HEART & STROKE FOUNDATION

CANADIAN Stroke BEST PRACTICE RECOMMENDATIONS

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Stroke Rehabilitation Evidence Tables

Range of Motion and Spasticity in the Shoulder, Arm and Hand

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on Behalf of the Canadian Stroke Best Practice Recommendations
STROKE REHABILITATION Writing Group

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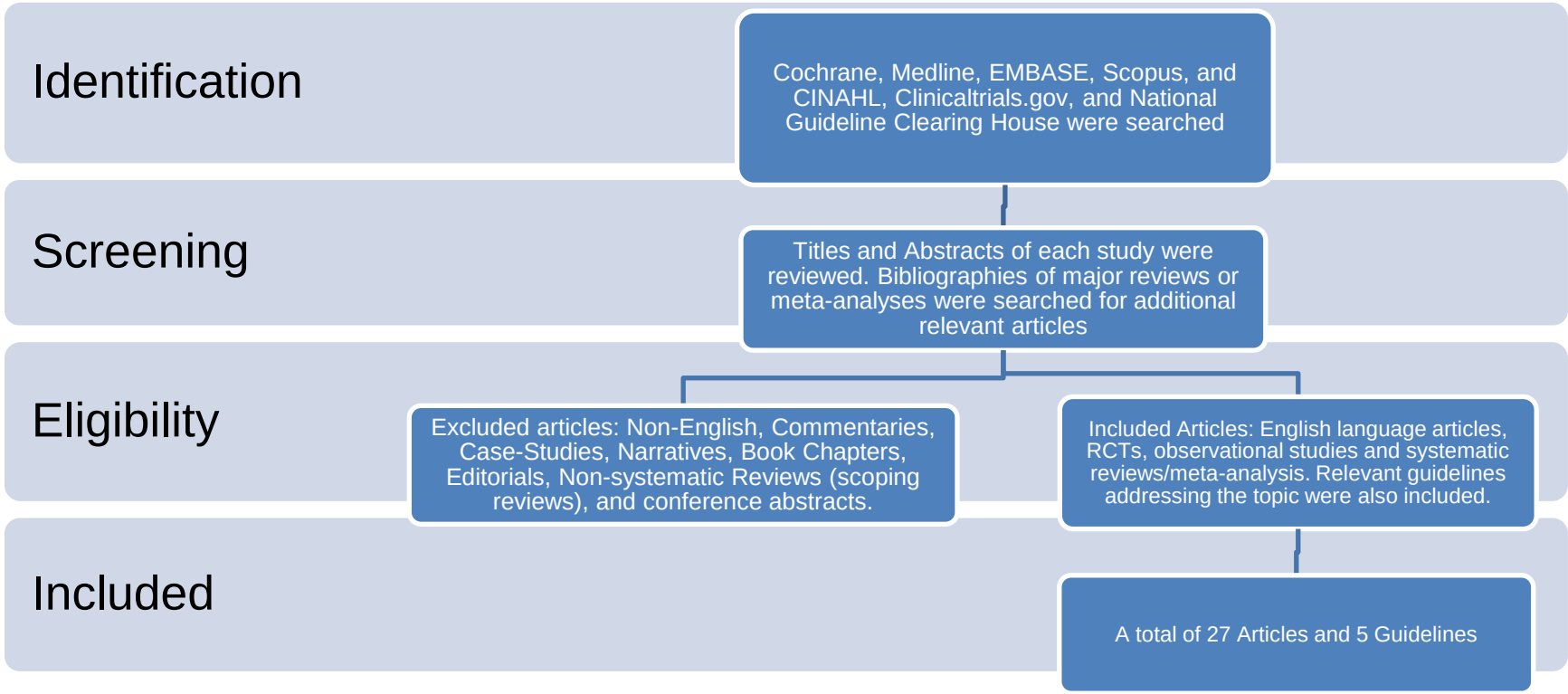
Table of Contents

Search Strategy



Cochrane, clinicaltrials.gov, Medline, EMBASE, CINAHL and Scopus were searched using the keywords: Stroke AND (“spasticity” OR “contracture”) AND (“upper extremity” OR “upper limb”) AND (rehabilitation OR therapy OR intervention). Two new sections, stimulation and robotics, were added for the 2014 update. The same databases were searched to identify paediatric related evidence using additional keywords: (stroke OR CVD OR cerebrovascular disease) AND (rehabilitation OR intervention OR therapy) AND (paediatric OR paediatrics OR youth OR child OR children OR young) AND ("upper limb" OR "upper extremity" OR shoulder OR hand OR arm).Titles and abstract of each article were reviewed for relevance. Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, non-systematic review, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review. A total of 27 articles and 5 guidelines were included and were separated into categories designed to answer specific questions.

