liu et al. 2009 Hong Kong 5 (RCT)	35 acute stroke admitted for inpatient rehabilitation were randomly assigned to the mental imagery (MI; n=18) or conventional functional rehabilitation (FR; n=17) group. The interventions were provided for 1 hour/day for 3 weeks (15 sessions). The main outcome measure was gains in performance on 8 tasks on trained (n=5) and untrained tasks (n=3) in the training and novel environments at the end of treatment.	Patients in the MI group demonstrated significantly improved performance on 4 of 5 trained tasks compared with improvement in only 1 task in the FR patients when assessed within the training environment. Patients in the MI group performed significantly better on the 3 trained and 2 untrained tasks carried out in the novel environment.
Page et al. 2009 USA 4 (RCT)	10 chronic stroke subjects exhibiting stable, affected arm motor deficits were recruited from the community and received modified constraint-induced therapy (mCIT), consisting of structured therapy emphasizing affected arm use in functional activities 3 days/week for 10 weeks and less affected arm restraint 5 days/week for 5 hours. 5 subjects were randomly assigned to receive an additional co-intervention-mental practice (MP) for 30 minutes/day which required daily cognitive rehearsal of the activities of daily living practiced during mCIT clinical sessions. Outcomes assessed the Action Research Arm test (ARAT) and Fugl-Meyer (FM)	Subjects in the mCIT+MP group exhibited significantly greater gains on both outcomes after intervention. 1) ARAT: +15.4 vs. 8.4, (p<0.001); 2) FM: +7.8 vs. +4.1, p=0.01). These changes were sustained 3 months after intervention.
Riccio et al. 2010 Italy 5 (RCT)	36 stroke patients underwent a 6 week inpatient rehabilitation program. Patients were randomly assigned to receive 3 weeks of mental practice (MP) + conventional rehabilitation (CV)(3	There were statistically significant differences favouring the group that received CV+MP at the 3-week crossover point on all outcomes assessed. There were no significant differences between groups at the end of treatment period, after which all patients had received

	hrs/day x 5 days/week) followed by 3 weeks of CV or CR for 3 weeks and then CV + MP for the next 3 weeks. Outcome assessments were conducted at baseline, 3 weeks (crossover point) and at 6 weeks and included Motricity Index (upper extremity sub score), Arm Function Test-Functional Ability Scale and Time.	MP +CV.
Bovend'Eerdt et al. 2010 The Netherlands 8 (RCT)	50 patients undergoing either inpatient or outpatient rehabilitation following stroke were randomized to receive a 6-week program consisting of conventional therapy + mental practice (total of 6.5 hrs) or to conventional therapy only. Assessments were conducted at baseline, after 6 weeks (post intervention), and after 12 weeks (follow-up). Outcomes included Goal Attainment Scaling, BI, Rivermead Mobility Index, Nottingham Extended ADL, Action Research Arm Test and Timed up & Go.	Patients in both groups improved over time, but there were no significant differences between groups on any of the outcomes assessed. Compliance with advised treatment was poor in 85% of the therapists and in 72% of the patients.
Ietswaart et al. 2011 UK 7 (RCT)	121 stroke patients with a residual upper limb weakness within 6 months following stroke (on average <3 months post stroke) were randomized to one of 3 groups that received treatment 3 days a week for 45 min x 4 weeks: motor imagery group (n=41), attention placebo control (n=39) and usual care control (n=41). Patients in the motor imagery group mentally rehearsed upper-limb movements while patients in the attention placebo group performed equally intensive non-motor mental rehearsal. The primary outcome measure the Action Research Arm test assessed before and after treatment.	There were no differences among the treatment groups at baseline or following treatment on the Action Research Arm Test or on any of the secondary outcome measures.
Page et al. 2011 USA 6 (RCT)	29 subjects with chronic stroke, exhibiting stable, mild hemiparesis participated in 30-minutes of task-specific therapy 3 days/week for 10 weeks. Directly after these sessions, patients were randomly selected to receive audiotaped mental practice for 20, 40, or 60 minutes. Subjects assigned to a	Mental practice duration significantly predicted changes in FM scores (P = 0.05), with increasing duration related to larger increases (5.4 point score increase for the 60-minute duration group). There was a non-significant trend in ARAT score increases favoring the 20-minute dosing condition (4.5 point increase). Regardless of dosing condition, subjects who received mental practice exhibited markedly

	control group received an audiotaped sham intervention. Outcome measures included Fugl-Meyer (FM) motor assessment and Action Research Arm Test (ARAT) and were conducted twice at baseline and after treatment.	larger increases in both FM and ARAT scores than subjects not receiving mental practice, although the differences were not statistically significant.
Lee et al. 2012 Korea 5 (RCT)	26 patients within 6 mos of stroke were randomized to an experimental group (n = 13) or control group (n = 13). Patients in both groups participated in a standard rehabilitation program, 60 min, twice a day, and 5 days a week for 4 weeks. Patients in the experimental groups received an additional 25 min session of mental practice, twice a day. The Fugl-Meyer Assessment (FMA), Brunnstrom motor recovery stage, and Manual Function Test were used to assess changes in upper-limb motor recovery and motor function before and after intervention.	Patients in both groups improved over the study period, but patients in the experimental group achieved significantly greater gains in mean scores of: FMA (shoulder/elbow/forearm items, 9.54 vs. 4.61; wrist items, 2.76 vs. 1.07; hand items, 4.43 vs. 1.46, respectively); Brunnstrom stages for upper limb and hand (by 1.77 vs. 0.69 and 1.92 vs. 0.50, respectively); and Manual Function Test score (shoulder item, 5.00 vs. 2.23; hand item, 5.07 vs. 0.46, respectively).

Discussion

Page et al. (2000, 2001, 2005, 2007,2011) used a tape-recorded (guided) imagery intervention to enable mental practice, whereby patients would sit in a room quietly and listen to a male voice encouraging them to first relax (warm-up) and then to mentally perform a series of tasks (reaching for a cup). Patients mentally practised both at home and during supervised therapy sessions. Patients in both the control and intervention groups also received occupational therapy. Page et al. reported significant improvement in Fugl-Meyer scores (2000; 2007) and Action Research Arm tests (2005; 2007) between treatment and control subjects. A dose-response effect was observed among patients randomized to receive 20, 40 or 60 minutes of mental practice in terms of impairment, but not disability. Patients who received 60 minutes of mental practice achieved higher Fugl Meyer scores than patients who had received 40, who, in turn, received higher scores compared with those who had received 20 minutes. The same trend was not observed in Action Research arm test scores, although, as a group patients who had received any mental practice has higher scores on both tests compared to those who had received none. Patients in the study by Dijkerman et al. (2004) were asked to read a set of instructions directing them through a series of tasks. A placebo mental imagery condition was also used where patients were asked to describe a series of pictures, which had been presented previously. There was no difference between groups with respect to ADL performance, measured by the Barthel Index. The studies by Liu et al. (2004, 2009) had patients in the mental practice group practice a different series of mental tasks each week (i.e. week 1: wash the dishes, prepare tea, fold laundry) while patients in the control group (functional training program) practiced the same tasks having the therapist first demonstrate the task. This study reported a benefit of treatment in terms of improvement in ADL performance. Page et al. (2005) also demonstrated that mental practice, where patients cognitively rehearse ADL activities, improved motor function in the affected upper limbs of chronic stroke patients. The author suggests that the technique induces use-dependent brain reorganization to achieve the improvements in motor function. Mental practice also appeared to provide additive benefit when combined with the co-intervention of modified constraint-induced therapy (Page et al. 2009). Bovend'Eerdt et al. (2010) suggested that the poor compliance with the therapy was instrumental in the failure of patients to achieve significantly better outcomes. Ietswaart et al. (2011) reported there was no evidence of benefit associated with mental imagery. This study was larger than any of the previous ones and evaluated the potential benefit of mental in the absence of combined physical practice.

Conclusions Regarding Mental Imagery

There is conflicting (level 4) evidence that mental practice may improve upper-extremity motor and ADL performance following stroke.

Mental practice may result in improved motor and ADL functioning after stroke.

10.2.9 Hand Splinting

There are many aims when applying splints. These include: reduction in spasticity, reduction in pain, improvement in functional outcome, prevention of contracture, and prevention of edema (Lannin & Herbert, 2003).

The effectiveness of the use of splints to improve function is reviewed in this section. The use of splints to prevent the development of contracture, or reduce spasticity following stroke is reviewed in section 10.5.1.

In a systematic review of hand splinting for adults with stroke, Lannin and Herbert (2003) included the results from 19 studies, of which only 4 were RCTs. The authors concluded that there was insufficient evidence to either support or refute the effectiveness of hand splinting for a variety of outcomes for adults following stroke.

Tyson & Kent (2011) conducted a systematic review on the effect of upper limb orthotics following stroke, which included the results from 4 RCTs representing 126 subjects. The treatment effects associated with measures of disability, impairment, range of motion, pain, and spasticity were small and not statistically significant.

Table 10.17 Splinting the Upper Extremity

Author/ Country Pedro Score	Methods	Outcomes
Poole et al. 1990	18 patients with hemiplegia were matched according to upper extremity	No difference in motor function (Fugl-Meyer) in the wrist and hand after wearing the

5 (RCT)	motor scores on the Fugl-Meyer. Within each pair, subjects were then randomly assigned to either a non-splint or splint condition. The intervention group wore an inflatable pressure splint which positioned the shoulder in 90 degrees of flexion and maximum external rotation with full elbow extension (hand and wrist not enclosed in the splint) for 30 minutes/day.	inflatable pressure splint.
Lannin et al. 2003 Australia 8 (RCT)	28 rehabilitation patients were randomized to either control or experimental groups. Subjects in both groups participated in routine therapy for individual motor training and upper limb stretches 4 days a week. In addition, patients in the experimental group wore an immobilizing hand splint on a daily basis, for a maximum of 12 hours each night, for 4 weeks.	No difference in contracture formation in the wrist and finger flexor muscles between groups.
Lannin et al. 2007 Australia 7 (RCT)	63 stroke patients within 8 weeks of stroke onset were randomly allocated to receive 1 of 3 therapies: i.) no splint control group (n=21), ii.) a neutral splint group (n=20), or iii.) an extension splint group (n=21). All patients received routine rehabilitation. Splints were worn 12 hours overnight for the 4-week treatment period. The Primary Outcome was muscle extensibility of the wrist and fingers, assessed before/after treatment and at 6 weeks.	There were no significant differences between groups or within groups. Splinting did not reduce wrist contractures.
Bürge et al. 2008 Switzerland 5 (RCT)	30 hemiparetic patients with sub acute hemiparesis and severe upper limb deficits were randomized to 1) a standard rehabilitation program without orthosis 2) an experimental orthosis in addition to their standard rehabilitation program. The orthosis group wore the neutral functional realignment orthosis for at least 6 hours daily. Outcome measures assessed before, and at 13 weeks at the end of treatment included hand pain at rest (visual analog scale), wrist range of motion (Fugl-Meyer Assessment subscale), and edema of hand and wrist (circumferences).	At baseline, 2 patients in each group complained about a painful hand. After 13 weeks, 8 subjects in the control group and 1 subject in the orthosis group complained of hand pain. The number of patients presenting with a loss of wrist mobility increased in the control group (from 1 at baseline to 8 at 13 weeks) while remaining unchanged in the orthosis group (which remained at 4). In terms of hand edema, it remained unresolved in the one subject in the orthosis group while the number of subjects with hand edema increased from 1 to 2 in the control group.
Barry et al. 2012 USA 7 (RCT)	19 participants with moderate hemiparesis, an average of 4.5 yrs post stroke were randomly assigned to receive therapy while wearing a dynamic wrist-hand orthosis	There were no significant between-group differences for any of the measures. Within-group differences showed that the SaeboFlex group had a significant improvement in the ARAT score (mean = 2.2; P = 0.04). The MAT

	(SaeboFlex), or to a manual assisted therapy group (MAT), where participants performed therapy assistance from a therapist. Both groups participated in 1 hour of therapy per week for 6 weeks and were prescribed exercises to perform at home 4 days per week. Pre- and post training assessments included grip strength, the Action Research Arm Test (ARAT), Box and Blocks (B&B) test, and Stroke Impact Scale (SIS).	group had a significant improvement on the percent recovery on the SIS (mean = 9.3%; P = 0.03) and approached a significant improvement on the ARAT (mean = 1.4; P = 0.08).

Discussion

Since splinting has not been shown to effectively reduce spasticity or prevent contracture formation (see section 10.5.1), it is not surprising that it also appears not to be effective to help improve active function following stroke.

The use of the commercially available splint, the Saebo-flex has been evaluated in a single RCT (Barry et al. 2012). In this study, where the device was compared with a therapist assisted manual program that focused on grasp and release tasks, there were modest improvements in function for patients in both groups. However, on average, patients in neither group gained enough points to meet the minimal clinically important difference on either the ARAT or the Box or Block test.

Conclusions Regarding Splinting to Improve Hand Function

There is strong (Level 1a) evidence that hand splinting does not improve impairment or reduce disability.

Hand splinting does not improve motor function or reduce contractures in the upper extremity.

10.2.10 Constraint-Induced Movement Therapy

Constraint-Induced Movement Therapy (CIMT) refers to a new set of rehabilitation techniques designed to reduce functional deficits in the more affected upper extremity of stroke survivors. The two key features of CIMT are restraint of the unaffected hand/arm and increased practice /use of the affected hand/arm (Fritz et al. 2005). Since stroke survivors may experience "learned non-use" of the upper extremity within a short period of time (Taub 1980), CIMT is designed to overcome learned non-use by promoting cortical reorganization (Taub et al. 1999). While the biological mechanism(s) responsible for the benefit are unknown and the contribution from intense practice is difficult to disassociate from the contribution of constraining the good limb, this form of treatment shows promise, especially for survivors with moderate disability following stroke.

Several reviews have been published on the effectiveness of CIMT (Taub & Morris, 2001, Barreca et al. 2003, Hakkennes & Keating 2006, Bonaiuti et al. 2007) and while the results have been generally positive, uncertainty of its effectiveness remain due to the small number of trials published, the small sample sizes of the studies and heterogeneous patient characteristics, duration and intensity of treatment, and outcomes assessed. A meta-analysis conducted by Van Peppen et al. (2004) concluded that CIT was associated with improvements in dexterity, measured by the Arm Motor Activity Test or the Action Research Arm test, but not in performance of ADL, measured by FIM or Barthel Index scores. A more recent review by Hakkenes and Keating (2006) included the results from 14 RCTs and concluded that there was a benefit associated with treatment although larger well-designed studies are still required. Several treatment contrasts were examined including traditional CIT vs. alternative therapy or control, modified CIT vs. alternative therapy or control and traditional CIT vs. modified CIT, although pooled estimates of the treatment sizes for the subgroups were not provided. The associated pooled effect sizes for all of the included RCTs were: Action Research Arm test 1.51 (95% CI 0.27, 2.74), Fugl Meyer Assessment 1.16 (95% CI –0.18, 2.52) and the Wolf Motor Function Test 0.50 (95% CI –0.28, 1.27).

Taub et al. (2003) noted that constraint-induced movement therapy has limitations in that the improvement seen does not restore the stroke patients' movement to their motor status prior to the stroke. The same authors note that constraint-induced movement therapy "*produces a variable outcome that depends on the severity of initial impairment. If patients with residual motor function are categorized on the basis of their active range of motion, the higher functioning individuals tend to improve more than persons who are more disabled (Taub et al. 1999)…. For patients with the lowest motor functioning, constraint-induced therapy does improve movement at the shoulder and elbows. Because these people have little or no ability to move the fingers, there is no adequate motor basis for carrying out training of hand function. Consequently, because most daily activities that are carried out by the upper extremity are performed by the hand, there is relatively little translation of the therapy induced movement in proximal joint function into an increase in the actual amount of use of the more affected extremity in the real life situation… Thus, constraint-induced therapy is clearly not a complete answer to motor deficits after stroke. The work so far does show that motor function in a large percentage of patients with chronic stroke is substantially modifiable.*" (Taub et al. 2003). Van der Lee (2001) suggests that the positive results attributed to CIMT may simply reflect a greater intensity of training of the affected arm and questions the concept of non-use implying that it may not be a distinct entity, but rather the result of sensory disorders or hemineglect.

According to Dromerick et al. (2000), constraint of the unaffected arm by use of a mitten (6 hours per day for 14 days), and 'forced use' of the affected arm soon after stroke (mean six days), is feasible. However, trials reporting small, but significant reductions in arm impairment, especially for patients with sensory disorders and hemi-neglect (van der Lee et al. 1999, Ploughman & Corbett 2004), have also reported a high number of deviations from the randomized treatment schedule, due to patients' non compliance. This has led to trials investigating the effectiveness of modified or shorter periods of constraint induced therapy treatment.

There is promising evidence that the drawbacks to stroke patient participation in CIMT (i.e., required practice intensity and duration of restraint) may be overcome through modifications to the basic procedures. They include a less intense, modified CIMT (mCIMT) that combines structured functional practice sessions with restricted use of the less affected upper limb (Page et al., 2004), and also forced-use therapy (FUT) which employs constraint without intensive training of the affected arm ("shaping") (Ploughman & Corbett, 2004). Page et al. (2002, 2004 and 2005) provide one example of the distinction between CIMT and mCIMT: CIMT is defined by the i) restriction of a patient's less affected upper-limb during up to 90% of waking hours during a 2-week period and ii) participation in an intensive upper-extremity therapy program for 6 hours per day, using the affected limb during the same 2-week period. In contrast, mCIMT involves the restriction of the unaffected limb for periods of 5 hours a day, 5 days a week for 2 weeks combined with structured, ½ hour therapy sessions, 3 days a week. However, other criteria for defining mCIMT have also been used, which overlap with CIMT, blurring the distinction. Lin et al. (2007) cite mCIMT as providing 2 hours of therapy a day for 10-15 consecutive weekdays + restraint for 6 hours per day. There are also examples of trials, presented in the following tables, which provided the intervention for periods of up to 10 weeks.

There is some evidence, too, for the beneficial effect of donepezil, a primarily central acetylcholinesterase inhibitor, as an adjuvant therapy (Nadeau et al., 2004; Richards et al. 2006). Taub et al. (2005) recently reported that the benefits associated with CIMT could be achieved with the use of an automated device (AutoCITE). The optimal timing of treatment remains uncertain. While there is evidence that patients treated in the acute phase of stroke may benefit preferentially (Taub & Morris 2001), there is also evidence that it may, in fact, be harmful (Dromerick et al. 2009). Grotta et al. (2004) suggest that the greatest benefit is likely to be conferred during the chronic stages of stroke and that the treatment has been shown to be harmful in animal studies of "forced use" immediately post stroke.

The results from the largest and most rigorously conducted trial-*The Extremity Constraint Induced Therapy Evaluation (EXCITE)*, may provide the strongest evidence of a benefit of CIMT treatment, to date. The study recruited 222 subjects with moderate disability 3 to 9 months following stroke, over 3 years from 7 institutions in the US. Treatment was provided for up to 6 hours a day, 5 days a week for 2 weeks. Patients were reassessed up to 24 months following treatment. At 12 months, compared with the control group who received usual care, subjects in the treatment group had significantly higher scores on sections of the Wolf Motor Function test and the Motor Activity Log. At 24 months these gains were maintained. While these results are encouraging, as Cramer (2007) points out, the number of patients for whom this treatment may be suitable for, remains uncertain. In the EXCITE trial, only 6.3% of patients screened were eligible. While larger estimates of 20-25% have been suggested, it remains uncertain if subjects with greater disability would benefit from treatment.

A recent Cochrane review (Sirtori et al. 2009) examined the benefit of all forms of CIMT including studies that used the traditional protocol as described by Taub, in addition to trials of modified CIMT and forced use. The review included the results from 19 trials involving 619 subjects. The primary outcome was disability. The authors reported that there was a significant improvement in arm motor function, assessed immediately following the intervention, but not at 3-6 months post-intervention. A subgroup analysis compared the benefit of CIMT in terms of time since stroke onset (0-3 months and >9 months). No studies were included that measured disability 3-9 months following stroke. The associated effect sizes were not statistically significant for either subgroup. The authors caution that the findings cannot be considered robust due to the small sample sizes and poor methodological quality of the primary studies.

The same group of authors (Corbetta et al. 2010) updated their Cochrane review and included the results from 4 recently published trials. Disability was the primary outcome. Among the 8 studies (n=276) that included an upper extremity assessment of function, or an ADL instrument, there was no significant treatment effect associated with CIMT. There was a moderate treatment effect associated with arm motor function. However, this review did not include sub analysis based on chronicity of stroke or type of CIMT treatment (i.e. forced use vs. traditional CIMT vs. modified CIMT).

Shi et al. (2011) conducted a review examining modified CIMT compared with traditional rehabilitation strategies. The results from 13 RCTs (278 patients) were included. The mean differences in scores favoured patients in the CIMT group on the following outcome measures: Fugl-Meyer Assessment (7.8), Action Research Arm test (14.2) FIM (7) and the Motor Activity Log (amount of use: 0.78), suggesting that the treatment can be used to reduce post stroke disability. The authors noted that none of the included RCTs included information on compliance with the study protocol.

Nijland et al. (2011) conducted a systematic review of CIMT, limited to trials that evaluated the effectiveness of treatment initiated within the first 2 weeks of stroke. The review included the results from 5 RCTs (106 subjects). There was evidence of a benefit of treatment assessed using the Action Research Arm test, Fugl-Meyer (arm section) and the Motor Activity Log. Although there were only a small number of studies that examined the contrast, the authors suggested that low-intensity (<3 hours of therapy/day) CIMT was superior to high-intensity (>3 hours of therapy/day) CIMT.

Peurala et al. (2011) examined the impact of CIMT and mCIMT on activity and participation measures, as defined by the ICF. The review included the results from 30 trials. The authors identified 4 broad categories of treatment intensity: 60-72 and 20-56 hours over 2 weeks, 30 hours over 3 weeks and 15-30 hours over 10 weeks. Significant improvements were associated with Motor Activity Log scores for all intensity categories. Of the other outcomes examined, including the FIM, Wolf Motor Function test scores, Action Research Arm test and the Stroke Impact Scale, not all treatment categories were represented. Action Research Arm test scores were significantly improved at both treatment intensity categories that were assessed (20-56 hrs x 2 weeks & 15-30 hrs x 10 weeks). FIM scores were significantly increased in only 1 of 3 treatment intensity categories (15-30 hours x 10 weeks) and there were no significant improvements in SIS scores, regardless of treatment intensity.

Studies examining modified CIMT and CIMT, as well as several studies that examined forced use therapy are presented in Table 10.18.

Table 10.18 Studies Evaluating Constraint-Induced Movement Therapy

Author, Country Pedro Score	Methods	Outcomes
Taub et al. 1993 USA 6 (RCT)	9 patients randomized to either have their unaffected upper extremity restrained in a sling during waking hours for 14 days with 10 of those 10 days patients given 6 hours of practice in using impaired upper extremity or to receive several procedures designed to focus attention on use of the impaired upper extremity (control).	Restraint group showed significantly greater improvement in quality of movement and functional ability compared to control on Emory Test and the Arm Motor Activity Rest test at the end of treatment. Motor Activity Log indicates that the restraint group showed a marked increase in their ability to use their affected upper extremity. Gains made during treatment period were maintained during 2 year follow up.
van der Lee et al. 1999 Netherlands 7 (RCT)	In an observer blind trial, 66 patients were randomized to receive either forced use therapy with immobilization of the unaffected arm combined with intensive treatment or to receive intensive bimanual training based on Neuro-Development Treatment.	Mean improvement on Action Research Arm in patients with sensory disorder was significantly greater in those receiving forced use rather than bimanual training. During treatment, force use patients also showed greater clinical significant improvement on Motor Activity Log than bimanual training patients.
Dromerick et al. 2000 USA 6 (RCT)	20 acute, stroke inpatients were randomized to receive either CI movement therapy or traditional upper extremity therapies for two weeks.	Total Action Research Arm scores were significantly higher in patients who received CI treatment. FIM score for upper body dressing was also significantly improved.
Sterr et al. 2002 UK 4 (RCT)	15 stroke patients with chronic hemiparesis were randomized to 2 training groups for 14 days -group 1: standard receive constraint–induced movement therapy (CIMT) plus 6 hours of daily 'shaping procedure' 2: CIMT plus 'shaping procedure' for 3hrs/day. Assessments of Motor Activity Log (MAL) and Wolf Motor Function Test (WMFT).	Assessments were performed at baseline, pre-treatment, post-treatment and weekly follow-up for 4 weeks. MAL: Both groups improved over time ($p<0.01$), with a greater treatment effect for the 6 hrs group, compared to the 3 hr group. ($p<0.05$).
Page et al. 2002 USA 5 (RCT)	14 stroke patients an average of 4.4 months post stroke were randomized to receive one of three treatments: 1) modified constraint-induced therapy (mCIT): 30 min each of physical and	After the intervention mCIT patients had significantly improved Fugl-Meyer scores (+11, p=.02). Patients in the mCIT group also improved 11 points on the Action Research Arm test. Patients in the TR and CON groups

	occupational therapy 3x per week for 10 weeks + mCIT program, 2) traditional rehab (TR) :30 min each of physical and occupational therapy for 10 weeks or 3) Control (CON): no therapy.	did not demonstrate significant improvement.
Wittenberg et al. 2003 USA 5 (RCT)	16 stroke patients more than 1 year post stroke with significant impairment indicated by the Motor Activity Log were randomized to receive intense or less intense CIMT. The intense group received CIMT for 10 continuous inpatient days for 6 hrs/day (4 hrs/day on weekends). The less intense group received CIMT 3 hrs/day on weekdays only. Outcome measures included: Wolf Motor function test, Motor activity Log, Assessment of Motor and Process Skills, transcranial Magnetic stimulation and Positron emission tomography.	There was no significant difference between groups on the Wolf Motor function test, the Assessment of Motor and Process Skills, transcranial Magnetic stimulation or Positron emission tomography. However, both groups did show statistically significantly improvements in the above outcome measurements. There was however a significant difference in favour of the more intense CIMT group in the Motor activity Log scores.
Alberts et al. 2004 USA 6 (RCT)	10 right-handed stroke patients (3-9 months post stroke) from the ongoing EXCITE trial (with 222 patients in total) were randomized to 1 of 2 groups: 1) immediate constraint-induced therapy (CIT): patients began CIT approximately 3 days after pre-intervention evaluations or 2) delayed CIT: patients received CIT approximately 1 year after pre-intervention evaluations; therapy took place over a 2 week period and patients wore a soft mitt for a goal of 90% of waking hours.	Overall change in WMFT median time was nearly significant (p=0.07). The immediate CIT group reduced movement time to perform the key-turning task to 47% after CIT, whereas the delayed group required 15% more time after CIT. The maximum precision grip force and maximum strength from pretest to post-test were statistically significant group-by-time interactions for the intermediate group.
Atteya et al. 2004 Saudi Arabia 3 (RCT)	6 stroke patients (<6 months post stroke) were randomly divided into 3 groups of 2: 1) constraint induced therapy (CIT): patients received 30 min of physical therapy and occupational therapy 3x per week for 10 weeks + mCIT program, 2) traditional rehab (TR): 30 min of physical and occupational therapy for 10 weeks or 3) Control (CON): no therapy	The CIT group showed substantial improvements on the Fugl-Meyer Assessment of Recovery After Stroke, the Wolf Motor Function Test and the Motor Activity Log from pre to post treatment. No tests of statistical significance were conducted.
Page et al. 2004 USA 6 (RCT)	17 patients with chronic stroke (1 year post stroke) were randomly assigned to one of 3 groups: 1) modified constraint-induced therapy (mCIT): 30 min each of physical and occupational therapy 3x per week for 10 weeks + mCIT program, 2) traditional rehab (TR) :30 min each of physical and occupational therapy for 10 weeks or 3) Control	The mCIMT patients had significantly greater motor changes on the Fugl-Meyer scores and on the Action Research Arm test than those in the two other groups.

	(CON): no therapy.	
Ploughman & Corbett 2004 Canada 5 (RCT)	23 stroke patients were randomized into a forced-use therapy (FUT; constraint without shaping) group (n=10) and a control group (conventional treatment for the upper extremity; n=13).	FUT participants had greater recovery of postural control (Chedoke McMaster Impairment Inventory, CMII) (p=.04), and more shoulder pain, than did controls. CMII mean scores suggested greater clinical recovery for the arm and hand for FUT participants, but the results were not statistically significant.
Suputtitada et al. 2004 Thailand 6 (RCT)	69 chronic stroke patients were allocated either to constraint-induced movement technique (CIMT) (n = 33) or conservative treatment (n = 36). The CIMT group received 6 hours of daily affected-upper-extremity training and restrained unaffected upper extremities for 5 days per week, totally 2 weeks. The control group received bimanual-upper-extremity training by conservative neurodevelopmental technique without restrained unaffected upper extremities for 2 weeks. Assessments included the Action Research Arm Test (ARA test), hand grip strength, pinch strength of affected upper extremity	ARA scores, pinch strength of affected upper extremities were significantly higher for CIMT patients compared to the control group. There were no statistically significant differences between the groups in hand grip strength.
Brogårdh & Bengt 2006 Sweden 7 (RCT)	16 chronic stroke patients underwent 2 weeks of constraint-induced movement therapy in groups of 2-3 patients per therapist for 6 hours/day. Each wore a mitt on the unaffected hand for a target of 90% of waking hours. Patients were randomly assigned into 1 of 2 groups: 1) Using the mitt at home for an additional 3 months every other day, 2) no further treatment.	There was significant improvement for the Modified Motor Assessment Scale (p=0.003), the Sollerman Hand Function Test (p=0.037), and the Motor Activity Log (p<0.001) after the 2 week CIMT treatment period. However, there were no significant differences between groups at the end of 3 months.
Page et al. 2005 USA 5 (RCT)	10 acute stroke patients with upper limb hemiparesis and within 14 days of stroke were randomized to receive constraint-induced movement therapy (CIT) or regular rehabilitation. Patients in the CIT group received ½ hr therapy sessions, 3X/week for 10 weeks. During this time patients' unaffected arm and hand was restrained everyday for 5 hours. Patients in the regular rehabilitation group received standard therapy for their affected limbs. Fugl-Meyer, Action Research Arm test and Motor Activity Log tests were conducted at week 10.	Improvements in both Action Research Arm test and Fugl Meyer Scale from pre to post treatment. No between group differences were reported.
Ro et al. 2006 USA	8 patients within 14 days of stroke were randomly assigned to receive two	The mean GPT and FM scores were higher among patients in the control group at both

6 (RCT)	weeks of CIMT (3 hrs/day x 6 days/week) or traditional therapy. Motor performance was assessed before and after treatment and at follow-up (3 months) and included the Grooved Pegboard test (GPT), Fugl-Meyer Assessment (FM) and the 30-item Motor Activity Log.	the end of treatment and follow-up (1 patient in the control group did not complete the 3-month follow-up). There were no differences in the mean MAL scores at either assessment point.
Taub et al. 2006 USA No score	41 chronic stroke patients (>1 yr post-stroke) were assigned either to a constraint-induced movement therapy for patients with mild to moderate deficit following stroke (n=21) or a placebo control group who underwent a general fitness program (n=20). CI therapy received intensive training of the more affected upper extremity for 6 hours/day, for 10 consecutive days which included 'shaping' procedures, restraint of less affected extremity for a target of 90% waking hours during a 2-treatment period.	There were significant improvements in the Wolf Motor Function Test, the Motor Activity Log, and the Actual Amount of Use from pre-treatment to post-treatment. In addition, females showed greater gains on MAL then males in the CI therapy group (p=0.02). At 2-year follow-up significant improvements were still seen on the MAL relative to post-treatment for the treatment group.
Richards et al. 2006 USA 7 (RCT)	39 chronic unilateral stroke individuals with hemiparesis were randomly assigned to receive traditional CIMT plus donepezil or placebo (CIMT-6), who underwent the standard 6 hours of therapist-guided, in-clinic task practice (n=16) or shortened CIMT along with repetitive transcranial magnetic stimulation or sham stimulation (CIMT-1) who underwent a single hour of in-clinic task practice (n=19). Treatment continued for 2 weeks. Outcome Measures included the Wolf Motor Function Test and the Motor Activity Log and were assessed before/after treatment and at 6 months.	The CIMT-6 group showed significant improvement in use (P<0.001) and movement quality (p<0.004) compared to the CIMT-1 group. However, after 2 weeks of therapy motor skill gains for both groups were equivalent and at six months both groups did not maintain the gains made.
Wolf et al. 2006 USA 8 (RCT) EXCITE Trial	222 patients between 3 to 9 months post stroke received either CIMT (n=106) or usual care (no treatment, home care or outpatient programs) (n=116). The CIMT group wore a mitt on the less-affected hand while performing repetitive task practice and behavioural shaping with the hemiplegic hand). Outcome measures included the Wolf Motor Function Test (WMFT), Motor Activity Log (MAL), functional ability measures, a measure of the quality and frequency of the performance of 30 standard daily activities. Assessments were conducted before/after treatment and at 4, 6 and	The CIMT group significantly improved in the WMFT (log performance time, functional ability 0-5 scale (p<0.001), the MAL Amount of Use (p<0.001) and the MAL Quality of Movement (p<0.001) and caregiver MAL. (Group x time interaction).

