CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Rehabilitation, Recovery and Community Participation Following Stroke

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

7th edition, update 2025

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

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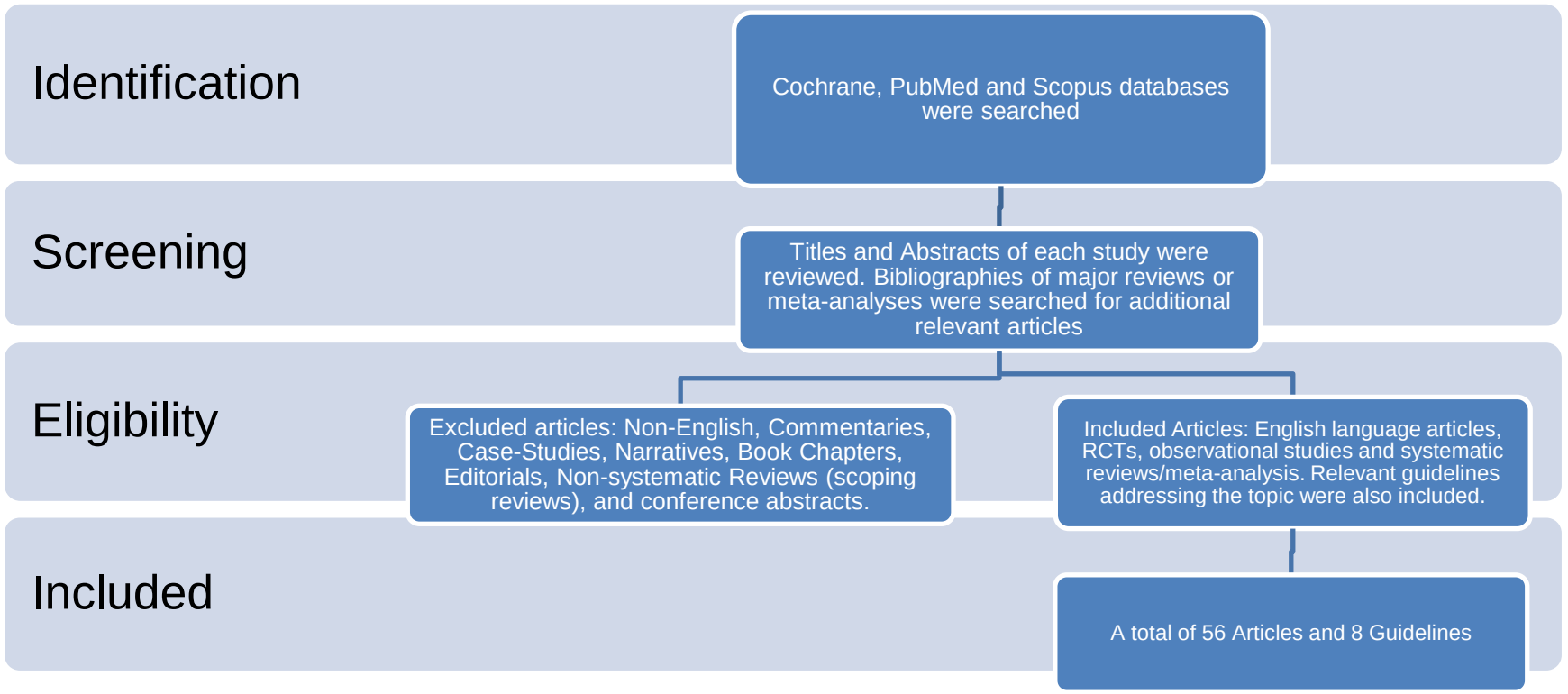
Search Strategy



Cochrane, PubMed and Scopus databases were searched using terms such as (Stroke OR Cerebrovascular accident) AND (“spasticity” OR “contracture”) AND (“upper extremity” OR “upper limb”) AND (rehabilitation OR therapy OR intervention). Titles and abstract of each article were reviewed for relevance. Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, non-systematic review, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review. A total of 56 articles and 8 guidelines were included and were separated into categories designed to answer specific questions.