Published Guidelines

Guideline	Recommendations
Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with stroke: rehabilitation, prevention and management of complications, and discharge planning. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2010 Jun. 101 p.31	**4.9.1 Summary of recommendations** **Not recommended** routine resting splinting of the upper limb *Clostridium botulinum* toxin type A **Insufficient evidence** routine functional electrical stimulation robot-mediated passive therapy oral antispasticity agents intrathecal antispasticity agents alcohol neurolysis tibial nerve neurotomy
Management of Stroke Rehabilitation Working Group. VA/DoD clinical practice guideline for the management of stroke rehabilitation. Washington (DC): Veterans Health Administration, Department of Defense; 2010. p. 87	Use of antispastic positioning, range of motion exercises, stretching, splinting, serial casting or surgical correction for spasticity. **C** Use of tizanidine (in chronic stroke patients), dantrolene, and oral baclofen for spasticity **B** Avoid drugs with central nervous system effects that may impair recovery **D** Use of botulinum toxin improves spasticity **B** Use of intrathecal baclofen for chronic stroke patients **B** Use of certain neurosurgical procedures **I**
Clinical Guidelines for Stroke Management 2010. Melbourne (Australia): National Stroke Foundation; 2010 Sep. p. 99.	Interventions to decrease spasticity other than an early comprehensive therapy program should NOT be routinely provided for people who have mild to moderate spasticity (i.e. spasticity that does not interfere with a stroke survivor's activity or personal care) **GPP** In stroke survivors who have persistent moderate to severe spasticity (i.e. spasticity that does not interfere with a stroke survivor's activity or personal care): Botulinum toxin A should be trialed in conjunction with rehabilitation therapy which includes setting clear goals. **B**

Guideline	Recommendations
	Electrical stimulation and/or EMG biofeedback can be used. **C** **Contracture** Conventional therapy (i.e. early tailored interventions) should be provided for stroke survivors at risk who have developed contracture. **GPP** For stroke survivors at risk of, or who have developed contractures and are undergoing comprehensive rehabilitation, the routine use of splints or prolonged positioning of muscles in a lengthened position is NOT recommended. **C** Overhead pulley exercises should NOT be used routinely to maintain ROM of the shoulder **C** Serial casting can be used to reduce severe, persistent contracture when conventional therapy has failed. **GPP**
Duncan PW, Zorowitz R, Bates B, Choi JY, Glasberg JJ, Graham GD, Katz RC, Lamberty K, Reker D. Management of adult stroke rehabilitation care: a clinical practice guideline. Stroke, 2005;36:e100-e143.	Use of antispastic positioning, range-of-motion exercises, stretching, splinting, serial casting, or surgical correction for spasticity. **C** Use of tizanidine (in chronic stroke patients), dantrolene, and oral baclofen for spasticity. **D** Use of central nervous system effects may deteriorate recovery. **B** Use of botulinum toxin and phenol/alcohol to treat spasticity. **B** Use of intrathecal baclofen for chronic stroke patients **C** Use of certain neurosurgical procedures. **I**
Intercollegiate Stroke Working Party. *National clinical guideline for stroke,* 4th edition. London: Royal College of Physicians, 2012.	*6.10.1 Recommendations* A Any patient with motor weakness should be assessed for the presence of spasticity as a cause of pain, as a factor limiting activities or care, and as a risk factor for the development of contractures. B For all the interventions given below, specific goals should be set and monitored using appropriate clinical measures (eg numerical rating scales for ease of care (eg Arm Activity measure (ArmA)) or pain (eg 10-point numerical rating scale), the modified Ashworth scale, and range of movement). C In any patient where spasticity is causing concern, the extent of the problem should be monitored and simple procedures to reduce spasticity should be started. This may include positioning, active movement and monitoring range of movement for deterioration of function, passive movement and pain control. D Patients with persistent or progressing troublesome focal spasticity affecting one or two joints and in whom a therapeutic goal can be identified (usually ease of care also referred to as passive function) should be given intramuscular botulinum toxin. This should be in the context of a specialist multidisciplinary team service accompanied by rehabilitation therapy or physical maintenance strategies (eg splinting or casting) over the next 2–12 weeks following botulinum toxin injection. functional assessment should be carried out at 3–4 months post injection and further botulinum toxin and physical treatments planned as required. E For patients experiencing troublesome general spasticity after initial treatment, antispastic drugs should be tried unless contraindicated. Either baclofen or tizanidine should be tried first. Other drugs and combinations of drugs should only be started by people with specific expertise in managing spasticity. F Intrathecal baclofen, intra-neural phenol and other rare procedures should only be used in the context of a specialist multidisciplinary spasticity service or a clinical trial.

Guideline	Recommendations
	6.11.1 Recommendations A Any patient who has increased tone sufficient to reduce passive or active movement around a joint should have their range of passive joint movement assessed and monitored. B Splinting of the arm and hand should not be used routinely after stroke.