	12 months.	
Underwood et al. 2006 USA 8 (RCT)	The results from 41 individuals recruited from a single centre of the EXCITE trial were evaluated. Outcome measures were assessed before and after treatment including the pain scale of the Fugl-Meyer test for upper extremity and the WMFT.	Fatigue and pain scores for all participants were low. Patients receiving CIMT did not have significantly increased pain or fatigue compared with those in the control group.
Uswatte et al. 2006 USA No Score	18 chronic stroke patients were consecutively assigned to 1 of 4 groups: i.) Sling and Task-practice (n=4), ii.) Sling and Shaping (n=5), iii.) Half-glove and Shaping, iv.) Shaping Only (n=4). Task-practice occurred 6 hr/day for 2 weeks and incorporated using the affected arm to carry out repetitive arm training on functional tasks. Patients who underwent shaping treatment were given feedback immediately after tasks preformed and tasks became increasingly more demanding over the 2 week period. Outcome measures included Motor Activity Log and the Wolf Motor Function Test and were assessed before/after treatment and at 1-month and 2 years.	One form of treatment did not emerge as superior. For all groups combined there was a significant improvement from pre-treatment in MAL scores (1.6 vs. 3.1 at 2 years, $p<0.05$).
Boake et al. 2007 USA 5 (RCT)	23 patients within 2 weeks of stroke were randomly assigned to receive either 2 weeks of CIMT (n=10) or traditional rehabilitation (n=13). Both given at the same frequency of up to 3 hours daily. Outcome measures include Fugl-Meyer (FM) Assessment, Grooved Pegboard Test, and Motor Activity Log (MAL), assessed before/after treatment and at 3 months.	Patients in both groups improved but there were no statistically significant differences between groups, although there was a trend in favour of CIMT over traditional therapy.
Burns et al. 2007 UK No Score	In an A-B-A designed trial, 10 subjects with a mean onset time of 6.1 months post stroke wore a constraint mitten on the unaffected upper limb for 9 waking hours/day for two weeks to encourage use of the hemiplegic arm. Existing levels of therapy continued during the entire study. The primary outcome measure was the Action Research Arm Test (ARAT), which was assessed twice at baseline and at 4 and 6 weeks following intervention.	A mean improvement in ARAT scores of 4.0 points (95% confidence interval 1.7 to 6.2; P=00.016) was found following intervention (correcting for background recovery). The improvement was just below that associated with a clinically significant improvement. Mean compliance was 6.7 hours/day
Lin et al. 2007 Taiwan 7 (RCT)	32 patients with a mean post-stroke onset time of 16.3 months were randomized to receive modified CIMT (restraint of the unaffected limb or	There were moderate and significant effects of modified CIMT compared with the control group on the following kinematic variables: reaction time, percentage of movement time

	traditional rehabilitation for three weeks). Kinematic analysis was used to assess motor control characteristics as patients reached to grasp a beverage can. Functional outcomes were evaluated before and after treatment using the Motor Activity Log (MAL) and FIM.	where peak velocity occurs. The mCIMT group also showed significantly improved functional performance on the MAL (amount of use: 2.04 vs. 0.93 and quality of movement: 2.30 vs. 0.99) and FIM scores (113 vs. 106).
Wu et al. 2007a) Taiwan 5 (RCT)	26 stroke patients (0.5 to 31 months post stroke) were randomized to receive 3 weeks of either modified CIMT (mCIMT) (n=13) or traditional occupational therapy (n=13). Both groups received 2-hour therapy sessions 5 days a week. The patients in the mCIMT group received intensive therapy combined with the use of a restraining mitt on the unaffected hand. Outcome Measures: Fugl-Meyer (FM) Assessment, FIM instrument, Motor Activity Log (MAL), and Stroke Impact Scale (SIS) were assessed before and after treatment.	Significantly greater improvements were seen for the mCIMT group in FM, FIM, MAL and 3 components of the SIS.
Wu et al. 2007 b) Taiwan 6 (RCT)	30 stroke patients (mean of 18 mos post stroke) were randomized to receive a course of modified CIMT with intensive therapy for 2 hrs, 5 x/wk for 3 weeks + wearing a mitt for 6 hours a day or traditional rehabilitation. Kinematic analyses and clinical assessments including the FIM and the Motor Assessment Log (MAL) were measured before and after treatment.	Patients receiving mCIMT showed greater improvements in reaching kinematics, although the effect was modest. MAL scores were also significantly higher for both amount of use (2.32 vs. 1.45) and quality of movement (2.32 vs. 1.63). FIM scores were significantly higher in the treatment group (107 vs. 98).
Wu et al. 2007 c) Taiwan 6 (RCT)	47 patients with stroke onset of 3 weeks to 37 months (mean 12 months) were randomized to receive either CIMT (restraint of the less affected hand combined with intensive training of the more affected upper extremity) or traditional intervention (control treatment) during the study. The treatment intensity was matched between the 2 groups (2h/d, 5d/wk for 3wk) + the treatment group wore a mitt for 6 hours a day during the study period. Outcomes assessed before and after treatment included kinematic variables of reaching movement used to describe the control strategies for reaching, the Fugl-Meyer Assessment (FMA) and the Motor Activity Log (MAL).	After treatment, the CIMT group showed better strategies of reaching control than the control group as demonstrated by a bell-ringing test. MAL scores were also significantly higher in the mCIMT group for both amount of use (1.85 vs. 0.81) and quality of movement (1.85 vs. 1.08). There were no significant differences in FMA scores (47 vs. 45).
Dahl et al. 2008	30 patients with mean stroke onset of 17 months were randomized to receive	At the end of treatment, the CIMT group showed a significantly shorter performance

Norway 8 (RCT)	CIMT training: 6 hours of arm therapy for 10 consecutive weekdays, while using a restraining mitten on the unaffected hand for 90% of waking time (n=18) or community-based rehabilitation (n=12). Primary outcome assessed at the end before and after treatment and at 6 month follow-up was the Wolf Motor Function Test (WMFT). Secondary outcomes were the Motor Activity Log (MAL), FIM and Stroke Impact Scale (SIS).	time (4.76 seconds versus 7.61 seconds, p= 0.030) and greater functional ability (3.85 versus 3.47, P= 0.037) than the control group (n=12) on the WMFT. At follow-up the CIMT group maintained their improvement, but as the control group improved even more, there were no significant differences between the groups on any measurements. There were no significant differences between the groups at either the end of treatment, or at follow-up on any of the secondary outcomes.
Wolf et al. 2008 USA 8 (RCT)	Further results from the EXCITE trial, which assessed outcomes at 24 months. Only the 106 patients who were randomized to receive immediate CIMT were included in this analysis.	The drop out rate was 34% at 24 months. The effects at 24 months either improved or remained stable compared with those at 12 months for all domains of the WMFT, the MAL and for all domains of the SIS scale, except memory and thinking.
Sawaki et al. 2008 USA 3 (RCT)	30 subjects (>3 and <9 months poststroke) were randomized into 2 groups: 1) the experimental group received CIMT immediately after baseline evaluation, 2) the control group where subjects received CIMT after 4 months. The primary outcome measure, the Wolf Motor Function Test (WMFT) was assessed at baseline, 2 weeks after baseline, and at 4-month follow-up	Both experimental and control groups demonstrated improved hand motor function 2 weeks after baseline. The experimental group showed significantly greater improvement in grip strength after the intervention and at follow-up, but not on the overall WMFT or on the force-based measure.
Myint et al. 2008 Hong Kong 7 (RCT)	43 patients, 2-16 weeks post stroke with hemiparesis of the affected limb, were randomized to receive a program of 10 days upper extremity training (4 hours per day) with the unaffected limb being restrained in a shoulder sling (intervention group, n=23) or to a control group which received an equivalent duration of conventional rehabilitation therapy (n=20). Primary outcomes were assessed at baseline, post-intervention and at 12 weeks follow-up and included the Motor Activity Log (MAL), Action Research Arm Test (ARAT) and modified Barthel Index (BI).	The intervention group scored higher over the study period on both subscales of the MAL test and on total ARAT scores. They also scored higher on all of the subscales of the ARAT at the end of intervention: grasp, grip, pinch and gross, although only grip subscale scores were significantly better at 12 weeks follow-up.
Page et al. 2008 USA 5 (RCT)	35 patients with chronic stroke (onset >12 mos) were randomized to 1 of 3 groups for a 10 week course of treatment: i) mCIMT group (n=13), ii) a traditional rehab group (n=12) and iii) a no treatment control group (n=10). Outcome measures were assessed before and after treatment	There was no significant treatment effect for FM scores. Controlling for pre-intervention scores there was a significant treatment effect on ARAT scores favouring the mCIMT group (40 vs. 29. vs. 25)

	and included the Fugl Meyer (FM) scale scores and the Action Research Arm Test (ARAT)	
Lin et al. 2008 Taiwan 5 (RCT)	22 chronic stroke patients (mean time post onset of stroke = 18.9 months) were randomized to receive CIMT (restraint of the less affected limb combined with intensive training of the affected limb) or traditional intervention (control treatment) for 2h/d, 5d/wk for 3 wk. Both groups of patients received restraint of the less affected limb outside rehabilitation. Outcomes assessed before and after treatment included Fugl-Myer Assessment (FMA), the Motor Activity Log (MAL), FIM and the Nottingham extended activities of daily living scale (NEADL).	The mean improvement was greater for subjects in the CIMT group in terms of FMA and FIM scores. There were no significant differences between groups on the outcomes of MAL and NEADL, with the exception of the mobility subsection.
Hammer & Lindmark 2009a Sweden 6 (RCT)	30 patients, between 1 and 6 months post stroke, were randomized to a forced use or conventional therapy group. The patients of both groups participated in two weeks of daily training on weekdays. In addition, the forced use group wore a restraining sling on the non-paretic arm for up to 6 hours per weekday. The primary outcome measure was the Motor Activity Log (MAL), assessed one and three months after intervention.	Subjects in both groups received similar amounts of therapy. The mean duration of sling wear was 37.4 hours. There were no significant differences between groups. There was a trend towards higher scores in the forced-used group immediately post-intervention, but these small differences also leveled out up to the three-month follow-up, with both groups earning an approximately 1.0 score point on both scales of the MAL (amount of use and quality of use).
Hammer & Lindmark 2009b Sweden 6 (RCT)	Additional outcomes reported. The Fugl-Meyer (FM) test, the Action Research Arm Test, the Motor Assessment Scale (MAS) (sum of scores for the upper limb), a 16-hole peg test (16HPT), a grip strength ratio (paretic hand to nonparetic hand), and the Modified Ashworth Scale were used to obtain measurements.	There were no significant between group differences on any of the outcomes assessed. Subjects in both groups demonstrated improvements over the study period.
Brogårdh & Bengt 2009a Sweden 7 (RCT)	4-year follow-up from 2006 study. 14 of the original 16 subjects participated. However, the 2 original study groups (continued mitt use for 21 days vs. no mitt use) following 12 days of CIT were collapsed to one.	There was no significant change in the median score of the Sollerman hand function test (50.1 points after CIT therapy, with a gain of 2.3 points 4 years later). Both components of the Motor Activity Log scale had decreased significantly over time: Median Amount of use MAL score before CIT was 2.8, which decreased by 0.6. Median Quality of Movement score was 2.6 after CIT and decreased by 0.4 points.
Brogårdh et al. 2009b Sweden 5 (RCT)	24 subjects, an average of 7 weeks post stroke with mild to moderate impaired hand function, were randomized to mitt use or no mitt use	Patients in both groups showed significant improvements in arm and hand motor performance and on self-reported motor ability after 2 weeks of therapy and at 3

	on the less affected hand for 90% of waking hours for 12 days. All patients received 3 hours of arm and hand training per day for 2 weeks. Assessments included the modified Motor Assessment Scale, the Sollerman hand function test, the 2-Point Discrimination test and Motor Activity Log test.	months follow-up. However, no statistically significant differences between the groups were found in any measures at any point in time.
Lin et al. 2009 Taiwan 5 (RCT)	32 patients within 6 to 40 months after onset of a first stroke were randomized to 2 groups: CIT (restraint of the less affected limb combined with intensive training of the affected limb) for 2 hours daily 5 days per week for 3 weeks and restraint of the less affected hand for 5 hours outside of the rehabilitation training) or a conventional intervention with hand restraint for the same duration (similar protocol to 2008a study). Outcomes assessed before and after treatment included Fugl-Myer Assessment (FMA), the Motor Activity Log (MAL), FIM and the Nottingham extended activities of daily living scale (NEADL) and Stroke Impact Scale (SIS).	The mean improvement was greater for subjects in the CIMT group in terms of FMA, FIM, NEADL, and total SIS scores. There were no significant differences between groups on MAL.
VECTORS Dromerick et al. 2009 USA 6 (RCT)	Very Early Constraint-Induced Movement during Stroke Rehabilitation (VECTORS). 52 subjects were randomized to one of 3 groups an average of 9.7 days following stroke: 1) standard CIMT received 2 hours of shaping therapy and wore a mitt for 6 hours per day; 2) high-intensity CIMT, 3 hours of shaping exercise /day + wearing mitt 90% of waking hours; or 3) control treatment consisting of 1 hour of ADL training and 1 hour of UE bilateral training exercises. All treatment was provided for 2 weeks. The primary endpoint was the total Action Research Arm Test (ARAT) score on the more affected side at 90 days after stroke onset.	All groups improved with time on the total ARAT score. There was a significant time x group interaction. Subjects in the standard CIMT and control treatment groups achieved similar gains in total ARAT score (24.2 and 25.7, respectively), while subjects in the high-intensity CIMT group gained an average gain of only 12.6 points.
Azab et al. 2009 Jordan No Score	27 stroke subject an average of 81-87 days post stroke received outpatient therapy for 4 weeks (40 minutes 3x/week). Subjects received either conventional or CIMT therapy. The experimental/treatment group received traditional therapy with the CIMT where the intact contralateral upper limb was placed in a removable cast for 6 hours a	At the end of treatment the CIMT group had achieved higher BI scores compared with the control group (96 vs. 79, $p<0.05$).

	day during waking hours. The control group received traditional therapy only. Both groups were assessed using the Barthel Index on admission and on discharge from rehabilitation.	
Lin et al. 2010 Taiwan 5 (RCT)	13 patients at least 3 months post stroke were randomized to 2 groups: CIT (restraint of the less affected limb combined with intensive training of the affected limb) for 2 hours daily 5 days per week for 3 weeks and restraint of the less affected hand for 5 hours outside of the rehabilitation training) (n=5) or a conventional intervention with hand restraint for the same duration (similar protocol to 2009 study)(n=8). Outcome measures included the Fugl-Meyer Assessment (FMA), the Motor Activity Log (MLA), and functional magnetic resonance imaging (fMRI) examination assessed before and after treatment.	Patients in the CIT group had significantly higher scores on both the FMA and MAL at the end of treatment compared with the control group. The fMRI data showed that distributed form of constraint-induced therapy significantly increased activation in the contralesional hemisphere during movement of the affected and unaffected hand. The control intervention group showed a decrease in primary sensorimotor cortex activation of the ipsilesional hemisphere during movement of the affected hand.
Wolf et al. 2010 USA 8 (RCT)	Further results reported from the EXCITE trial whereby the outcomes of subjects who received treatment immediately following randomization (3 to 9 months) were compared with those who received delayed treatment (15 to 21 months). The primary outcomes were the Wolf Motor Function Test (WMFT) and the Motor Activity Log (MAL). The secondary outcome was the Stroke Impact Scale (SIS). Outcomes were assessed before and after treatment and at 4, 8, and 12 months later.	106 subjects received early treatment and 86, delayed. The earlier CIMT group showed significantly greater improvement compared with the delayed group on the WMFT and the MAL. SIS Hand and Activities domains scores were also significantly higher among subjects in the early group. Early and delayed group comparison of scores on these measures 24 months after enrollment showed no statistically significant differences between groups.
Hayner et al. 2010 USA 4 (RCT)	12 community-dwelling adults with chronic stroke were randomized to a program of either bilateral arm training (BAT) or modified CIMT for 6 hr each day for 10 days plus additional home practice. Assessments included the Wolf Motor Function Test (WMFT) and the Canadian Occupational Performance Measure (COPM) and were administered before and after treatment and at 6-mo follow-up.	Over the study period patients in both groups experienced significant improvement on both outcomes, but there were no significant between-group differences.
Wu et al. 2011 Taiwan 5 (RCT)	66 chronic stroke patients (mean of 16 months post onset) with mild to moderate motor impairment were randomized to a regimen of distributed constraint-induced movement therapy (dCIT), bilateral arm training (BAT), or	The dCIT and BAT groups had smoother reaching trajectories in the unilateral and bilateral tasks than the CT group. The BAT group, but not the dCIT group, generated greater force at movement initiation than the CT group during the unilateral and bilateral

	routine therapy (control group)(CT). Each group received treatment for 2 h/d and 5 d/wk for 3 weeks. Assessments were conducted before and after the treatment period and included reaching kinematic variables in unilateral and bilateral tasks, the Wolf Motor Function Test (WMFT), and the Motor Activity Log (MAL).	tasks. Patients in the dCIT group performed better on the MAL and WMFT compared with patients in either the control or BAT groups.
Wang et al. 2011 China 4 (RCT)	30 hemiparetic patients an average of 11 weeks following stroke were randomly divided into 3 groups that received treatment 5 days a week for 4 weeks: conventional rehabilitation (45 min/day) , intensive conventional rehabilitation (3 hrs/day), and modified constraint-induced movement therapy (CIMT)(3 hrs/day). Motor function was assessed using the Wolf Motor Function Test (WMFT) before treatment, and 2 weeks and 4 weeks after treatment.	Patients in the CIMT group and intensive groups improved their WMFT significantly more than the conventional rehabilitation group after 2 weeks of treatment ($p < 0.05$), but all groups reached comparable levels at the end of 4 weeks of intervention. The median performance time of the Wolf Motor Function Test decreased significantly in all groups after 4 weeks of treatment ($p < 0.05$), but only the modified constraint-induced movement therapy group showed significant improvements both 2 and 4 weeks after the initiation of treatment.
Khan et al. 2011 Switzerland 6 (RCT)	44 patients with minimal to moderate arm function an average of 10 months following stroke were referred for inpatient rehabilitation and were randomized to one of three groups: conventional neurological therapy, CIMT or therapeutic climbing. Patients in all groups received 15-20 hours per week of therapy for an average of 4 weeks. Primary outcomes were the Wolf Motor Function Test (WMFT) and the Motor Activity Log (MAL) assessed at baseline, post intervention and at 6 months.	Patients in the CIMT group demonstrated the greatest improvement on the WMFT compared with patients in the other two groups and were less likely to report shoulder pain at the end of 6 months.
Fuzaro et al. 2011 Brazil 5 (RCT)	37 patients an average of 25 months following stroke were randomized to a forced use (FU) group, and were fitted with a tubular mesh stocking fitted over the non-paretic hand and arm for 23 hrs a day, 6 days a week for 4 weeks or to a mCIMT group that received 50 min of therapy/day for 5 weeks in addition to the restraint. Outcomes were assessed at baseline, and then weekly until the end of the treatment period and at 1, 2 and 3 months follow up. The focus of this study was on balance and gait improvements. Outcomes were the Berg Balance Scale, the Stroke Impact Scale, 10 m walk test and Timed Up & Go.	Patients in both groups improved over the treatment period. Improvements were maintained at follow-up.
Huseyinsinogl	24 patients with stroke onset within the	Although patients in both groups improved

u et al. 2012 Turkey 6 (RCT)	previous 12 months were randomized to receive constraint-induced movement therapy for 3 hours/day x 10 weekdays with the less affected hand restrained for 90% of waking hours for 12 days or Bobath concept training for 1 hour/day x 10 weekdays. The primary outcome was the Wolf Motor Function Test assessed before and after treatment. Secondary measures included Motor Activity Log-28, the Motor Evaluation Scale for Arm in Stroke Patients and FIM.	over the treatment period, there were no significant differences between groups on any of the outcomes except for the MAL, for both amount of use and quality of movement (P = 0.003; P = 0.01, respectively).
Treger et al. 2012 Israel 7 (RCT)	28 patients an average of 23 and 40 days post stroke admitted for inpatient rehabilitation were randomized to receive conventional rehabilitation 1 hour/day each weekday (control group) or, in addition to receive dose-matched mCIMT for 2 weeks (wearing a mitt for 4 hours/day + a series of functional tasks). Outcomes, assessed at baseline and 1 month follow up included performance on 3 tasks (peg transfer, ball grasping and eating with a spoon).	Patients in the mCIMT group performed significantly better on all 3 tasks compared to patients in the control group.
Krawczyk et al. 2012 Poland 6 (RCT)	47 patients, both < and > 6 months following stroke were randomized to receive a course of CIMT therapy for 5 hrs/day x 15 days using either a hemisling worn for 5 hours/day or voluntary constraint. Outcomes were assessed at baseline, the end of treatment and at 1 year and included the Rivermead Motor Assessment Arm scale, 30-item Motor Activity Log - Quality of Movement.	Patients in both groups improved over the treatment period and maintained the gains at 1 year. There were no significant differences between groups after therapy or at 1 year on any of the outcomes.
Smania et al. 2012 Italy 8 (RCT)	66 patients 3-24 months poststroke from 9 centers who could extend the wrist and several fingers at least 10° were randomly assigned to mCIMT or conventional rehabilitation. Patients in both groups received 10 (2 h/day) treatment sessions 5 days/wk for 2 weeks). Patients in the mCIMT group wore a splint on their unaffected arm for at least 12 hours of their waking day. Outcomes were assessed before and after treatment and 3 months later and included the Wolf Motor Function Test (WMFT-FA and WMFT-T), the Motor Activity Log (MAL-AOU and MAL-QOM), and the Ashworth Scale.	Patients in the mCIMT group achieved greater overall improvement compared with the control group on the WMFT-FA, MAL-AOU, and MAL-QOM at the end of treatment and at follow-up. 40% of participants did not complete the 3-month assessment.

Discussion

To enable better examination of the included studies, they were classified according to type of treatment (CIMT or modified CIMT) and to chronicity of the stroke (acute vs. chronic). We used the author's own declaration of the type of therapy that was provided (i.e. mCIMT or CIMT).The results are summarized in tables 10.19 to 10.22.

Table 10.19 Summary of RCTs Evaluating CIMT in the Acute Phase Following Stroke

Author/ PEDro Score	Intervention	Intensity/Duration	Main Outcome(s) Result
Dromerick et al. 2000 6 (RCT)	CIMT vs. traditional upper extremity therapy	2 hrs/day x 5 days/wk x 2 wks	Total Action Research Arm and pinch sub score (+) FIM score (-) Upper body dressing (+)
Ro et al. 2006 6 (RCT)	CIMT vs. traditional rehabilitation	3 hrs/day x 6 days/wk x 2 wks	Grooved Pegboard test (+) Fugl-Meyer (+) Motor Activity Log (-)
Boake et al. 2007 5 (RCT)	CIMT vs. traditional rehabilitation	3 hrs/day x 6 days/wk x 2 wks	Fugl-Meyer Assessment of Motor Recovery (-) Grooved Pegboard Test (-) Motor Activity Log (+ for quality)
Dromerick et al. 2009 6 (RCT)	Standard CIMT vs. high-intensity CIMT vs. traditional upper extremity therapy	2 hrs/day x 5 days/wk x 2 wks	Total Action Research Arm (-)

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Dromerick et al. (2000) reported significant improvements in total Action Research Arm test scores and on the FIM subset of upper extremity dressing. Extrapolation from animal studies suggests that CIMT therapy is most appropriate in the early recovery following stroke to minimize the effects of learned non-use and could prevent shrinkage. However, the findings of the Boake study do not support these conclusions. These authors reported that patients receiving CIMT experienced no greater motor function recovery compared with patients receiving inpatient (followed by outpatient) rehabilitation at follow-up of 3-4 months. Since the authors reported a trend towards greater improvement in the CIMT group, it is unclear if the study was simply underpowered to detect a significant difference. In a more recent study (Dromerick et al. 2009) including 2 CIMT groups (standard and high intensity), subjects in the higher-intensity group fared, on average, worse than those in either the control group or the standard CIMT group, demonstrating an inverse dose-response curve. This result ran counter to the authors' hypothesis, predicting the greatest gains in the most intensive group. The authors proposed too soon timing of the intervention following stroke, overtraining and a practice schedule that better resembled a blocked, rather than distributed one as possible explanations for their findings.

Since subjects in both groups received task-specific therapy directed at the hand and arm in the study authored by Brogårdh et al. (2009), we considered it a study examining forced-use rather than CIT.

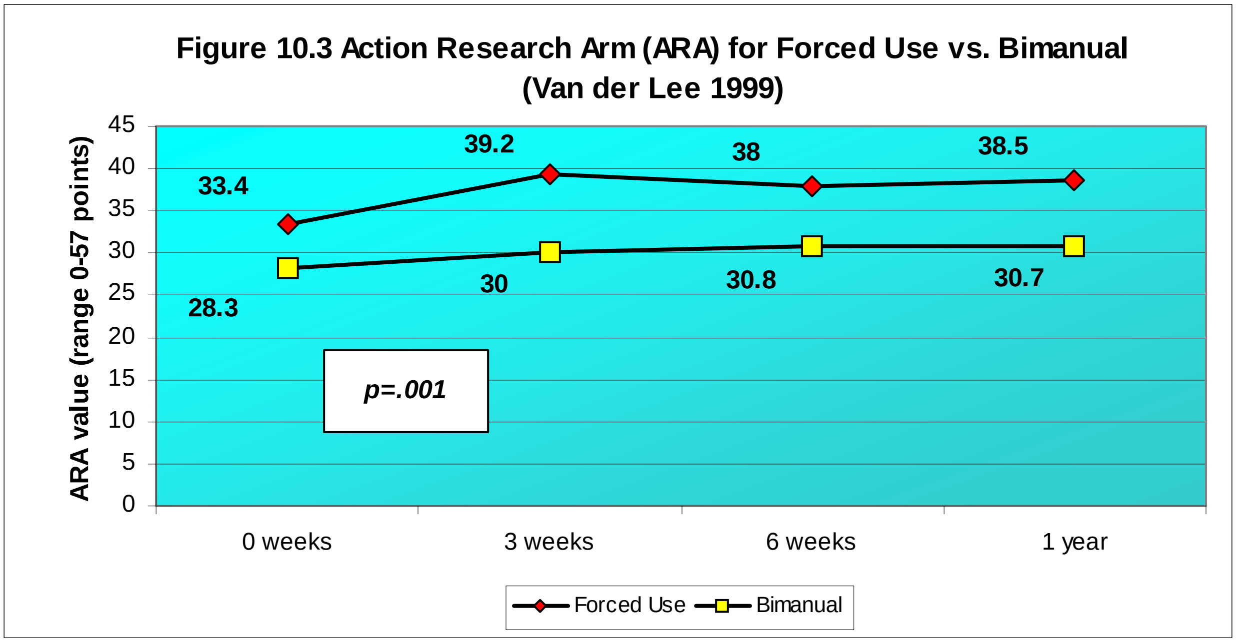
A summary of the results from RCTs that evaluated CIMT in the subacute or chronic stages of stroke is presented in Table 10.19. The author's own declarations of whether mCIMT or CIMT were used to classify studies.

Table 10.20 Summary of RCTs Evaluating CIMT in the Chronic Phase Following Stroke

Author/ PEDro Score	Intervention	Intensity/Duration	Main Outcome(s) Result
Wolf et al. 2006, 2008 8 (RCT) EXCITE	CIMT + a mitt on the un-affected hand + 'shaping procedure vs. usual care	6 hrs/day x 5x/wk x 2 wks	Wolf Motor Function Test (+) Motor Activity Log (+ amount of use and quality of movement) Functional ability measures (-) Quality/frequency of performance of 30 daily activities (-)
Dahl et al. 2008 Norway 8 (RCT)	CIMT vs. community-based rehabilitation	6 hrs/day x 5x/wk x 2 wks	Wolf Motor Function Test End of treatment (+) 6 months (-) Motor Activity Log (-) FIM (-) SIS (-)
Sawaki et al. 2008 3 (RCT)	Early vs. delayed CIMT	14 consecutive days (wearing mitt for 90% of the day)	Wolf Motor Function Test (+ grip strength) (-total score, lift weight)
Underwood et al. 2006 8 (RCT)	Subgroup from EXCITE	6 hrs/day x 5 day/wk x 2 wks	Pain scale of Fugl-Meyer test for upper extremity (-) Wolf Motor Function test (-)
Richards et al. 2006 7 (RCT)	Traditional CIMT plus donepezil or placebo (CIMT-6) vs. shortened CIMT along with repetitive transcranial magnetic stimulation (CIMT-1)	CIMT-6: 6 hrs/day in clinic x 5 days/wk x 2 wks CIMT-1: 1 hr/day in clinic + 5 hours home practice x 5 days/wk x 2wks All groups wore a padded mitt on unaffected arm for 90% of waking hours	Wolf Motor Function Test (-) Motor Activity Log (+ in use and movement quality for CIMT-6)
van der Lee et al. 1999 7 (RCT)	Intensive forced use therapy + immobilization of the unaffected arm (n=33) vs. intensive bimanual training based on NDT (n=33)	6 hrs/day x 5 days/wk x 2 wks	Action Research Arm (+ at end of treatment) Motor Activity Log (+ during treatment)
Wu et al. 2007 c) 6 (RCT)	CIMT (n=24) vs. regular interdisciplinary rehab (n=23)	2 hrs/day x 5 days/wk x 3 wks	Motor Activity Log (+) Fugl Meyer Assessment (-)
Alberts et al.	Immediate CIT (n=5) vs.	6 hrs/day x 5 days/wk x	Maximum precision grip (+)

2004 6 (RCT)	delayed CIT (n=5)	2 wks	Wolf Motor Function Test (-) Arm and Hand Section (-)
Suputtitada et al. 2004 6 (RCT)	CIMT (n=33) vs. bimanual-upper-extremity training based on NDT approach (n=36)	6 hrs/day x 5 days/wk x 14 days or daily weekday therapy for an unspecified time for 2 weeks	Action Research Arm (+) Pinch test (+)
Taub et al. 1993 6 (RCT)	Unaffected upper extremity restrained in a sling + practice using impaired upper extremity (n=4) vs. procedures designed to focus attention use of impaired upper extremity (control) (n=5)	6 hrs/day x 5 days/wk x 2 wks	Emory Test (+ at end of treatment and 2 yr) Arm Motor Activity Rest test (+ at end of treatment and 2 yr) Motor Activity Log (+ increase in ability to use affected upper extremity)
Wittenberg et al. 2003 USA 5 (RCT)	Intense CIMT (n=9) vs. less intense CIMT (n=7)	6 hrs/day (4hrs on weekends) or 3 hrs/day on weekdays only) x 10 days	Motor Activity Log (+) Wolf Motor Function Test (-) Assessment of Motor and Process Skills (-) (All at end of therapy)
Lin et al. 2008/09/10 5 (RCT)	CIT vs. traditional therapy (neurodevelopmental)	2 hrs/day x 5days/week x 3 weeks	Fugl-Meyer (+) FIM (+) Motor Activity Log (-)
Sterr et al. 2002 4 (RCT)	Longer CIMT + 'shaping procedure' (n=7) vs. shorter CIMT + 'shaping procedure' (n=8)	6 hrs/day for a target of 90% of waking time or 3hrs/day x 2 wks.	Motor Activity Log (+ after treatment and at weekly follow-up for 4 wks) Wolf Motor Function Test (+ after treatment and at weekly follow-up for 4 wks)
- Indicates non-statistically significant differences between treatment groups *+ Indicates statistically significant differences between treatment groups*			

Thirteen RCTs evaluated the benefit of CIMT in the subacute or chronic phase of stroke. There was great variability in the chronicity of stroke. The median time of stroke onset in the study by Taub et al. (1993) was 4+ years, while patients in the EXCITE Trial, the largest and most methodologically rigorous study recruited patients within 3 to 9 months following stroke. The results from these RCTs reported a positive treatment effect for the patients receiving constraint-induced movement therapy (Figure 10.3). However, functional benefit appears to be largely confined to those individuals with some active wrist and hand movement. It is particularly useful for those individuals with sensory deficits and neglect consistent with a "disuse" concept. The selective benefit within certain subsets of stroke patients raises concerns as to the treatment's generalizability. Promising research trends are that more recent studies have included improved control treatments that have helped determine the specificity of treatment effects to CIMT, and patients whose levels of impairment and disability are more typical of all who participate in stroke rehabilitation. Results from the Lin et al (2010) trial demonstrated that the apparent benefits of CIMT could be attributed to plastic reorganization, as evidenced by fMRI data.



The majority of studies included patients with less severe levels of impairment, typically characterised by a patients' ability to demonstrate at least 200 of wrist extension and 100 of each metacarpophalangeal and interphalangeal joint of the involved upper extremity. Bonifer et al. (2005) included patients with moderate-to severe upper extremity paresis and reported significant improvement in functional ability, although noting that there were issues of compliance with some patients.