Published Guidelines

Guideline	Recommendations
Management of Stroke Rehabilitation Working Group. VA/DoD clinical practice guideline for the management of stroke rehabilitation. Washington (DC): Veterans Health Administration, Department of Defense; Version 5.0 – 2024. **Available at:** https://www.healthquality.va.gov/guidelines/Rehab/stroke/	24. We suggest botulinum toxin for patients with focal spasticity depending on patient characteristics and preferences. Weak (for) 25. There is insufficient evidence to recommend for or against the use of acupuncture or dry needling for spasticity management. Neither for nor against 26. There is insufficient evidence to recommend for or against whole body or localized muscle vibration for spasticity management. Neither for nor against 27. There is insufficient evidence to recommend for or against extracorporeal shock wave therapy for spasticity management. Neither for nor against
National Clinical Guideline for Stroke for the UK and Ireland. London: Intercollegiate Stroke Working Party; 2023 May 4. **Available at:** www.strokeguideline.org**.**	**New for 2023** People with spasticity in the upper or lower limbs after stroke should not be treated with electrical stimulation to reduce spasticity. People with spasticity in their wrist or fingers who have been treated with botulinum toxin may be considered for electrical stimulation (cyclical/neuromuscular electrical stimulation) after the injection to maintain range of movement and/or to provide regular stretching as an adjunct to splinting or when splinting is not tolerated. People with stroke at high risk of contracture should be monitored to identify problematic spasticity and provided with interventions to prevent skin damage, or significant difficulties with hygiene, dressing, pain or positioning.
Minelli C, Luvizutto GJ, Cacho RO, Neves LO, Magalhães SCSA, Pedatella MTA et al. **Brazilian practice guidelines for stroke rehabilitation: Part II.** ***Arq Neuropsiquiatr*. 2022 Jul;80(7):741-758.**	**Spasticity (upper limb and lower limb)** High LOE (Level A): • The application of botulinum toxin to target muscles is recommended for the treatment of spasticity. • Transcutaneous electrical nerve stimulation is recommended to reduce muscle spasticity in the lower limbs. • Functional electrical stimulation of spastic muscles may be helpful. • Treatment with intrathecal baclofen may be helpful in refractory cases. • Acupuncture, electroacupuncture, and functional bandaging may be helpful. • Oral medications such as baclofen, tizanidine, and benzodiazepines do not seem to be effective; however, they may be helpful considering their adverse effects. • The effects of botulinum toxin on function are uncertain. • Splints and positioning orthoses have uncertain effects. Moderate LOE (Level B): • Kinesiotherapy has shown controversial effects but might sometimes be helpful.

Guideline	Recommendations
Miyamoto S, Ogasawara K., Kuroda S, et al. **Japan Stroke Society Guideline 2021 for the Treatment of Stroke** ***Int J Stroke 2022*; 17(9): 1039–1049.**	**Chapter 7, Section 2-5. Spasticity** High LOE, strong recommendation: • To alleviate post-stroke upper/lower limb spasticity or improve the motor function of the limbs, it is recommended to perform botulinum toxin injection. • It is recommended to perform transcutaneous electrical nerve stimulation. High LOE, Moderate recommendation: • It is reasonable to administer an oral muscle relaxant while paying attention to adverse events. Moderate LOE, Moderate recommendation: • While the injection is often performed in the chronic phase, it is also reasonable to perform it in the subacute phase. • It is reasonable to perform motor point block with phenol. • It is reasonable to perform orthotic bracing. • To alleviate spasticity or improve ADL, it is reasonable to perform intrathecal baclofen pump therapy.
Zhang T, Zhao J, Li X, Bai Y, Wang B, Qu Y et al. **Chinese Stroke Association guidelines for clinical management of cerebrovascular disorders: executive summary and 2019 update of clinical management of stroke rehabilitation.** ***Stroke Vasc Neurol.* 2020 Sep;5(3):250-259.** **(selected)**	The Modified Ashworth Scale and Modified Tardieu Scale are recommended for the evaluation of spasticity (Grade I recommendation, Level B evidence). Normal limb position, passive stretching, range of motion training and Chinese medical massages are recommended to alleviate spasticity (Class I recommendation, Level C evidence). Combined transcranial direct current stimulation, repetitive transcranial magnetic stimulation and transcutaneous electrical nerve stimulation (TENS) with conventional physiotherapy is reasonable to relieve spasticity (Grade IIa recommendation, Level B evidence).
Clinical Guidelines for Stroke Management 2017. Melbourne (Australia): National Stroke Foundation. Section 5. Rehabilitation	**Spasticity** • Hand and wrist orthoses (splints) should not be used as part of routine practice as they have no effect on function, pain or range of movement. (strong recommendation). • For stroke survivors with upper limb spasticity, Botulinum Toxin A in addition to rehabilitation therapy may be used to reduce spasticity, but is unlikely to improve activity or motor function. (weak recommendation). • For stroke survivors with spasticity, acupuncture should not be used for treatment of spasticity in routine practice other than as part of a research study. (weak recommendation). • For stroke survivors with spasticity, adjunct therapies to Botulinum Toxin A, such as electrical stimulation, casting and taping, may be used. (weak recommendation). • For stroke survivors, the routine use of stretch to reduce spasticity is not recommended. (weak recommendation).