GPP Good Practice Point

SUMMARY OF UPPER-EXTREMITY SPASTICITY INTERVENTIONS AND ASSOCIATED STRENGTH OF EVIDENCE FROM SELECTED GUIDELINE DOCUMENTS

Intervention	CBPR 2013	SIGN 118 2010*	NSF 2010*	VA/DoD 2010 *	AHA/ASA 2005*	RCP 2012
Positioning/ROM exercises	Recommended [Early – C; Late – C]	Not included	Not included	C	C	Recommended
Splinting	Not recommended [Early – A; Late – B]	A Not recommended	B Not recommended for contracture	C	C	Not Included
BT-type A	Recommended [Early – C; Late – A]	Not recommended	B	B	B	Recommended
Phenol/alcohol	Not included	I	Not included	Not included	B	Not Included
Oral agents	Recommended Tizanidine [Early–C; Late–B] Baclofen [Early-C; Late-C]	I	Not included	B (Tizanidine for chronic), oral baclofen)	B (Tinzanidine, dantrolene, oral baclofen)	Recommneded (baclofen, Tizanidine)
Benzodazepines	Not recommended [Early-C; Late-C]	Not included	Not included	D Not recommended	Not included	Not Included
Electrical stimulation	Not included	I	C	Not included	Not included	Not Included
Robotic devices	Not included	I	Not included	Not included		Not Included
Intrathecal agents	Not included	I	Not included	No recommendation for UE	C	Not Included
Surgery	Not included	I	Not included	I (spasticity) C (contracture)	I	Not Included

I: Insufficient evidence to recommend for/against providing intervention
* General recommendations regarding spasticity, not specific to UE

Evidence Tables

Splinting and Orthotics

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Basaran et al. 2012 **Turkey** **RCT**	CA: ☑ Blinding: assessor ☑ ITT:☒	39 subjects, 5-120 months post stroke with a wrist MAS score of ≥1	Examination of a 5 week, home-based exercise program. Patients were advised to stretch wrist and finger flexors for 10 repetitions and to try reaching and grasping an object for 10 repetitions 3x/day in addition to conventional therapy. 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	**Primary Outcome:** MAS Outcomes were assessed before and after treatment, at least 2 hours after the splint had been removed.	No significant differences within or among the groups on any of the outcomes assessed.
Lanin et al. 2007 **Australia** **RCT**	CA: ☑ Blinding: assessor ☑ ITT: ☑	63 subjects who had experienced a stroke in the previous 8 weeks with no active wrist extension.	Comparison of 2 different splints. Subjects in all groups received routine therapy. Subjects in the interventions groups wore one of 2 custom-made, static, palmar mitt splints-one placed the subject's wrist in a neutral position, the other, in an extended position (>45^{o}). Subjects wore the splints for up to 12 hours overnight for 8. Subjects in the control group received therapy only.	**Primary Outcome:** Extensibility of the wrist and finger flexor muscles. **Secondary Outcomes:** Motor Assessment Scale, Tardieu Scale, Disabilities of the Arm, Shoulder and Outcome Measure (DASH) Assessments were conducted at baseline, at the end of treatment (4 weeks) and 6 weeks.	There were no statistically significant differences between groups on any of the outcomes over the study period. Mean changes in wrist extensibility (degrees) from baseline to 6 weeks: Neutral splint group: 62.1 ± 16.4 to 48.8 ± 14.5 Extended splint group: 65.2 ± 15.0 to 42.5 ± 14.9 Control group: 64.5 ± 10.1 to 39.4 ±17.8 Mean changes in UE-MAS from baseline to 6 weeks: Neutral splint group: 0.3 ± 0.9 to 0.9 ± 2.0 Extended splint group: 0.3 ± 0.4 to 0.8 ± 2.0 Control group: 0.1 ± 0.3 to 0.5 ± 0.8 Mean changes in DASH scores from baseline to 6 weeks: Neutral splint group: 57.6 ± 24.0 to 56.5 ± 22.9 Extended splint group: 62.8 ± 24.4 to 58.0 ± 18.9 Control group: 60.8 ± 21.7 to 67.0 ± 19.8

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Doucet et al. 2013 **USA** **Pre-Post**	N/A	6 subjects, on average, 67.92 months post stroke	Custom fitted dynamic progressive wrist extension orthotic worn for 4 hr daily, 4 times a week for 12 weeks.	**Primary Outcome:** MAS of wrist. Outcomes were assessed at baseline and 12 weeks.	3/6 MAS scores were non-significant. 3/6 MAS scores showed negative trends.
Andringa et al. 2013 **The Netherlands** **Pre-Post**	N/A	6 subjects, on average 64 months (range: 22-110) post stroke	Custom made dynamic orthotic worn 8 hr daily, every day for 6 months.	**Primary Outcome:** MAS of elbow, wrist and fingers Outcomes were assessed at baseline, 3 months and 6 months.	No significant differences within or among groups on MAS.