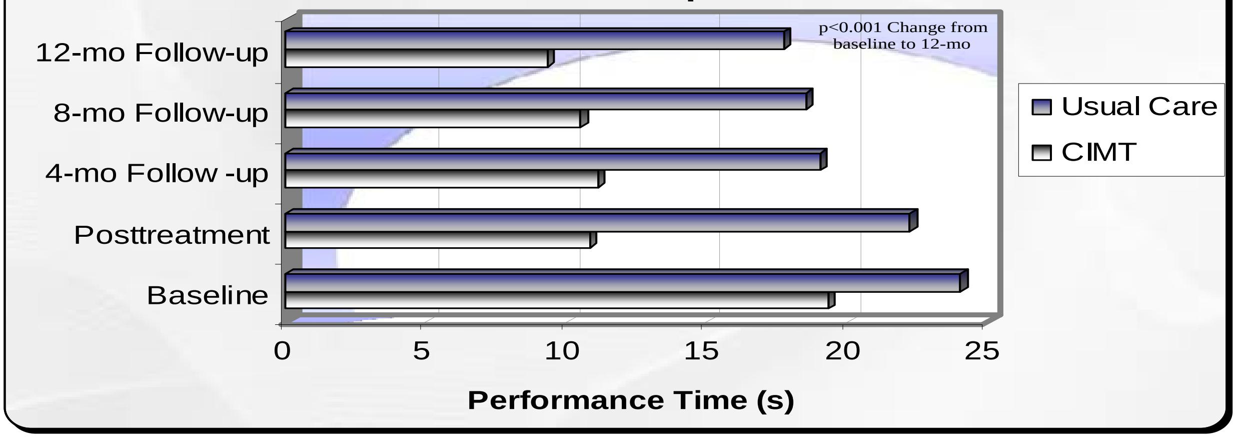
Three studies assessed the benefit of modified CIMT provided in the acute phase of stroke (Table 10.21).

Table 10.21 Summary of RCTs Evaluating Modified CIMT in the Acute Phase Following Stroke

Author/ PEDro Score	Intervention	Intensity/Duration	Main Outcome(s) Result
Myint et al. 2008 7 (RCT)	mCIMT vs. traditional rehabilitation	4 hrs/day x 10 days	Total ARAT and subscale scores (+) MAL (+)
Treger et al. 2012 7	mCIMT vs. traditional rehabilitation	Less affected arm restrained for 4 hrs/day x 2 days/wks + practice of functional tasks for 1 hr/day	Peg transfer task (+) Ball grasping (+) Eating with a spoon (+)
Page et al. 2005 5 (RCT)	mCIMT (n=5) vs. traditional motor rehab (n=5), consisting of structured therapy emphasizing more	Less affected arm restrained for 5 hrs/day x 5 days/wk x 10 weeks or motor rehabilitation of the upper extremity for	Between group comparisons not reported

	affected arm use in valued activities strategies with the unaffected limb. The TR regimens occurred 3 d/week for 10 weeks.	0.5hr x 3days/wk x 10 weeks	
- *Indicates non-statistically significant differences between treatment groups* + *Indicates statistically significant differences between treatment groups*			

Figure 10.4 Effect of Constraint-Induced Movement Therapy (CIMT) vs. Usual Care on WMFT Performance Time at Baseline Through 12-Month Follow-up



Page et al. (2005) reported that the mean change in Fugl-Meyer and Action Research Arm tests for patients randomized to the m-CIMT group were greater than previously reported for patients receiving m-CIMT therapy in the subacute period of stroke. The treatment was well tolerated and there were no losses at follow-up. Myint et al. (2008) reported a beneficial effect of treatment in a small group of Chinese stroke patients where rest and recuperation have been traditionally favoured following an acute illness compared with intensive therapy. Hayner et al. (2010) included patients who were more impaired. There were no minimum criteria for wrist and finger extension. This was one of the few studies examining CIMT that included a control group which received the same duration, frequency and intensity of therapy as the treatment group. The authors suggested that the intensity, rather than the type of therapy explained the gains that subjects in both groups made, as well as the lack of difference between groups. The addition of a third group consisting of conventional therapy at a lower intensity may have helped to elucidate the effect of treatment.

Ten RCTs evaluated the effectiveness of mCIMT in the subacute and chronic phases of stroke (Table 10.22). While all the studies reported improvements in functional outcomes, the sample sizes were generally small and the treatment intensities varied considerably among studies.

Table 10.22 Summary of RCTs Evaluating Modified CIMT in the Sub-acute or Chronic Phase Following Stroke

Author/ PEDro Score	Intervention	Intensity/Duration	Main Outcome(s) Result
Smania et al. 2012 8 (RCT)	Modified CIMT vs. dose-match task-specific therapy	2 hrs/day x 5 days/wk x 2 wks	Wolf Motor Function Test (+) Motor Activity Log (+)
Lin et al. 2007 7 (RCT)	Modified CIMT vs. traditional rehab	6 hrs/day x 5 hrs/day x 3 wks.	MAL (+) FIM (+)
Wu et al. 2007 b) 6 (RCT)	Modified CIMT vs. regular occupational therapy	2 hrs/day x 5 days/wk x 3 wks	MAL (+) FIM (+)
Page et al. 2004 6 (RCT)	Modified CIT + physical and occupational therapy (n=7) vs. traditional rehab (n=4) vs. no therapy (n=6)	5 hrs/day x 5 days/wk x 10 wks. or 1 hr therapy 3x/wk x 10wks or 0 hrs of therapy.	Fugl-Meyer (+ in modified CIMT group only after intervention) Action Research Arm test (+ in modified CIMT group only after intervention)
Huseyinsinoglu et al. 2012 6 (RCT)	CIMT vs. Bobath	CIMT for 3 hrs/dayx10 days (n=11) or 1 hr Bobath for10 days (n=11)	MAL (AOU+ QOM) + CIMT WMFT (-) FIM (-)
Page et al. 2002 5 (RCT)	Modified CIT + physical and occupational therapy (n=4) vs. traditional rehabilitation (n=5) vs. no therapy (n=5)	5 hrs/day x 5 days/wk x 10 wks. or 1 hr therapy 3x/wk x 10wks or 0 hrs of therapy.	Fugl-Meyer (+ in modified CIMT group only after intervention) Action Research Arm test (+ in modified CIMT group only after intervention)
Page et al. 2008 5 (RCT)	Modified CIMT (n=13) vs. conventional therapy (n=12) vs. no therapy (n=10)	5 hrs/day x 5 days/wk x 10 wks. or 1/2 hr therapy 3x/wk x 10wks or 0 hrs of therapy.	Fugl-Meyer (-) Action Research Arm Test (+)
Wu et al. 2007 5 (RCT)	Modified CIMT (mCIMT) + a restraining mitt on the unaffected hand (n=13) or traditional therapy (n=13).	2 hrs/day x 5 days/wk x 3 wks	Fugl-Meyer Assessment (+) FIM instrument (+) Motor Activity Log (+) Stroke Impact Scale (+ improvement in strength, ADLS/IADLs, and stroke recovery)
Wang et al. 4 (RCT)	mCIMT vs. intensive conventional therapy vs. conventional therapy	3 hrs/day x 5 days/wk x 4 wks	Wolf Motor Function test (+ mCIMT)
Hayner et al. 2010 4 (RCT)	mCIMT vs. bilateral training	Both groups practiced for 6 hrs/day x 10 days.	WMFT (-) COPM (-)
- Indicates non-statistically significant differences between treatment groups *+ Indicates statistically significant differences between treatment groups*			

In addition to the studies that examined either modified CIMT or CIMT, 4 studies were included that assessed the use of forced-use therapy, in which the unaffected arm was restrained without a shaping, or more intense exercise component (Wolf et al. 1989, Ploughman & Corbett 2004, Burns et al. 2008, Hammer & Lindmark 2009 a,b). Among the 2 RCTs examining this intervention, neither demonstrated a statistically significant benefit (Ploghman & Corbett 2004, Hammer & Lindmark, 2009 a,b), although both reported trends in favour of the treatment group. The sample sizes in both of these studies were small. A fifth study, evaluated the effectiveness of the continued use of a mitt following a 2-week course of CIMT (Brogårdh & Bengt 2006, 2009). There was no additional benefit of therapy associated with the continued use of a mitt for several weeks either 3 months or 4 years following the initial course of treatment.

Conclusions Regarding Constraint-Induced Movement Therapy

There is conflicting (Level 4) evidence of benefit of CIMT in the acute stage of stroke.

There is strong (Level 1a) evidence of benefit of mCIMT in the acute/subacute stage of stroke.

There is strong (Level 1a) evidence of benefit of CIMT and mCIMT in comparison to traditional therapies in the chronic stage of stroke. Benefits appear to be confined to stroke patients with some active wrist and hand movements, particularly those with sensory loss and neglect.

Constraint-induced movement therapy is a beneficial treatment approach for those stroke patients with some active wrist and hand movement.

10.2.11 Mirror Therapy

Mirror therapy is a technique that uses visual feedback about motor performance to improve rehabilitation outcomes. It has been adapted from its original use for the treatment of phantom limb pain as a method to "re-train the brain" as a means to enhance upper-limb function following stroke and to reduce pain. In mirror therapy, patients place a mirror beside the unaffected limb, blocking their view of the affected limb, creating the illusion that both limbs are working normally. It is believed that by viewing the reflection of the unaffected arm in the mirror that it may act as a substitute for the decreased or absent proprioceptive input.

The effectiveness of mirror therapy was evaluated recently in a Cochrane review (Thieme et al. 2012). The results from 14 RCT (567 subjects) were included. A modest benefit of treatment was reported in terms of motor function, but the treatment effect was difficult to isolate due to the variability of control conditions. Improvement in performance of ADLs (SMD=0.33, 95% CI 0.05 to 0.60, p=0.02), pain (SMD=-1.1, 95% CI -2.10 to -0.09, p=0.03) and neglect (SMD=1.22, 95% CI 0.24 to 2.19, p=0.01) were also noted.

Table 10.23 Studies Evaluating Mirror Therapy

Author, Year Country PEDro Score	Methods	Results
Altschuler et al. 1999 USA (RCT) Letter-insufficient info to score	9 subjects with stroke onset of > 6 mos were randomly assigned to spend the first 4 weeks using either a mirror or transparent plastic then crossed over to the other treatment for the next 4 weeks. Patients practiced for 15 min 2x/day 6 days a week, moving the paretic hand as much as they were able while watching the unaffected arm in the mirror, or the paretic arm through the plastic. 2 Neurologists assessed change from baseline movement ability in terms of range of motion, speed and accuracy, using a -3 to + 3 scale (0 is no change)	Both raters agreed that 7/9 patients in the control group did not improve. Two patients in the control group improved by 0.5 or 1 point. In the mirror group, at least one of the raters reported that every patient had improved by at least 0.5 points.
Yavuzer et al. 2008 Turkey 7 (RCT)	40 inpatients all within one-year of stroke were randomized to a program of either 30 minutes of mirror therapy (n=20) a day consisting of wrist and finger flexion and extension movements or sham therapy (n=20) in addition to conventional stroke rehabilitation program, 5 days a week, 2 to 5 hours a day, for 4 weeks. Outcomes including the modified Ashworth Scale (MAS) and the Brunnstrom stages of motor recovery were assessed before and after treatment and at 6 months.	The scores of the Brunnstrom stages for the hand and upper extremity and the FIM self-care score improved more in the mirror group than in the control group after 4 weeks of treatment (by 0.83, 0.89, and 4.10, respectively; all $P<.01$) and at the 6-month follow-up (by 0.16, 0.43, and 2.34, respectively; all $P<.05$). There were no significant differences in change scores between the groups at either the end of treatment or at follow-up. (4 week change MAS: 0.12 vs. 0.11, $p=0.89$; 6 months: 0.18 vs. 0.21, $p=0.876$).
Dohle et al. 2009 Germany 7 (RCT)	36 patients with severe hemiparesis due to first-ever ischemic stroke in the territory of the middle cerebral artery were enrolled, no more than 8 weeks after the stroke. They completed a protocol of 6 weeks of additional therapy (30 minutes a day, 5 days a week), with random assignment to either mirror therapy (MT) or an equivalent control therapy (CT). The primary outcome measures were the Fugl-Meyer sub scores for the upper extremity, (arm, hand and finger function) were evaluated before and after treatment.	There were no significant differences in the mean FM sub scores of any of the FM sub scores at the end of treatment. In the subgroup of 25 patients with distal plegia at the beginning of the therapy, MT patients regained more distal function than CT patients. Furthermore, across all patients, MT improved recovery of surface sensibility.
Michielsen et al. 2011 The Netherlands	40 chronic stroke patients (mean of 3.9 years post onset) were randomly assigned to the mirror group (n = 20) or the control group (n = 20) and then	Patients in the mirror group achieved more gains in FMA points compared with those in the control group, although they did not persist at follow-up. There were no significant

7 (RCT)	participated in a 6-week training program, led by physiotherapist at the rehabilitation center and practiced at home 1 hour daily, 5 times a week. The primary outcome measure was the Fugl-Meyer motor assessment (FMA). The grip force, spasticity, pain, dexterity, hand-use in daily life, and quality of life at baseline-post treatment and at 6 months-were all measured by a blinded assessor.	differences on any of the other outcomes at either the end of treatment or follow-up (ARAT, ABILIHAND, grip force, Tardieu scale).
Yun et al. 2011 Korea 4 (RCT)	60 patients admitted to an inpatient rehabilitation unit within 30 days of stroke were randomized to receive NMES + mirror therapy (n=20), NMES only (n=20) or mirror therapy only (n=20). Each treatment was done five days per week, 30 minutes per day, for three weeks. NMES was applied on the surface of the extensor digitorum communis and extensor pollicis brevis for open-hand motion. Muscle tone, Fugl-Meyer (FM) assessment, and power of wrist and hand were evaluated before and after treatment.	Patient in all treatment groups improved. The mirror + NMES group showed significantly greater improvements in the FM scores of hand, wrist, coordination and power of hand extension compared to the other groups. There were no significant differences among the three groups for the power of hand flexion, wrist flexion, or wrist extension muscle tone.
Thieme et al. 2012 Germany 8 (RCT)	60 patients, within 3 months of first stroke, with a severe paresis of the arm were randomized to one of 3 treatment groups: 1) individual mirror therapy, (2) group mirror therapy and (3) control intervention with restricted view on the affected arm. Patients in all groups received standard inpatient therapy. In all 3 groups, patients received a maximum of 30 minutes of mirror therapy or control therapy-a minimum of 20 sessions. The main outcomes, assessed before and after treatment included the Fugl-Meyer Assessment and the Action Research Arm Test.	Although patients in all groups demonstrated modest improvements over the treatment period there were no significant differences among groups on the primary outcomes. There was significant improvement on the Star Cancellation test for patients in the individual mirror therapy compared to control group could be shown.

Mirror therapy is a treatment for which there is a limited body of evidence in its application to stroke rehabilitation. In the 3 RCTs that included only 2 study groups (treatment and control), there was an improvement in motor function reported in one trials (Yavuzer et al. 2008), no improvement in the third trial (Dohle et al. 2009) and mixed results in the fourth (Michielsen et al. 2011). The fifth study included an additional group that included a co-intervention of NMES (Yun et al. 2011).

Conclusions Regarding Mirror Therapy

There is conflicting (Level 4) evidence that mirror therapy improves motor function following stroke and moderate

(Level 1b) evidence that it does not reduce spasticity.

10.2.12 Feedback

As with athletic performance, feedback can be used as a means to improve motor learning following stroke. There are two types of feedback, intrinsic and extrinsic. Intrinsic feedback refers to the use of a person's own sensory-perceptual information to enhance their performance during a given task. It may take the form of touch, sound, pressure, and/or proprioception. Extrinsic feedback can augment the effect of intrinsic and refers to feedback provided from the environment. Extrinsic feedback can be both verbal and non-verbal. Comments from a therapist would be an example of extrinsic verbal feedback. Extrinsic feedback can be further classified as either knowledge of results (KR) or knowledge of performance (KP). KR is often given at the end of a task and is feedback related to the outcome of the performance of that task. A patient's time performing a timed-walk test is an example of KR. KP is information about the movement characteristics that led to the performance outcome. Two reviews have been published on the topic of feedback. Van Vliet & Wulf (2006) concluded that visual feedback can be used to provide information about weight distribution that can improve balance performance and auditory feedback can improve sit-to-stand performance. Subramanian et al. (2010) included the results from 9 studies and reported that there was evidence that external feedback, particularly KP, in the forms of verbal, virtual environments, videotape, robotics, audition or vision, improved motor learning of the more affected limb.

Table 10.24 Studies Evaluating Feedback

Author, Year Country PEDro Score	Methods	Results
Winstein et al. 1999 USA No Score	40 stroke subjects approximately 2 years post onset) and 40 age-matched controls practiced a rapid, spatially and temporally constrained programmed action under one of two augmented feedback practice conditions. Participants in the stroke group used the upper limb ipsilateral to the lesion. After an extended practice period (198 trials), acquisition, retention, and reacquisition performance was assessed for accuracy and consistency and compared over trials, between groups and feedback conditions.	Both stroke and control groups demonstrated significant improvement in accuracy and consistency over practice with relative persistence of these changes during retention. There were no differences between groups (stroke vs. control) in performance patterns across trials for acquisition, retention, or reacquisition phases. In addition, there were no differential effects of the two augmented feedback conditions on performance and no interactions of feedback condition with group. However, independent of feedback condition, the stroke group performed with more error than did the control group during all experimental phases (i.e., acquisition, retention, reacquisition)
Cirstea et al. 2006 Canada	37 chronic stroke patients, no longer receiving active therapy were randomized to one of 3 groups: 1)	Patients in the KP group made faster, less segmented and less variable movements, which were maintained at follow-up.

6 (RCT)	Knowledge of Results (KR) (n=14) practiced a reaching task involving 75 repetitions per day, 5 days per week for 2 weeks, with 20% KR about movement precision; 2) Knowledge of Performance (KP) (n=14) trained on the same task and schedule as KR but with faded KP about joint motions; and (3) control (C) (n=9) practiced a nonreaching task. Outcomes were assessed before and after treatment and at 1-month and included motor, cognitive, neuropsychological and kinematic measures.	
Cristea & Levin 2007 6 (RCT)	28 chronic stroke survivors were randomly assigned to 2 groups that practiced 10 sessions of 75 pointing movements. During practice, groups received either 20% Knowledge of Results (KR) about movement precision or faded (26.6% average) Knowledge of Performance (KP) about arm joint movements. A nondisabled control group (n = 5) practiced the same task with KR. Outcomes were assessed before and after treatment and at 1-month and included Fugl-Meyer (FM) scale, the Composite Spasticity Index (CSI) and the TEMPA and kinematic measures.	Patients in the KP group increased the range of shoulder movements and improved elbow and shoulder temporal interjoint co-ordination to a greater degree than patients in the KR group, immediately following treatment.
Gilmore & Spaulding 2007 Canada 5 (RCT)	10 patients undergoing inpatient rehabilitation, who were unable to don their own socks and shoes independently, received a maximum of 10 training sessions in addition to routine therapy. Patients were randomized to one of two groups. In the experimental group, participants were videotaped and received both verbal feedback and viewed the tapes from the training sessions. Patients in the control group received verbal feedback only. The main outcome, assessed before and after each treatment, was the socks and shoes subtests of the Klein-Bell Activities of Daily Living Scale. The Canadian Occupational Performance Measure was assessed before and after treatment.	There was no significant difference between the two groups at either the start, or the end of treatment. Patients in both groups improved. However, the group that received videotape feedback thought they performed better and were more satisfied with their ability to don shoes.
Piron et al. 2010 Italy 8 (RCT)	50 chronic stroke subjects with upper arm paresis were randomized to receive a program of either reinforced feedback in a virtual environment or	In the per protocol analysis, there were no significant differences between groups on any of the outcomes assessed. In an intention-to-treat analysis with imputed data for 3 missing

	conventional therapy, based on Bobath principles for 1 hour of therapy daily (5 days/week) x 4 weeks. The outcomes were assessed before and after treatment and included FIM Fugl Meyer –UE (FM) and kinematic analysis of reaching.	subjects, from the control group, assuming the best possible outcome, there was a significant difference in FM scores following treatment, favouring the treatment group.

Conclusions Regarding Extrinsic Feedback

There is strong (Level 1a) evidence that extrinsic feedback helps to improve motor learning following stroke.

10.2.13 Action Observation

Action observation is a form of therapy whereby a motor task is performed by an individual while watching another individual perform the same task, in mirror image. The therapy is designed to increase cortical excitability in the primary motor cortex. Although it has been evaluated mainly in healthy volunteers, a limited number of studies have evaluated its benefit in motor relearning following stroke.

Table 10.25 Studies Evaluating Action Observation

Author, Year Country PEDro Score	Methods	Results
Celnik et al. 2008 USA 5 (RCT)	8 chronic stroke subjects received, in random order, 3 treatments: physical therapy, physical therapy + concurrent AO (watching a video of a healthy subject perform hand movements in the same direction) or incongruent AO (watching a video of a healthy subject perform hand movements in the opposite direction). Motor memory formation and kinematic assessments were performed before and after each treatment.	Patients in the PT congruent group performed better than those in the other 2 groups.
Franceschini et al. 2012 Italy 8 (RCT)	102 patients with recent stroke who were receiving inpatient rehabilitation were randomly assigned to the experimental (EG) or control group (CG) and received 20 sessions over 4 weeks (2 x15 minute sessions/day). EG participants watched video footage of daily routine tasks (actions) carried out with the upper limb in order to prepare to imitate the presented action. At the end of each sequence, a therapist prompted the patient to	Subjects in the EG group performed better than those in the other 2 groups on the BBT. (8.5, 20, 25.6 vs. 8.3, 14.5, 18.70). The mean differences in blocks moved were statistically significant from baseline to the end of treatment (+5.2, p=0.003) and from baseline to 4-5 months after treatment ended (5+5.7, p=0.01). There were no significant differences between groups on the other outcomes.

	perform the same movement for 2 minutes. Static images were shown to the CG. At the end of each sequence, the CG executed movements that simulated the shoulder and elbow joint mobilization activities performed by the EG. Outcomes were evaluated before and after treatment and at 4-5 months and included the Box & Block Test (BBT), Frenchay Arm test, Modified Ashworth Scale, and Functional Independence Measure Motor items.	

Conclusions Regarding Action Observation

There is moderate (Level 1b) evidence that action observation improves performance on the Box & Block test.

10.3 Robotic Devices for Movement Therapy

Robotic devices can be used to assist the patient in a number of circumstances. First of all, the robot can aid with passive range of motion to help maintain range and flexibility, to temporarily reduce hypertonia or resistance to passive movement. The robot can also assist when the patient has active movements, however, cannot complete a movement independently. Robotics may be most appropriate for patients with dense hemiplegia, although robotics can be used with higher-level patients who wish to increase strength by providing resistance during the movement. According to Lum et al. (2002), "even though unassisted movement may be the most effective technique in patients with mild to moderate impairments, active- assisted movement (with robotic devices) may be beneficial in more severely impaired patients…especially during the acute and subacute phases when patients are experiencing spontaneous recovery." Krebs et al. (2002) noted that robotic devices rely on the repetition of specific movements to improve functional outcomes. While the majority of robotic devices focus on retraining of the upper extremity, specifically shoulder, elbow and wrist movements, researchers have recently begun to investigate the potential use of robotic devices for the fingers and legs (Krebs et al. 2002, Lum et al. 2002).

A recent systematic review of robot-aided therapy on recovery of the hemiparetic arm on recovery of the hemiparetic arm was conducted (Prange et al. 2006). The authors included the results from 8 studies evaluating the MIT-Manus, MIME and ARM Guide and concluded that robotic devices improved short and long term motor function of the paretic shoulder and elbow beyond that which could be achieved through therapy alone.

Kwakkel et al. (2008) conducted a systematic review of RCTs that evaluated robotic devices in the management of upper extremity hemiplegia following stroke. The results from 10 studies involving 218 subjects were identified. Pooling the results from 7 trials assessing improvement in motor function revealed a nonsignificant benefit of robotic treatment. The summary effect size was 0.65 (95% CI -0.02 to 1.33, p=0.06). When one of the studies (Hesse et al. 2005) was removed in sensitivity analysis, there was a significant treatment effect. In the 5 studies that evaluated improvement in ADL, no significant beneficial treatment effect was found.

A recent Cochrane review, authored by Mehrholz et al. (2012) included the results from 19 trials (328 subjects) evaluating electromechanical and robot-assisted arm training devices. Compared with routine therapy, usually conventional physical therapy, the authors reported significantly greater improvement in activities of daily living (SMD=0.43; 95% CI 0.11 to 0.75, p <0.009) and arm function (SMD=0.45; 95% CI 0.20 to 0.69, p<0.001), but not arm strength (SMD=0.48; 95% CI -0.04 to 0.04, p=0.82).

The results of studies that have assessed a variety of these devices are presented in tables 10.26 to 10.33.

10.3.1 MIT-Manus

MIT-Manus was one of the first robotic devices to be developed. It features a 2-degree-of-freedom robot manipulator that assists in shoulder and elbow movement by guiding the patient's hand in a horizontal plane, while visual, auditory and tactile feedback is provided during goal-directed movements. A commercially available unit (InMotion[2]) of this device is also available.

Table 10.26 Studies Evaluating MIT-Manus Robotic Device

Author, Year Country PEDro Score	Methods	Results
Volpe et al. 1999 USA 6 (RCT)	20 patients admitted to rehabilitation were randomized to either robot or sham treatment. All patients received similar standard physical and occupational therapy. For 1 hr/day, 5 days/wk, patients in the robot group moved the handle of a robot, which provided visual feedback of the movement. The robot provided assistance if the patient did not produce movement. Nearly 3 years after discharge and without further robot training, 12 of the patients were re-examined.	The robot-trained group showed significant improvement on the MSS (motor status scores) for shoulder/elbow at discharge and 3 year follow up and from admission to discharge for the Motor Power score. Both groups showed comparable changes in the FM for shoulder/elbow and for wrist/hand and MSS for the wrist/hand over both intervals. These data show that the advantages conferred by robot training were specific to the muscle groups trained and were persistent. The motor scores for both groups improved 3 years after stroke, which showed that for some patients, improvements may continue long after discharge.
Volpe et al. 2000 USA 6 (RCT)	56 patients with stroke and hemiparesis or hemiplegia received standard poststroke multidisciplinary rehabilitation, and were randomly assigned either to receive robotic training (at least 25 hours) or exposure to the robotic device without training. Patients were assessed before treatment began and at the end of treatment, with the upper extremity	At the end of treatment, the robot-trained group demonstrated improvement in motor outcome for the trained shoulder and elbow (Motor Power score, p < 0.001; Motor Status score, p < 0.01) that did not generalize to the untrained wrist and hand. The robot-treated group also demonstrated significantly improved functional outcome (Functional Independence Measurement–Motor, p < 0.01).

	component of the Fugl-Meyer Motor Assessment, the Motor Status score, the Motor Power score, and Functional Independence Measurement.	
Stein et al. 2004 USA 5 (RCT)	Stroke patients (n=46) capable of doing resistance training were randomized to receive either robot-aided progressive resistance training or active-assisted robot-aided exercises. There was no control for robot assistance.	The incorporation of robot-aided progressive resistance exercises into a program of robot-aided exercise did not favourably or negatively affect motor control or strength.
Day et al. 2005 USA 5 (RCT)	12 moderate to severe chronic stroke survivors were randomized to one of two treatments: robotics and motor learning (ROB-ML) or functional neuromuscular stimulation and motor learning (FNS-ML). Treatment was 5 h/d, 5 d/wk for 12 wk. ROB-ML group had 1.5 h per session devoted to robotics shoulder and elbow (S/E) training. FNS-ML had 1.5 h per session devoted to functional neuromuscular stimulation (surface electrodes) for wrist and hand (W/H) flexors/extensors. The primary outcome measure was the functional measure Arm Motor Ability Test (AMAT).	There was a significant reduction in mean AMAT scores between the beginning and end of treatment for subjects in the ROB-ML group but not for those in the control group (-475 vs. -242).
Daly et al. 2005 USA 5 (RCT)	13 chronic stroke subjects living in the community were randomized to receive a 12-week program (5 hrs/day x 5 days/week) of robotics (InMotion[2]) + motor learning or motor learning + functional neuromuscular stimulation. Outcome measures, assessed before and after treatment, included the Arm Motor Ability Test (AMAT) + shoulder/elbow (SE) and wrist hand (WH) subsections, the Fugl-Meyer (FM) scale and motor control measures of target accuracy.	The results of between group comparisons are not reported. Subjects in the robotic group achieved significant improvements on the AMAT (Total) and AMAT (S/E subsection), FM scores and target accuracy. Subjects in control group improved significantly on AMAT (W/H) and FM scores only.
Volpe et al. 2008 USA 5 (RCT)	21 chronic stroke patients were randomized to receive a course of intensive upper-extremity treatment that was provided by either a therapist or a robotic device (InMotion[2]). Treatment consisted of 1 hr sessions, 3x/week for 6 weeks. Primary outcome was the Fugl-Meyer (FM) score for shoulder/elbow. Secondary outcomes were the FM wrist/hand and the Motor Power Scale for Shoulder/elbow. Assessments were conducted monthly	Patients in both groups demonstrated improvement over time, which was maintained at 3 months; however, there were no significant between group differences on either the primary or secondary outcomes.

	for 3 months.	
Rabadi et al. 2008 USA 5 (RCT)	30 acute stroke patients (< 5 weeks) admitted for inpatient rehabilitation were randomized to 1 of 3 groups: 1) Occupational therapy (OT) group (control) (n = 10), 2) arm ergometer (n = 10) or 3) robotic (n = 10) therapy group. All patients received standard, inpatient, post-stroke rehabilitation training for 3 hours a day, plus 12 additional 40-minute sessions of the activity-based therapy. The primary outcome measures, assessed before and after treatment, were discharge scores in the Fugl-Meyer (FM) Assessment Scale for upper limb impairment, Motor Status Scale and FIM.	After adjusting for age, stroke type and outcome measures at baseline, a similar degree of improvement in the discharge scores was found in all of the primary outcome measures. Overall, the OT group experienced the greatest gains.
Lo et al. 2010 USA 7 (RCT)	127 patients with moderate-to-severe upper-limb impairment 6 months or more after a stroke, were randomly assigned to receive intensive robot-assisted therapy (n=49), intensive comparison therapy (n=50), or to usual care (n=28). Therapy consisted of 36, 1-hour sessions over a period of 12 weeks. The primary outcome was the Fugl-Meyer Assessment (FM) at 12 weeks. Secondary outcomes were scores on the Wolf Motor Function Test and the Stroke Impact Scale. Secondary analyses assessed the treatment effect at 36 weeks.	At 12 weeks, subjects in the robot assisted group had gained more FM points, compared to subjects in the usual care group (1.11 vs. -1.06, p=0.08). Subjects in the intensive therapy group gained more FM points compared with subjects in the robot-assist group (4.01 vs. 3.87, p=0.92). No other treatment comparisons were significant at 12 weeks. No serious adverse events were reported.
Conroy et al. 2011 USA 6 (RCT)	62 chronic stroke patients were randomized to one of 3 groups that received treatment for 1 hour, 3x/week over 6 weeks (18 sessions total) Groups included robot-assisted planar reaching (gravity compensated), combined planar with vertical robot-assisted reaching, both using the InMotion Linear Robot) or intensive conventional arm exercise program. The primary outcome was the UE Fugl-Meyer Assessment (FMA). Evaluations were conducted at baseline, midway and at the end of treatment and at 12 weeks follow-up.	Patients in all groups showed modest gains in the FMA from baseline to final with no significant between group differences.

10.3.2 Mirror-Image Motion Enabler Robots (MIME)

MIME is a 6 degree of freedom robotic device developed "*to provide therapy that combines bimanual movements with unilateral passive, active-assisted* *and resisted movements of the hemiparetic upper extremity"* (Burgar et al. 2011). The unit applies force to the more affected forearm during goal-directed movements.

Table 10.27 Studies Evaluating MIME Robotic Device

Author, Year Country PEDro Score	Methods	Results
Burgar et al. 2000 USA 5 (RCT)	21 chronic stroke subjects were randomized to a course of treatment using either a robotic device (n=11) or to a control group (n-10) that received a physical therapy program of stretching, weight bearing, facilitation games and activities. 24, 1 hr sessions were provided over 2 months. Motor function was assessed using the Fugl-Meyer (FM) Assessment and ADLs were assessed using FIM and BI.	There were no significant differences between the groups on either of the ADL assessments while subjects in the robotic group exhibited a trend towards greater improvement in FM scores. These differences achieved statistical significance if only the shoulder and elbow portions of the FM test were considered.
Lum et al. 2002 USA 6 (RCT)	27 patients with chronic hemiparesis (> 6 months post-stroke) were randomly allocated to receive either robot assisted movement training or conventional therapy. The robot group practiced shoulder and elbow movements assisted by a robot manipulator while the control group received NDT and 5 minutes of exposure to the robot in each session.	After the first and second months of treatment, the robot group had significantly larger improvements in the proximal movement portion of the Fugl-Meyer test. The robot group also had larger gains in strength and larger increases in reach extent after 2 months of treatment. At 6 months, no significant differences were seen between the two groups on the Fugl-Meyer test, however, the robot group did have significantly larger improvements on the FIM.
Lum et al. 2006 USA 4 (RCT)	30 subacute stroke patients were randomized to receive 1 of 4 treatments: i.) robot-unilateral group (n=9), ii.) robot-bilateral group (n=5), iii.) robot-combined group – unilateral + bilateral (n=10), or iv.) conventional therapy (n=6). Over 4 weeks patients in each group received 15 one-hour treatment sessions. Main measures included Fugl-Meyer Assessment (FM), Motor Status Score (MSS), Functional Independence Measure (FIM), modified Ashworth scale and were assessed pre and post intervention and at 6 months.	Significantly greater gains were attained at post treatment for the robot-combined group in proximal FM and MSS synergy scale compared to the control group. However, these gains were not maintained at 6 months follow-up. Also, a significantly greater improvement was seen for the robot-unilateral group compared to the robot-combined group for distal FM ($P<0.05$).
Burgar et al. 2011 USA 5 (RCT)	54 acute, (within 17 days of stroke) hemiparetic inpatients were randomized to either a control group (n=18) or to one of 2 robotic groups, high intensity (n=17) or low intensity (n=19). Patients in the low dose robotic group were scheduled to	Actual mean duration of study treatment was 8.6, 15.8, and 9.4 hours for the low-dose, high-dose, and control groups, respectively. There were no significant differences in the mean gains in FMA scores among the groups at either the end of treatment or at 6 months. Post treatment: 14.0 vs. 6.8 vs. 14.4 for the

	receive 15 hours or training, while those in the hi-dose group were to receive 30 hours. The primary outcome measure was the Fugl-Meyer Assessment (FMA). The secondary outcome measures were the Functional Independence Measure (FIM), Wolf Motor Function Test, Motor Power, and Ashworth scores, assessed at admission, discharge, and 6-month follow-up.	control, low and high dose groups, respectively. Patients in the high-dose group had gained significantly more upper FIM scores at the end of treatment compared with the controls (21.5 vs. 15.9, p=0.04); however, the differences were no longer significant at 6 months. At the 6-month point, the only significant differences among groups was the mean Ashworth scores, although they were all less than one, indicating only slight spasticity. When the 2 robot groups were combined, there was a strong correlation between treatment intensity and admission FMA scores at the end of treatment and at 6 months (r-0.45, p=0.005; r=0.66, p<0.001).