Guideline	Recommendations
	• For stroke survivors at risk of developing contracture, routine use of splints or prolonged positioning of upper or lower limb muscles in a lengthened position (stretch) is not recommended. (strong recommendation). **Contracture** • For stroke survivors, serial casting may be trialled to reduce severe, persistent contracture when conventional therapy has failed. • For stroke survivors at risk of developing contracture or who have developed contracture, active motor training or electrical stimulation to elicit muscle activity should be provided.
Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC et al; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research. **Guidelines for adult stroke rehabilitation and recovery: A guideline for healthcare professionals from the American Heart Association/American Stroke Association.** ***Stroke* 2016;47:e98–e169**	Resting hand/wrist splints, along with regular stretching and spasticity management in patients lacking active hand movement, may be considered. **(C)** Use of serial casting or static adjustable splints may be considered to reduce mild to moderate elbow and wrist contractures. **(C)** Surgical release of brachialis, brachioradialis, and biceps muscles may be considered for substantial elbow contractures and associated pain. **(B)** The use of overhead pulley exercises is not recommended. **(C)** Targeted injection of botulinum toxin into localized upper limb muscles is recommended to reduce spasticity, to improve passive or active range of motion, and to improve dressing, hygiene, and limb positioning. **(A)** Oral antispasticity agents can be useful for generalized spastic dystonia but may result in dose-limiting sedation or other side effects. **(A)** Physical modalities such as NMES or vibration applied to spastic muscles may be reasonable to improve spasticity temporarily as an adjunct to rehabilitation therapy. **(A)** Intrathecal baclofen therapy may be useful for severe spastic hypertonia that does not respond to other interventions. **(A)** The use of splints and taping are not recommended for prevention of wrist and finger spasticity after stroke. **(B)**
Intercollegiate Stroke Working Party. *National clinical guideline for stroke,* 5th edition. London: Royal College of Physicians, 2016.	*4.15.1 Recommendations* A. People with motor weakness after stroke should be assessed for spasticity as a cause of pain, as a factor limiting activities or care, and as a risk factor for the development of contractures. B. People with stroke should be supported to set and monitor specific goals for interventions for spasticity using appropriate clinical measures for ease of care, pain and/or range of movement. C. People with spasticity after stroke should be monitored to determine the extent of the problem and the effect of simple measures to reduce spasticity e.g. positioning, passive movement, active movement (with monitoring of the range of movement and alteration in function) and/or pain control. D. People with persistent or progressive focal spasticity after stroke affecting one or two areas for whom a therapeutic goal can be identified (e.g. ease of care, pain) should be offered intramuscular botulinum toxin. This should be within a specialist multidisciplinary team and be accompanied by rehabilitation therapy and/or splinting or casting for up to 12 weeks after the injections. Goal attainment should be assessed 3-4 months after the injections and further treatment planned according to response.

Guideline	Recommendations
	E. People with generalised or diffuse spasticity after stroke should be offered treatment with skeletal muscle relaxants (e.g. baclofen, tizanidine) and monitored for adverse effects, in particular sedation and increased weakness. Combinations of antispasticity drugs should only be initiated by healthcare professionals with specific expertise in managing spasticity. F. People with stroke should only receive intrathecal baclofen, intraneural phenol or similar interventions in the context of a specialist multidisciplinary spasticity service. G. People with stroke with increased tone that is reducing passive or active movement around a joint should have the range of passive joint movement assessed. They should only be offered splinting or casting following individualised assessment and with monitoring by appropriately skilled staff. H. People with stroke should not be routinely offered splinting for the arm and hand.

Evidence Tables

Stretching Programs +/- Splinting to Prevent Contracture

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Salazar et al. 2019 **Brazil** **Systematic review & meta-analysis**	Median PEDro score was 6 with scores ranging from 4-9.	10 RCTs including persons recovering from stroke in the acute/subacute stage (7 RCTs, 210 participants and chronic stage (3 RCTs, 57 participants). Mean age ranged from 36 to 75.4 years.	3 trials compared wrist and hand static stretching vs. positioning orthoses to treat spasticity. In these trials, therapy was delivered for 20-42 minutes/session, 6-7 days/week x 3-4 weeks. 7 trials compared static stretching with simple positioning + conventional physiotherapy vs. conventional physiotherapy. In these trials, stretching was delivered for 30-120 minutes, 5 or 7 days a week x 4-to 8 weeks.	**Primary Outcomes:** Spasticity (assessed using conventional scales) **Secondary Outcomes:** Passive Range of Motion (assessed by goniometry)	Using data from 3 trials, static stretching with positioning orthoses was associated with reduced wrist-flexor spasticity compared with no therapy or conventional physiotherapy (MD= -1.89, 95% CI -2.44 to -1.34). Using data from 7 trials, static stretching with simple positioning (without any device), with or without other therapies, was not associated with significant improvements in PROM of shoulder external rotation, shoulder flexion, or wrist extension versus conventional physiotherapy.
Harvey et al. 2017 **Australia** **Cochrane Review**	The risk of bias was high in ≥1 domain in all trials.	49 RCTs (2,135 participants) including persons with neurological condition, advanced age, those with a history of trauma and those with underlying joint or muscle pathology. 11 trials included stroke cohorts treated for upper limb impairments.	Trials evaluated the effect of stretching programs (casting, splinting, self-administered, positioning, and sustained passive stretch) on preventing contractures. Intervention comparisons included stretch vs. no stretch, stretch vs. placebo or sham, and stretch plus co-intervention vs. co-intervention, including splints. The total cumulative time that stretch was administered ranged from 23 minutes to 1,456 hours (median 168 hours, IQR 24	**Primary Outcomes:** Joint mobility (active range of motion, passive range of motion, passive joint stiffness) **Secondary Outcomes:** Pain (VAS), spasticity (Modified Ashworth Scale, Tardieu Scale), activity limitation (Functional Independence Measure, Motor Assessment Scale)	**Stroke specific results (upper & lower limbs combined)** *Joint mobility* Stretching was not associated with significant improvement in joint mobility in the short term (MD=0.56 degrees, 95% CI -1.56 to 2.68, n=11 trials148 participants) or long term (MD=-0.32 degrees, 95% CI -4.09 to 3.44, n=4 trials, 70 participants). *Pain* Stretching was not associated with significant improvement in pain in either the short term (SMD=0.31, 95% CI -0.03 to 0.66, n=4 trials, 135 participants) or long term (SMD=-0.03, 95% CI -0.41 to 0.47, n=4 trials, 132 participants). *Spasticity*