Stretching Programs to Prevent Contracture

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Horsley et al. 2007 **Australia** **RCT**	CA: ☑ Blinding: assessor ☑ ITT: ☑	40 patients admitted for inpatient rehabilitation > 40 days on average, who were unable to actively extend their wrist past the neutral position.	Patients in the experimental group received 30 minutes of stretch of wrist and finger flexors 5 days a week for 4 weeks. Patients in both groups received conventional task-specific therapy from physiotherapists and occupational therapists.	**Primary Outcome:** Passive wrist extension **Secondary Outcomes:** Pain (10 cm VAS), Motor Assessment Scale Assessments were conducted at baseline, weeks 4, 5 and 9.	There were no statistically significant differences between groups on any of the outcomes over the study period. Mean changes in passive wrist extensibility (degrees) from baseline to 9 weeks: Stretch group: 69.5± 13.6 to 63.4 ± 14.7 Control group: 65.7 ± 13.1 to 57.0 ± 15.9 Mean Δ change = 3.5 degrees, 95% CI -4.6 to 11.7 Mean changes in pain at rest from baseline to 9 weeks: Stretch group: 1.1 ± 1.8 to 1.5 ± 2.6 Control group: 0.4 ± 1.1 to 1.5 ± 2.6 Mean Δ change = 0.2, 95% CI -1.5 to 2.0 Mean changes in UE-MAS from baseline to 9 weeks: Stretch group: 0.9 ± 1.8 to 5.9 ± 6.6 Control group: 0.3 ± 0.6 to 1.9 ± 3.3 Mean Δ change = 2.3, 95% CI -0.7 to 5.3

Centrally Acting Oral Agents

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Simpson et al. 2009 **USA** **RCT**	CA: ☑ Blinding: assessor ☑ patient ☑ ITT: ☑	60 patients with stroke or traumatic brain injury of at least 3 months duration with a MAS score of ≥3 of the wrist flexors and difficulty with dressing or hygiene	Comparison of BT-A vs. tizanidine vs. placebo Subjects were randomized to 1 of 3 groups: BT-A + oral placebo (n=20), oral tizanidine + placebo injection (n=21) or placebo injection + oral placebo (n=19). Patients in the BT-A group received a single injection of BT-A (Botox), (average of 400U). The wrist flexors were the primary target site, although muscles in the shoulder or fingers could also be injected at the discretion of the investigator. Patients in the tizanidine group received a maximum daily dose of 36 mg/day, which was achieved by day 28 if increments (4 mg q 3-4 days were tolerated). No mention of additional therapy Study duration was 22-24 weeks.	**Primary Outcome:** MAS (wrist) **Secondary Outcomes:** Disability Assessment Scale, Modified Frenchay Scale, grip strength Assessments were conducted at baseline, 3, 6,12 and 18 weeks	Mean change from baseline to week 3 in MAS scores: BT-A: -1.55 ± 1.2; tizanidine: -0.25 ± 0.64; placebo: -0.67 ± 0.91, p<0.001 (BT-A was more effective compared with other 2 groups). The differences persisted at week 6, but by weeks18 and 22 there appeared to be no differences between the groups. Results from inferential statistics not reported, but by looking at figure, the mean reductions were <1 in all study groups. Mean change from baseline to week 6 in Principal Therapeutic Target of DAS scores: BT-A: -1.13 ± 1.1; tizanidine: -0.47 ± 1.18; placebo: -0.67 ± 1.08, p=0.20 Frenchay Scale scores to be reported in future publication Early terminations: BT-A group: 6; tizanidine group: 8; placebo: 5 Number of adverse events: BT-A group: 8; tizanidine group n=15; placebo group: n=10
Gelber et al. 2001 **USA** **Single group intervention study**	Blinding: assessor ☑	47 subjects at least 6 months post stroke with moderate spasticity (MAS scores of 2 or 3 in major muscle groups) with functional limitations or pain as a result	Open label study where subjects received a maximum daily dose of 36 mg/day, titrated in 2 mg increments Subjects were tapered off the drug after 16 weeks	**Primary Outcomes:** MAS (elbow, wrist, finger), **Secondary Outcomes:** NIHSS, muscle strength assessed using the British Medical Research Council scale, ARAT, Pain (0-4 scale) BI, physician assessed functional disability (0-4 scale)	Total Mean UE MAS score: Baseline: 9.03 ± 0.41 Week 16: 6.47 ± 0.54 Week 18 (off-meds): 7.46 ± 0.49 Changes from baseline were statistically significant. There were no significant decreases in muscle strength using any of the BMRC sub scales. No significant improvement in any of the 4 domains of the ARAT. Mean improvement for grasp, grip, pinch and gross movement scores ranged from 0 to 0.4. No significant decrease in the frequency of pain, but

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				Outcomes were assessed at baseline and weeks 16 and 18.	there was a decrease in the intensity of pain at week 16 (1.6 ± 0.20 to 1.4 ± 0.23, p=0.038). Significant improvement in disability assessed by the physician ay week 16 (2.5 ± 0.12 to 1.9 ± 0.19, p<0.0001). No significant improvement in BI scores at week 16 (80.2 ± 2.7 to 81.1 ± 2.9, p=ns) Adverse events: 89% of subjects reported at least 1 adverse event. 28% of subjects discontinued the study due to an adverse event.