10.3.3 Assisted Rehabilitation and Measurement (ARM) Guide

This unit uses a motor and chain drive to move the user's hand along a linear rail, which assists reaching in a straight-line trajectory.

Table 10.28 Studies Evaluating ARM Guide

Author, Year Country PEDro Score	Methods	Results
Kahn et al. 2006 USA 4 (RCT)	19 Chronic (>1 year post stroke) patients were randomly assigned to receive 24 sessions of either active-assistive reaching exercise using a robotic device (n=10) or a task-matched amount of reaching without assistance (n=9). Both groups completed an 8-week therapy program involving a total of 24, 45-minute sessions. Main outcomes measures include the Rango Los Amigos Functional Test of Upper Extremity Function, range, smoothness and straightness of unsupported arm movement, and speed and range of supported reaching, assessed at baseline, post intervention and 6 months.	Significant improvements were attained with training for functional ability movement, velocity and range of motion of supported reaching and straightness of unsupported reaching. No significant differences existed between groups. The group without assistance with reaching exercises showed a greater improvement in smoothness of arm movement compared to the robot-assisted group.

10.3.4 Bi-Manu-Track

This arm-training device enables bilateral and passive and active practice of forearm and wrist movement.

Table 10.29 Studies Evaluating the Bi-Manu-Track Device

Author, Year Country PEDro Score	Methods	Results
Hesse et al. 2005 Germany 8 (RCT)	44 subacute stroke patients with severe arm paresis were randomized to computerized arm training (AT) enabling repetitive practice of passive and active bilateral forearm and wrist movement cycle (yielding 800 repetitions) or electromyography-initiated electrical stimulation (ES) of the paretic wrist extensor. 60-80 wrist extensions were achieved with each ES session. The therapy was conducted for 20 minutes/5 days a week for 6 weeks.	At the end of 3 months Fugl-Meyer scores among patients in the AT group improved to a greater degree than those in the ES group. Upper limb motor power scores also improved more among patients in the AT group compared to the ES group.
Hesse et al. 2008 Germany 8 (RCT)	54 patients enrolled in a comprehensive inpatient rehabilitation program, within 4-8 wks from stroke onset were randomized to practice with an arm trainer (AT) or to receive electrical stimulation (ES) (75 Hz, 0.5 msec, 0-80 mA). The arm trainer device (Reha-Slide) consists of 2 handles spaced .75 m apart and connected by a rod and mounted on 2 parallel tracks. The patient can move the handles forwards and backwards, as well as sideways. The handles are yoked. Both groups received treatments for 20-30 mins, 5x/week x 6 wks (30 sessions). Primary outcome was the Fugl-Meyer (FM) assessment. Secondary outcomes were the Box and Block test, the Medical Research Council and the modified Ashworth scale, assessed at enrollment, after 6 wks, and at 3-mos follow-up.	Patients in both groups improved over time but there was no significant difference in FM scores between groups. FM scores improved from a mean of 8.8 at baseline to 28.9 at follow up (AT group) and from 8.6 to 18.4 (ES group). No patient could transport a block initially, but at completion significantly more arm trainer patients were able to transport at least three blocks (five vs. zero, P = 0.023).
Hsieh YM et al. 2011 8 (RCT) Taiwan	18 patients with severe upper extremity impairment (mean Fugl-Meyer Assessment (FMA) of 37 to 44) were randomized to receive higher intensity robot-assisted therapy (RT), lower intensity RT, or conventional (CR) intervention for 4 weeks. Patients in all groups completed 20 training sessions lasting from 90-105 min, 5 days/week. The dose of the higher intensity RT was twice the number of repetitions in the lower intensity RT. Outcome measures were	There were significant differences in mean FMA scores among the groups (p=0.04), with patients in the high-intensity RT group improving more than those in the low-intensity group (p=0.04). There was no difference in mean FMA scores between patients in the low-intensity RT group and the CR group. There were also significant differences in MAL-QOU scores (p=0.03) among the groups. Patients in the high-intensity RT group did better than those in the CR group. There were no other significant differences among groups in the other outcomes.

	assessed before and after treatment. Primary outcomes were the FMA and Medical Research Council (MRC) scale.	
Liao et al. 2011 Taiwan 7 (RCT)	20 patients an average of 22 months following stroke were randomized to receive 20 training sessions over 4 weeks with the Bi-Manu-Trak (n = 10) or dose-matched active control therapy (n = 10). All patients received either of these two therapies for 90-105 minutes each day. Outcome measures were assessed before and after training and included arm activity ratio (the ratio of mean activity between the impaired and unimpaired arm, measured by accelerometers), the Fugl-Meyer Assessment (FMA), FIM, Motor Activity Log and ABILHAND questionnaire.	The mean ratio change over the study period was significantly higher in the robot-assisted therapy group compared with the control group (0.047 vs. 0.007, p=0.026). The mean changes in FMA, MAL and ABILIHAND scores were also significantly better in the robot-assisted therapy group.
Hsieh et al. 2012 Taiwan 7 (RCT)	54 chronic (> 6 months) stroke patients were randomized to a 4-week intervention of higher-intensity, lower-intensity therapy using the Bi-Manu-Track device, or control treatment. Patients received treatment for 90-105 min/day x 5 days a week. Patients in the high intensity group performed twice as many repetitions as patients in the low intensity group. Patients in the control group received dose-matched therapy. The primary outcome, the Fugl-Meyer Assessment, was administered at baseline, midterm, and post treatment. Secondary outcomes included the Medical Research Council scale, the Motor Activity Log, and the physical domains of the Stroke Impact Scale.	Patients in all 3 groups improved over the study period. There was a significant time x group interaction effect. The higher-intensity group showed significantly greater improvements on the Fugl-Meyer Assessment than the lower-intensity and control treatment groups at midterm (p=0.003 and p=0.02) and at post treatment (p=0.04 and p=0.02). Patients in all groups made significant gains on the secondary outcomes, but the differences among the 3 groups were not significant.

10.3.5 Neuro-Rehabilitation-Robot (NeReBot)

The NeReBot device was developed in Italy designed to produce sensorimotor stimulation. The 3 degrees of freedom device can perform spatial movements of the shoulder and elbow, is portable and can be used when the patient is either prone or sitting.

Table 10.30 Studies Evaluating the NeReBot Device

Author, Year Country PEDro Score	Methods	Results
Masiero et al. 2006 Italy 5 (RCT)	20 acute stroke patients with hemiplegia or hemiparesis all received traditional multidisciplinary rehabilitation following stroke and they were randomized to receive either additional sensory motor training 4 hours per week for 4 wks or exposure to a robotic device without training. Assessments conducted before/after treatment and at 3 months included the Fugl-Meyer scale (FM), upper-Motricity Index (MI), motor FIM and Medical Research Council (MRC) scale.	At the end of treatment patients in the experimental group achieved significantly better scores on the shoulder/elbow section of the FM (shoulder elbow coordination) ($p<0.05$) and the motor FIM ($p<0.02$) compared to patients in the control group. These improvements were still evident at 3-month follow-up, as well as significantly greater improvement in MI scores ($p<0.04$)
Masiero et al. 2007 Italy 5 (RCT)	35 acute stroke patients were randomly assigned to either an experimental group (n=17) who received an additional 5 weeks of early sensorimotor robotic training for 4 hours/ wk or a control group (n=18) who performed exercises with their unaffected upper limb 30 min a week for 2 weeks using the robotic device. Main outcome measures included: Fugl-Meyer Assessment (FMA), the Medical Research Council (MRC) score (specifically MRC deltoid, MRC biceps and MRC wrist flexors), FIM instrument, Trunk Control Test (TCT) and Modified Ashworth Scale (MAS) assessed at the end of treatment and at 3 and 8 months follow-up.	There were significant gains made for the treatment group in functional recovery and motor impairment of the upper extremity following robot-assisted training seen in MRC deltoid and biceps, FMA for the upper proximal extremity, FIM motor score and FIM instrument. These gains were maintained at 3 and 8 months follow-up. No significant differences were found for the MAS and TCT.
Masiero et al. 2011 Italy 5 (RCT)	21 patients, less than 12 days following stroke were randomized to an experimental or control group. Patients in the control group (n=10) received 2 hours of conventional therapy, 5 days a week for 5 weeks. Patients received specific arm training for 40 minutes a day. The experimental group (n=11) substituted the conventional arm training with the robotic device. Outcomes were assessed before and after treatment and at 3 months follow-up. Outcomes included Medical Research Council (MRC), Fugl-Meyer	At the end of treatment, patients in both groups had improved significantly on all outcomes assessed. The only significant difference between groups was the MRC wrist flexor score, favouring the experimental group. At follow-up there were no significant differences between groups.

	Assessment, FIM, Modified Ashworth Scale, Frencahy Arm test, Box and Block test and the tolerability of treatment	

10.3.6 Continuous Passive Motion (CPM)

Passive range of motion is a standard therapeutic technique, considered to be effective in the prevention of contractures. Two studies evaluated the effectiveness of the device in maintaining gleno-humeral joint mobility.

Table 10.31 A Study Evaluating a CPM Device

Author, Year Country PEDro Score	Methods	Results
Volpe et al. 2004 USA 4 (RCT)	2 studies reported. Study 1: Patients with acute stroke (within 3 weeks) and hemiparesis randomly assigned to one of 2 groups: i) Continuous Passive Motion (CPM) group: 25 min/day of CPM training + standard post-stroke therapy (minimum 3.5 hrs/day of physical, occupational, and speech therapy) or ii) Control group: standard post-stroke therapy + extra 25 min/day of occupational therapy Study 2: Chronic stroke patients received interactive robotic arm training – lasted 1 hr/day, 3 days/wk for 6 wks. Patients assigned to two groups: i) moderate stroke severity, ii) severe stroke severity. Patients in both groups performed over 1000 flexion extension movements of the paralyzed arm with gravity eliminated to move the end of a robotic arm in the direction represented by eight points of a compass. Evaluations included Fugl-Meyer for shoulder/elbow and coordination; Motor Power; Motor Status Scale of shoulder and elbow; Joint stability; Ashworth score; Fugl-Meyer for pain; Functional Independence Measure. Evaluations-3 baseline 2 months prior to start of training, a midpoint evaluation, and a discharge evaluation	Study 1: no significant differences in improvement between CPM and Control group. Study 2: Within group comparisons-both groups showed significant improvement in motor function (p=.01) and power in the trained shoulder and elbow (p=.0001).
Hu et al. Hong Kong 2009 5 (RCT)	27 hemiplegic subjects with chronic stroke were randomly assigned to receive 20-sessions of wrist training with a continuous electromyography (EMG)-driven robot (interactive	Subjects in the Interactive group demonstrated statistically greater improvement in the following outcomes: FMA: shoulder/elbow, MAS elbow and MAS wrist, compared with subjects in the passive group.

	group, n = 15) and a passive motion device (passive group, n = 12), completed within 7 consecutive weeks. Training effects were evaluated with clinical scores by pretraining and post training tests (Fugl-Meyer Assessment [FMA] and Modified Ashworth Score [MAS]).	

10.3.7 GENTLE/s

This is a three-degree of freedom haptic interface arm with a wrist attachment mechanism, two embedded computers, a monitor and speakers and an overhead arm support system. The affected arm is de-weighted through a free moving elbow splint attached to the overhead frame. The subject is connected to the device by a wrist splint. Exercises such as hand-to-mouth and reaching movements can then be practised, while feedback is provided.

Table 10.32 A Study Evaluating the GENTLE/s Device

Author, Year Country PEDro Score	Methods	Results
Coote et al. 2008 UK 6 (RCT)	Following a baseline period, 20 subacute and chronic stroke patients were crossed over to receive robot-mediated therapy or a sling suspension phase which acted as the control condition. In robot-mediated therapy, they practiced three functional exercises with haptic and visual feedback from the system. In sling suspension, they practiced three single-plane exercises. Each treatment phase was three weeks long. Main measures included range of active shoulder flexion, the Fugl-Meyer (FM) motor assessment and the Motor Assessment Scale (MAS) were measured at each visit.	Each subject had a varied response to the measurement and intervention phases. The rate of recovery was greater during the robot-mediated therapy phase than in the baseline phase for the majority of subjects. The rate of recovery during the robot-mediated therapy phase was also greater than that during the sling suspension phase for most subjects.

10.3.8 Other Devices

Table 10.33 Studies Evaluating Other Robotic Devices

Author, Year Country PEDro Score	Methods	Results
Fazekas et al. 2007 Hungary	30 patients with spasticity following stroke were divided randomly into 2 groups: robotic and control. Subjects	Patients in both groups improved significantly on the Rivermead arm score, FM, FIM and ROM (elbow). There was no significant change

3 (RCT)	from both groups received 30 minutes of Bobath therapy sessions on 20 consecutive work days. Patients in the robotic group received an additional 30 minutes of robot-mediated therapy on the same days with the aim of reducing spasticity. Outcomes assessed before and after treatment included the Rivermead Arm Score, MAS of the shoulder adductors and elbow flexors, Fugl-Meyer (FM) (shoulder-elbow subsection), ROM and FIM (self-care).	in either group's ROM (shoulder). MAS scores of the shoulder adductors and elbow were significantly higher in the robotic group. No between group comparisons were conducted or reported.
Kutner et al. 2010 USA 7 (RCT)	17 subjects 3 to 9 months poststroke were randomized to receive 60 hours of therapist-supervised repetitive task practice (RTP) or 30 hours of RTP + 30 hours of robotic-assisted therapy over 3 weeks. The primary outcome measure was the Stroke Impact Scale (SIS), assessed at baseline, post intervention and 2 months post intervention.	The combined therapy group had a significantly greater increase in rating of mood from preintervention to post intervention compared with the RPT group while the RTP group had a greater increase in rating of social participation from preintervention to follow-up compared with the combined group.
Abdullah et al. 2011 Canada 5 (RCT)	20 patients admitted to an inpatient stroke rehabilitation following acute stroke unit were randomly allocated to receive 45 min of training with a robot designed to provide assistive therapy to the upper limb 3 x/week until discharge or to a dose-matched control group that received conventional therapy. The Chedoke Arm and Hand Activity Inventory (CAHAI-7) and the Chedoke McMaster Stroke Assessment of the Arm and Hand (CMSA) were assessed at admission and discharge.	Patients in the robotic therapy group improved their CMSA scores by an average of 62% compared with an improvement of 30% for those in the control group. The results were significant for the arm and hand scores. There were no significant differences between groups in pain or CAHAI-7 scores.
Hwang et al.2012 Korea 6 (RCT)	17 patients, an average of 6.5 mos following stroke were randomized to receive 20 sessions of active robot-assisted therapy for 40 min/day 5x/week for 4 weeks or 10 sessions of early passive therapy followed by 10 sessions of active robot-assisted intervention. Assessments were conducted at baseline, and at 2, 4 and 8 weeks after starting therapy and included the Jebsen-Talyor hand function (JTHF) test, the Fugl-Meyer Assessment, the Ashworth Scale, the 9-hole peg test (9HPT) and the Stroke Impact Scale.	Compared to baseline, patients in both groups showed improved results for the Jebsen-Taylor test, the wrist and hand sub portion of the Fugl-Meyer arm motor scale, active movement of the 2nd metacarpophalangeal joint, grasping, and pinching power ($P < 0.05$ for all) at each time point (2, 4 and 8 weeks), with a greater degree of improvement for the patients that received 20 sessions of robot-assisted therapy. There were no between-group differences in any of the outcomes.
Kim et al.	15 chronic stroke subjects with Fugl-	In addition to improvements on kinematic

2012 USA (RCT)	Meyer Scores between 16- 39, Mini Mental Status Exam score >19, between 27 and 70 years of age were randomly assigned to a bilateral robotic training or unilateral robotic training. The device under study was a seven degree of freedom (DOF) upper limb exoskeleton robot (UL-EXO7). Both patient groups played eight therapeutic video games over twelve sessions (90 minutes, two times a week). In each session, patients intensively played the different combination of video games that directly interacted with UL-EXO7 under the supervision of research assistant. At each session, all of the joint angle data was recorded for the evaluation of therapeutic effects.	performance, patients in both groups also gained an average of 4 points on the Fugl-Meyer Assessment.

Discussion

Robotic therapies show promise for helping to provide safe and intensive rehabilitation to patients who have mild to severe motor impairment. Robotic devices can be used to provide rehabilitation that is of high-intensity, repetitive and task-specific in a manner that is similar to physical therapy. Summarizing the results from the above studies can be challenging as a variety of devices were assessed using patients in the acute, sub acute and chronic stages of stroke.

A summary of the studies evaluating any form of robotic training is presented in table 10.34.

Table 10.34 Summary of Results From Studies Evaluating Sensorimotor Training: Robotic Devices

Author/ PEDro Score	n	Intervention	Main Outcome(s) Result
Kutner et al. 2010	17	Hand Mentor	Stroke Impact Scale (Mood +)
Rabadi et al. 2009 5 (RCT)	30	Robot-unilateral group vs. ergometer (bilateral) group vs. conventional therapy	Fugl-Meyer Assessment (-)
Coote et al. 2008 8 (RCT)	20	Robot-aided therapy vs. sham robot-aided therapy	Fugl-Meyer Assessment (+)
Volpe et al. 2008 5 (RCT)	21	Robot assisted movement training vs. conventional therapy	Fugl-Meyer Assessment (-)
Lum et al. 2006 4 (RCT)	30	Robot-unilateral group vs. robot-bilateral group vs. robot-combined group vs. conventional therapy	Fugl-Meyer Assessment (+ robot-groups vs. control at post-treatment) (+ robot-unilateral vs. robot-combined) Motor Status Score (+ robot-groups vs. control at post-treatment) FIM (-) Modified Ashworth Scale (-)
Masiero et al. 2007	35	Additional Robotic Training 4	Fugl-Meyer Assessment

5 (RCT)		hrs/wk x 5 wks vs. exposure to robotic device 30 min/wk x 2 wks	(+ upper extremity) (- wrist) Medical Research Council (+ deltoid and biceps) (- wrist) FIM (+) Trunk Control Test (-) Modified Ashworth Scale (-) (All outcomes are taken at the end of treatment)
Masiero et al. 2006 5 (RCT)	20	Additional sensorimotor robotic training or exposure to robotic device with no training	Fugl-Meyer scale (+ shoulder and elbow) upper-Motricity Index (+) Functional Independence Measure (+ motor component) Medical Research Council scale (-)
Kahn et al. 2006 4 (RCT)	19	Robot-assisted training vs. reaching unassisted	Biomechanical Assessment (- range) (- speed) (- straightness) (+ smoothness at d/c) Rangos Los Amigos Functional Test (-)
Hesse et al. 2005 8	44	Computerized arm training enabling repetitive practice v. electrical stimulation	Fugl-Meyer Assessment (+)
Fasoli et al. 2004 6	56	Robot assisted movement training vs. robot exposure	Fugl-Meyer Assessment (+ from adm-hospital d/c) Motor Status score for shoulder/elbow (+)
Lum et al. 2002 6 (RCT)	27	Robot assisted movement training vs. conventional therapy	Fugl-Meyer Assessment (+ at 1 and 2 months) (- at 6 months) Upper Extremity Strength (+ at 2 months) Upper Extremity Reach (+ at 2 months) FIM (+ at 6 months)
Volpe et al. 2000 6 (RCT)	56	Robotic training (at least 25 hrs) vs. exposure to the robotic device without training	Motor Power score (+ shoulder and elbow) (- wrist and hand) Motor Status score (+ shoulder and elbow) (- wrist and hand) FIM–Motor (+) (All outcomes are taken at the end of treatment)
Volpe et al. 1999 6 (RCT)	20	Robot vs. sham treatment	Motor status Scores (+ for shoulder/elbow at discharge and 3 yr follow up) (- for wrist/hand at discharge and follow-up) Motor Power Score (+ for shoulder and elbow at discharge)

			Fugl-Meyer (- for shoulder/elbow and wrist/hand at discharge and follow-up)
Stein et al. 2004 5 (RCT)	49	Robot-aided vs. robot assisted program	Motor control (-) Strength (-)
Volpe et al. 2004 4 (RCT)	32	Continuos Passive Motion Device vs. control	Fugl-Meyer pain (-) Motor Status scores (- elbow/shoulder) Ashworth scale (-)
	36	Interactive Robotic Therapy	Fugl-Meyer elbow/shoulder (+) Motor Power (+)
- Indicates non-statistically significant differences between treatment groups *+ Indicates statistically significant differences between treatment groups*			

Conclusions Regarding Robotics in the Rehabilitation of the Upper Extremity

There is strong (Level 1a) evidence that sensorimotor training with robotic devices improves upper extremity functional outcomes, and motor outcomes of the shoulder and elbow.

There is strong (Level 1a) evidence that robotic devices do not improve motor outcomes of the wrist and hand.

Sensorimotor training with robotic devices improves functional and motor outcomes of the shoulder and elbow; however, it does not improve functional and motor outcomes of the wrist and hand.

10.4 Virtual Reality Technology

Virtual reality, also known as virtual environment, is a technology that allows individuals to experience and interact with three-dimensional environments. The most common forms of virtual environments simulators are head-mounted displays (immersion) or with conventional computer monitors or projector screens (nonimmersion) (Sisto et al. 2002). According to Merians et al. (2002), a computerized virtual environment has opened the doors to an "…exercise environment where the intensity of practice and positive feedback can be consistently and systematically manipulated and enhanced to create the most appropriate, individualized motor learning approach. Adding computerized VR to computerized motor learning activities provides a three-dimensional spatial correspondence between the amount of movement in the real world and the amount of movement seen on the computer screen. This exact representation allows for visual feedback and guidance for the patient."

Henderson et al. (2007) conducted a systematic review that included 6 studies evaluating immersive and nonimmersive VR technology in the rehabilitation of the upper extremity. The authors concluded that immersive VR might be more effective compared no therapy, while the results from studies examining nonimmersive VR were conflicting.

Saponsik & Levin (2011) conducted a systematic review and meta-analysis of virtual reality including the results from 12 studies, 5 of which were RCTs. In an analysis restricted to RCTs, VR was associated with significant improvements of 13.7% to 20% in impairment level measures (Fugl-Meyer scores, speed of arm movement, range of motion and force) compared with improvements of 3.8% to 12.2% among patients in the control groups. In the analysis restricted to observation studies with no control group, there was a 14.7% improvement in terms of impairment-level measures and 20.1% in motor function.

The results of a Cochrane review, (Laver et al. 2011) included the results from 19 RCTs (565 subjects), of which 8 examined upper-limb training, reported a moderate treatment effect for arm function (SMD=0.53, 95% CI 0.25 to 0.81). Only two of the studies used readily available commercial devices (Playstation EyeToy, and Nintendo Wii), the remainder used customised VR programs.

Table 10.35 Studies Evaluating Virtual Reality Technology

Author, Year Country PEDro score	Methods	Results
Jang et al. 2005 Korea 5 (RCT)	Controlled trial evaluating virtual reality (VR) training for 60 min/day x 5 days/week x 4 weeks vs. no VR intervention. 10 chronic stroke patients participated. Outcome measures included the box and block test (BBT), Fugl-Meyer (FM) and the Manual function test (MFT). Qualitative information on the amount of use and the quality of movement was also collected. Functional MRI was also conducted. VR was designed to provide a virtual rehabilitation scene where the intensity of practice and sensory feedback could be systematically manipulated to provide the most appropriate, individualized motor retraining program.	Following treatment VR patients scored significantly higher, compare to controls on BBT, FMA and MFT scores. Cortical activation by the affected movements were reorganized from contralateral (before VR) to ipsilateral (after VR), in the laterality index.
Lam et al. 2006 Israel 4 (RCT)	58 stroke patients were randomly assigned to 1 of 3 groups: i.) 2DVR computer based training programme for training in mass transit railway (MTR) skills, ii.) video modelling-based psychoeducational programme of similar structure and content, or iii.) control. Assessments were made using a questionnaire on the demographic characteristics of the patients, a behavioural rating scale on using MTR skills and an MTR self-efficacy rating scale.	Over a 4-wk interval significant improvements were seen for subjects in both treatments groups in MTR knowledge, skills and self-efficacy ($p<0.01$). However, the control group failed to improve and remained stable in skills and self-efficacy in using MTR.
Fischer et al. 2007 USA 4 (RCT)	15 chronic stroke patients with upper extremity hemiparesis were randomly assigned to 1 of 3 groups: i.) digit extension assisted by a novel cable orthosis (n=5), ii.) digit extension assisted	Participants demonstrated a significant decrease in time to perform functional tasks for the WMFT ($p = .02$), an increase in the number of blocks successfully grasped and released during the BB ($p =$

	by a novel pneumatic orthosis (n=5), iii.) or no assistance provided. The training consisted of 6 weeks of therapy (1 hour sessions held 3 x/week). Each session required patients to grasp and release virtual and actual objects. Outcome measures included Wolf Motor Function Test (WMFT), Rancho Los Amigos Functional test of the Hemiparetic Upper Extremity (RLA), Box and Blocks Test (B&B), Upper Extremity Test Fugl-Meyer Test (FM), and Biomechanical Assessments. Assessments were conducted before/after and at one and 6 months post intervention.	.09), and an increase for the FM score (p = .08). There were no statistically significant changes in time to complete tasks on the RLA or any of the biomechanical measures. Assistance of extension did not have a significant effect.
Broeren et al. 2008 Sweden 3 (RCT)	22 subjects with chronic stroke living in the community in their own homes were randomized to receive extra rehabilitation by training on a computer 3 times a week during a 4-week period or to continue their previous rehabilitation (no extra computer training). The VR training consisted of challenging games which provided a range of difficulty levels. An additional group of 11 right-handed, aged matched individuals without history of neurological or psychiatric illnesses served as reference subjects. Outcomes were assessed before and after treatment and included a semi-structured interview, Box & Block test (BBT), ABILIHAND, Trail Making Test (to assess executive function and attention) and kinematic analyses.	All the participants in the VR group reported that they enjoyed using the system. There were no significant differences between the control and the VR group on tests of manual ability or executive function. There were significant improvements in some of the kinematic measurements associated with reaching.
Yavuzer et al. 2008 Turkey 6 (RCT)	20 hemiparetic inpatients, all within 12 months post stroke, received 30 minutes of treatment with ''PlayStation EyeToy Games'' per day, consisting of flexion and extension of the paretic shoulder, elbow and wrist as well as abduction of the paretic shoulder or placebo therapy (watching the games for the same duration without physical involvement into the games) in addition to conventional program, 5 days a week, 2-5 hours/day for 4 weeks. Brunnstrom's staging and self-care sub-items of the functional independence measure (FIM) were performed at baseline, 4 weeks (post-treatment), and 3 months follow-up.	There was a significantly greater improvement in both mean hand and UE components of the Brunnstrom scale and FIM scores following treatment among subjects in the EyeToy group. The improvement in FIM self-care scores remained significantly greater at follow-up among subjects in the EyeToy group (5.5 vs. .1.8, p=0.018).
Housman et al. 2009 USA 6 (RCT)	34 chronic stroke subjects were randomized to receive 24 treatment sessions using either an arm orthosis using the Therapy Wilmington Robotic Exoskeleton (T-WREX), which supports	At the end of 6 months, subjects in the T-WREX group achieved and maintained a higher FMA score compared with control (3.6 vs. 1.5 points, p<0.045). There were no other significant between group

	the arm against gravity and measures arm movement and trace hand grasp as users interact with computer games (n=14) or to a control group (n=14) whereby subjects participated in conventional exercises (self range of motion stretches and active range of motion strengthening exercises). Outcomes assessed before and after treatment and at 6 month follow-up included the Fugl-Meyer Assessment, ADL assessment, Motor Activity Log and grip strength.	differences.
Piron et al. 2009 Italy 7 (RCT)	36 patients with mild arm motor impairments due to ischemic stroke in the region of the middle cerebral artery were randomized to one of 2, 4-week outpatient treatment programs. Treatment lasted for 1 hr/day x 5 days/ week. The experimental treatment was a virtual reality-based system delivered via the Internet, which provided motor tasks to the patients from a remote rehabilitation facility (Telerehab). The control group underwent traditional physical therapy for the upper limb. Outcomes were assessed one month prior to therapy, at the beginning and end of therapies and one month post-therapy, with the Fugl-Meyer (FM) Upper Extremity, the ABILHAND and the Ashworth scales.	Both rehabilitative therapies significantly improved all outcome scores after treatment. Subjects in the Telerehab group had a higher FM score at the end of treatment compared with control (53.6 vs. 49.5, $p<0.05$), although the difference was no longer significant at 3 months (53.1 vs. 48.8). A similar pattern was observed for the ABIHAND, whereby the Telerehab group had significantly better scores after the first 2 assessments but not at follow-up. There were no differences in Ashworth Scores between groups at any point.
Saposnik et al. 2010 Canada 7 (RCT)	22 patients within 2 months of stroke receiving standard rehabilitation were randomized to receive either 8, 60 minutes sessions with either the Nintendo Wii gaming system (VRWii) or recreational therapy (playing cards, bingo, or "Jenga"). The primary feasibility outcome was the total time receiving the intervention. Efficacy was evaluated with the Wolf Motor Function Test, Box and Block Test, and Stroke Impact Scale at 4 weeks after intervention.	The interventions were successfully delivered in 9 of 10 participants in the VRWii and 8 of 10 in the recreational therapy arm. Participants in the VRWii arm had a significant improvement in mean motor function of 7 seconds (Wolf Motor Function Test, 7.4 seconds. There were no differences on any of the other outcomes.
Crosbie et al. 2012 UK 8 (RCT) (pilot study)	18 subjects with an average stroke onset of 10.8 months were randomized to a virtual reality group or a conventional arm therapy group for nine sessions over three weeks. Primary outcome measures were The Motricity Index (MI) upper limb and the Action Research Arm Test (ARAT) assessed at baseline, post intervention and six weeks follow-up.	Patients in both groups improved but there were no statistically or clinically significant differences between groups at the end of follow-up. Patients in both groups demonstrated 7-8 point gains in MI scores and an average of 4 points on the ARAT. Clinically significant differences for these measures are 10 and 6, respectively.

Virtual reality training is an innovative new treatment approach, which may enhance cortical reorganization following stroke. To date only a few RCTs have been conducted. One of the studies included in this review used virtual reality technology as a more efficient method to test the efficacy of a device used to improve finger extension (Fisher et al. 2007). Two trials used popular gaming systems--the Playstation EyeToy and the Ninetendo Wii gaming system, both inexpensive video game devices to improve upper-extremity function following stroke, with equivocal results. The authors hypothesized that the beneficial effect could be attributed to the avoidance of learned nonuse behaviour or by repeated practice of functional tasks. The results from the remaining RCTs indicated that virtual reality treatment was of benefit for chronic stroke patients in the improvement of motor function.

Table 10.36 Summary of RCTs Evaluating Virtual Reality Technology

Author/ PEDro Score	N	Intervention	Main Outcome(s) Result
Crosbie et al. 2012 8	18	Virtual reality training of 9 sessions over 3 weeks vs. conventional therapy	Motricity Index (-) ARAT (-)
Saposnik et al. 2010 7 (RCT)	20	Nintendo Wii gaming system (VRWii) vs. recreational therapy	Wolf Motor Function Test (+) Box & Block test (-) Stroke Impact Scale (-)
Yavuzer et al. 2008 6 (RCT)	20	Playstation EyeToy games vs. conventional therapy	Brunnstrom score (-) FIM self-care (+)
Jang et al. 2005 Korea 5 (RCT)	10	Virtual reality training for 60 min/day x 5x/wk x 4 wks vs. no Virtual reality training.	Box and block test (+) Fugl-Meyer test (+) Manual function test (+)
Lam et al. 2006 Israel 4 (RCT)	58	2DVR computer based training programme vs. video modelling-based psychoeducational programme vs. control	Mass Transit Railway (- skills) (- self-efficacy)
Broeren et al. 2008 Sweden 3 (RCT)	22	Semi-immersive workbench with haptic and stereoscopic glasses vs. no VR treatment	Box & Block Test (-) ABILIHAND (-) Trail Making Test (-) Kinematics (+)

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Conclusions Regarding Virtual Reality Technology in the Treatment of Stroke

There is strong (Level 1a) evidence that virtual reality treatment can improve motor function in the chronic stages of stroke.

Virtual reality therapy may improve motor outcomes post stroke.