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			to 672).		Stretching was not associated with significant improvement in spasticity in either the short term (SMD=0.05, 95% CI -0.29 to 0.39, n=5 trials, 134 participants) or long term (SMD=-0.5, 95% CI -1.12 to 0.11, n=1 trial, 21 participants). *Activity limitation* Stretching was not associated with significant improvement in activity limitation in either the short term (SMD=0.27, 95% CI -0.09 to 0.63, n=5 trials, 170 participants) or long term (SMD=0.14, 95% CI -0.29 to 0.58, n= 4 trials, 136 participants).
Choi et al. 2016 **Korea** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☒ ITT: ☒	30 persons 2-6 months post stroke with pain, edema and paralysis of the hand. Mean age was 62.5 years, 57% were men. Mean chronicity of stroke was 3.5 months	Participants in the experimental group wore resting hand splints for a max 10hr/d for 12wk. The control group did not receive splinting therapy. All participants received general rehabilitation for 30min/d, 5d/week for 12 weeks.	**Primary Outcomes:** Pain (VAS), hand edema (voltmeter), spasticity (MAS) of the wrist. Outcomes were assessed before and after the intervention.	There were significant differences between groups favouring the experimental group for the outcomes of pain (mean difference from baseline =-1.53 vs. -0.27) and volume of hand (mean difference from baseline (24.3 vs. -3.67), but there were no differences in change in mean MAS scores (-0.73 vs. -0.40).
Lannin et al. 2007 **Australia** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	63 persons who had experienced a stroke in the previous 8 weeks with no active wrist extension. Mean age was approximately 70 years, 52% were women. Mean chronicity of stroke was 28 days.	Participants were randomized 1:1:1 to 2 intervention groups and a control group. Participants in the intervention 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}) for up to 12 hours overnight for 4 weeks. Participants in the control group did not wear a splint. Persons in all groups received conventional therapy.	**Primary Outcome:** Extensibility of the wrist and finger flexor muscles. **Secondary Outcomes:** Upper limb function (assess using the Motor Assessment Scale), spasticity (assessed using the Tardieu Scale) and disability (assessed using the 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

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Horsley et al. 2007 **Australia** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	40 adult patients admitted for inpatient rehabilitation with stroke (n=19) or stroke-like brain injury (n=1) who were unable to actively extend their wrist past the neutral position. Mean age was 61.5 years, 47.5% were men.	Patients were randomized 1:1 to receive 30 minutes of stretch of wrist and finger flexors 5 days a week for 4 weeks + conventional task-specific therapy (experimental group) or conventional therapy only (control group).	**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 3 persons were lost to follow-up (exp group =2; control group=1).

Botulinum Toxin-Type A (BTX-A)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Jia et al. 2020 **China** **Systematic review & meta-analysis**	The risk of bias was high in 4 trials (assessed using Cochrane risk-of-bias method)	10 RCTs, including 950 participants recovering from stroke, with upper limb spasticity. Mean age ranged from 59 to 66.5 years. The percentage of women ranged from 32.2% to 66.7%.	Trials compared the use of BTX-A (Dysport, Botox or Xeomin) vs. placebo or any kind of routine care. The duration of treatment was between 12 weeks and 12 months	**Primary Outcomes:** Modified Ashworth Score (MAS) of the elbow, finger and wrist, pain and Barthel Index (BI)	Botulinum toxin was not associated with significant improvements in spasticity of the elbow (SMD=-0.27, 95% CI -0.56 to 0.01), or the wrist (SMD=-0.20, 95% CI -0.67 to 0.28), but did improve spasticity in the finger (SMD=-0.57, 95% CI -0.99 to -0.15). Botulinum toxin was not associated with significant improvement in pain (SMD=-0.03, 95% CI -0.17 to 0.10).

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					Botulinum toxin was not associated with significant improvement in BI scores (SMD=0.01, 95% CI -0.13 to 0.15). In subgroup analysis, the reduction in mean MAS scores at the wrist was significantly better with Dysport vs. Botox (SMD = -.39 vs. SMD=0.08). In sub-group analysis, the improvement in MAS scores at the elbow was greater for persons <65 years compared with those more ≥ 65 years (SMD=-0.32 vs. SMD=-0.16).
Andringa et al. 2019 **Netherlands** **Systematic review & meta-analysis**	PEDro scores ranged from 4 to 10.	40 RCTs, (28 included in pooled analysis) including adult patients with upper-limb spasticity post stroke. Mean/median age ranged from 39 to 69 years. Chronicity of stroke was ≥3 months in 36 trials.	Trials compared BTX-A injections in the upper limb vs. a control condition (13 placebo, 1 intraarticular injections of triamcinolone acetonide and 2 oral tizanidine) or BTX-A + a rehabilitation program, including electrical stimulation, robotic training, or range of motion exercises vs. rehabilitation only (19 trials)	**Primary outcomes:** Spasticity related pain, grip strength, passive and active ROM, self care	*4-8 weeks after injection* BTX-A was not associated with significant reduction in spasticity-related pain in the shoulder or arm. Overall, BTX-A was associated with significant improvement in passive ROM in the shoulder, elbow or wrist (effect size=0.28, 95% CI 0.02-0.55) and resistance to passive movement (effect size=0.72, 95% CI 0.51-0.92) Overall, BTX-A was not associated with significant improvement in active ROM in the elbow, wrist or finger (effect size=0.09, 95% CI -0.13-0.32). BTX-A was associated with significant improvement in self care (effect size=0.36, 95% CI 0.02-0.61). BTX-A was not associated with significant improvement in motor function or grip strength. *12 weeks after injection* BTX-A was not associated with significant reduction in spasticity-related pain in the shoulder (effect size=0.34, 95% CI -0.04-0.72), but was effective for pain in the arm (effect size=0.22, 95% CI 0.0-0.44). Overall, BTX-A was associated with significant improvement in passive ROM in the shoulder,