Botulinum Toxin-Type A (BT-A)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Hesse et al. 2012 **Germany** **RCT**	CA: ☒ Blinding assessor: ☒ patient: ☑ ITT: ☑	18 subjects with upper limb spasticity (MAS=1-2) who were 4-6 months post stroke	Subjects were randomized into two groups: 1) 150 U botulinum toxin type-A injected into the deep and superficial finger (100 U) and wrist flexors (50 U), or 2) no injection.	**Primary Outcomes:** MAS of finger Outcomes were assessed at baseline, 4 weeks and 6 months.	Individuals in the treatment group experienced significantly less finger flexor stiffness at 4 weeks (p<0.001) and 6 months (p=0.025).
Shaw et al. 2012 **UK** **RCT**	CA: ☑ Blinding: assessor ☑ patient ☒ ITT: ☑	333 subjects < 1 month following stroke with spasticity of the elbow (MAS>2) and/or spasticity of the shoulder, wrist or hand with reduced arm function	Comparison of BT-A vs. therapy Subjects were randomized to receive 100 or 200 U BT-A (Dysport) (n=170) + a standardized therapy program (1 hour/day, 2x/week for 4 weeks) vs. therapy program only (n=163). Subjects in the BT-A group received injections injected into the shoulder, arm, wrist, elbow and/or fingers Repeat injections were	**Primary Outcome:** A successful outcome-defined as an increase in score of ≥3 ARAT points for subjects with initial ARAT scores of 0 to 3; ≥6 points for subjects with initial scores of 4 to 51 and a final ARAT score of 57 for baseline scores between 52 and 56. **Secondary Outcomes:** MAS, Motricity Index (arm), grip strength, 9-Hole Peg Test, BI, Pain (0-10 verbal rating Scale)	At 1 month, there was no significant difference in the proportion of subjects who achieved a successful outcome between groups. 25.1% in BT-A group vs. 19.5% in control group, p=0.232. There were no significant differences at months 3 or 12. There was a significant reduction in MAS scores at 1 month favouring the BT-A group (median change score of 0 vs. -1, p=0.001), but not at 3 or 12 months (median change score 0 vs. 0). There were no significant differences between groups for the following outcomes at any of the assessment points for either group: Motricity Index (median change 0 vs. 3 at 1 month, 0 vs. 4 at 3 months and 5 vs. 5 at 12 months), 9-hole Peg Test (median change 0 vs. 0 at all assessment points),

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			available to subjects in the intervention group at 3, 6 and 9 mos. 2 therapy menus were available depending on baseline arm function. Subjects with no active arm function participated in stretching (20 minutes), positioning (10 minutes) and passive/active assisted upper arm activity (20 minutes), while subjects with some arm function participated in stretching (10 minutes) and task-oriented practice (40 minutes).	Outcomes were assessed at baseline, 1,3 and 12 months following randomization	grip strength (median change score of 0 vs. 0 at 1 and 3 months, 0.5 vs. 0 at 12 months), BI (median change score of 0 vs. 0 at months 1 and 3, -1 vs. -1 at 12 months). There was a significant decrease in pain score at 12 months favouring the BT-A group (0 vs. -2, p=0.004). 12 month assessments were completed for 92 subjects in the control group and 170 subjects in the BT-A group. Adverse events: There were 52 serious adverse events in the BT-A group and 50 in the control group. Only 1 serious adverse event was believed to have been related to BT-A treatment.
McCrory et al. 2009 **USA** **RCT**	CA: ☑ Blinding: assessor ☑ patient ☑ ITT: ☑	102 subjects with moderate to severe spasticity of the arm, (minimum MAS score of 2 in at least 2 out of the 3 of the wrist, elbow and finger flexor muscles and a minimum of 1+ in the third area) an average of 6 years following stroke	Comparison of BT-A (n=54) vs. placebo (n=42) First treatment: Placebo vs. 750 to 1,000 U Dysport injected into elbow, wrist and fingers muscles under EMG guidance. Second treatment at 12 weeks: additional 500 to 1,000 U Dysport into same sites Concurrent therapy: none stated	**Primary Outcome:** Assessment of Quality of Life (AQoL) (0 to 1.0) **Secondary Outcomes:** Pain (100-mm VAS), Depression (Hospital Anxiety and Depression Scale), goal Attainment Scaling (GAS), spasticity (MAS), (Modified) Motor Assessment Scale, Patient Disability Scale (PDS), Carer Burden Scale (CBS) Outcomes were assessed at baseline, weeks 8, 12, 20 and 24	Between group differences from baseline to week 20 (mean Δ, 95% CI). AQoL: -0.03, -0.09 to 0.02, p=0.27 Pain: 10.14, -8.1 to 27.4, p=0.25 HADS: -0.07, -0.87 to 1.47, p=0.61 GAS: -5.20, -9.08 to 1.28, p<0.001 (favours BT-A group) There must be a typo in this reporting. Significant p value not possible given 95% CI MAS across all joint: 1.59, 0.98 to 2.00, p<0.001 (favours BT-A group) MMAS: -0.22, -0.75 to 0.31, p=0.41 PDS: -0.01, -0.27 to 0.25, p=0.94 CBS: -0.02, -0.65 to 0.61, p=0.95 20-week assessments were completed for 37 subjects in the control group and 53 subjects in the BT-A group. Adverse events: Treatment related adverse events were reported in 5.55 of subjects in the BT-A group and 9.5% in the placebo group. Most adverse events were mild.
Coban et al. 2014	CA: ☑ Blinding	17 patients with upper limb spasticity at least 1 year post-stroke.	Two preparations of Botox and Dysport were used (the dilution was	**Primary Outcomes:** MAS of elbow flexors, forearm pronators, wrist	Only forearm pronators showed a statistically significant change in MAS scores between the 1st versus 2nd injection (p=0.021) and 1st versus 5th