10.5 Treatment for Spasticity or Contracture in the Upper Extremity

Stroke survivors often display a constellation of signs and symptoms that together constitute the upper motor neuron syndrome. The syndrome consists of negative signs including: weakness, loss of dexterity, fatigue and positive signs including increased muscle stretch reflexes, abnormal cutaneous reflexes and spasticity. Spasticity is classically defined as a velocity dependent increase of tonic stretch reflexes (muscle tone) with exaggerated tendon jerks. Spasticity can be painful, interfere with functional recovery in the upper extremity and hinder rehabilitation efforts. However, Gallichio (2004) cautioned that a reduction in spasticity do not necessarily lead to improvements in function. Van Kuijk et al. (2002) noted that for most stroke patients, "…spasticity is a variable phenomenon in time and apparent in only certain muscle groups, and therefore, low threshold and "reversible" focal treatment techniques seem to be the preferable first option."

A study by Watkins et al. (2002) reported that 39% of patients with a first-ever stroke were spastic 12 months after their stroke. More recently, a study by Sommerfeld et al. (2004) reported that of 95 patients assessed initially (mean 5.4 days) after an acute stroke, 77 (81%) were hemiplegic and 20 (21%) were spastic. Overall, upper extremity spasticity alone (n=13) was more common than lower extremity spasticity alone (n=1) or spasticity in both upper and lower extremities (n=6). At three months post-stroke, 64 patients (67%) were still hemiparetic, and 18 (19%) were still spastic. At that point, there were more patients with spasticity in both extremities (n=10) than in the upper extremity alone (n=7) or in the lower extremity alone (n=1). The authors also reported that severe disabilities were found in almost the same number of nonspastic patients as spastic patients.

There are a number of interventions used for limb spasticity. These include oral antispasticity agents, injection of phenol to motor nerves or alcohol to muscle bellies, and physical modalities such as stretching, orthoses, casting, cold application and surgery. The mainstay of treatment for spasticity has been physical therapy. Traditional pharmacotherapies for spasticity include centrally acting depressants (baclofen, benzodiazepines, clonidine, and tizanidine) and muscle relaxants (dantrolene). There is evidence from RCTs published in the 60's and 70's that these treatments are only partially effective in treating spasticity and have negative side effects of weakness and sedation. More recently, Tizanidine hydrochloride was used to successfully treat spasticity among 47 chronic stroke patients, although, due to side effects, only a small percentage of patients reached the maximum daily dose (Gelber et al. 2001). Motor point or nerve blocks with phenol or alcohol have been used but are often associated with variable success rates, and high rates of neuropathic pain. Botulinum toxin type A, a potent neurotoxin that prevents the release of acetylcholine from the preseynaptic axon, has more recently been studied as a potentially useful treatment for stroke related spasticity. Intrathecal drug therapy refers to the injection of a drug into the subarachnoid space of the central nervous system and requires the implantation of a programmable device into the subcutaneous tissue surrounding the abdominal wall. Intrathecal baclofen, the most commonly used intrathecal drug for relieving spasticity associated with stroke has not been well studied, particularly for spasticity of the upper extremity.

10.5.1 Splinting

Splints have been widely-used in clinical practice with the aim of the prevention of contractures and reducing of spasticity; however, they have not been well-studied.

In a systematic review by Steultjens et al. (2003), the authors also concluded that based on the results of 2 RCTs (Langlois et al.1991, Rose et al. 1987), 2 case-controlled trails (McPherson et al. 1982, Poole et al. 1990) and one uncontrolled trial (Gracies et al. 2000) that there was insufficient evidence that splinting was effective in decreasing muscle tone. Tyson & Kent (2011) conducted a systematic review on the effect of upper limb orthotics following stroke, which included the results from 4 RCTs representing 126 subjects. The treatment effects associated with measures of disability, impairment, range of motion, pain, and spasticity were small and not statistically significant.

Table 10.37 Splinting the Upper Extremity

Author/ Country Pedro Score	Methods	Outcomes
Rose et al. 1987 4 (RCT)	30 patients with spastic wrist flexors resulting from a diagnosed stroke, no more than 6 months post-stroke. Subjects were randomly assigned to either of two experimental groups (predominantly dorsal or predominantly volar static orthosis) or to the control group (no orthosis). Both of the intervention groups had hand splinting in the functional position for 2 hours using either volar or dorsal splints.	The patients in the intervention groups had significant increases in passive range of wrist extension and a decrease in hypertonus compared with the control group. No significant difference in passive range of motion or resistance to passive extension was found between the dorsal and volar splinting groups. There was a significant difference between spontaneous flexion between dorsal and control groups, but not volar and control groups.
Langlois et al. 1991 3 (RCT)	9 patients within 12 months of acute stroke were randomly allocated to one of 3 groups: wearing a finger spreader splint for 6 hrs, 12 hrs or 22 hrs per day for a period of 2 weeks.	No significant differences were found in spasticity reduction between groups; however, all 3 groups demonstrated a reduction in spasticity. No significant differences were found between groups on measures of expectation or satisfaction and the reduction of spasticity (Expectation and Satisfaction Questionnaire that was developed specifically for this study), or on reported compliance and prescribed wearing schedule at 2 weeks. There was a significant association between expectation and compliance.
Lannin et al. 2003 Australia 8 (RCT)	28 rehabilitation patients were randomized to either control or experimental groups. Subjects in both groups participated in routine therapy for	No difference in contracture formation in the wrist and finger flexor muscles between groups.

	individual motor training and upper limb stretches 4 days a week. In addition, patients in the experimental group wore an immobilizing hand splint on a daily basis, for a maximum of 12 hours each night, for 4 weeks.	
Harvey et al. 2006 Australia 8 (RCT)	44 community-dwelling patients, 14 with chronic stroke with uni or bilateral thumb web-space contractures were randomized to wear a splint each night for 12 weeks. The splint stretched the thumb into an abducted position. Subjects in the control group were not splinted. Thumb web-space was measured as the carpometacarpal angle during the application of a 0.9 Nm abduction torque before and after intervention.	There was no significant difference between groups of 1 degree (95% CI, -1 to 2). The mean increase in thumb web-space after 12 weeks was 2 deg in the experimental group and 1 degree in patients in the control group.
Lannin et al. 2007 Australia 7 (RCT)	63 stroke patients within 8 weeks of stroke onset were randomly allocated to receive 1 of 3 therapies: i.) no splint control group (n=21), ii.) a neutral splint group (n=20), or iii.) an extension splint group (n=21). All patients received routine rehabilitation. Splints were worn 12 hours overnight for the 4-week treatment period. The Primary Outcome was muscle extensibility of the wrist and fingers, assessed before/after treatment and at 6 weeks.	There were no significant differences between groups or within groups. Splinting did not reduce wrist contractures.
Basaran et al. 2012 Turkey 6 (RCT)	39 subjects, 5 to 120 months post stroke onset were randomized to 1 of 3 groups and received a 5 week, home-based exercise program. Patients in 2 groups wore either a volar or dorsal splint for up to 10 hours overnight throughout the study period. Patients in the control group did not wear a splint. Outcomes assessed before and after treatment included the Modified Ashworth Scale (MAS), Hmax: Mma x of the flexor carpi radialis muscle and passive range of motion.	There were no significant differences within or among the groups on any of the outcomes assessed.

Six RCTs were identified examining the benefit of splinting. The focus of each of these studies was different (finger, wrist and elbow). One of the trials (Lai et al. 2009) assessed a dynamic splint, which progressively increases torque to reduce contracture and maintain the joint at its end range. The remaining trials assessed resting or static splints. Most of the studies failed to support the benefit of splinting in reducing spasticity of avoiding contracture. It has been suggested that short treatment periods, typically from 4-6 weeks and underpowered studies may have contributed to the negative findings.

Conclusions Regarding Treatment of Spasticity: Hand Splinting

There is strong (Level 1a) evidence that hand splinting does not reduce the development of contracture, nor reduce spasticity.

Hand splints to not reduce spasticity or prevent contracture.

10.5.2 Stretching Programs to Prevent Contracture

Spastic contracture following stroke is the expression of hypertonicity or increased active tension of the muscle. Contracture may also occur as a result of atrophic changes in the mechanical properties of muscles. Since surgery is the only treatment option once a contracture has developed, prevention is encouraged. Stretching may help to prevent contracture formation and, although well-accepted as a treatment strategy, has not been well-studied.

Table 10.38 Stretching Programs to Prevent Contracture

Author/ Country Pedro Score	Methods	Outcomes
Turton & Britton 2005 UK 6 (RCT)	In addition to usual care, 13 subjects on a stroke rehabilitation unit, admitted within 4 weeks post stroke and with no hand function, received two 30-min stretches for wrist and finger flexors and two 30-min stretches targeting shoulder adductors and internal rotators, per day for up to 12 weeks post stroke. Therapists and nursing staff carried out stretches. 12 patients in the control group received standard care.	There were no significant effects of treatment. By eight weeks post stroke the mean range of wrist extension and shoulder external rotation lost on the affected side in both groups was approximately 30 degrees. Compliance was variable. Only 6 patients completed the full treatment. Patients declined to participate or were unavailable and staff was also non-compliant.
Tseng et al. 2007 Taiwan 7 (RCT)	59 bedridden older stroke survivors in residential care were randomly assigned to usual care or one of two intervention groups. The 4-week, twice-per-day, 6 days-per-week range-of-motion exercise protocols were similar in both intervention groups, and consisted of full range-of-motion exercises of the upper and lower extremities. To test the effect of different degrees of staff involvement, in intervention group I, a Registered Nurse was present to supervise participants performing the exercises, while intervention group II involved a Registered Nurse physically assisting participants to achieve maximum range-of-motion within or beyond their present abilities. Assessments conducted before and after the intervention included joint angles of the shoulder, elbow and wrist and FIM and pain score.	Both intervention groups had statistically significant improvement in mean joint angles, activity function, perception of pain and depressive symptoms compared with the usual care group ($P < 0.05$). Post hoc comparison revealed that the joint angles in intervention group II were statistically significantly wider than in both the other groups ($P < 0.01$).

Only two RCTs have been published examining the benefit of stretching regimes to help prevent contracture formation. One was conducted during the acute stage of stroke (Turton & Britton 2005) and the other, during the chronic stage (Tseng et al. 2007). The development of contracture formation was not reported, therefore the outcomes assessed focused on joint angles, ADL performance and pain.

Conclusions Regarding Stretching Programs to Prevent Contracture Formation

There is moderate (Level 1a) evidence that a nurse-led stretching program can help to increase range of motion in the upper extremity and reduce pain in the chronic stage of stroke.

10.5.3 Botulinum Toxin Injections

Botulinum works by weakening spastic muscles through selectively blocking the release of acetylcholine at the neuromuscular junction. The benefits of botulinum injections are generally dose-dependent and last approximately 2 to 4 months (Simpson et al. 1996, Bakheit et al. 2001, Smith et al. 2000, Francisco et al. 2002, Brashear et al. 2002). One of the advantages of botulinum is that it is safe to use on small, localized areas or muscles, such as those in the upper extremity. Unlike chemical neurolysis with either phenol or alcohol, botulinum toxin is not associated with skin sensory loss or dysesthesia (Suputtitada & Sunanwela 2005). Dynamic EMG studies can be helpful in determining which muscles should be injected (Bell and Williams 2003).

van Kuijk et al. (2002) evaluated the benefit of botulinum toxin for the treatment of upper extremity spasticity with focal neuronal or neuromuscular blockade. The review included 10 studies (4 RCTs and 6 uncontrolled observational studies). The authors found that there was evidence of the effectiveness of botulinum toxin treatment on reducing muscle tone (modified Ashworth Scale) and improving passive range of motion at all arm-hand levels in chronic patients for approximately 3 to 4 months. However, the authors concluded that while overall, the effectiveness on improving functional abilities was not justified, specific stroke groups may benefit from botulinum injections in the upper extremity.

While many controlled studies have demonstrated a reduction in spasticity following treatment with botulinum toxin, usually BTX-A (Botox or Dysport), measured using the Modified Ashworth Scale or range of motion, it is less clear whether treatment is associated with an improvement in upper extremity function. Francis et al. (2004) suggested several reasons why this might be so. These authors suggested that underlying muscle weakness and not spasticity contribute to the limitation in function. However, they speculated that the most likely reasons were insufficiently sensitive outcome measures chosen and under-powered studies. A meta-analysis authored by the same authors included the results from two RCTs (Bakheit et al. 2000, 2001), suggested that there was a benefit, albeit modest of BTX-A on improved function. The authors of this review pooled the data and assessed the effect on the arm section of the Barthel Index (dressing, grooming and eating) and reported a modest improvement in upper arm function following botulinum toxin.

Pooling was only possible for two RCTs due to heterogeneity of interventions and outcomes.

Cardoso et al. (2005) conducted a meta-analysis investigating botulinum toxin type A (BTX-A) as a treatment for upper limb spasticity following stroke. They included five RCTs (Simpson et al. 1996; Smith et al. 2000; Bakheit et al. 2000; Bakheit et al. 2001; Brashear et al. 2002) and reported that there was a significantly greater reduction in spasticity for patients who underwent BTX-A treatment compared to patients receiving the placebo treatment, as measured by the modified Ashworth Scale and the Global Assessment Scale. They concluded that BTX-A reduces spasticity and that the treatment was tolerated well, although the effects of long-term use of BTX-A are unknown. Levy et al. (2007) reported additional benefits when a course of constraint-induced movement therapy followed treatment with BTX-A. Unfortunately the gains in motor function were lost at the end of 24 weeks when spasticity returned.

The results from controlled and uncontrolled studies, which evaluated the effect of botulinum toxin on spasticity, were reviewed. The results are presented in Table 10.39.

Table 10.39 Botulinum Toxin Injection and Spasticity in Upper Extremity Post Stroke

Author/ Country PEDro Score	Methods	Outcomes
Simpson et al. 1996 USA 8 (RCT)	A double blind, placebo controlled trial of 37 patients randomized to receive either a single treatment of either 75 units, 150 units or 300 units of total doses of BTX-A or placebo into the biceps, flexor carpi radialis and flexor carpi ulnaris muscles.	Treatment with 300-unit BTX-A dose resulted in clinical significant mean decrease in wrist flexor tone at 2, 4 and 6 weeks post-injection. BTX-A groups reported significant improvement on physician and patient Global Assessment of Response to Treatment at weeks 4 and 6 post-injection.
Smith et al. 2000 UK 7 (RCT)	Double blind placebo trial of 25 patients randomized to receive 500 Mu, 1000 Mu or 1500 Mu of botulinum toxin by intra-muscular injection, or placebo of an equal volume of sterile saline.	Combining data from active treatment, botulinum toxin showed significantly greater improvement in modified Ashworth scale at fingers, passive range of movement at the wrist, and finger curl distance at rest. Only significant difference between dose groups in favour of 1500 Mu for improved movement at the elbow.
Bakheit et al. 2000 UK 8 (RCT)	International, multi-center, randomized, double-blind placebo-controlled trial of 82 patients randomized to one of four groups (500 U of Dysport, 1000 U of Dysport, 1500 U of Dysport or placebo). Injections were made to the biceps brachii, flexor digitorum profundus and flexor digitorum superficialis, flexor carpi ulnaris and flexor carpi radialis muscles.	All 3 groups receiving Dysport showed significant reduction in MAS (Modified Ashworth Scale) scores in any joint at week 4 compared with placebo. At 16 weeks, the MAS scores were significantly reduced in the hemiparetic arm for all doses in the elbow and wrist and also in the fingers in the 1000 U Dysport group. No significant differences were found between groups on the Rivermead Motor Assessment, pain scores, or Barthel Index scores.
Bhakta et al. 2000	40 patients with stroke and spasticity in a functionally useless arm (median	There was a significant reduction in disability at 2 and 6 weeks, but not at 12 weeks post

UK 7 RCT	duration 3.1 years) were randomized to receive intramuscular botulinum toxin type A (BT-A; Dysport) (n=20) or placebo (n=20) in a total dose of 1000 MU divided between elbow, wrist, and finger flexors. Spasticity was assessed using the modified Ashworth scale (MAS). Muscle power, joint movement, and pain, disability and carer burden were also assessed. Two baseline and three post-treatment assessments were conducted at weeks 2, 6, and 12 weeks.	treatment. Caregiver burden was significantly reduced throughout the study period. MAS scores were reduced significantly at 2 weeks (finger and elbow), 6 weeks and 12 weeks (finger only). There was no significant improvement in grip strength or reduction in pain associated with BT-A treatment.
Bakheit et al. 2001 UK 8 (RCT)	International, multi-center, randomized, double-blind placebo-controlled trial of 59 patients who received either placebo injections or a total of 1000 IU of BtxA (Dysport) into 5 muscles of the affected arm.	The group who received Dysport had a significant reduction in the summed Modified Ashworth Scale score at week 4 compared with the placebo group. The magnitude of benefit over the 16 week follow-up period was significantly reduced for the BTX-A group in the wrist and finger joints compared with the placebo group. No significant difference was noted between the groups in the joint ROM, muscle pain, goal-attainment or the Barthel Index scores at week 4 of the study. At week 16, the BTX-A group showed significantly greater improvement in elbow PROM.
Brashear et al. 2002 USA 7 (RCT)	126 stroke patients were randomized to receive a single injection of BTX-A (n=64) or placebo (n=64) (50 units injected in each of 4 wrist and finger muscles).	122 patients completed the study. The primary outcome was improvement in the 4-point Disability Assessment scores at 6 weeks (hygiene, dressing, pain and limb position). Six weeks after injection with BTX-A 83% of subjects reported at least a one-point improvement of DAS score compared to 53% of patients who were treated with placebo (p=0.007).
Francisco et al. 2002 USA 7 (RCT)	13 patients (10 strokes) with Modified Ashworth Scores (MAS) of 3 or 4 were randomized to receive either high volume BTX-A (50 units/1 mL saline:1.2 mL delivered per 4 muscles) or low volume BTX-A (100 units/1 mL saline delivered per 4 muscles). On average, patients in the high volume group received 417 units BTX-A compared to patients in the low volume group (432 units).	Assessments were completed at 4, 8 and 12 weeks post injection. MAS scores of both wrist and finger flexors were assessed. While MAS scores decreased significantly in both treatment groups, there were no differences between the low and high volume BTX-A regimens.
Bakheit et al. 2004 UK No Score	An open label study in which 51 patients with established post stroke upper limb spasticity received 1000 units of BtxA (Dysport) into five muscles of the affected arm. Treatment was repeated every 12, 16, or 20 weeks as clinically indicated. Each patient received a total of three	41 subjects completed all 3 treatment cycles. Improvement from the cycle one baseline was observed in all the outcome measures. 100% of subjects achieved at least a 1- point decrease on MAS scores in at least 1 joint. By the end of the 3rd cycle, 98% had achieved a 1-point reduction. 90% of subjects who completed the 3 cycles reported that the

	treatment cycles. Efficacy of treatment was assessed using the Modified Ashworth Scale. Patients were assessed on study entry and on week 4 and 12 of each treatment cycle for all safety and efficacy parameters. Blood samples for BtxA antibody assay were taken at baseline and on completion of the trial.	treatment had been beneficial. Mild to moderately severe treatment related adverse events were reported in 24% of cases. No BtxA antibodies were detected
Brashear et al. 2004 USA 7 (RCT)	15 stroke patients were randomized to receive a single Botox type B injection (10,000U) in the elbow, wrist, finger and thumb (n=10) or placebo (n=5). Measures were recorded at 2, 4, 8, 12 and 16 weeks.	There was no significant decrease in muscle tone in the elbow, wrist, or finger. A decrease in Ashworth scale scores was observed at the wrist at week 2 in the treatment group. Improvement was also observed at week 4 for the elbow (p=.039), wrist (p=.002), finger (p=.001) and thumb (p=.002) in the treatment gr. Improvements were not sustained.
Gordon et al. 2004 USA No Score	Additional component of study by Brashear et al. 2002. 111 patients who completed the study entered into an open label study of BTX-A and received up to four treatments. The mean dose was 220U. The longest interval between cycles was 24 weeks.	Compared to baseline values from the double-blind portion of the study, there were significant improvements in each of the four domains of the Disability Assessment Scale. There were also improvements in Modified Ashworth Scores.
Childers et al. 2004 USA 7 (RCT)	91 patients were randomized to 4 groups: (1) 90U Botox type A; (2) 180U Botox; (3) 360U Botox; (4) placebo. Efficacy outcome measures were completed for the 4 groups as follows: (1) n=16; (2) n=15; (3) n=18; (4) n=18.	A dose-dependent response in muscle tone was generally observed in tone reduction in the wrist (p<.03), elbow (p<.04, and finger (p<.04), but not in pain, FIM scores, or SF-36 scores.
Suputtitada & Suwanwela 2005 Thailand 6 (RCT)	Patients received either a placebo (n=15) or one of three does of Dysport (350 U n=15, 500 U n=15, 1000 U n=15) into five muscles of affected arm by anatomical and electromyography guidance. Efficacy was assessed throughout the 6-month study period by the Modified Ashworth Scale (MAS), the Action Research Arm Test (ARA), the Barthel Index (BI) and the Visual Analogue Pain Scale (VAS).	All doses of Dysport studied showed a significant reduction from baseline of muscle tone and pain compared to placebo. However, the effect of functional disability was best at a dose of 500 U and the peak improvement was at week 8 after injection. A dose of 1000 U Dysport produced such an excess degree of muscle weakening that the number of randomized patients was reduced to five. BI and ARA of all patients were decrease after injection. No other adverse event was considered related to the study medication.
Slawek et al. 2005 Poland No Score	Open-label study of 21 stroke patients with onset of symptoms from 3 months to less than 3 years. Patients received an average dose of botulinum toxin-A of 255 U, based on individual spasticity. Outcome assessed included Modified Ashworth scores, finger flexion scale,	There were statistically significant improvements in baselines scores to week 16 for MAS (elbow and wrist), Bhahkta finger scale in passive movements and muscle tone analyses. The only significant result for active movement analysis was MAS (arm). Pain was present only in 11 patients and did not

	nine-hole peg test and Motor Assessment Scale, assessed up to week 16.	significantly improve following treatment. Individualized BTX-A injection regimens may be an effective, reversible and safe new treatment option for patients with spasticity. Nevertheless, functional improvement may be reached only in selected patients.
Jahangir et al. 2007 Malaysia 6 (RCT)	27 patients, at least 3 months following stroke, with focal spasticity of the wrist and fingers were randomized to receive a single injection of 40 U of botulinum toxin (Botox) or placebo. 20 U were injected into the wrist and finger flexors. All subjects received physical therapy for 1 hour, twice a week for 3 months. Assessments were performed at baseline and 1 and 3 months after injection and included the Modified Ashworth Scale (MAS), Barthel Index (BI) and EQ-5D and EQ VAS for quality of life.	At the end of 3 months there were significant improvements favouring the Botox group in terms of MAS score of both the wrist and finger, but no significant differences on any of the other outcomes assessed. No serious Botox related adverse effects were reported.
Bhakta et al. 2008 UK 9 (RCT)	Additional results from 2000 study evaluating the impact of associated reactions on activities of daily living. Associated reactions were measured using hand dynamometry. The effort used was measured using maximum voluntary grip in the unaffected arm. Measurements were recorded at 2 pre-treatment and 3 post-intervention times. Activities that patients felt caused associated reactions and activities that were affected by associated reactions were recorded.	Peak associated reactions force was reduced at week 6 with botulinum toxin A compared with placebo (mean group difference 19.0 N; 95% confidence interval (CI): 7.2, 30.9; $p < 0.01$) and week 2 ($p = 0.005$), with the effect wearing off by week 12 ($p = 0.09$). 31 patients noted associated reactions on a regular basis and 24 said that these movements interfered with daily activities. Ten of 12 patients receiving botulinum toxin A and 2 of 12 receiving placebo reported reduction in interference with daily activities ($p = 0.02$)
Kanovsky et al. 2009 Czech Republic 8 (RCT)	148 chronic stroke patients from 23 sites in 3 European countries with wrist and finger flexor spasticity and with at least moderate disability in their principal therapeutic target of the Disability Assessment Scale (DAS) were treated either with NT 201 (Xeomin)(median, 320 U) or placebo and followed up for up to 20 weeks. Outcomes assessed included the Ashworth Scale, DAS, Carer Burden Scale and the global assessment of benefit, as identified by the investigators, carers and patients.	A significantly higher proportion of patients treated with NT 201 had improved by at least 1 point on the Ashworth Scale score on the wrist flexors, compared with the placebo group at the end of 20 weeks (39.7% vs. 19.2%, $p=0.007$). The proportion of responders for all other muscle groups (clenched fist, thumb-in-palm, flexed elbow and pronated forearm) was significant greater for patients in the active drug group, at 4 weeks. On all of the other outcomes assessed, patients in the active drug group fared better than patients in the control group on at one assessment point.
McCrory et al. 2009 Australia 9 (RCT)	96 patients an average of 5.9 years post stroke were randomized to receive either 500-1,000U botulinum toxin type A or placebo into the affected distal upper limb muscles on 2 occasions, 12 weeks apart. Assessment was	There were no significant between group differences in AQoL change scores, pain, mood, disability or carer burden. However, patients treated with botulinum toxin type A had significantly greater reduction in spasticity (MAS) ($p < 0.001$), higher GAS

	undertaken at baseline, 8, 12, 20 and 24 weeks. The primary outcome measure was the Assessment of Quality of Life scale (AQoL) assessed at week 20. Secondary outcome assessments included Goal Attainment Scaling (GAS), pain, mood, global benefit, Modified Ashworth Scale (MAS), disability and carer burden.	scores ($p < 0.01$) and greater global benefit ($p < 0.01$).
Meythaler et al. 2009 USA 6 (RCT)	21 subjects with stroke onset more than 6 months with tone greater than 3 on the Ashworth Scale for 2 joints in the involved upper extremity were randomized in a crossover trial to receive either 100 U BTX-A combined with a defined therapy program or placebo injection combined with a therapy program in two 12-week sessions. The primary functional outcome measure was the Motor Activity Log (MAL), assessed at baseline and at the end of treatment. Subjects were also assessed on physiologic measures including tone (Ashworth Scale), range of motion, and motor strength.	The use of BTX-A combined with therapy as compared with therapy only improved the functional status of the subjects on the MAL Quality of Movement subscale ($P=.0180$). There was a trend toward significance in the Amount of Use subscale ($P=.0605$). After each 12-week period, tone had largely returned to baseline ($P>.05$).
Turner-Stokes et al. 2010 UK 9 (RCT)	Additional analysis from McCrory et al. 2009. Main outcome measures were: individualized goal attainment and its relationship with spasticity and other person-centred measures - pain, mood, quality of life and global benefit.	Goal-attainment scaling outcome were highly correlated with reduction in spasticity ($rho=0.36$, $p=0.001$) and global benefit ($rho=0.45$, $p<0.001$), but not with other outcome measures. Goals related to passive tasks were more often achieved than those reflecting active function.
Sun et al. 2010 Taiwan 6 (RCT)	32 patients (≥1 year after stroke) with ability to actively extend >10 degrees at metacarpophalangeal and interphalangeal joints and 20 degrees at wrist of the affected upper limb were randomized to receive BtxA + modified constraint-induced movement therapy (CIMT) (combination group) (n=16) or BtxA + conventional rehabilitation (control group) (n=16) for 2 hours/day, 3 days/week for 3 months. The primary outcome assessed spasticity on the Modified Ashworth Scale (MAS) at 6 months. Secondary outcomes assessed were Motor Activity Log (MAL), Action Research Arm Test (ARAT), and patients' global satisfaction.	The combination group showed significantly greater improvements in elbow, wrist, and finger spasticity ($P = .019$, $P = .019$, and $P < .001$, respectively), MAL and ARAT scores than the control group at 6-month postinjection. Patients reported considerable satisfaction and no serious adverse events occurred.
Bensmail et al. 2010 France	15 outpatients with spastic hemiparesis and 9 healthy controls were included in this single-site, open-labeled study of	Significant differences were found between hemiparetic patients and healthy participants for all kinematic parameters. All parameters

No Score	Botox with dosages specific to each participant. The trajectories of reaching movements were recorded, and kinematic variables were computed. A clinical evaluation included the Motor Activity Log, the Action Research Arm Test (ARAT), and the Box and Block Test (BBT). Patients were assessed before (M0), 1 month after a first (M1), and 1 month after a second BTI (M4, at 4 months) in proximal and distal muscles.	tended to improve after Botox. This effect was significant for velocity and smoothness. Functional scores also tended to improve. Improvements were greater at M4 than at M1, although the differences were not significant. There were no significant improvements from baseline to follow-up on any of the functional assessments.
Kaji et al. 2010 Japan 9 (RCT)	109 subjects with upper limb spasticity following chronic stroke were randomized to receive a single treatment with lower-dose (120–150 U)(n=21) or placebo (n=11) or higher dose (200–240 U) (n=51) BoNTA or placebo (n=26). The tone of the wrist flexor was assessed at baseline and at weeks 0, 1, 4, 6, 8 and 12 using the Modified Ashworth Scale (MAS) for wrist, finger, thumb and disability in activities of daily living (ADL) was rated using the 4-point Disability Assessment Scale (DAS).	Higher dose BoNTA was associated with greater reductions in MAS and DAS scores associated with limb positioning compared with a lower dose, or placebo at 12 weeks. There were no differences in the number of adverse events reported among the treatment or placebo groups.
Cousins et al. 2010 UK 5 (RCT)	30 subjects following stroke within the previous 3 weeks with impaired grasping ability were randomized to receive a single injection of either one-quarter, or half standard dose botulinum toxin, or placebo (saline) to prevent the development of spasticity. Arm function, active and passive movement, and spasticity at elbow and wrist were recorded at baseline, and at 4, 8, 12 and 20 weeks post intervention. A pre-planned subgroup analysis included only subjects with no arm function at baseline (Action Research Arm Test score = 0).	Arm function, assessed using the ARAT improved in all three groups between baseline and week 20, but there were no significant differences among groups. In the subgroup analysis restricted to subjects without arm function at baseline, there were no significant differences among groups except for the active range of elbow flexion, which was greater in the ¼ dose group compared with the other 2 groups.
Barnes et al. 2011 Portugal 5 (RCT)	A non-inferiority study. 125 patients with spasticity of mixed etiology (stroke=88%) of at least 6 months duration were randomized to receive a single injection of either 50 or 20 U/ml NT 201 (Xeomin) dilutions. The maximum total NT 201 dose was 495 units. The primary outcome was improvement in the primary target of the Disability Assessment Scale (DAS). Spasticity was assessed using the Ashworth Scale.	At 4 weeks post-injection, at least a 2 point reduction was observed on the DAS in 57.1%, and on the Ashworth scale in 62.2% of patients. The 20 U/ml NT 201 dilution was non-inferior to the 50 U/ml NT 201 dilution.

Shaw et al. 2011 UK 8 (RCT)	333 patients with at least 1 month post stroke with upper limb spasticity and reduced arm function were randomized to receive injection(s) with 100 – 200 U botulinum toxin type A plus a 4-week therapy program (n=170) or a therapy program alone (n=163). Repeat injection(s) and therapy were available at 3, 6, and 9 months. The primary outcome was successful outcome, defined as either a 3-point gain on the Action Research Arm Test (ARAT) for those with baseline scores of 0-3, a gain of at least 6 points for those with baseline scores of 4-51, and a final ARAT score of 57 for those with baseline scores of 52-57at 1 month. Secondary outcomes included measures of impairment, activity limitation, and pain at 1, 3, and 12 months.	There was no significant difference in the percentage of patients who has achieved a successful outcome: 25% of patients in the treatment group had achieved a successful outcomes compared with 19.5% of patients in the control group; P=0.232. Significant differences in favor of the intervention group were seen in muscle tone at 1 month; upper limb strength at 3 months; basic arm functional tasks (hand hygiene, facilitation of dressing) at 1, 3, and 12 months; and pain at 12 months.
Kanovsky et al. 2011 Czech Republic 8 (RCT)	Patients from 2009 study were invited to participate in an extension of the study. 145 patients received up to 5 additional sets of NT 201 injections for an open-label extension period of up to 69 weeks	Mean cumulative dose of NT 201 was 1120 U. The proportion of treatment responders (≥1-point improvement on the Ashworth scale) for flexors of wrist, elbow, finger, and thumb, and forearm pronator ranged from 49% to 80%. The proportion of treatment responders (≥1-point improvement on the Disability Assessment Scale) ranged from 43% to 56%. The majority of investigators, patients and caregivers rated NT 201 efficacy as very good or good (56-84%). Adverse events considered treatment-related occurred in 11% of patients. Formation of neutralizing antibodies was not observed in any patient after repeated treatments.
Hesse et al. 2012 Germany 7 (RCT)	18 patients admitted for inpatient rehabilitation within 4-6 weeks of stroke with a non-functional arm, Fugl-Meyer arm score <20, with the beginning of elevated finger flexor tone were randomly allocated to receive 150 units BTX-A (Xeomin) injected into the deep and superficial finger (100 units) and wrist flexors (50 units) or no injection. The primary outcome, asses at baseline, weeks 4 and 6 months was the Modified Ashworth Scale (MAS) of the finger flexors. Secondary measures REPAS (a summary rating scale for resistance to passive movement), Fugl-Meyer Assessment (FMA) arm score, and a 6-item disability scale (DS).	4 weeks following treatment, patients in the BTX-A group had experienced significantly greater improvement on MAS, REPAS and total DS scores compared with controls. At 6 months MAS and DS scores remained significantly better.
Wolf et al. 2012	25 patients with stroke onset within the previous 3-24 months, who could	Performance on the WMFT improved in both groups, but there were no significant

USA 9 (RCT)	initiate wrist extension, were included. Patients participated in 12-16 standardized exercise sessions and received either 300 U BTX-A (300 U max) or placebo. Evaluations were conducted at baseline and then 3 more times, approximately 1 month apart. The primary outcome measure was the Wolf Motor Function Test (WMFT). Secondary measures were the Stroke Impact Scale (SIS), modified Ashworth scale (MAS), active range of motion (AROM).	differences between them. There were no significant differences between groups for wrist AROM. Only for the emotion domain of the SIS was there a significant difference between groups favouring BTX-A.