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					(effect size=0.44, 95% CI 0.05-0.82) and resistance to passive movement (effect size=0.49, 95% CI 0.28-0.70). Overall, BTX-A was not associated with significant improvement in active ROM in the elbow, wrist or finger (effect size=-0.18, 95% CI -0.46-0.10). BTX-A was associated with significant improvement in self care (effect size=0.36, 95% CI 0.12-0.59). BTX-A was not associated with significant improvement in motor function or grip strength.
Sun et al. 2019 **China** **Systematic review & meta-analysis**	Jadad scores ranged from 2 to 5.	27 RCTs, including adult participants with limb spasticity following stroke, of which 18 trials included persons with upper limb spasticity. In trials of the upper limb, mean age ranged from 49.3 to 63.2 years. The percentage of men ranged from 40% to 79.2%. Time since stroke ranged from >24 hours to 83 months.	Trials compared BTX-A injections (Botox, Dysport, Xeomin) in the upper limb vs. placebo. Doses of Botox ranged from 70U to 500U, doses for Dysport ranged from 500-1,500 and for Xeomin (1 trial), the dose was 400U. The duration of follow-up ranged from 4 to 16 weeks.	**Primary outcomes:** Muscle tone, active upper limb function, physician global assessment, and disability	Treatment with BTX-A was associated with significant improvement in muscle tone (SMD=-0.76; 95% CI -0.97 to -0.55), physician global assessment (SMD=0.51; 95% CI 0.35-0.67) and disability assessment scale (SMD=-0.30; 95% CI -0.40 to -0.20; P<0.001), with no significant improvement on active upper limb function (SMD=0.49; 95% CI -0.08 to 1.07).
Elovic et al. 2016 **USA** **RCT**	CA: ☒ Blinding: Patient ☑ Assessor ☑ ITT: ☒	317 adults with upper limb spasticity (Ashworth Scale ≥2) following a stroke that occurred >3 months previously. Mean age was approximately 56 years, 46% were men. Median time since stroke was 28 months. Mean duration of spasticity was 12 months.	Patients were randomized to receive a single total dose of 400U BTX-A (n=210) or placebo (n=107). A primary target clinical pattern (PTCP) was determined that included the elbow (200U), wrist (150U) or wrist for injection (100U). Muscles other than the PTCP the investigators discretion was used.	**Primary Outcomes:** Ashworth Scale (AS) on the PTCP, Investigator's Global Impression of Change (IGIC), assessed at week 4 **Secondary Outcomes:** Disability Assessment Scale (DAS). Assessments were conducted at baseline, 4wk, 8wk, and 12wks.	At week 4, treatment with BTX-A was associated with significantly greater improvement in PTCP AS scores (least-squares mean change –0.96 vs. –0.5), and more persons were PTCP AS responders (1-point improvement) with BTX-A (69.6% vs. 37.5%). Improvements were maintained at 8 and 12 weeks for both outcomes. IGIC was significantly higher in the experimental group than the placebo group at 4 weeks (p<0.05). A significantly higher proportion of persons in the BTX-A group were considered to be responders on DAS (1- point improvement of the principal target