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Turkey **Pre-Post**	assessor: ☑ patient: ☑ ITT: ☑		standardized: one vial of Botox 100 U was diluted with 2 or 4 ml normal saline; one vial of Dysport 500 U was diluted with 2.5 ml normal saline), the injection were administered in one distal part of upper limb (the upper limb spasticity group, 15 patients) and patients injected one distal part of lower limb (the lower limb spasticity group, 12 patients).	flexors and finger flexors. Outcomes were assessed after the 1st, 2nd and 5th injection.	injection (p=0.021).
Santamoto et al. 2013 **Italy** **Pre-Post**	CA: ☒ Blinding assessor: ☒ patient: ☒ ITT: ☑	25 patients with upper limb spasticity (AS ≥2) who were ≥ 6 months post stroke	Subjects received one set of injections of botulinum toxin type-A NT 201, in their hypertonic upper and lower limb; maximum total dosage in the upper limbs was 840 U (ranged from 750 to 840 U).	**Primary Outcomes:** Disability Assessment Scale (DAS) Outcomes were assessed 30 and 90 days post injections.	Mean DAS scores decreased at 30 and 90 days after treatment (p<0.05). However, the rate of response was higher for investigators than patients; 40% of investigators and 28% of patients rated their clinical picture as “marked improvement.”
Takekawa et al. 2013 **Japan** **Pre-Post**	CA: ☒ Blinding assessor: ☒ patient: ☒ ITT: ☑	190 subjects with upper limb spasticity 64.8 months post stroke.	Botulinum toxin type-A was injected into the elbow flexors, wrist flexors, forearm pronators or finger flexors with a total dosage less than 240 U. After the injection, subjects participated in one-on-one home-based functional training for 15 min with an occupational therapist.	**Primary Outcomes:** MAS of elbow flexors, wrist flexors, forearm pronators and finger flexors. Outcomes were assessed at baseline, and at 1-, 3- and 6-month follow-up	A significant reduction in MAS scores were noted in all muscles examined, at 1-, 3-, and 6-month follow-up compare to baseline (p<0.001 for all).

Intrathecal Baclofen (ITB)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Meythaler et al. 2001 **USA** **Randomized crossover screening period followed by open-label follow-up**	Screening period: assessor ☑ patient ☑ Open-label portion: assessor ☒ patient ☒ ITT: ☒	21 subjects with disabling and painful intractable hypertonia (defined by an Ashworth Scale score of at least 3 in one affected extremity or an average spasm score of at least 2 in the affected extremities on the day of screening) following stroke of at least 6 months duration, and failure to respond to oral antispasticity medications.	Subjects were randomized to receive a screening bolus trial of either 50 µg baclofen or saline placebo. 17 subjects responded to the active drug and were then implanted with a continuous-infusion pump and continued to receive treatment for up to a year. Subjects were initiated to continued treatment at 100 µg/day with dose increases up to an average of 268 ± 175 µg/day.	**Primary Outcome:** Ashworth Scale **Secondary Outcomes:** 5-point Penn Spasm Frequency Scale, 6-point reflex scale (elbow) 13 subjects were followed for 1 year, 4 for 6 months.	Mean (± sd) scores at baseline and 12 months Ashworth scores: 3.2 ± 1.1 to 1.8 ±0.09, p<0.0001. Spasm score: 0.7±1.0 to 0.5, p=ns (12 month result extrapolated from figures) Reflex Score: 2.4 ±0.8 to 1.5, p=ns (12 month result extrapolated from figures) Adverse events: Several mild and transient adverse events were reported.