A summary of the results from the "good" quality RCTs is presented in Table 10.40.

Table 10.40 Summary of Botulinum Toxin Injection and Spasticity in Upper Extremity Post Stroke

Author/ PEDro Score	n	Intervention	Main Outcome(s) Result
Kaji et al. 2010 9	109	120 U Botox vs. placebo & 200 U Botox vs. placebo	Modified Ashworth Scale (+ hi dose Botox vs. placebo, - low dose Botox vs. placebo) Disability Assessment Scale (+ both groups)
McCrory et al. 2009 9	96	500-1,000U of Dysport vs. placebo x 2 occasions	The Assessment of Quality of Life scale (- at week 20)
Wolf et al. 2012 9	25	300U Botox + therapy vs. placebo +therapy	Wolf Motor Function test (-)
Shaw et al. 2011 8	333	100-200 U Dysport + 4 weeks therapy vs. therapy only	ARAT scores (-) Modified Ashworth Scale (+)
Kanovsky et al. 2009 8 (RCT)	148	Median of 320 U Zeomin vs. placebo	Ashworth Scale scores (-/+)
Bakheit et al. 2000 8	82	500 U of Dysport vs.1000 U of Dysport vs. 1500 U of Dysport vs. placebo	Modified Ashworth Scale (+ for all three groups at wk 4 and week 16 in the elbow and wrist and in the fingers in the 1000U group compared to placebo group) Rivermead Motor Assessment (- at 4 and 16 weeks)
Bakheit et al. 2001 8	59	Total of 1000 IU of BtxA (Dysport) into 5 muscles of the affected arm vs. placebo injections	Summed Modified Ashworth Scale score (+ at week 4) Magnitude of benefit in wrist and finger joints (+ over 16 wk follow-up period) Joint ROM (- at wk 4) Muscle pain (- at wk 4) Goal-attainment (- at wk 4) Barthel Index (- at wk 4) Elbow PROM (+ at 16 wks)

Simpson et al. 1996 8	37	Single treatment of 75 units vs. 150 units vs. 300 units of BTX-A or placebo	Decrease in wrist flexor tone (+ in 300 BTX-A group at 2,4 and 6 wks post-injection) Global Assessment of Response to Treatment (+ with all BTX-A groups at 4 and 6 wks post-injection)
Simpson et al. 2009 8	60	Up to 500 U of BT-X vs. tinzanidine vs. placebo	Decrease in wrist flexor tone (+ at 6 weeks-favouring BT-X)
Hesse et al. 2012 7	18	150U Xeomin + therapy vs. therapy only	Modified Ashworth Scale score (+) REPAS (+)
Bhakta et al. 2000, 2008 7	40	Total of 1000 IU Dysport (n=20) vs. placebo (n=20) divided between elbow, wrist, and finger flexors.	Disability (+ at 2 & 6 weeks) Caregiver burden (+ at 2, 6 & 12 weeks) MAS (finger) (+ at 2,6 &12 weeks) MAS (elbow) (+ at 2 weeks) Pain (-) Associated reactions (+)
Brashear et al. 2002 7	126	Injection of botulinum toxin A (50 units) vs. placebo	Disability Assessment scores (+ at 6 weeks)
Smith et al. 2000 7	25	500 units vs. 1000 units vs. 1500 units of botulinum toxin or placebo	Modified Ashworth Scale at fingers (+ for all botulinum groups) Passive range of movement at wrist (+ for all botulinum groups) Finger curl distance at rest (+ for all botulinum groups) Only significant difference between dose groups was seen in improved movement at the elbow (+ 1500 Mu group)
Francisco et al. 2004 7	13 (10 stroke)	High volume BTX-A (50 units/1 mL saline:1.2 mL delivered per 4 muscles) vs. low volume BTX-A (100 units/1 mL saline	Modified Ashworth Scale (-at 4, 8 and 12 weeks post injection)
Brashear et al. 2004 7	15	10000 U of BTX-B or placebo	Modified Ashworth scale (+ at week 2, - at weeks 4, 8, 12, and 16) Global Assessment of Change (-)
Childers et al. 2004 7	91	Up to 2 treatments of placebo, or 90, 180, or 360U of BTX.	Muscle tone (+ at weeks 1-6) FIM (-) SF-36 (-)
Meythayler et al. 2009 6	21	100 U Botox + therapy vs. saline + therapy	Motor Activity Log (Quality of Use) (+) Motor Activity Log (Amount of Use) (-) Ashworth Scale (-)
Sun et al. 2010 6	32	1,000 U Dysport + mCIMT vs. 1,000 U Dysport + conventional rehab	MAS (+) Motor Activity Log (amount of use) (+)
Jahangir et al. 2007 6	27	50 U Botox vs. placebo	Modified Ashworth Scale (+ at 3 months) Barthel Index (-) EQ-5D (-)

Suputtitada & Suwanwela 2005 6	60	Single dose of either placebo or one of 3 doses of BTX-A (350, 500 or 1,000U)	Modified Ashworth scale (+ in 500 and 1,000 U groups) ARAT (+ at 8 and 24 weeks 500 U) BI (+ at 8 and 24 weeks 500 U)
- Indicates non-statistically significant differences between treatment groups + Indicates statistically significant differences between treatment groups			

Discussion

Assessing the effectiveness of botulinum toxin in the treatment of upper limb spasticity was difficult owing to the broad range of doses and types of agents administered. Among the RCTs reviewed, many assessed the between a single dose, administered to several sites, of botulinum toxin A as either Dysport ®, Botox® or Xeomin® vs. placebo. A single trial assessed the benefit of BT-type B (Brashear et al. 2004-10,000 U BT-B). The dose equivalent is approximately 300-500 Units of Dysport equal 100 units of Botox (O'Brian 2002). Among these trials, the results were ambiguous. The greatest benefit appeared to be realized in the patients who received Botox (Brashear et al. 2002) who had reductions in tone and also experienced improvement in functional outcome. Patients treated with BT-B (MyoBloc) appeared to have the poorest response to treatment (Brashear et al. 2004). One trial, the most methodically rigorous (McCrory et al. 2009) evaluated the effectiveness of 2 doses of Botox, given 12 weeks apart, compared with placebo. The most recent trial (Shaw et al. 2011) failed to find a benefit of treatment with BT-A on function, assessed by the Action Research Arm Test, although spasticity was significantly reduced as was pain at one-year following injection.

Several trials assessed the effect of several doses of botulinum toxin compared with placebo (Bakheit et al. 2000, Simpson et al. 1996, Smith et al. 2000, Childers et al. 2004, Suputtitada & Suwanwela 2005). Due to the small sample sizes, many of the authors of these studies grouped the treatments together and compared the effects with the placebo. This approach presented difficulties when attempting to determine if escalating doses were associated with greater reductions in spasticity. Generally all doses of BT resulted in reduction in muscle tone; however, increasingly higher doses were associated with muscle weakening.

Conclusion Regarding Botulinum Toxin Injection in the Upper Extremity

There is strong (Level Ia) that treatment with BTX alone or in combination with therapy significantly decreases spasticity in the upper extremity in stroke survivors.

There is conflicting (Level 4) evidence that treatment with BTX alone or in combination with therapy significantly improves upper limb function or quality of life.

Botulinum Toxin decreases spasticity and increases range of motion; however, these improvements do not necessarily result in better upper extremity function.

10.5.4 Electrical Stimulation Combined with Botulinum Toxin Injection

A single study evaluated the efficacy of botulinum toxin injection combined with electrical stimulation.

Table 10.41 Electrical Stimulation Combined with Botulinum Toxin (BTX) Injection in the Upper Extremity

Author/ Country Pedro Score	Methods	Outcomes
Hesse et al. 1998 Germany 7 (RCT)	A placebo controlled trial of 24 patients randomized to one of four groups: 1000unit BTX-A + electrical stimulation (Group A); 1000 units of BTX-A (Group B); Placebo + electrical stimulation (Group C); and Placebo (Group D). Intra-muscular injection of either BTX-A or placebo into six upper limb flexors. Electrical stimulation of the injected muscles with surface electrodes, was conducted three times, ½ hr each day for three days (Group A and C).	Significant muscle tone reduction of the elbow joint was most prominent for Group A. Group A experienced fewer difficulties while cleaning the palm of the hand, when compared to Group B and Group D. Patients in the BTX-A groups experienced fewer difficulties when putting the involved arm through a sleeve, compared to patients in groups C & D.

Table 10.42 Summary of Combined Therapy with Botulinum Toxin Injection in the Upper Extremity

Author/ PEDro Score	N	Intervention	Main Outcome(s) Result
Hesse et al. 1998 7 (RCT)	24	1000unit Btx A + electrical stimulation (Group A) vs. 1000 units of Btx A (Group B) vs. Placebo + electrical stimulation (Group C) vs. and Placebo (Group D).	Muscle Tone Reduction (- elbow joint for group A) Reduction in difficulties while cleaning palm (+ group A compared to group B and D) Difficulties putting arm through a sleeve (+ reduction between botulinum groups and placebo)

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Conclusions Regarding Treatment of Spasticity: Botulinum Toxin Injections

There is moderate (Level 1b) evidence that electrical stimulation combined with Botulinum Toxin injection is associated with reductions in muscle tone.

Botulinum Toxin in combination with electrical stimulation improves tone in the upper extremity.

10.5.5 Nerve Block and Spasticity

One method of decreasing spasticity is by injecting alcohol or phenol into a specific nerve (i.e. the musculocutaneous nerve) thus decreasing spasticity of the innervated muscles. One of the side effects of this treatment is a loss of sensation; therefore, this form of treatment is not widely used in clinical practice. A commonly reported side effect is temporary pain (Kong and Chau 1999).

Table 10.43 Nerve Block and Spasticity in Upper Extremity

Author/ Country Pedro Score	Methods	Outcomes
Kong and Chau 1999 Singapore No Score	20 patients received musculocut-aneous nerve block of hemiplegic upper extremity with 50% ethyl alcohol. Outcome measures included spasticity severity as measured by the Modified Ashworth Scale (MAS) and the elbow passive range of motion (PROM) of the elbow.	There was statistically significant improvement in MAS and PROM. The mean baseline MAS score was 3.7, which improved to 1.7, 2.0 and 2.1 at 4 weeks, 3 months, and 6 months respectively. The elbow PROM was 87.3 degrees, 104.3, 103.8 and 101.6 degrees, respectively. Four subjects had concomitant improvement of finger flexor spasticity and another four had relief of shoulder pain
Kong and Chua 2002 Singapore No Score	30 patients with mean onset since stroke of 8.3 months and with complications secondary to flexion spasticity of the wrist and fingers were given intramuscular neurolysis or motor point blocks of the finger flexors of the hemiplegic upper extremity with 50% ethyl alcohol. Assessments included the Modified Ashworth Scale (MAS), passive range of motion (PROM) of the interphalangeal joints of the second and fifth digits. Assessments were conducted before treatment and at 4 weeks, 3 and 6 months.	20 patients had significant swelling over their forearm associated with treatment. MAS scores improved significant from baseline 4.0 to 2.0 (4 wks), and then fell slightly to 2.2 (3 months) and 2.6 (6 months). Baseline PROM values were not reported.

Conclusions Regarding Treatment of Spasticity: Nerve Block

There is limited (Level 2) evidence that treatment with ethyl alcohol improves elbow and finger PROM and can decrease spasticity in the upper extremity in stroke survivors.

More research is needed to determine whether nerve blocks decrease spasticity in the upper extremity.

10.5.6 Physical Therapy in the Treatment of Spasticity

As previously mentioned, physical therapy is a mainstay in the treatment of spasticity. Common physical modalities used in the treatment of spasticity include stretching, orthoses, casting, and cold application.

Table 10.44 Physical Therapy and Spasticity in Upper Extremity

Author/ Country Pedro Score	Methods	Outcomes
Carey 1990 USA 4 (RCT)	24 patients were randomly assigned to either a no treatment control group or to a treatment group in which manual stretch was applied to the extrinsic finger flexor muscles for 5 minutes between the pre-test and post-test. A joint-movement tracking test (JMTT) quantified control of active finger extension movement at the metacarpophalangeal joint of the index finger within the available range of active movement, and a force tracking test (FTT) quantified control of isometric finger extension force at the same joint within the subject's available force range.	The JMTT and FTT performances of both control and experimental groups were significantly subnormal on the pretest. The JMTT improvement on posttest was significantly greater ($p < 0 .05$) in subjects than in controls. However, the change in FTT performance was not significantly different between the two groups
Miller et al. 1997 USA No score	9 patients performed 10 quick and forceful isometric contractions of the biceps with the sequence of pre-test, graded resistive exercise (GRE) and post-test applied to both paretic and on-paretic arm. Testing was randomized to which arm was started first. Treatment and no-treatment occurred on two consecutive days in counterbalanced order and at the same time of day.	Although no differences between tasks were noted, there was a trend in favour of the GRE suggesting that it is not detrimental to post-stroke spastic muscles.
Horsley et al. 2007 Australia 8 (RCT)	40 patients admitted to a rehabilitation service (19 with stroke) received routine upper-limb retraining five days a week. In addition, the experimental group (n=20) received 30 minutes daily stretch of the wrist and finger flexors five days a week for four weeks. The primary outcome was contracture, measured as torque-controlled passive wrist extension with the fingers extended. Secondary outcomes were pain at rest measured on a 10-cm visual analogue scale, and upper-limb activity measured using the Motor Assessment Scale. Outcomes were assessed at baseline, post-intervention, and one and five weeks after cessation of intervention.	There were no significant differences between groups on any of the outcomes assessed either immediately following the treatment or at follow-up.

Conclusions Regarding Treatment of Spasticity: Physical Therapy

There is strong (Level 1a) evidence that physical therapy does not reduce spasticity in the upper extremity.

Physiotherapy does not decrease spasticity in the upper extremity.

10.5.7 Electrical Stimulation

Electrical stimulation as an addition to physical therapy has been found to be an effective treatment for lower-limb spasticity (see Module 9). The mechanism of action appears to the relaxation of agonist muscles and strengthening of the antagonist muscles (Sahin et al. 2012). The treatment has not been well studied in the upper extremity. To date, there is only 1 RCT on the subject.

Table 10.45 Electrical Stimulation and Spasticity in Upper Extremity

Author/ Country Pedro Score	Methods	Outcomes
Sahin et al. 2012 Turkey 5 (RCT)	44 hemiplegic patients with MAS scores of 2-3 in the wrist muscles were randomized to received a course of 20 sessions over a 1 month period of applied stretching plus neuromuscular electrical stimulation (NMES) to the wrist extensors, in the form of pulsed current, 100 Hz, with a pulse duration of 0.1 msec, and a resting duration of 9 seconds, for 15 minutes to provide the maximum muscular contraction or to stretching only. The outcomes evaluated before and after treatment included using MAS, Fmax/Mmax ratio, Hmax/Mmax ratio, wrist extension range of motion (ROM), FIM and Brunnstrom motor staging.	The average chronicity of stroke was over 2 years. Patients in both groups improved significantly over the treatment period. Patients in the NMES groups experienced greater reductions in MAS scores (-1.4 vs. -1.0, p<0.001), increased gains in wrist extension (16.5 vs. 15.9 degrees, p<0.001), greater improvement in Brunnstrom upper scores (1.2 vs. 0.9, p=0.04) and greater FIM gains (2.1 vs. 1.0, p=0.028)

Conclusions Regarding Treatment of Spasticity with Electrical Stimulation

There is moderate (Level 1b) evidence that neuromuscular electrical stimulation can reduce spasticity and improve motor function in the upper extremity.

10.5.8 Shock Wave Treatment

Shock wave therapy has been demonstrated to effectively treat a variety of bone and tendon diseases by reducing hypertonia and may be an attractive treatment option for stroke patients instead of botulinum toxin. A single study, which investigated the effects of shock wave therapy, was reviewed.

Table 10.44 Shock Wave Therapy and Spasticity in Upper Extremity

Author/ Country Pedro Score	Methods	Outcomes
Manganotti et al. 2005 Italy (No Score)	20 patients with severe hypertonia associated with chronic stroke received one sham treatment and one active treatment with extracorporeal shock wave therapy, given one week apart. The National Institutes of Health Stroke Scale (NIHSS) and Ashworth Scale were assessed at 1, 4	Ashworth scores for wrist flexors and finger flexors decreased significantly after active treatment The positive effects persisted for finger flexors at 12 weeks, but not for wrist flexors. Passive range of motion increase following active treatment. The benefit was maintained

	and 12 weeks following active treatment.	for 4 weeks. There were no changes in the NIHSS scores following treatment.

A single treatment of shock wave therapy among a small group of patients with spasticity in the hand was effectively reduced for a period of more than 12 weeks, with no adverse effects. This may be a promising new treatment.

Conclusions Regarding Treatment of Spasticity: Shock Wave Therapy

There is limited (Level 2) evidence that shock wave therapy can reduce tone in the upper extremity.

10.5.8 Centrally Acting Muscle Relaxants (tolperisone)

Tolperisone is a centrally acting muscle relaxant, similar in action to lidocaine, which acts by reducing sodium influx through nerve membranes. It may be superior to other muscle relaxants in that it does not cause sedation or muscle weakness, nor does it impair attention-related brain functions. Tolperisone and its analogue epersione have been used successfully in patients with spinal cord injuries.

Table 10.46 Tolperisone in the Treatment of and Spasticity in Upper Extremity

Author/ Country Pedro Score	Methods	Outcomes
Stamenova et al. 2005 Bulgaria/Germany 8 (RCT)	120 acute stroke patients (having suffered from a stroke within the previous 2 months) with spasticity were randomized to receive either a daily dose of 300-900 mg of tolperisone or placebo for 12 weeks. Outcomes assessed at the end of treatment included Ashworth Scale scores.	Patients treated with tolperisone had a greater decrease in mean Ashworth Scores (1.03 +/- 0.71 vs. 0.47 +/- 0.54). 78.3% of the patients on tolperisone vs. 45% of the placebo patients experienced a reduction by at least 1 point on the Ashworth Scale. Functional and overall assessments of efficacy confirmed superior efficacy of tolperisone. Adverse events occurred more frequently in the placebo group compared to treatment (26 vs. 19) and were mostly of mild-to-moderate intensity.
Tariq et al. 2005 Pakistan No Score	26 stroke patients with hemiparesis were alternatively assigned to receive either a 3-week treatment of Eperisone (t.i.d) (n=13) or one-hour of physical therapy daily (n=13). Tone was assessed at the end of the treatment period.	17 patients completed the study; 8/13 in the epersione group and 9/13 who received physiotherapy. No inferential statistics were conducted or reported. Tone was improved in 6/8 patients who received eperisone and in 4/9 patients who received phsyio. Although tone was assessed in both the upper and lower extremities it is unclear what the reduction in tone was in the upper extremity.

Conclusions Regarding Centrally Acting Muscle Relaxants

There is moderate (Level 1b) evidence that tolperisone can reduce spasticity following stroke.

10.6 EMG/Biofeedback

EMG biofeedback uses instrumentation applied to the patient's muscle(s) with external electrodes to capture motor unit electrical potentials. As the instrumentation converts the potentials into visual or audio information, the patient is able to have a visual picture or auditory indication of how much they are activating the muscle. In 1994, Moreland and Thomson published their research overview and meta-analysis on the efficacy of electromyographic biofeedback compared with conventional physical therapy for upper-extremity function in stroke patients. They concluded that neither therapy was superior to the other.

Eleven RCTs evaluating EMG/biofeedback therapy were identified. The results are presented in Tables 10.47 and 10.48.

Table 10.47 EMG/Biofeedback Studies

Author/ Country Pedro Score	Methods	Outcomes
Lee et al. 1976 USA 4 (RCT)	18 patients with reduced deltoid muscle strength were randomly assigned to 1 of 6 possible treatment orders of 3 interventions conditions, over 3 consecutive days in a crossover designed study. i) True myofeedback ii) Placebo myofeedback iii) No myofeedback with conventional training. Each daily training section consisted of 20 consecutive contractions of the deltoid muscle for 5 sec with a rest interval of 10 sec. Peak amplitude of the averaged myolectric signal maintained for 1 sec were collected.	There were no significant differences between the 3 treatment conditions.
Mroczek et al. 1978 USA 5 (RCT)	5 chronic stroke patients received 4 weeks of biofeedback therapy followed by 4 weeks of physical therapy while 4 patients received training in the opposite order. Active range of motion (ROM) was assessed at baseline and weeks 4, 7, 10 and 12.	ROM improved following treatment with both physical therapy and EMG therapy. When the results were pooled there no significant differences between treatment conditions.
Smith 1979 Australia 4 (RCT)	12 stroke patients with movement disorder were randomly assigned to receive a biofeedback therapy or physiotherapy for 6 weeks.	Greater improvements reported for patients receiving biofeedback therapy in the areas of sensation, muscle tone, voluntary isolated movement, synergistic movement pattern, functional activities, gross motor abilities and coordination. However, no inferential statistics were

		reported.
Greenberg and Fowler 1980 USA 5 (RCT)	20 stroke patients were randomized to receive either conventional OT (n=10) or audiovisual kinaesthetic biofeedback associated with active elbow extension (n=10). All subjects were treated 30 min x 2/week x 4weeks.	There were no differences in active elbow extension measured on three occasions by a conventional goniometer.
Hurd et al. 1980 6 (RCT)	24 hemiplegic inpatients were randomized to receive 10 sessions over a two-week period of either actual or simulated myofeedback	There were no statistically significant differences in either active range of motion or muscle activity between the two groups.
Prevo et al. 1982 Netherlands 3 (RCT)	28 patients were assigned to receive either EMG biofeedback (n=9), confined to augmenting the reduced muscle activity in one proximal and one distal agonist, and to decreasing the excessive activity in one proximal agonist and in two distal muscle groups or to conventional physical therapy (n=9) for 2.5 months.	EMG feedback therapy had no specific effect on proximal and distal agonists of the hemiplegic arm compared to conventional therapy.
Basmajian et al. 1982 Canada 6 (RCT)	37 hemiplegic stroke patients were randomized to receive physical therapy + EMG biofeedback or physical therapy using a general neurophysiological approach, for 40 min x 3x/week for 5 weeks.	There were no differences between the groups on any of the outcome measures (Upper Extremity Function Test, Minnesota rate of manipulation test, 9-hole peg test, grip and pinch test).
Wolf et al. 1983 USA No Score	22 chronic stroke patients who each received 60 EMG feedback training sessions. EMG data were compared with changes measured from a Control Group of 9 (no treatment) patients.	Those patients receiving feedback training showed significant improvements in numerous neuromuscular measures but not in functional measures.
Inglis et al. 1984 5 (RCT)	30 patients with stroke onset of at least 6 months were randomized to receive 20 sessions of EMG biofeedback treatments + routine physiotherapy or to routine physiotherapy. Patients in the control group were then crossed over to receive the experimental therapy. Assessments of muscle strength, active range of motion, picture goniometry and Brunnstrom's staging were conducted at baseline and at the end of treatment.	Patients in the experimental condition demonstrated significant improvements in all measured parameters compared to patients in the control condition.
Turczynski et al. 1984 Germany No Score	12 chronic stroke patients with hemiparesis received electromyographic feedback exercises applied to upper extremity muscles. Outcomes measures included objective and standardized tests of motor skills.	The standardized tests of motor skills could only be performed properly in 6 patients. The test scores of those 6 patients were not significant from pre- to post-treatment.
Basmajian et al. 1987 Canada 6 (RCT)	29 hemiparetic stroke patients were randomized to receive either integrated behavioural and physical therapy (including EMG) (n=13) or physical therapy based on neurofacilitatory techniques (n=16), of 45 min x 3	There were no differences between the groups on any of the outcome measures (Upper Extremity Function Test, finger oscillation tests).

	days/week x 5 weeks.	
Crow et al. 1989 UK 8 (RCT)	40 stroke patients were randomized to receive routine physical therapy + EMG biofeedback (n=20) or sham treatment + routine physical therapy, for 12 weeks.	After 6 weeks of treatment, the difference between the groups was statistically significant for both outcome measures (ARA-Action Research Arm test and BFM-Brunnstrom-Fugl Meyer test). However, following an additional 6 weeks without the treatment, there were no significant differences between the groups.
Bate et al. 1992 Australia 4 (RCT)	16 stroke patients recruited from day hospitals or rehabilitation hospitals were randomized to receive EMG biofeedback from the spastic elbow flexor muscles during movement practice or to a control condition, which did not receive EMG in a single training session. Patients practiced a pursuit tracking task by following a moving target with elbow flexion and extension, simultaneously attempting to reduce the activity of elbow flexors.	Both groups tracked the target more accurately following training. Transfer tests failed to demonstrate effects of feedback on accuracy of tracking or on electromyographic activity during performance of the practiced task without feedback. Moreover, the group that was trained with electromyographic feedback exhibited negative transfer on variants of the practiced task: tracking faster or less predictable targets
Armagan et al. 2003 Turkey 7 (RCT)	27 patients with hemiparesis resulting from stroke 3-6 months previously were randomized to i) an exercise program (Brunnstrom approach) + EMG biofeedback or to the same intervention but with placebo EMG therapy (machine turned on, but to feedback to patient). Both treatments were applied 5x/week for 20 days. Evaluations included: Goniometric measurements for wrist extension (range of motion), scale for judging the performance of drinking from a glass, Brunnstrom's stages of recovery for hand, and surface EMG potentials, assessed before and after treatment.	No significant difference between the groups in Brunnstrom stages of hand recovery or scale for judging the performance of the movement complex of drinking from a glass. Significant between group differences for active range of motion scores and changes in EMG surface potentials.
Hemmen & Seelen 2007 Netherlands 7 (RCT)	27 patients with stroke onset of greater than 3 weeks were randomized to receive conventional electrostimulation (n=14) or to a group that received arm-hand function training based on EMG-biofeedback combined with movement imagery. In both groups training was carried out for 3 months (5 days/wk, 30 min) in addition to usual therapy. Outcomes were assessed at baseline, 12 months and 12 months and included Fugl-Meyer (FM) scores and the Action Research Arm (ARA) test.	There were no significant differences between groups on either of the outcomes assessed; however, patients in both groups experienced significant improvement from baseline to one-year follow-up.

Table 10.48 Summary Table of RCTs for EMG/Biofeedback Therapy and the Hemiparetic Upper Extremity

Author PEDro Score	n	Intervention	Main Outcome(s) Result
Crow et al. 1989 8 (RCT)	40	EMG/Biofeedback Therapy vs. Sham EMG/biofeedback	Action Research Arm test post-treatment (+) 6 weeks follow-up (-)
Hemmen & Seelen 2007	27	EMG biofeedback + movement imagery vs. conventional electrostimulation	Fugl-Meyer (-) Action Research Arm test (-)
Armagan et al. 2003 7 (RCT)	27	EMG/Biofeedback Therapy vs. Sham EMG/biofeedback	Active range of motion (+) Changes in EMG surface potentials (+) Brunnstrom stages (-) Complex movement (-)
Basmajian et al. 1987 6 (RCT)	29	EMG/Biofeedback Therapy vs. Physical Therapy using neuro-facilitatory	Upper extremity function test (-) Finger Oscillation test (-)
Hurd et al. 1980 6 (RCT)	24	Actual myofeedback vs. simulated myofeedback	Active range of motion (-) Muscle activity (-)
Basmajian et al. 1982 6 (RCT)	37	EMG/Biofeedback Therapy vs. Physical Therapy using neuro-physiological approach	Upper extremity function test (-) Minn rate of manipulation test (-) 9-hole peg test (-)
Inglis et al. 1984 5 (RCT)	30	EMG/Biofeedback+ physiotherapy vs. Physiotherapy	Active range of motion (+) Brunnstrom (+) Muscle strength (+)
Bate et al. 1984 4 (RCT)	16	EMG vs. no EMG	Tracking task (-)
Greenberg & Fowler 1980 5 (RCT)	20	EMG/Biofeedback Therapy vs. Conventional Occupational Therapy	Active elbow extension (-)
Smith 1979 Australia 4 (RCT)	12	Biofeedback therapy vs. Physiotherapy	No inferential statistics were reported.
Mrocek et al. 1978 5 (RCT)	9	EMG biofeedback vs. Physical therapy	Range of Motion (-)
Lee et al. 1976 4 (RCT)	18	True myofeedback vs. Placebo myofeedback vs. No myofeedback with conventional training.	Peak amplitude (-)
Prevo et al. 1982 3 (RCT)	28	EMG/Biofeedback Therapy vs. Conventional Therapy	Proximal and distal agonists (-)

- Indicates non-statistically significant differences between treatment groups
+ Indicates statistically significant differences between treatment groups

Conclusions Regarding Efficacy of EMG/Biofeedback Therapy

There is strong (Level 1a) evidence that EMG/Biofeedback therapy is not superior to other forms of treatment.

EMG/Biofeedback therapy is not superior to other forms of treatment in the treatment of the hemiparetic upper extremity.

10.7 Electrical Stimulation

10.7.1Transcutaneous Electrical Nerve Stimulation (TENS)

The application of electrical stimulation at a sensory level may help to enhance plasticity of the brain, which in turn may help with motor recovery (Sonde et al. 1998). Robbins et al. (2006) described the TENS current intensity to be beneath motor threshold, although capable of generating a "pins-and-needles sensation." Similar to acupuncture, transcutaneous electrical nerve stimulation is one method of achieving increased afferent stimulation (Sonde et al. 1998).

Laufer et al. (2011) conducted a systematic review of the effectiveness of TENS for motor recovery, including the findings from 15 studies. Seven of these studies examined treatments focused on the upper extremity, while two included both the upper and lower extremities. The majority of studies recruited subjects in the chronic stage of stroke. The outcomes assessed in these studies included movement kinematics during reaching, pinch force, the Jebsen-Talyor Hand Function test and the Action Research Arm test, the Barthel Index and the Modified Motor Assessment Scale. The authors stated while there was much variability in the stimulation protocols and the timing and selection of outcome measures to enable definitive conclusions, there was still evidence that TENS treatment, when combined with rehabilitation therapies may help to improve motor recovery.

Several trials have examined the use of TENS treatment in the restoration of motor function following stroke.