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					domain at 4 weeks (46.2% vs. 28.4%). There were 7 losses to follow-up/dropouts in the placebo group and 11 in the BTX-A group.
Gracies et al. 2015 **USA** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	243 adults with chronic hemiparesis and spasticity following stroke (n=215) or traumatic brain injury, recruited from 34 rehabilitation centers across Europe and USA. Mean age was 53 years, 63% were men. The chronicity of stroke was approximately 5 years for persons with stroke.	Participants were randomized 1:1:1 to receive BTX-A 500U vs. BTX-A 1,000U vs. placebo into the most hypertonic muscle group among the elbow, wrist, or finger flexors and into at least two additional muscle groups from the elbow, wrist, or finger flexors or shoulder extensors	**Primary Outcomes:** Modified Ashworth Scale (MAS) at 4 weeks **Secondary Outcomes:** Physician Global Assessment (PGA), Disability Assessment Scale (DAS) at 4 weeks	Mean baseline MAS score was 3.9 in all groups. At 4 weeks, the mean MAS score and change from baseline in the placebo group was 3.7 and -0.3. The corresponding values for the BTX-A groups were 2.7 and -1.2 for the 500U group and 2.6 and -1.4 for the 1,000U group (placebo vs. 500U, p<0.0001 and placebo vs. 1,000U, p<0.0001). At 4 weeks, the mean PGA scores for the placebo, 500U and 1,000U groups were 0.6, 1.4 and 1.8, respectively (placebo vs. 500U, p=0.003 and placebo vs. 1,000U, p<0.0001). Mean baseline DSA scores were 2.6 (placebo), 2.6 (500U) and 2.5 (1,000U). At 4 weeks, the mean PGA score and change from baseline in the placebo group was 2.1 and -0.5. The corresponding values for the BTX-A groups were 1.9 and -0.7 for the 500U group and 1.8 and -0.7 for the 1,000U group (placebo vs. 500U, p=n/s and placebo vs. 1,000U, p=n/s). There were 3 serious adverse events in each group. Adverse events that were thought to be treatment related occurred in 2%, 7% and 9% of patients in the placebo, 500U, and 1,000U groups, respectively.
Wissel et al. 2016 (pain) **Ward et al. 2014 (function)** **International** **RCT** ***BOTOX®***	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☑	273 persons with post-stroke spasticity. Mean age was 62 years, 41% were women. 86% of participants had their stroke >12 months previous. 74.3% of patients reported pain at baseline. Persons with upper and lower-limb	Participants were randomized to receive a single dose of BTX-A or placebo in addition to usual care. Dosing and site of injection was based on clinician judgement. An optional second dose was administered ≥ 12 weeks after the first injection. The double-blind phase lasted for 22 to 34	**Primary outcome:** Physician Assessment of Success, as Determined by Percentage of Patients Who Achieve Their Principal Active Functional Goal at Week 24 **Secondary outcomes:**	The median first and optional second injection doses of BTX-A were 340 U and 365 U. *Function* There were no significant differences between the groups at weeks 12, 24 or 52 with respect to the percentage of patients who achieved their principal active functional goal (33.1% vs. 28.9%; 40.9% vs. 33.3% and 45.0% vs. 52.4%, respectively).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Economic Spasticity Trial (BEST)		spasticity were included.	weeks, depending on the timing of the second injection, followed by an open label extension through week 52.	Pain, HRQoL	There were no significant differences between groups in the number of persons who achieved their secondary active functional goals. A higher number of persons in the BTX-A groups achieved their secondary passive functional goals at 24 weeks, (60.6% vs. 38.6%, p=0.016), but not at weeks 12 or 52. The mean change from baseline in resistance to passive movement Scale Summated total score in persons with upper-limb spasticity was –4.3 (95% CI –5.7 to –2.8) in the BTX-A group and –1.7 (95% CI –2.9 to –0.4) in the placebo group. *Pain* Mean pain reduction from baseline at week 12 was significantly greater with BTX-A group (-0.77, 95% CI -1.14 to -0.40) than placebo (-0.13, 95% CI -0.51 to -0.24; P < 0.05). Higher proportions of patients with pain in the BTX-A group achieved ≥30% and ≥50% reductions in pain at week 12 (53.7% and 37.0%, respectively) compared with placebo (28.8% and 18.6%, respectively; P < 0.05).
Shaw et al. 2011 **UK** **RCT (BoTULS)**	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☑	333 patients with spasticity of the elbow (MAS>2) and/or spasticity of the shoulder, wrist or hand with reduced arm function following a stroke occurring > 1 month. Median age was 66 years, 67% were men. Median chronicity of stroke was approximately 300 days.	Participants were randomized to receive 100 or 200 U BTX-A (Dysport) (n=170) + a standardized therapy program (1 hour/day, 2x/week for 4 weeks) vs. therapy program only (n=163). Persons in the BTX-A group received injections injected into the shoulder, arm, wrist, elbow and/or fingers Repeat injections were available to subjects in the	**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	At 1 month, there was no significant difference in the proportion of subjects who achieved a successful outcome between groups. 25.1% in BTX-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 BTX-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

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			intervention group at 3, 6 and 9 months. Two therapy menus were available depending on baseline arm function. Persons with no active arm function participated in stretching (20 minutes), positioning (10 minutes) and passive/active assisted upper arm activity (20 minutes), while those with some arm function participated in stretching (10 minutes) and task-oriented practice (40 minutes).	(arm), grip strength, 9-Hole Peg Test, BI, Pain (0-10 verbal rating Scale) Outcomes were assessed at baseline, 1,3- and 12-months following randomization	(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), 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 BTX-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 BTX-A group. Adverse events: There were 52 serious adverse events in the BTX-A group and 50 in the control group. Only 1 serious adverse event was believed to have been related to BTX-A treatment.
McCrory et al. 2009 **USA** **RCT**	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☑	102 persons 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) following stroke. Mean age was 58 years, 57% were women. Mean chronicity of stroke was 6 years.	Patients were randomized to receive BTX-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	**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	There were no significant differences between groups from baseline to week 20 (mean Δ, 95% CI) for the outcomes of AQoL: -0.03, -0.09 to 0.02, p=0.27; pain: 10.14, -8.1 to 27.4, p=0.25; or HADS: -0.07, -0.87 to 1.47, p=0.61 GAS: -5.20, 95% CI -9.08 to 1.28, p<0.001 (favours BTX-A group) There must be a typo in this reporting, since 95% CI crosses zero. Treatment with BTX-A was associated with a significant reduction in mean MAS scores across all joint from baseline to 20 weeks (1.59, 95% CI 0.98 to 2.00, p<0.001). There were no significant differences between groups from baseline to week 20 (mean Δ, 95% CI) for the outcomes of: MMAS: -0.22, 95% CI -0.75 to 0.31, p=0.41; PDS: -0.01, 95% CI -0.27 to 0.25, p=0.94; or CBS: -0.02, 95% CI -0.65 to 0.61, p=0.95. 20-week assessments were completed for 37