Alcohol or Phenol Neurolysis

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Kong & Chua 1999 **Singapore** **Single group intervention study**	Blinding: assessor ☒ patient ☒	20 subjects an average of 12 months following stroke with severe elbow flexor spasticity causing fixed contracture and flexion deformity	The musculocutaneous nerve was localized and blocked with a solution of 50% ethyl alcohol in water at a rate of 1-2 mL/mm until muscle contraction ceased (mean total volume was 4 mL). No mention of concurrent therapy	**Primary Outcome:** MAS (elbow) **Secondary Outcomes:** Passive ROM(elbow), Medical Research council (MRC) scale Outcomes were assessed at baseline (t0), 4, weeks (t1), 3 (t2) and 6 months (t3) post treatment.	Mean (± sd) scores at t0, t1, t2 & t3 were MAS: 3.7 ± 0.6, 1.7±1.0, 2.0±0.8, 2.1±0.8, p<0.001) PROM (degrees): 87.3±20.2, 104.3±20.1, 103.8±18.9, 101.6± 19.7, p=0.018 MRC: 0.6 ±0.8, 0.6±0.8, 0.6±0.8, 0.6±0.8, p=ns Adverse events: 3 subjects reported pain over the lateral aspect of the forearm

Robotics

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Sale et al. 2014 **Italy** **RCT**	CA: ☒ Blinding: assessor ☑ patient☒ ITT: ☒	53 subjects, on average 30±7 days post stroke.	Subjects randomized into two groups; both groups received standard therapy. Experimental group received 30 additional sessions of robot-assisted therapy, while the control received an additional 30 sessions of usual therapy.	**Primary Outcome:** MAS of shoulder and elbow Outcomes were assessed after 15 sessions and after 30 sessions.	A significant improvement was noted for the experimental group on MAS for shoulder (p=0.004) and elbow (p=0.018).
Hu et al. 2013 **Hong Kong** **Pre-Post**	N/A	10 subjects, on average 7.2 months post stroke	20-session hand EMG robot-assisted upper limb training with a training intensity of 3-5 sessions per week for 7 consecutive weeks.	**Primary Outcome:** MAS of fingers Outcomes were assessed at baseline and after 20 sessions.	A significant reduction in spasticity of the fingers was reported as measured by the MAS (p<0.05).

Electrical Stimulation

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Gunduz et al. 2014 **Spain** **Systematic Review**	N/A	7 studies in the subacute phase of stroke; participants ranged from a few months to almost 20 years post stroke.	A review of the literature to identify studies evaluating the safety and effectiveness of non-invasive brain stimulation (primarily rTMS and tDCS). The review assessed a variety of neurological disorders (stroke, multiple sclerosis, spinal cord injury and cerebral palsy).	Outcomes assessed included spasticity, upper limb functioning, gait and activities of daily living. Assessment time points ranged from 1 to 4 weeks after treatment.	Several studies found a significant improvement in spasticity and upper limb functioning with low- and high-frequency rTMS. Anodal and cathodal tDCS has been found effective. These results are dependent on hemisphere of administration, Effectiveness is dependent on the underlying neurological pathology and if it is applied as a unique intervention or in combination with medical and/or physical therapy.
Karakus et al. 2013 **Turkey**	CA: ☑ Blinding: assessor ☑	28 patients, on average 3.3 months post stroke.	A standard rehabilitation program was applied to control group (n=14), and a standard rehabilitation	**Primary Outcome:** MAS of elbow, wrist and finger.	There were no significant difference in MAS scores between the two groups for elbow (p=0.513), wrist (p=0.119) or finger flexor spasticity (p=0.655).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
RCT	patient☒ ITT: ☑		program plus functional electrical stimulation of wrist and finger extensors were applied to the other group (n=14).		
de Jong et al. 2013 **Netherlands** **RCT**	CA: ☑ Blinding: assessor ☑ Patient ☒ ITT: ☑	46 subjects, 2-8 weeks post-stroke	Subjects were randomized into a control or experimental group. The experimental group received arm stretch positioning combined with NMES for 2, 45-min sessions a day, 5 days a week, for 8 weeks. Control participants received sham treatments.	**Primary Outcome:** Modified Tardieu Scale (MTS), Leeds Adult/Arm Spasticity Impact Scale (LEEDS)	There were no significant between group differences on the LEEDS (p=0.485) or MTS (p=0.89).
Boyaci et al. 2013 **Turkey** **RCT**	CA: ☒ Blinding: assessor ☑ patient ☑ ITT: ☒	31 subjects, who were ≥ 4 weeks post stroke	Subjects were randomized into three groups: 1) NMES (n=11), passive NMES (n=10), or sham. Stimulation lasted 45 min, 5x per week for 3 weeks.	**Primary Outcome:** MAS of wrist and finger. Outcomes were assessed at baseline and 3 weeks.	Wilcoxon's signed-rank test showed significance between group 1 and group 3 (p=0.0008) for wrist flexor spasticity and no significant differences for finger flexor spasticity between any of the groups.
Wu et al. 2013 **USA** **RCT**	CA: ☑ Blinding: assessor ☑ patient ☑ ITT: ☑	90 subjects, 2-12 months post stroke	Subjects were randomized into two groups: 1) tDCS to the primary sensorimotor cortex of the affected side for 20 minutes per day, 5 days per week, for 4 weeks, or 2) sham stimulation. Both groups received conventional physical therapy.	**Primary Outcome:** MAS of elbow and wrist. Outcomes were assessed at admission, after treatment and at 4-week follow-up.	Compared with the sham tDCS group, the active tDCS group had significantly more patients with a clinically important difference after treatment (80% and 78% vs 6% and 9%) and at 4-week follow-up (84% and 82% vs 7% and 4%),
Ochi et al. 2013 **Japan** **RCT**	CA: ☑ Blinding: assessor ☑ patient ☑ ITT: ☒	18 subjects, ≤6 months post stroke	Subjects received two interventions, comprising 1) anodal tDCS to the affected hemisphere with arm training (AT) (tDCS(a)+AT) and 2) cathodal tDCS to the unaffected hemisphere with AT (tDCS(c)+AT) for	**Primary Outcome:** MAS of elbow, wrist and finger. Outcomes were assessed at baseline and post intervention.	MAS scores for elbow, wrist, and finger significantly improved between baseline and post treatment for both groups ($p<0.05$ for all). However, the only between-group difference occurred on finger MAS scores where tDCS(c) + AT improved more than tDCS(a) + AT ($p<0.05$) for right hemispheric lesions but not left hemispheric lesions.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			5 days in a cross-over manner.		