Table 10.49 TENS in the Treatment of Upper Extremity

Author, Year Country PEDro	Methods	Outcomes
Potisk et al. 1995 Slovenia No Score	20 stroke patients with hemiplegia (>3 months post-stroke) had surface electrodes placed over the affected limbs' sural nerve. The patients then received 20 minutes of TENS with impulse frequency of 100 Hz. Evaluation measures included resistive torques, spasticity, and electromyography (EMG) stretch reflex activity.	18 of the 20 patients significantly decreased in resistive torques at all frequencies of passive ankle movements after 20 min of applying TENS. This significant reduction persisted 15, 30 and 45 minutes following TENS, but was not significant 60 minutes after TENS. The decrease in resistive torques was frequently linked with a reduction in reflex electromyographic activity.
Sonde et al. 1998 Sweden 5 (RCT)	44 patients randomized to receive either physiotherapy or to receive in addition to physiotherapy of the upper extremity 2 x/ week, low-intensity, low-	Fugl-Meyer scores of patients in the treatment group increased significantly compared to patients in the control group. No changes in spasticity or pain associated

	frequency (1.7Hz) transcutaneous electrical stimulation (TENS) for 60 minutes, 5 days per week for 3 months, for treatment of a paretic arm.	with the treatment were observed. Barthel scores did not change significantly.
Tekeoðlu et al. 1998 Turkey 6 (RCT)	A double blind randomized controlled trial of 60 patients. Patients received either basic neurophysiological rehabilitation or received in addition to the basic neurophysiological rehab treatment, active TENS for 40 sessions over 8 weeks with a frequency of 100Hz at intensity that patients could tolerate.	At 8 weeks, patients in both groups had significantly improved their BI scores compared to baseline. Patients in the treatment group experienced greater improvement in BI scores compared to the control group (80 vs. 60, $p<0.01$). Significant reduction in Ashworth scores was observed in both groups.
Johansson et al. 2001 Sweden 8 (RCT)	150 patients were randomized to receive acupuncture (including electroacupuncture), high-intensity, low frequency TENS or subliminal high-frequency, low intensity transcutaneous electrostimulation (control).	No significant differences were observed between groups on any of the outcome measures (Rivermead Mobility Index, Walking Ability, Barthel Index, Nottingham Health Profile, and Nine Hole Peg Test).
Sonde et al. 2000 Sweden 5 (RCT)	Three-year follow-up of 28 from 1998 study.	Motor function of the paretic arm had deteriorated in both groups. Increased spasticity was seen in both groups. ADL scores remained at a similar level in the low TENS group, whereas the control group had deteriorated during the same time period.
Conforto et al. 2002 USA 6 (RCT)	8 chronic stroke patients participated in two 2-hour sessions, randomly ordered, in which stimulation was delivered to wrist by (1) median nerve stimulation (MNS), in which, stimulus intensity increased until patients reported strong paresthesias in the median nerve territory in the absence of pain, and (2) control simulation, in which, stimulus intensity kept immediately below that required to elicit paresthesias.	A significant increase in pinch muscle strength was observed during the MNS sessions; however, no significant changes were noted in the CS sessions.
Peurala et al. 2002 Finland No score	Cutaneous stimulation was delivered to 59 patients with chronic stroke, twice daily for 20 min, as part of their 3-week, yearly, inpatient rehabilitation program. 32 patients received treatment of their affected hand, while 8 received a no treatment control (sham). 19 patients received treatment in their affected foot.	Modified Motor Assessment Scale, 10-metre walking test, paretic hand function, upper limb skin sensation and somatosensory evoked potentials, normality classification of paretic upper limb and paretic lower limb improved significantly in the treatment group. When active hand treatment and placebo hand treatment were compared, a significant improvement in the sensory and motor function was observed only in the actively treated group.
Rorsman & Johansson 2006 Sweden 8 (RCT)	54 patients were randomized to 1 of 3 groups: 1) acupuncture + electroacupuncture, 2) high intensity, low-frequency transcutaneous electrical nerve stimulation (TENS) group or 3) low-intensity subliminal high-frequency TENS (control). Treatment sessions	No significant differences were found between the control group and the experimental groups for Activities of Daily Living (Barthel Index) or overall motor function (Rivermead Mobility Index). Although significant differences were seen in patients emotional status for a variety of

	were 30 min, 2 days/week for 10 weeks Outcome Measures included: cognition performance and emotional functioning.	tests.
Wu et al. 2006 USA 6 (RCT)	9 chronic stroke patients participated in a crossover study with 3 treatment conditions. Patients received a single 2-hour peripheral nerve stimulation session, separated by a 24-hour period, of the affected arm and hand and no stimulation. Outcome was assessed by the Jebsen-Taylor Hand Function Test (JTHFT) before and after each treatment.	JTHFT time was shorter following hand stimulation compared to either leg stimulation or no stimulation treatment conditions. The greatest improvement occurred in patients with the greatest level of impairment.
Yozbatiran et al. 2006 Turkey No Score	36 acute stroke patients were assigned in a ranked order to either a TENS group of a control group. Patients in both groups received an hour per day for 10 days of physical therapy according to the Bobath method. The treatment group received 1 hour of electrical stimulation of the finger and wrist extensors. Evaluations performed at the beginning and the end of treatment included kinaesthesia and position sense tests, and hand function and movement scales.	There were significant between group differences in mean changes in the hand function test, favouring the TENS group (2.38 vs. 1.22, p=0.044).
Celnik et al. 2007 Germany 6 (RCT)	9 patients with subcortical stroke with onset of at least 1-year participated in this crossover designed study. After a familiarization session each subject returned to take part in sessions 2,3 and 4. These sessions each performed on a different day started with the Jebsen-Taylor Hand Function Test (JTHFT) after which subjects received 2 hours of nerve stimulation (ulnar and median nerves of the affected hand), no stimulation or asynchronous nerve stimulation. The JTHFT was assessed 1 and 24 hrs later. Subjective reports of fatigue, attention, perceived difficulty of task performance were assessed using VAS.	Reduction in JTHFT time at 1 and 24 hrs relative to pre-test were only significant in the nerve stimulation group. There were no differences among conditions with respect to reductions in fatigue, attention or perceived difficulty.
Conforto et al. 2007 Brazil No Score	11 patients with chronic cortical stroke participated in a crossover study whereby subjects received 2 hrs of somatosensory stimulation in the form of median nerve stimulation at 2 different intensities (suprathreshold and subthresthold) and a control condition of sham stimulation. The interval between treatments was at least 60 days. The primary outcome was the	Improvement in performance in the JTT after somatosensory stimulation and after motor training was significantly greater in the MNS session than in the CS session. Patients who received MNS in the second session maintained the beneficial effects of training 30 days later.

	Jebsen-Taylor test (JTT).	
Klaiput et al. 2009 Thailand 8 (RCT)	20 stroke patients with stroke onset less than 6 months previously, who could voluntarily pinch the thumb to the index finger were randomized to receive 2 hours of real (10Hz- to the level of appreciating paresthesias) or sham (stimulation to the level of perception only) electrical stimulation over the median and ulnar nerves at the wrist. Pinch strength of the thumb pad to tip and to lateral side of the index finger of the paretic hand and the Action Research Arm test were tested before and immediately after the stimulation.	There were no changes in either group in ARAT scores from beginning to end of treatment. Scores were 56.2 in real stimulation group and 56.9 in sham group. There were significant between group differences favouring the real stimulation group in lateral and tip pinch strength. Mean lateral pinch strength of real stimulation and sham groups was 1.24 +/- 0.54 and 0.20 +/- 0.28 pounds, respectively. Mean increase tip pinch strength of real and sham groups were 1.00 +/- 0.72 and 0.37 +/- 0.36 pounds, respectively.
Koesler et al. 2009 Germany 5 (RCT)	12 chronic subcortical stroke subjects performed index finger and hand tapping movements as well as reach-to-grasp movements with both the affected and unaffected hand prior to and following 2 hrs of electrical somatosensory stimulation (trains of five pulses at 10 Hz with 1 ms duration delivered at 1 Hz with an intensity on average 60% above the individual somatosensory threshold) of the median nerve of the affected hand or 2 hrs of idle time on separate occasions at least 1 week apart. The order of sessions was counterbalanced across subjects.	Somatosensory stimulation of the median nerve of the affected hand, but not a period of idle time, enhanced the frequency of index finger and hand tapping movements and improved the kinematics of reach-to-grasp movements performed with the affected hand, compared with baseline.
Conforto et al. 2010 Brazil No Score	22 patients were pseudo-randomized within the second month after stroke to receive application of 2-hour repetitive peripheral nerve sensory stimulation (RPSS) at 1 of 2 stimulus intensities (sub sensory and suprasensory) immediately preceding motor training, 3 times a week, for 1 month. All patients received conventional rehabilitation therapies on an outpatient basis, once a week. Jebsen-Taylor test (JTT), pinch force and FIM, were measured before and after the end of the treatment month and 2-3 months later.	At the end of treatment, JTT scores in the sub sensory group had improved significantly greater compared with the suprasensory group (sub sensory: 114 to 49.5 vs. suprasensory: 93 to 61.4, p=0.026). The differences between groups were no longer significant at 2-3 months. There were no differences between groups in terms of pinch force or FIM scores at either the end of treatment, or at follow-up.
Ikuno et al. 2012 Japan 8 (RCT)	22 patients, an average of 3 months following stroke, in addition to 2 weeks of conventional inpatient rehabilitation were randomly assigned to receive peripheral sensory nerve stimulation combined with task-oriented training in the first week, followed by another	From baseline to one week, patients in the immediate group showed larger improvements than the delayed groups in the WMFT timed test (mean decrease from 41.9 to 30.6 sec. vs. 46.8 to 42.9 sec, respectively). The mean improvements in the WMFT Functional Ability Scale for

	week with task-oriented training alone (immediate group). Patients in the other group underwent the same training in reverse order (delayed group). Outcome measures included the Wolf Motor Function Test (WMFT) and fatigue and were assessed at baseline, one and two weeks.	patients in the immediate group were also better for patients in the immediate group (60 to 63.3 vs. 58.3 to 59.3). There was no difference in fatigue between groups.

In five studies the effect of TENS was investigated in both upper and lower extremity functioning (Tekeoðlu et al. 1998, Johansson et al. 2001 and Peurala et al. 2002, Rorsman and Johansson 2006, Potisk et al. 1995).

Nine RCTs examined the effectiveness of TENS treatment on motor recovery following stroke. Their results are summarized in Table 10.50.

Table 10.50 Summary of the RCTs Evaluating TENS in the Treatment of Upper Extremity

Author/PEDro	N	Intervention	Outcome
Johansson et al. 2001 8	150	Acupuncture vs. TENS vs. control	Barthel Index (-) Nottingham Health Profile (-) Nine Hole Peg Test (-)
Ikuno et al. 2012 8	22	Peripheral sensory nerve stimulation + task-specific therapy vs. task-specific therapy	Fugl-Meyer Assessment (-)
Klaiput et al. 2009 8 (RCT)	20	Real vs. sham electrical stimulation	Action Research Arm test (-)
Celnik et al. 2007 6 (RCT)	9	Single session of peripheral nerve stimulation vs. no stimulation vs. asynchronous nerve stimulation	Jebsen-Taylor Hand Function Test (+)
Wu et al. 2006 6 (RCT)	9	Single session of peripheral nerve stimulation vs. no stimulation	Jebsen-Taylor Hand Function Test (+)
Conforto et al. 2002 6 (RCT)	8	Single session of medial nerve stimulation vs. sham stimulation	Pinch muscle strength (+)
Tekeoðlu et al. 1998 6	60	Rehabilitation + TENS vs. rehabilitation	Barthel Index improvement (+)
Sonde et al. 1998 5	44	TENS + physiotherapy vs. physiotherapy	Fugl Meyer (+) Pain (-) Barthel Index (-)

Conclusions Regarding Transcutaneous Electrical Nerve Stimulation

There is conflicting (Level 4) evidence that treatment with TENS in the upper extremity improves motor recovery, and performance of ADLs.

It is uncertain whether TENS improves outcomes post stroke.

10.8 Neuromuscular electrical stimulation (NMES)

Neuromuscular electrical stimulation (NMES) can be used to improve motor recovery, reduce pain and spasticity, strengthen muscles and increase range of motion following stroke. Functional electrical stimulation (FES) refers to the application of NMES to help achieve a functional task. FES is a technique that uses bursts of short electrical pulses to generate muscle contraction by stimulating motor neurons or reflex pathways. Three forms of NMES are available: 1) cyclic NMES, which contracts paretic muscles on a pre-set schedule and does not require participation on the part of the patient; 2) EMG triggered NMES, which may be used for patients who are able to partially activate a paretic muscle and may have a greater therapeutic effect; 3) neuroprosthetic applications of NMES, which can ultimately improve or restore the grasp and manipulation functions required for typical ADLs (Popovic et a. 2002).

Several reviews and meta-analyses examining the benefit of NMES have been conducted. A meta-analysis of four studies concluded that FES enhanced strength (Glanz et al. 1996). However, conclusions are limited by the methodology of the trials (small sample size, inadequate blinding) and it was difficult to link improved strength with improved function.

A systematic review by de Kroon et al. (2002) assessed the effect of therapeutic electrical stimulation of the affected upper extremity in improving motor control and functional abilities after stroke. The authors included 6 RCTs in their review. The authors concluded that there is a positive effect of electrical stimulation on motor control, but that no conclusions could be drawn regarding its effect on functional abilities.

Studies included in de Kroon et al. (2002)

De Kroon et al. 2002
Chae et al. 1998
Francisco et al. 1998
Sonde et al. 1998
Powell et al. 1999
Cauraugh et al. 2000
Bowman et al. 1979

A Cochrane review (Pomeroy et al. 2006) examined the use of all forms of electrostimulation (ES) in the recovery of functional ability following stroke. This review assessed the efficacy of functional electrical stimulation (both as a form of neuromuscular retraining and as a form of neuroprosthesis/orthosis), transcutaneous electrical nerve stimulation, EMG and electroacupuncture. Twenty-four RCTs evaluating the efficacy of treatment on both the upper and lower extremities were included. Among the trials of upper extremity interventions, the primary outcome included nine measures of functional motor ability and two ADL measures. The review included four planned treatment contrasts:1) ES vs. no treatment; 2) ES vs. placebo stimulation; 3) ES vs. conventional therapy and 4) One type of ES vs. an alternative type of ES. With respect to the assessment of treatments specific to the upper extremity, five outcomes were associated with a statistically significant treatment effect. With one exception, all of the pooled analyses were based on the results from only one study. The results from pooled analyses with positive results are presented in Table 10.50. The authors concluded that there was insufficient evidence to guide practice on the efficacy of ES.

Table 10.51 Pooled Analysis from 2006 Cochrane Review Assessing Efficacy of ES as a Therapy for the Upper Extremity

Treatment Contrast Outcome Assessed	**Standardized Mean Difference (95% CI)**
ES vs. No treatment	
Motor reaction time	1.18 (0.00, 2.37)
Isometric torque	1.02 (0.46, 1.59)
Box & Block test	1.28 (0.00, 2.56) *
Upper Extremity Drawing test	-1.40 (-2.25, -0.56) (favours no treatment)
ES vs. Placebo	
Jebsen Hand Function test feeding	1.36 (0.24, 2.48)
ES vs. Conventional Therapy	No outcomes were statistically significant
Comparison of Different Forms of ES	No comparisons conducted or reported
** All 3 studies included in the pooled analysis were authored by the same person (Cauraugh)*	

Meilink et al. (2008) examined the effectiveness of EMG-triggered NMES applied to the extensor muscles of the forearm to improve hand function following stroke. The review included the results of 8 studies (157 patients). Compared with usual care, there was a non-statistically significant treatment effect for all outcomes assessed (Fugl-Meyer scores, Box & Block test, Action Research Arm test, reaction time and sustained contraction). The authors speculated that one of the reasons for the null findings was that the majority of studies had included subjects in either the sub acute or chronic stages of stroke. They hypothesized that there may be a critical 5 week time window following stroke during which dexterity is most likely to be regained.

Table 10.52 FES Studies in the Upper Extremity

Author/ Country Pedro Score	Methods	Outcomes
Bowman et al. 1979 USA 3 (RCT)	30 acute stroke patients were randomly assigned to receive conventional treatment of hand and wrist (n=15) or conventional treatment + positional feedback stimulation therapy (n=15) for 30 min x 5 days/week x 4 weeks.	With the wrist positioned at 30^0 flexion, the average isometric extension torque had increased by 280% compared to a 70% increase in the control group (p<0.25). Study group patients achieved a 200% gain in selective range of motion over baseline levels, compared to a 50% gain in the control group patients (p<0.05).
Kraft et al. 1992 USA No Score	22 right-handed patients were assigned to one of 4: 1) EMG-electrical stimulation (es)(n=6), 2) low intensity es (n=4), 3) proprioceptive nerve	The aggregate Fugl-Meyer (FM) scores for the groups receiving treatment was significantly increased from baseline to post-treatment and the improvements were maintained at 9

	facilitation (PNF) (n=3) or 4) no treatment control (n=5). Patients received treatment for 3 months and were assessed at 3 and 9 months following treatment.	months follow-up (p<0.005). There was no significant improvement in grip strength at 3 or 9 months. There were no significant improvements in either grip strength or FM scores among the control patients.
Faghri et al. 1994 USA 4 (RCT)	26 acute stroke patients were randomized to receive FES + conventional therapy, or only conventional therapy.	After treatment, the FES group showed significant increased arm function, tone and EMG activity compared with the control group.
King 1996 USA 4 (RCT)	21 chronic stroke subjects were randomized to receive a single 10 min session of either neuromuscular electrical stimulation (NMES) or passive stretch as a means to reduce tone.	Subjects in the NMES group experienced significantly greater reduction in tone, measure by a torque meter (9.6 cm/kg vs. 4.6 cm/kg).
Faghri and Rodgers 1997 USA 4 (RCT)	26 acute stroke patients were randomized to receive either conventional therapy + FES, daily for 6 weeks (n=13) or conventional therapy (n=13).	Weekly evaluation of arm and shoulder muscle function showed significant improvement. Significantly improved function assessed by range of motion at 4/7 testing times, shoulder muscle tone at 5/7 testing times, and EMG activity of the posterior deltoid muscle at 3/7 testing times.
Heckermann et al. 1997 Germany 4 (RCT)	28 stroke patients with severe hemiparesis were randomized to receive EMG-triggered FES + inpatient physical therapy (n=14) or physical therapy alone based on the Bobath method (n=14). Each patient was treated by a physiotherapist for 45 min x 5 days/week. FES treatment was delivered to the target muscles (upper arm extensors, knee flexors and ankle extensors. Each group of muscles was stimulated 15 times per session, 5 days/ week x 4 weeks. Outcomes included spasticity, range of motion and Barthel Index.	All patients improved from baseline to post treatment. The only significant between group result was improvement in the range of motion of the hand extensors.
Hummelsheim et al. 1997 Germany No Score	12 stroke patients were studied using a multiple baseline design. Following a baseline phase (phase A) that lasted between one and three weeks, all patients received electrical nerve stimulation for 20 min 2x/day x 2 weeks (phase B), followed by two weeks of a standardized training programme (phase C) emphasizing repetitive motor training, in addition to routine therapy.	Non-statistically significant improvement in Modified Ashworth and Rivermead Motor Assessment scores over the treatment period. A statistically significant improvement was reported in functional motor capacity during Phase C (p<0.008).
Pandyan and Granat 1997 UK No Score	11 stroke patients received 2 weeks of regular rehabilitation, followed by 2 weeks with electrical stimulation + rehabilitation, followed by 2 weeks of rehabilitation only.	Passive extension of the wrist had improved significantly immediately following treatment, but were lost both at 1 hour post treatment and at 2 weeks. The measures of resting wrist angle showed the same trend, whereby there was an improvement shown right after treatment, but

		which quickly declined.
Chae et al.1998 USA 6 (RCT)	46 acute stroke rehabilitation inpatients were randomized to receive surface neuromuscular stimulation to produce wrist and finger extension exercises in addition to routine rehabilitation (n=14) or to sham stimulation + routine rehabilitation (n=14), for 1 hr/day x 15 sessions. 18 subjects were excluded after randomization.	Treatment group had significantly greater gains in upper extremity Fugl-Meyer scores compared to controls immediately following treatment (13.1 vs. 6.5, p=0.05), at 4 weeks (17.9 vs. 9.7, p=0.05), but not at 12 weeks (20.6 vs. 11.2, p=0.06) following treatment.
Francisco et al. 1998 USA 5 (RCT)	9 acute stroke rehabilitation inpatients were randomized to receive EMG-electrical stimulation + standard therapy (n=4), for 30 min/day x 5 days/week for the duration of hospital stay or to standard therapy alone (n=5).	Treatment patients had significantly greater gains in upper extremity Fugl-Meyer (27 vs. 10.4, p=0.05) and upper extremity FIM scores (6.0 vs. 3.4, p=0.02), compared to controls.
Powell et al. 1999 UK 7 (RCT)	60 hemiparetic stroke patients, 2-4 weeks post stroke were randomized to receive standard rehabilitation+ electrical stimulation (ES) of wrist extensors for 30 min/day x 3x/week x 8 weeks (n=25) or to routine rehabilitation (n=23).	Change in isometric strength of wrist extensors was significantly greater in the ES group, at 8 and 32 weeks (p=0.004 and p=0.014). Grasp and grip scores on the Action Research Arm test had increased significantly in the ES group at 8 weeks (p=0.013 and p=0.02).
Cauraugh et al. 2000 USA 4 (RCT)	11 patients, greater than one-year post stroke onset, with upper extremity impairment were randomized to receive either passive range of motion and stretching exercises + electrical stimulation (ES), 30 min x 12 sessions (n=7) or to a control group without ES (n=4).	ES group moved significantly more blocks on the Box and Block test (p<0.05). No differences on the Motor Assessment Scale and the Fugl-Meyer (upper extremity) test.
Wang et al. 2002 China 5 (RCT)	32 hemiplegic stroke patients were placed into either a short or long-duration group, depending on the length of their hemiplegia and then subjects in each group were randomly assigned to either control or experimental condition. Subjects in experimental sub groups were treated in an A-B-A design that consisted of FES training (A), routine therapy or regular daily activity without FES (B) and another FES training (A). Each period lasted for 6 wks.	Patients in the short duration group demonstrated significant improvement in Fugl-Meyer scores compared to patients in the control group after the first 6 weeks of therapy, during the following 6 weeks of no therapy and again following an additional 6 weeks of therapy. There was no significant improvement for patients receiving FES in the long-duration group at any point, compared to the control group.
Cauraugh and Kim 2003 USA 5 (RCT)	26 stroke patients with chronic hemiparesis were randomly assigned to one of three groups: 1) 0 sec stimulation, 2) 5 sec stimulation, and 3) 10 sec stimulation. Stimulation was applied to the back of the impaired forearm. All patients completed 4 days (90 min/day) of rehabilitation training	Both the 5 sec and 10 sec groups moved significantly more blocks (Box and Block Test), significantly decreased their reaction times across test sessions, and significantly improved muscle contraction, while the 0 sec group did not show significant improvement on any of the outcome measures.

	over a 2 wk period. Outcome measures included: Box and Block Test (manual dexterity), Reaction time, and sustained wrist/finger contraction.	
Popovic et al. 2003 Denmark 6 (RCT)	28 patients with acute stroke were divided into lower functioning and higher functioning groups (LFG, HFG) and randomized to receive functional electrical therapy (FET) + conventional therapy or regular inpatient therapy. Time from stroke onset to randomization ranged from 4-11 weeks. Patients in the FET group performed 30 min exercise with the paretic arm and hand, facilitated with a neural prosthesis that controlled the opening and closing of the hand regular therapy +.everyday for 3 weeks. Patients in the control group received similar treatment, less electrical stimulation. Assessments at study start, 3,6,12, and 26 weeks included the Upper Extremity Function test (UEFT), drawing test (DT), coordination of elbow and shoulder movements, spasticity and a structured interview (Reduced Upper Extremity Motor Activity Log)	Patients in both the HFG/FET and LFG/FET groups picked up significantly more objects in 2 min (UEFT) at all testing intervals, except baseline, compared to controls. Patients in the HFG/FET group had significantly higher DT scores compared to control at all testing intervals, except baseline, compared to controls. DT differences between treatment and control groups were only significantly different at one testing point (week 13).
Popovic et al. 2004 Denmark 6 (RCT)	41 acute stroke patients were randomized to receive 3 weeks of daily FES treatments lasting 30 min each, either immediately or following a delay of 52- 56 weeks. All subjects also participated in a consecutive 3-week task-oriented therapy training program in addition to routine rehabilitation. The outcomes assessed were the Upper Extremity Function Test (UEFT), the Drawing Test (DT), the Modified Ashworth Scale (MAS), range of movement, and the questionnaire estimating the patients' satisfaction with the usage of the paretic arm. Assessments were conducted at baseline, at 78 weeks and several other times during the study period, which varied by outcome.	Patients who participated in the FES during the acute phase of hemiplegia reached functionality of the paretic arm, on average, in less than 6 weeks, and maintained this near-normal use of the arm and hand throughout the follow-up. The gains in all outcome scores were significantly larger in the early group after FES and at all follow-ups compared with the scores before the treatment. Subjects in the delayed group also experienced gains on all outcomes assessed, although they were not statistically significant. The speed of recovery was larger during the period of the FES compared with the follow-up period. The gains in the immediate FES group were significantly greater compared with the gains made by subjects in the delayed group.
Kimberly et al. 2004 USA 7 (RCT)	16 chronic stroke patients were randomized to receive intensive neuromuscular electrical stimulation (NMES) at home (6 hrs/day for 10 days over a 3-week period) or a similar (sham) treatment. Patients were then crossed over to the other treatment arm. Time from stroke onset to	There was statistically significant improvement in strength only from pre-test to post-test. Following the active treatment, patients improved significantly on the BB test,2 components of the MAL (amount of use score and how well score) and two components of the JTHFT (page turning and feeding). Using fMRI and a finger-tracking task, an index of cortical

	randomization was 7-58 months Pre-test, post-testing included Block & Box test (BB), Motor Activity Log (MAL), Jebsen Taylor Hand Function Test (JTHFT), isometric strength of the index finger extension finger movement control and fMRI.	intensity in the ipsilateral somatosensory cortex increased significantly from pre-test to post-test following treatment.
De Kroon et al. 2004 Netherlands 6 (RCT)	30 chronic stroke patients with spastic paresis were randomized to one of two treatment programs i) Alternating electrical stimulation of the extensor and flexor muscles of the hand or ii) Electrical stimulation of the extensors only. Treatment lasted for 6 wks, with stimulation time increased gradually from 20 min/session to 1 hr/session. Assessed immediately before start of treatment, at the end of 6-wk treatment period, and after a follow-up period of 6 wks. Primary outcome was Action Research Arm test. Secondary: grip strength; Motricity Index; Ashworth Scale; and range of motion of the wrist.	No significant differences between the groups.
Ring & Rosenthal 2005 Israel 6 (RCT)	22 chronic stroke patients with moderate to severe upper extremity hemiparesis were randomized to receive home-based neurostimulation with a 5-electrode neuroprosthetic device or to a no device control condition. Patients in the treatment group received FES treatments which peaked at 50 min, 3x per day for 6 weeks. All patients participated in a day hospital outpatient rehabilitation program. Assessments included modified Ashworth Scale, Blocks and Box test and 3 items on the Jebsen-Taylor assessment.	Patients in the FES group experienced significant improvement in reduction of spasticity and improved performance on the Box and Block test and 2/3 items on the Jebsen-Taylor assessment, relative to the control group. Among the few number of patients with edema and pain, only those in the FES group reported improvement.
Gabr et al. 2005 USA 4 (RCT)	In a crossover designed study, 12 chronic stroke patients with muscle contraction in their affected wrist, but with no movement were randomized to begin with a home-based electromyographic-triggered neuromuscular stimulation, twice daily for 35 minutes for 8 weeks or to a home exercise program. Outcomes included the Action Research Arm test, Fugl-Meyer and goniometry.	No statistically-based between group comparisons were reported. Patients who first received ETMS (n=8) gained 7 points on the FM scale following treatment (8 weeks), but the effects were lost when patients were switched to the home exercise program and reassessed at 16 weeks. They lost 9 points on FM from baseline. There were no changes in ARA scores. Patients who first received home exercise (n=4) gained less than a point on the FM scale at 8 weeks. When crossed over to the active therapy group and reassessed at 16 weeks, there was again a less than 1 point gain in FM points. There were no changes in ARA scores.

Hara et al. 2006 Japan 4 (RCT)	14 stroke patients (>1 yr post stroke) with spastic upper-extremity impairments were randomized to receive 4 mos of power-assisted FES (40 min sessions, once or twice a week for 4 mos) plus traditional therapy (n=8) or traditional therapy alone (n=6). Outcome was assessed before and after training included active range of motion (ROM), Modified Ashworth Scale and 2 clinical tests.	Patients in the hybrid FES group demonstrated significant improved active ROM in finger and wrist extension. There was a trend towards greater improvement in MAS among patients in the FES group.
Alon et al. 2007 USA 5 (RCT)	15 acute ischemic stroke patients were randomly assigned to receive 12 weeks of either FES along with task-specific upper extremity rehabilitation (n=7) or task-specific rehabilitation alone (control) (n=8). Outcome measures were recorded at baseline, 4, 8, and 12 weeks and they included Box and Block (B&B), Jebsen-Taylor light object lift (J-T) and modified Fugl-Meyer (mFM).	At 12 weeks the FES group moved significantly more blocks compared with the control group (42 vs. 26, p=0.049). Patients in the FES group completed the J-T task faster (6.7 vs. 11.8, p=0.049) and the mFM scores were higher among patients in the FES group (49 vs. 40, p=0.042).
Bhatt et al. 2007 USA 3 (RCT)	20 chronic stroke patients were randomly assigned to receive electrical stimulation (ES), tracking training (TR), combination (CM) group. All groups received 10 1-hr training sessions for over 2-3 weeks. Assessments included the Jebson Taylor tests of manual dexterity, Box and Block test and a finger-tracking test.	From pre-test to post-test on the Box and Block test and the Jebsen Taylor Test. There were no significant differences between groups.
Sullivan and Hedman 2007 USA No Score	10 chronic stroke patients with arm hemiparesis received an individualized home programme of neuromuscular and sensory amplitude electrical stimulation. All patients participated in stimulation-assisted task-specific exercises for 15 min 2-3 times daily, 7 days/wk for 8 wks. Patients with sensory deficits received 15 mins, twice daily of additional sensory stimulation. Assessments included the Action Research Arm Test (ARAT), the Stroke Rehabilitation Assessment of Movement and the Modified Ashworth Assessment (MAS) of Spasticity.	6 of the 10 participants improved significantly on the ARAT after treatment. 5 of the 10 patients improved significantly on the Stroke Rehabilitation Assessment of Movement and 4 of the 10 subjects attained a ≥10% change from pre- to post-test on the MAS.
Kowalczewski et al. 2007 Canada 6 (RCT)	19 subacute stroke subjects with severe upper-limb dysfunction were randomized to receive a program of either high (n=10) or low (n=9) intensity FES stimulation combined with an exercise workstation with instrumented objects were used to perform specific motor tasks with their	Improvements in the WMFT and CKS were significantly greater in the high-intensity group (effect size, .95) than the low-intensity group (effect size, 1.3). The differences in MAL and FMA were not statistically significant.

	affected upper extremity. Subjects in the high-intensity FES-ET group received treatment for 1 hour a day on 15 to 20 consecutive workdays, while subjects in the low-intensity FES-ET group received 15 minutes of sensory electric stimulation 4 days a week and on the fifth day they received 1 hour of FES-ET. The primary outcome measure included the Wolf Motor Function Test (WMFT). Secondary outcome measures included the Motor Activity Log (MAL), the upper-extremity portion of the Fugl-Meyer Assessment (FMA), and the combined kinematic score (CKS) derived from workstation measurements. Evaluations were performed before and after treatment and at 3 and 6-month follow-up.	
Alon et al. 2008 USA 3 (RCT)	26 severely impaired stroke patients were randomized an average of 20 days following stroke to receive either cyclic FES + task-specific exercise program or to an exercise-only group for 12 weeks. All participants trained with task-specific exercises, 30 min, twice daily. The FES group practiced the exercises combined with FES that enabled opening and closing of the paretic hand and continued with FES without exercises for up to 90 mins of additional time twice a day. Outcomes assessed included modified Fugl-Meyer (FM), Box & Blocks test (B&B) and the Jebsen-Taylor light object lift (JT). Outcomes were assessed at baseline and at 4, 8, and 12 wks.	At the end of 12 weeks, the mean FM scores were significantly higher among subjects in the FES group (24 vs. 14.2, p=0.05). There were non significant differences between groups on the B&B test, although subjects in the FES group were able to move more blocks (10.5 vs. 2.5). The JT task time did not differ significantly between groups. Eight (FES) compared with three (control) patients regained the ability to transfer five or more blocks (P = 0.051), and six (FES) compared with two (control) completed the J-T task in 30 sec or less after 12 wks of training (P = 0.09).
Hara et al. 2008 Japan 5 (RCT)	20 chronic stroke patients were randomized to a home-based 5-month program of FES or physical therapy. The FES group used a power-assisted FES device to induce greater muscle contraction by electrical stimulation in proportion to the integrated electromyography (EMG) signal picked up on surface electrodes. Target muscles were the extensor carpi radialis longus (ECRL) and extensor carpi radialis brevis (ECRB), extensor digitorum communis (EDC), extensor indicis proprius (EIP), and deltoid (Del). Patients underwent 30 approximately 60 min FES sessions at home about 6 days/week. Root mean square (RMS) of	The FES group displayed significantly greater improvements in RMS, active ROM, MAS and functional hand tests.

	ECRL, EDC and Del maximum voluntary EMGs, active range of motion (ROM) of wrist and finger extension and shoulder flexion, modified Ashworth scale (MAS), and clinical tests were investigated before and after FES training.	
De Kroon & Ijzerman 2008 Denmark 7 (RCT)	22 chronic stroke patients were randomly assigned to receive either cyclic (n=11) or EMG-triggered electrical stimulation (n=11) of the wrist and finger extensor muscles for a six-week period. The primary outcome measure was the Action Research Arm test (ARAT). Grip strength, Fugl-Meyer Motor Assessment and Motricity Index were secondary outcome measures. Assessments were made at the start of the treatment and after 4, 6 and 12 weeks.	Both groups improved on the Action Research Arm test. The group receiving cyclic stimulation improved by 2.3 points, and the group receiving EMG-triggered stimulation improved by 4.2 points. The difference in functional gain was not statistically significant. Differences in gain on the secondary outcome measures were also not significant.
Chae et al. 2009 USA 8 (RCT)	26 chronic stroke survivors were randomly assigned to receive percutaneous intramuscular ES for hand opening (n = 13) or percutaneous ES for sensory stimulation only (n = 13). The intramuscular ES group received cyclic, electromyography (EMG)-triggered or EMG-controlled ES depending on baseline motor status. All participants received 1 hour of stimulation per day for 6 weeks. After completion of ES, participants received 18 hours of task-specific functional training. The primary outcome measure was the Fugl-Meyer Motor Assessment. Secondary measures included the Arm Motor Ability Test and delay and termination of EMG activity. Outcomes were assessed at baseline, at the end of ES, at the end of functional training, and at 1, 3, and 6 months follow-up.	There were no significant differences between groups over the testing periods, although subjects in both groups improved on all measures over time.
Chan et al. 2009 Hong Kong 7 (RCT)	20 subjects, 6 months post stroke were randomized to receive 15 sessions of either FES (using a self-triggering mechanism) + bilateral tasks (20 minutes), + 10 min of stretching exercises and occupational therapy treatment (60 minutes), or the same duration of stretching and occupational therapy training + placebo FES during the bilateral tasks. The outcome measures assessed before and after intervention, included Functional Test for the Hemiplegic Upper Extremity	After 15 training sessions, the FES group had achieved significantly greater improvement in FMA (+7.7 vs. +2.1 points, P = .039), FTHUE (+1.3 vs. 0.3, P = .001), and active range of motion of wrist extension (+17 vs. 3.5 degrees, P = .020), when compared with the control group.