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					subjects in the control group and 53 subjects in the BTX-A group. Treatment related adverse events were reported in 5.5% of patients in the BTX-A group and 9.5% in the placebo group. Most adverse events were mild.
BTX-A + Cointerventions (Electrical Stimulation)					
Lee et al. 2018 **South Korea** **Prospective study**	NA	15 patients with finger and wrist flexor spasticity graded at least 1+ on the MAS, >6 months following stroke. Mean age was 44.7 years, 93% were men. Mean time since stroke was 12.8 months.	Two weeks after Botox injections into the finger and/or wrist flexors, patients received electrical stimulation (ES) of finger extensors while wearing a wrist brace for 4 weeks (5 days per week; 30-min sessions).	**Primary outcomes:** Box & Block Test (BBT), Action Research Arm Test (ARAT) **Secondary outcomes:** Spasticity of finger extension (MAS), active ROM (AROM) Assessments were conducted at baseline, immediately before Botox injections, and 2 and 6 weeks after injections	There were significant improvements in mean BBT and total ARAT scores over the intervention period. BBT: 3.07 (baseline), 3.60 (2 weeks) and 4.67 (6 weeks), p=0.039 ARAT: 11.33 (baseline) 11.27 (2 weeks) and 12.73 (6 weeks), p=0.043. There was significant improvement in mean wrist flexor/flexion and finger flexor/flexion MAS scores, but not in wrist of finger extensor/extension MAS scores. There was significant improvement in mean AROM-wrist flexors (degrees) and AROM wrist extensors (degrees).
Santamato et al. 2013 **Italy** **RCT** ***The Spasticity treated by Botulinum Toxin and ESWT (SBOTE) study***	CA: ☒ Blinding: Patient ☑ Assessor ☒ ITT: ☑	32 patients with focal spasticity of finger flexors measured as ≥ 2 on MAS, > 6 months post stroke. daily painful muscle spasms and pain at rest and during limb mobilization. Mean age was 64 years, 41% were men. Mean time since stroke was 10 months.	All patients received a single injection of BTX-A into the flexor digitorum superficialis muscle in the forearm (mean dose of Botox was 118 U). Patients were randomized to receive electrical stimulation using the Endomed 482 device applied for 30 min twice a day for 5 days (50–90 mA) or extracorporeal shock wave therapy (ESWT), administered immediately after BTX-A injection once a day for 5 days.	**Primary outcomes:** Spasticity (MAS), spams frequency, assessed using the spasm frequency scale (SFS) and pain (VAS)	15 days after treatment, there was significantly greater improvement in mean MAS scores in the ESWT group (mean MAS 1.37 vs. 2.37, p<0.0001). 30 days after treatment, there were significantly greater improvements in all outcomes in the ESWT group (mean MAS 1.75 vs. 2.18, SFS 0.8 vs. 1.5, and pain VAS 1.94 vs. 2.44). 90 days after treatment, there were significantly greater improvements in all outcomes in the ESWT group (mean MAS 1.58 vs. 2.18, SFS 0.25 vs. 1.06, and pain VAS 1.87 vs. 2.69).
Picelli et al. 2011	CA: ☒	24 patients with unilateral stroke with spasticity of	95 U Botox was injected into the BB and the abductor digiti	**Primary outcomes:** MAS (elbow) and ADM	Patients in the immediate group had significantly improved MAS scores from baseline to 4 weeks