Magnetic Stimulation

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Gunduz et al. 2014 **Spain** **Systematic Review**	N/A	7 studies in the subacute phase of stroke; participants ranged from a few months to almost 20 years post stroke.	A review of the literature to identify studies evaluating the safety and effectiveness of non-invasive brain stimulation (primarily rTMS and tDCS). The review assessed a variety of neurological disorders (stroke, multiple sclerosis, spinal cord injury and cerebral palsy).	Outcomes assessed included spasticity, upper limb functioning, gait and activities of daily living. Assessment time points ranged from 1 to 4 weeks after treatment.	Several studies found a significant improvement in spasticity and upper limb functioning with low- and high-frequency rTMS. Anodal and cathodal tDCS has been found effective. These results are dependent on hemisphere of administration, Effectiveness is dependent on the underlying neurological pathology and if it is applied as a unique intervention or in combination with medical and/or physical therapy.
Krewer et al. 2014 **Germany** **RCT**	CA: ☑ Blinding: assessor ☑ patient ☑ ITT: ☑	66 subjects, who were on average 26±71 weeks (experimental) or 37±82 weeks (control) post stroke.	Subjects were randomized into two groups to receive either 20 minutes repetitive peripheral magnetic stimulation or sham treatment and occupational therapy for 20 minutes, 2 times a day, for 2 weeks.	**Primary Outcome:** Modified Tardieu Scale (MTS) Outcomes were assessed at baseline, after 1st therapy, before 3rd therapy, after 2 weeks therapy, and 2 weeks after the intervention phase.	Compared with the sham stimulation group, the experimental group showed short-term effects on spasticity for wrist flexors (P=.048), and long-term effects for elbow extensors (P<.045) as measured by MTS.
Barros Galvao et al. 2014 **Brazil** **RCT**	CA: ☑ Blinding: assessor ☑ patient ☑ ITT: ☑	20 subjects, ≤6 months post stroke	Subjects were randomized into either a rTMS (10 sessions, 3d/wk) or sham stimulation group. Both groups also received physiotherapy.	**Primary Outcome:** MAS of wrist. Outcomes were assessed at baseline, after treatment and 4 week follow-up.	In the experimental group (control group), 90% (30%) of the patients at post intervention and 55.5% (22.2%) at follow-up showed a decrease ≥1 in MAS score.
Etoh et al. 2013 **Japan**	CA: ☑ Blinding:	18 subjects, on average 29.9 months post stroke	Subjects were randomized into either a rTMS or sham group and received	**Primary Outcome:** MAS of elbow, wrist, fingers	The MAS scores of the elbow, wrist and finger flexors did not show significant improvement during either real or sham stimulation (p>0.05).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Cross-over RCT	assessor ☑ patient ☑ ITT: ☑		therapy for two weeks. Subjects then crossed-over and received the other protocol.	Outcomes were assessed at baseline and 4 weeks.	

Glossary
RCT= Randomized Controlled Trial
N/A = Not Applicable
CA = Concealed Allocation
ITT = Intention to treat
OR = Odds Ratio
MD = Mean Difference
CI = Confidence Interval
IQR = Interquartile Range
MAS = Modified Ashworth Scale

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