	(FTHUE), Fugl-Meyer Assessment (FMA), grip power, forward reaching distance, active range of motion of wrist extension, FIM and Modified Ashworth Scale.	
Mangold et al. 2009 Switzerland 5 (RCT)	23 subjects with stroke onset of 2-18 weeks admitted for inpatient rehabilitation were randomly assigned to a 4-week intervention program of either FES or conventional therapy. Subjects in both groups received 3-5 occupational therapy sessions per week, each lasting 45 min each. FES training replaced 12 conventional training sessions in the intervention group. Outcomes assessed before and after treatment included the ADL sub score of the Extended Barthel Index (EBI), the Chedoke McMaster Stroke Assessment (CMSA) measured hand and arm function and shoulder pain and the Modified Ashworth Scale (MAS) score.	There were no statistically significant differences between groups on any of the outcome measures assessed. The EBI sub score and CMSA arm score improved significantly in both groups. The CMSA hand function improved significantly in the FES group. Resistance to passive movement of finger and wrist flexors increased significantly in the FES group. Shoulder pain did not change significantly. None of the outcome measures demonstrated significant differences in gains between the groups.
Thraher et al. 2009 Canada 5 (RCT)	21 subjects with onset of stroke 2-7 weeks admitted for inpatient rehabilitation were randomized to receive a 12-16 week program of either FES plus conventional occupational and physiotherapy (FES group) or only conventional therapy (control group) for 45 min x 5 days a week. FES was applied to proximal and then distal muscle groups during specific motor tasks. At baseline and at the end of treatment, grasping function was assessed using the Rehabilitation Engineering Laboratory Hand Function Test, Barthel Index, Fugl-Meyer (FM) scores, and Upper Extremity Chedoke-McMaster Stages of Motor Recovery.	The FES group improved significantly more than the control group in terms of object manipulation, palmar grip torque, pinch grip pulling force, Barthel Index, Upper Extremity Fugl-Meyer scores, and Upper Extremity Chedoke-McMaster Stages of Motor Recovery. There were no significant differences in FIM scores.
Hsu et al. 2010 Taiwan 6 (RCT)	66 acute patients receiving inpatient rehabilitation were randomized to 3 groups: high NMES, low NMES, or control. The low-NMES group received 30 minutes of stimulation per day, and the high-NMES group received 60 minutes per day, for 4 weeks. He control group received no additional treatment. Outcomes included the Fugl-Meyer Motor Assessment Scale (FM), Action Research Arm Test (ARAT), and Motor Activity Log and were assessed at	At 4 and 12 weeks, both NMES groups showed significant improvement on FM Assessment and ARAT scales compared with the control group. The results for the high and low NMES groups were similar.

	baseline, 4 weeks, and 12 weeks post baseline.	
Weber et al. 2010 USA 7(RCT)	23 chronic stroke patients received botulinum toxin-A injections + a home exercise program (60 min/day x 12 weeks) consisting of task-specific practice. Participants were then randomly assigned to receive additional treatment with FES during practice time or no FES. Outcomes assessed at baseline, 6 and 12 weeks included the Motor Activity Log (MAL)-Observation, Action Research Arm Test (ARAT) and MAL-Self-Report.	There were no statistically significant differences between groups on any of the outcomes assessed at any of the assessment points.
Lin & Yan 2011 China 6 (RCT)	46 patients within 3 months of first-stroke onset were randomized to a neuromuscular electrical stimulation (NMES) group or a control group. All patients received a standard rehabilitation program for 30 min, 5x/week for 3 weeks. Patients in the neuromuscular electrical stimulation group received additional NMES treatment for 30 min, 5x/week for 3 weeks. Outcomes were assessed before treatment, at the 2nd and 3rd week of treatment and 1, 3 and 6 months after treatment ended. Outcomes included the Modified Ashworth Scale (MAS), the upper extremity section of the Fugl-Meyer Assessment (FMA) and the BI.	Patients in both groups improved over the study period. The mean total FMA scores had improved significantly more from baseline to 6 months among patients in the NMES group compared with controls (from 8.4 to 29.8 vs. 8.2 to 20.3, $p<0.05$). The mean total BI scores had improved significantly more from baseline to 6 months among patients in the NMES group compared with controls (from 31 to 79.2 vs. 30.3 to 66.1, $p<0.05$). Mean MAS scores increased slightly over the study period from 0.53 to 1.67 in the NMES group and 0.5 to 1.86 in the control group.
Knutson et al. 2011 USA 6 (RCT)	21 patients < 6 months following stroke were randomized to receive 6 weeks of either contralaterally controlled functional electrical stimulation (CCFES) or cyclic neuromuscular electrical stimulation (NMES). Patients in both groups received daily treatment consisting of daily stimulation-assisted repetitive hand-opening exercise at home plus twice-weekly lab sessions of functional task practice. Assessments were made before and after treatment and at 1 month and 3 months follow-up. Outcomes included maximum voluntary finger extension angle, finger movement tracking error, upper extremity Fugl-Meyer score, Box and Blocks test, and Arm Motor Abilities test.	Although patients in the CCFES group demonstrated greater improvements over the study period, there were no significant differences on any the outcomes assessed after controlling for baseline scores. Maximum voluntary finger extension showed the largest treatment effect, with a mean group difference across the post treatment time points of 28 degrees more finger extension for CCFES.
Shindo et al. 2011 Japan	24 inpatients within 60 days of stroke received standard rehabilitation therapy which included 1 hr of OT and PT, 5	Compared with the control group, the HANDS group showed significantly greater gains in distal (wrist/hand) portion of the FMA (gain of

6 (RCT)	days a week during hospital stay. In addition 12 patients underwent hybrid assistive neuromuscular dynamic stimulation (HANDS) therapy, which combined NMES with a splint. Patients in this group wore the device for 8 hrs each day. Patients in the control group wore a wrist splint only. Outcomes included upper extremity portion of the Fugl-Meyer Assessment (FMA), Action Research Arm Test (ARAT), and Motor Activity Log-14 (MAL), assessed before and after treatment.	5.8 vs. 2.6, p=0.009, but not proximal (gain of 6.4 vs. 2.9, p=0.105. Mean ARAT gains were greater for patients in the HANDS group (1.99 vs. 1.51, p=0.043. The mean gain in the MAL did not differ between groups.
Tarkka et al. 2011 Finland 2 (RCT)	20 chronic stroke patients were randomized to receive FES or therapy only. All patients received twice daily sessions of therapy for 2 weeks. Hand motor function and neurophysiologic transcranial magnetic stimulation (TMS) tests were applied before and after the treatment and at 6-months follow-up.	Faster movement times were observed in the functional electrical therapy group but not in the conventionally treated group.
Page et al. 2012 USA 6 (RCT)	32 chronic stroke subjects participated in 30-, 60-, or 120-minute sessions of repetetive task-specific practice (RTP) + FES using the Bioness device every weekday for 8 weeks. The fourth group participated in a 30-minute per weekday home exercise program. Outcomes were evaluated using the UE section of the Fugl-Meyer Assessment of Sensorimotor Impairment (FM), the Arm Motor Ability Test (AMAT), the Action Research Arm Test (ARAT), and Box and Block (B&B) 1 week before and 1 week after intervention.	After intervention, subjects in the 120-minute group were the only ones to exhibit significant score increases on the FM (P=.0007), AMAT functional ability scale (P=.002), AMAT quality of movement scale (P=.0002), and ARAT (P=.02). They also exhibited the largest changes in time to perform AMAT tasks and in B&B score, but these changes were nonsignificant, (P=.15 and P=.10, respectively).

RCTs evaluating FES were categorized according to chronicity of stroke. Patients were considered to be acute if they had suffered a stroke within 6 months and chronic if their stroke had occurred greater than 6 months prior to inclusion in the study. The results are presented in Tables 10.53 and 10.54

Table 10.53 Summary Table for FES for the Hemiparetic Upper Extremity in Acute or Subacute Stroke (< 6 months)

Author PEDro Score	N	Intervention	Main Outcome(s) Result
Powell et al. 1999 7 (RCT)	60	Standard rehabilitation and electrical stimulation vs. standard rehabilitation	Grasp and grip scores of Action Research Arm test (+)
Shindo et al. 2011 6 (RCT)	24	NMES + splint vs. splint	Fugl-Meyer (+/-)
Lin & Yan 2011	46	Standard rehabilitation and	Fugl-Meyer (+)

6 (RCT)		electrical stimulation vs. standard rehabilitation	Barthel Index (+)
Hsu et al. 2010 6 (RCT)	66	High vs. low intensity FES vs. no treatment	Fugl-Meyer (hi and low FES +) Action Research Arm test (hi and low FES +) Motor Activity Log (-)
Kowalczewski et al. 2007 6 (RCT)	19	High vs. low intensity FES	Wolf Motor Function Test (+) Motor Activity Log (-) Fugl-Meyer (-)
Popovic et al. 2004 6 (RCT)	41	Early vs. delayed FES	Upper Extremity Function test (+ acute) Drawing test (+acute)
Popovic et al. 2003 6 (RCT)	28	Functional electrical therapy + therapy vs. standard therapy	Upper Extremity Function test (+) Drawing test (+)
Chae et al. 1998 6 (RCT)	46	Neuromuscular stimulation and routine rehabilitation vs. sham stimulation and routine rehabilitation	Fugl-Meyer: post-treatment (+) 12 weeks follow-up (-)
Mangold et al. 2009 5 (RCT)	23	FES vs. conventional therapy	ADL subscore of Extended Barthel Index (-) Chedoke McMaster Stroke Assessment (-)
Thrasher et al. 2009 5 (RCT)	21	FES+ conventional therapy vs. conventional therapy	Rehabilitation Engineering Laboratory Hand Function Test (+)
Alon et al. 2007 5 (RCT)	15	FES + task specific training vs. only task specific training	Box and Block (+) Jebsen-Taylor light object lift (+) Modified Fugl-Meyer (+ only at 12 weeks)
Francisco et al. 1998 5 (RCT)	9	Electrical stimulation and standard therapy vs. Conventional Therapy	Fugl-Meyer (+) Upper extremity FIM scores (+)
Faghri & Rodgers 1997 4 (RCT)	26	Conventional therapy and FES vs. conventional therapy	Range of motion (+) Shoulder muscle tone (+)
Heckermann et al. 1997 4 (RCT)	28	Functional electrical therapy + therapy vs. standard therapy	Range of motion (+)
Faghri et al. 1994 4 (RCT)	26	Conventional therapy and FES vs. Conventional Therapy	Arm tone (+) EMG activity (+)
Bowman et al. 1979 3 (RCT)	30	Conventional therapy + positional feedback stimulation therapy vs. conventional Therapy	Range of motion (+)
- Indicates non-statistically significant differences between treatment groups *+ Indicates statistically significant differences between treatment groups*			

Among the studies evaluating ES in the acute stage of stroke, most assessed the same treatment comparison, physical therapy plus FES (or sham FES) vs. physical therapy alone. The results most of the studies indicated that FES was an associated with improvements in motor function, ADL and dexterity. One study, Popovic et al. (2004) examined early vs. delayed treatment with FES and found that subjects who received FES acutely following stroke experienced improved recovery compared with those who received FES a year following stroke.

Conclusions Regarding the Efficacy of FES Therapy in Acute Stroke

There is strong (Level 1a) evidence that FES treatment improves upper extremity function in acute stroke.

Table 10.54 Summary Table for FES in the Hemiparetic Upper Extremity in Chronic Stroke

Author PEDro Score	N	Intervention	Main Outcome(s) Result
Chae et al. 2009 8 (RCT)	26	Percutaneous electrical stimulation (motor vs. sensory)	Fugl-Meyer (-)
Chan et al. 2009 7 (RCT)	20	Bilateral arm training + FES vs. bilateral arm training + sham FES	Fugl-Meyer (+) Functional test for the Hemiplegic Upper Extremity (+)
Weber et al. 2010 7	23	FES + BT-A + home based exercise program vs. BT-A + home-based exercise program	Motor Activity Log (-) Action Research Arm Test (-)
De Kroon & Ijzerman 2008 7 (RCT)	22	EMG-triggered vs. cyclic FES	Action Research Arm test (-)
Kimberly et al. 2004 7 (RCT)	16	NMES vs. sham	Box & Block test (+) Motor Activity Log (+) Jebsen Taylor Hand Function test (+)
Ring & Rosenthal 6 (RCT)	22	Neuroprothetic FES vs. control	Modified Ashworth Scores (+) Box & Block test (+) Jebsen Taylor Hand Function test (+)
De Kroon et al. 2004 6 (RCT)	30	Two different forms of ES	Arm Research Arm test (-) Motricity Index (-) Ashworth Scale (-)
Conforto et al. 2002 6 (RCT)	8	Electrical stimulation vs. Sham Stimulation	Pinch muscle strength (+)
Wu et al. 2006 6 (RCT)	9	3 electrical stimulation sessions vs. no treatment	Jebsen Taylor Hand Function test (+)
Cauraugh and Kim 2003 5 (RCT)	26	0 sec stimulation vs. 5 sec stimulation vs.10 sec stimulation	Box and Block Test (+ for both stim groups) Reaction time (+ for both stim groups) Sustained wrist/finger contraction (+ for both stim groups)
Hara et al. 2008 5 (RCT)	20	Power-assisted FES vs. control	ROM (+) Modified Ashworth Scale (+)
Gabr et al. 2005 4 (RCT)	12	Electromyography-triggered stimulation vs. home exercise	Fugl- Meyer (+) Action Research Arm test (-)

Hara et al. 2006 4 (RCT)	14	Power-assisted FES vs. control	Modified Ashworth Scale (-) Range of Motion (+) Root mean square (-)
Cauraugh et al. 2000 4 (RCT)	11	Passive range of motion and stretching exercises and electrical stimulation vs. passive range of motion and stretching	Box and Block test (+) Motor Assessment scale (-) Fugl-Meyer upper extremity (-)
King 4 (RCT)	21	NMES vs. passive stretch	Tone reduction (+)
Bhatt et al. 2007 3 (RCT)	20	Electrical stimulation vs. tracking training vs. combination group	Jebson Taylor tests (- of manual dexterity) Box & Block test (-) Finger tracking test (-)
- Indicates non-statistically significant differences between treatment groups *+ Indicates statistically significant differences between treatment groups*			

The treatment comparisons among studies evaluating electrical stimulation in the chronic stage of stroke were more heterogeneous. However, the weight of evidence suggested that there was a benefit of treatment.

Conclusions Regarding the Efficacy of FES Therapy in Chronic Stroke

There is strong (Level 1a) evidence that FES treatment improves upper extremity function in chronic stroke.

There is moderate (Level 1b) evidence that EMG-triggered FES is not superior to cyclic FES.

Functional Electrical Stimulation therapy improves hemiparetic upper extremity function.

10.9 Medications Used in Motor Recovery

Medications used following stroke to augment the rehabilitation process have mainly been examined for their potential benefit in terms of global recovery and depression. The results from these trials have been published in other chapters (Mobility, Depression, and Aphasia). However, a small group of studies that evaluated the efficacy of drugs for its effect on the upper extremity has also been identified. These drugs include stimulants (amphetamines and, methylphenidate), levodopa and anti-depressants (citalopram and reboxetine). A recent systematic review (Berends et al. 2009) evaluated the benefit of drugs influencing neurotransmitters on motor recovery following stroke. Six studies evaluating a broad range of drugs were included (antidepressant, amphetamine/methylphenidate and levodopa). The outcomes assessed included the BI and the FIM instrument. Methylphenidate, tarazadone and nortriptyline were associated with improved motor function. While recognizing that the studies differed from each other in many respects, they concluded that there was insufficient evidence to recommend their use.

10.9.1 Stimulants

Three RCTs have examined the effects of either amphetamine or methylphenidate on motor recovery in the upper extremity.

Table 10.55 The Use of Stimulants in Motor Recovery

Author, Year Country Pedro	Methods	Outcomes
Platz et al. 2005 Germany 9 (RCT)	31 patients with mild arm paresis, approx 5 weeks post stroke, were randomized to receive 10 mg d-amphetamine 2x per week x 3 weeks + arm training or placebo + arm training. Primary outcome was TEMPA scores assessed post intervention and at one-year.	A significant effect of active drug was observed immediately following treatment for total TEMPA scores, but was lost at the end of one-year. The study was terminated prematurely before reaching target recruitment of 60 partially because of lack of efficacy.
Tardy et al. 2006 France 9 (RCT)	8 male patients with stroke onset of 35 days or less with pure motor hemiparesis were randomized to receive a single dose of 20 mg of methylphenidate and placebo, 7 days later, in random order. The effect of drug on motor performance was measured using hand grip strength, number of taps completed in a finger tapping test and speed during a target pursuit task.	There was a significant treatment effect of methylphenidate with respect to the finger tapping test. Patients increased the number of taps completed in 10 s by almost 5, compared with the untreated condition. There was no treatment effect for either hand grip strength or the target pursuit task.
Schuster et al. 2011 Switzerland 9 (RCT)	16 patients within 14 to 60 days of first stroke patients, suffering from motor impairment of the arm, hand, leg and foot were randomized to the experimental group (EG, dexamphetamine + physiotherapy) (n=7) or control group (CG, placebo + physiotherapy)(n=9). Both groups received multidisciplinary inpatient rehabilitation. Dexamphetamine (10 mg oral) or placebo was administered 2 days per week before physiotherapy. ADL and motor function were measured using the Chedoke-McMaster Stroke Assessment (CMSA) twice during baseline, every week during the 5-week treatment period, and at follow-up 1 week, 6 months, and 12 months after intervention.	From the time period of to one-week follow-up, patients in the EG group had higher mean CMSA ADL sub scores ($p=0.023$) and CMSA hand scores ($p=0.02$) compared with patents in the control group. There were no other significant differences between groups on any other outcomes, or any other time periods

Amphetamines have shown promise in recovery following stroke as they have the potential to accelerate motor recovery following motor cortex lesions in the rat model (Feeney et al. 1982), especially when combined with task-specific training. A single RCT also examined the effect of methylphenidate (Tardy et al. 2006), the same class of drug as amphetamines, which has the advantage that it does not produce the same side effect profile as amphetamines (insomnia, lack or appetite).

Conclusions Regarding Stimulants

There is conflicting (Level 4) evidence that stimulants can improve upper extremity impairment following stroke.

10.9.2 Levodopa

Levodopa is a dopamine precursor which, once it crosses the blood-brain barrier, is converted to dopamine (dopamine cannot cross the blood-brain barrier). Levodopa is used as a prodrug to increase dopamine levels, most commonly in the treatment of Parkinson's disease. Levodopa may also improve arousal and motor initiation following stroke (Horowitz 2004).

Table 10.56 Levodopa in Motor Recovery

Author, Year Country Pedro	Methods	Outcomes
Restermeyer et al. 2007 Germany 9 (RCT)	10 patients > 6 months stroke onset participated. On two different occasions, patients were randomized to receive either 100 mg levodopa or placebo. Immediately afterwards, they participated in a 1-hour PT session aimed at an improvement of dexterity. Motor functions tests included: the Nine-Hole-Peg Test, grip strength (dynamometer) and Action Research Arm Test (ARAT). Outcomes were assessed before drug intake, 45 minutes after drug ingestion and after the physiotherapy.	There were no statistically significant differences among the groups at any of the testing times.
Rosser et al. 2008 Germany 5 (RCT)	18 patients with chronic motor dysfunction because of stroke were randomized to receive 3 doses of levodopa (100mg of levodopa plus 25mg of carbidopa) and placebo before 1 session of procedural motor learning in a crossover trial. The main outcome measure was a keyboard tapping test performed with the paretic hand.	Subjects in the levodopa condition performed significantly better on the performance test compared with the control condition.

Conclusions Regarding Levodopa

There is conflicting (Level 4) evidence that levodopa can improve upper extremity motor function following stroke.

10.9.3 Antidepressants

Beyond their ability to improve mood disturbances following stroke, antidepressants can be used to enhance upper extremity motor recovery through changes in neurotransmission. Two small RCTs have investigated the effect of 2 types of drugs-- selective serotonin-reuptake inhibitors (SSRI) and noradrenaline reuptake inhibitor (NARI). Both of these trials were conducted by the same author and examined the use of a single dose of the drug over a window of several hours for an off-label purpose in a small group of chronic stroke patients. A recent, larger RCT examined the efficacy of early initiation of fluoxetine in non-depressed patients for motor recovery. The results of the upper-extremity outcomes are reported here and the lower-extremity results are also presented in Module 9.

Table 10.57 Antidepressants in Stroke Recovery

Author, Year Country PEDro Score	Methods	Outcome
Robinson et al. 2000 USA 8 (RCT)	104 patients with stroke onset of less than 6 months were randomized to receive nortriptyline (max 100 mg/d), fluoxetine (max 40 mg/d) or placebo over 12 weeks of treatment. Both depressed and nondepressed patients were enrolled to determine whether improved recovery could be mediated by mechanisms unrelated to depression. Response to treatment of depression for individual patients was defined as a greater-than-50% reduction in scores on the Hamilton Rating Scale for Depression and no longer fulfilling diagnostic criteria for major or minor depression. Functional recovery was assessed using FIM, assessed before and after treatment.	Among patients who were depressed at study entry, those treated with nortriptyline had higher FIM scores compared with those treated with placebo or fluoxetine. Nortriptyline also produced a significantly higher response rate than fluoxetine or placebo in treating poststroke depression and anxiety. Among non-depressed patients, there was no difference in the FIM score among study groups.
Zittel et al. 2007 Germany 6 (RCT)	10 chronic hemiparetic subjects received a single 6 mg dose of the noradrenaline reuptake inhibitor reboxetine or placebo. Then the patients participated in one hour of physiotherapy focused on function of the paretic hand. Three different motor assessments (tapping speed, grip strength, dexterity evaluation) were performed before drug intake, 1.5 hours later and after the physiotherapy session.	Compared with placebo, reboxetine ingestion was followed by an increase of tapping speed and grip strength in the paretic but not in the unaffected hand.
Zittel et al. 2008 Germany 8 (RCT)	8 chronic stroke patients (>6 months onset) participated in a single-dose crossover experiment. Subjects received either 40 mg oral citalopram or placebo followed by a separation of at least 2 weeks. A single session of PT was given 2.5 hrs after drug/placebo. Motor function was assessed by nine-hole peg test, and measurements of hand grip-strength before drug intake, 2 hours after drug intake, and after 1 hour of PT.	Compared with placebo, citalopram intake was associated with significant improvement in performance of the nine-hole peg test for the paretic hand but not for the unaffected hand. Hand grip-strength remained unchanged.
Mikami et al. 2011 Japan RCT (8)	Additional analysis from Robinson et al. 2000 examining the effects of antidepressants on disability.	During the 1-year follow-up period, patients who had received either fluoxetine or nortriptyline had significantly greater improvement in modified Rankin Scale scores compared to patients who received placebo, regardless of

		whether they were depressed at baseline (2.2 and 2.4 vs. 3.4). The analysis adjusting for age, intensity of rehabilitation therapy, baseline stroke severity, and baseline Hamilton Depression Rating Scale.
Chollet et al. 2011 (FLAME) France 9 (RCT)	118 hemiplegic patients from 9 stroke centres in France who had experienced an ischemic stroke within 5-10 days and with Fugl-Meyer motor scale (FMMS) scores of 55 or less were included. Patients with existing depression or who were taking antidepressants were excluded. Patients were randomly assigned, to receive fluoxetine (20 mg once per day, orally, n=59) or placebo for 3 months starting (n=59). All patients received physiotherapy. The primary outcome measure was the change on the FMMS between day 0 and day 90 after the start of the study drug. Secondary outcomes included modified Rankin Scale scores (mRS) and NIHSS scores.	Total FMMS improvement at day 90 was significantly greater in the fluoxetine group (adjusted mean 34.0 points than in the placebo group (24.3 points; p=0.003). The increases in the upper limb FMMS sub scores were also significantly greater in patients in the fluoxetine group. There were no differences in NIHSS scores at day 90 between groups. A greater proportion of patients in the fluoxetine group had mRS score of 0-2 compared with those in the placebo group (15 vs. 9, p=0.021) after adjusting for age, history of stroke and baseline mRS scores. The frequency of incident depression was higher in the placebo group (17 vs. 4, p=0.002).

Conclusions Regarding Antidepressants

There is strong (Level 1a) evidence that a single dose of either a SSRI or NARI can enhance short-term manual dexterity in the affected hand following stroke.

There is moderate (Level 1b) evidence that a 90-day course of SSRIs initiated acutely following stroke improves motor recovery of the upper extremity.

10.10 Treatment of Hand Edema

Hand edema following stroke with hemiparesis is associated with pain and stiffness, which can lead to a decrease in active motion and disuse. Hand edema may be an isolated problem or occur as a symptom of shoulder-hand syndrome. The etiology of the development of hand edema is unclear. The most widely accepted explanation is of increased venous congestion related to prolonged dependency and loss of muscle pumping function in the paretic limb. (Leibovitz et al. 2007).

Diagnosis is difficult and depends, in part, on the method of assessment. Estimates of the incidence of hand edema vary widely. Tepperman et al. (1984) reported that 83% of 85 acute stroke patients suffered from hand edema not associated with shoulder-hand syndrome. More recently, Post et al. (2003) reported that based on volumetric assessments, 33% of 96 stroke patients had hand edema, compared to 50% of patients assessed through clinical evaluation. Volumetric assessments of the hand appear to provide the best estimation;

while the reliability of clinical evaluation through visual inspection is poor. A change of 12 mL or more is considered clinically significant (Post et al. 2003).

Using data from the same patient group as Post et al. (2003), Boomkamp-Koppen et al. (2005) reported a significant correlation between the presence of hand edema and measures of hand function (measured by the Frenchay arm test). Patients without hand edema were more likely to have good hand function. Significant predictor of hand function following stroke included the degree of motor impairment, hypertonia, tactile inattention and edema. In contrast, Gebruers et al. (2011) reported finding no relationship between activity limitations and the presence or edema in a cohort of 130 acute stroke patients followed over a period of 3 months. There were no statistically significant differences on a variety of clinical indications, including stroke severity and Fugl-Meyer Scale scores between the group of patients who developed edema and those who did not. The authors concluded that the theory suggesting that disuse in the paretic limb is the major cause of the development of hand edema is unlikely to be true. The incidence of edema was also lower in this study. Depending on the technique used for diagnosis, the incidence of hand edema ranged from 8% to 18%.

Leibovitz et al. (2007) compared the circumference of the hand in three places (mid-finger, hand and wrist) among subjects post stroke (m=188) and non-paretic institutionalized controls (n=70). Hand edema was detected in 37% of post stroke subjects compared with only 2% of control subjects.

Three different treatment approaches to aid in the reduction of hand edema following stroke have been studied, including passive motion exercises, neuromuscular stimulation and intermittent pneumatic compression. The results are presented in table 10.58.

Table 10.58 Treatment of Hand Edema

Author, Year Country PEDro Score	Methods	Outcome
Giudice 1990 USA No Score	16 patients with hand edema of greater than 4 months duration received two treatments on two consecutive days. The effect of a 30 minute treatment of continuous passive motion (CPM) exercises plus limb elevation was compared to limb elevation alone. Hand volume, finger circumference and finger stiffness were assessed.	11 patients in the study had suffered from a stroke. The treatment effect sizes for all 3 measures were large (>0.5) indicating that CPM was more effective than elevation alone.
Faghri 1997 USA No Score	8 patients with visible hand edema following stroke received neuromuscular stimulation (NMS)-induced contraction of the paralyzed muscles to produce an active muscle pump for removing excess fluid and compare its effect with elevation of the upper extremity. The effects of 30 minutes of NMS (stimulation frequency of 35 Hz) of the finger and wrist	No inferential statistics were reported. The reduction in mean hand volume (mL) of NMS and limb elevation were: –13.4 and + 1.9, respectively. Although NMS was more effective for reduction of hand edema than limb elevation alone, hand edema returned to pre-treatment levels within 24 hours.

	flexors and extensors were compared with the effects of 30 minutes of limb elevation alone. Each patient received both treatments, one on each of 2 consecutive days. Measures of hand and arm volume and upper and lower arm girth were taken before and after each treatment.	
Roper et al. 1999 UK 5 (RCT)	37 patients with first ever stroke and edema in their affected hand were randomized to receive intermittent pneumatic compression (INC) + standard physiotherapy 2 hours a day for one month or standard physiotherapy. Hand volume (measured by water displacement) and Motricity Index scores were assessed at the end of the treatment period.	There were no statistically significant between group differences reported.

Conclusion Regarding Intermittent Pneumatic Compression for Hand Edema

There is moderate (Level 1b) evidence that intermittent pneumatic compression does not reduce hand edema following stroke.

There is limited (Level 2) evidence that both neuromuscular nerve stimulation and continuous passive motion help to reduce hand edema compared to limb elevation.

Continuous passive motion and electrical stimulation might be effective treatments for hand edema, while intermittent pneumatic compression is not.

10.11 Summary

1. ***There is consensus (Level 3) opinion that in severely impaired upper extremities (less than stage 4) the focus of treatment should be on palliation and compensation. For those upper extremities with signs of some recovery (stage 4 or better) there is consensus (Level 3) opinion that attempts to restore function through therapy should be made.***

2. ***There is strong (Level 1a) evidence that neurodevelopmental techniques such as Bobath are not superior to other therapeutic approaches. There is moderate (level 1b) evidence that indicates compared to Bobath, motor relearning programs may result in improved short-term motor functioning and shorter lengths of hospital stay.***

3. ***There is moderate (Level 1b) evidence that both functional and neuropsychological approaches both help to improve dressing performance.***

4. ***There is conflicting (Level 4) evidence that enhanced therapies improve short-term upper extremity function. There is evidence that results may not be long-lasting. There is moderate (Level 1b) evidence that a program of daily stretch regimens does not prevent the development of contractures.***

5. ***There is strong (Level 1a) evidence that repetitive task-specific training techniques improve measures of upper extremity function.***

6. ***There is conflicting (Level 4) evidence that sensorimotor treatments improve upper extremity function.***

7. ***There is conflicting (Level 4) evidence that bilateral arm training is superior to unilateral training.***

8. ***There is conflicting (Level 4) evidence that specialized programs improve reaching.***

9. ***There is conflicting (level 4) evidence that mental practice may improve upper-extremity motor and ADL performance following stroke.***

10. ***There is strong (Level 1a) evidence that hand splinting does not improve impairment or reduce disability.***

11. ***There is conflicting (Level 4) evidence of benefit of CIMT in the acute stage of stroke.***

12. ***There is strong (Level 1a) evidence of benefit of mCIMT in the acute/subacute stage of stroke. Benefits appear to be confined to stroke patients with some active wrist and hand movements, particularly those with sensory loss and neglect. There is moderate (Level 1b) evidence that any intensity of CIMT will provide benefit.***

13. ***There is conflicting (Level 4) evidence that mirror therapy improves motor function following stroke and moderate (Level 1b) evidence that it does not reduce spasticity.***

14. ***There is moderate (Level 1b) evidence that action observation improves performance on the Box & Block test.***

15. ***There is strong (Level 1a) evidence that extrinsic feedback helps to improve motor learning following stroke.***

16. ***There is strong (Level 1a) evidence that sensorimotor training with robotic devices improves upper extremity functional outcomes, and motor***

outcomes of the shoulder and elbow. There is strong (Level 1a) evidence that robotic devices do not improve motor outcomes of the wrist and hand.

17. ***There is strong (Level 1a) evidence that virtual reality treatment can improve locomotor function in the chronic stages of stroke.***

18. ***There is strong (Level 1a) evidence that hand splinting does not reduce the development of contracture or reduce spasticity.***

19. ***There is moderate (Level 1a) evidence that a nurse-led stretching program can help to increase range of motion in the upper extremity and reduce pain in the chronic stage of stroke.***

20. ***There is strong (Level Ia) that treatment with BTX alone or in combination with therapy significantly decreases spasticity in the upper extremity in stroke survivors.***

21. ***There is conflicting (Level 4) evidence that treatment with BTX alone or in combination with therapy significantly improves upper limb function or quality of life.***

22. ***There is moderate (Level 1b) evidence that electrical stimulation combined with botulinum toxin injection is associated with reductions in muscle tone.***

23. ***There is moderate (Level 1b) evidence that electrical stimulation can reduce spasticity and improve motor function in the upper extremity.***

24. ***There is limited (Level 2) evidence that treatment with ethyl alcohol improves elbow and finger PROM and can decrease spasticity in the upper extremity in stroke survivors.***

25. ***There is strong (Level 1a) evidence that physical therapy does not reduce spasticity in the upper extremity.***

26. ***There is limited (Level 2) evidence that shock wave therapy can reduce tone in the upper extremity.***

27. ***There is moderate (Level 1b) evidence that tolperisone can reduce spasticity following stroke.***

28. ***There is strong (Level 1a) evidence that EMG/Biofeedback therapy is not superior to other forms of treatment.***

29. ***There is conflicting (Level 4) evidence that treatment with TENS in the upper extremity improves a variety of outcomes, including motor recovery, spasticity and ADLs.***

30. ***There is strong (Level 1a) evidence that FES treatment improves upper extremity function in chronic stroke.***

31. ***There is moderate (Level 1b) evidence that EMG-triggered FES is not superior to cyclic FES.***

32. ***There is conflicting (Level 4) evidence that stimulants can improve upper extremity impairment following stroke.***

33. ***There is conflicting (Level 4) evidence that levodopa can improve upper extremity motor function following stroke.***

34. ***There is strong (Level 1a) evidence that a single dose of either a SSRI or NARI can enhance short-term manual dexterity in the affected hand following stroke.***

35. ***There is moderate (Level 1b) evidence that a 90-day course of SSRIs initiated acutely following stroke improves motor recovery of the upper extremity.***

36. There is moderate (Level 1b) evidence that intermittent pneumatic compression does not reduce hand edema following stroke. There is limited (Level 2) evidence that both neuromuscular nerve stimulation and continuous passive motion help to reduce hand edema compared to limb elevation.

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