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Italy **RCT**	Blinding: Patient ☑ Assessor ☒ ITT: ☑	biceps brachii (BB) of ≥2 on MAS. Mean age was 63.7 years, 62.5% were men. Patients were recruited 6-18 months after stroke.	minimi (ADM) of the affected arm. Patients were randomized to receive electrical stimulation (ES) immediately after injection for 60 minutes or ES for 30 minutes a day for 3 consecutive days, beginning the day after injection.	compound muscle action potential (CMAP) amplitude Assessments were conducted immediately before and 4 weeks after injection	(mean 2.58 to 1.25 vs. 2.5 to 1.67) and better CMAP reductions (mean mV 11.60 to 4.36 vs. 12.41 to 7.24) than the delayed group at 4 weeks.
Weber et al. 2010 **USA** **RCT**	CA: ☒ Blinding: Patient ☑ Assessor ☒ ITT: ☒	23 patients with spastic hemiparesis following stroke (n=18) or brain injury (n=5) who had > 2 prior sessions of Botox injections. Mean age was significantly younger in the control group (41 vs. 54 years), 35% were men. Mean time since stroke was 4.3 years in the control group and 9.7 years in the FES group.	Patients were randomized to receive Botox injections (mean dose 328 U) + home-based task practice therapy + FES with an H200 device (worn during task practice) or Botox (mean dose 252 U) + task practice only. Patients were encouraged to complete the exercises for 60 minutes daily for 12 weeks.	**Primary outcome:** Motor Activity Log (MAL) observation **Secondary outcomes:** Action Research Arm Test (ARAT) and MAL-Self Report	18 patients completed the study. There were no significant differences in mean scores for any of the outcomes at baseline, week 6 or week 12. Overall, there were significant improvements in scores for both groups from baseline to week 6. From week 6 to 12, there was little change in scores for any of the outcomes.
BTX-A + Cointerventions (Motorized arm ergometer)					
Diserens et al. 2010 **Switzerland** **RCT (crossover)**	CA: ☒ Blinding: Patient ☒ Assessor ☒ ITT: ☒	8 patients with severe spastic hemisyndrome and spasticity (MAS ≥+1) following first-ever stroke who were able to tolerate 30 minutes of arm training. Mean age was 49 years. Mean time since stroke was 5.5 years.	All patients were injected with Botox (biceps brachii, brachioradialis, flexor digitorum superficialis and profundus, and the flexor carpi ulnaris and radialis muscles) at the beginning of the study and then a second time after 6 months. After 2 weeks, patients were randomized to train on a motorized arm ergometer 3 times per week for 30 minutes, for 3 months or played cards. After a 3-month washout period, patients crossed over to the other group.	**Primary outcome:** MAS **Secondary outcomes:** Rivermead Motor Stroke Assessment, ROM, Motricity Index (MI) Assessments were conducted 1 day before injection (time T1, time T3) and after 3 months of training or the control task (time T2, time T4). In addition, patients were examined clinically 2 weeks after BTX injection (time T1′, time	There were no significant differences between the study arms on any of the outcomes. In 4 patients with residual motor activity in the arm, there was significant improvement in MAS scores after arm ergometry, compared with the 4 patients without residual activity who showed worsening of their spasticity after use of the arm ergometer.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				T3′)	
BTX-A + Cointerventions (Dynamic splinting)					
Amini et al. 2016 **Iran** **Prospective study**	Downs & Black score 12/27	29 patients with chronic stroke and spasticity (MAS ≤3). Mean age was approximately 52 years, 48% were men. Mean time since stroke was 26 months.	Patients received one of 3 treatments: Botox injections into the wrist and finger flexors; Botox + Volar-Dorsal Wrist/Hand Immobilization splint, which immobilized the wrist in 10 degrees of extension, thumb in hyper-abduction and fingers in zero, (2 h/daytime plus night-time); or wearing the splint only for 3 months. All patients received occupational therapy, 3x/week for 3 months	**Primary outcomes:** Active and passive ROM of the elbow, wrist and metacarpophalangeal joints **Secondary outcomes:** MAS, Fugl Meyer Assessment (FMA) Assessments were conducted at baseline, after 1 month (T1), 2 months (T2) and 3 months (T3).	Generally, there was improvement in the primary and secondary outcomes over the study period in all 3 groups. There were no significant differences in mean changes from baseline to T1, T1 to T2 or T2 to T3, for any of the outcomes with one exception. There was significantly greater improvement in mean elbow AROM from T1 toT2 in the Botox group vs. splint only group (-17 degrees vs. 20, p=0.02).
Lai et al. 2009 **USA** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☒	36 patients with spasticity (MAS ≥ 2) of elbow flexors and range of movement deficit of > 24% in elbow extension. Mean age was 52 years, 57% were men. Time since stroke onset was >6 months.	All patients received BTX-A injections biceps (150 U), brachialis (75 U), and brachioradialis (75 U) muscles and occupational, manual therapy (2 x 1-hour sessions weekly for 16 weeks) including the use of moist heat, patient education and re-evaluation of symptoms, joint mobilization, passive and active ROM, proprio-neural facilitation, and therapeutic exercise. In addition, patients were randomized to receive adjunct treatment with Elbow Extension Dynasplint, which was worn for 6 to 8 hours during sleep, and education in use of the splint with change in tension prescribed twice a month vs. no splint.	**Primary outcomes:** Percent change in active range of movement (AROM) of the elbow extension and MAS of the elbow flexors	30 patients completed the trial. The mean change in AROM was significantly higher in the splinting group (33.5% vs. 18.7%). The mean change in MAS scores was similar between groups (9.3% splinting group vs. 8.6% control group).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
BTX-A + Cointerventions (Taping)					
Santamato et al. 2015 **Italy** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☒	70 patients with wrist and finger flexor muscle spasticity following stroke. Mean age was 56 years, 54% were men. Mean time since stroke was 12.4 months.	Patients in both groups received Xeomin injections into the wrist flexor muscles. They were then randomized 1:1 to receive adhesive taping (group A) or daily muscle manual stretching, passive articular mobilization of wrist and fingers, and palmar splint (group B) for 10 days.	**Primary outcome:** MAS, Disability Assessment Scale (DAS) Assessments were conducted at baseline (T_0) after two weeks (T1), and after one month (T2) from the treatment.	Mean finger MAS scores at T0, T1 and T2 Group A: 2.9, 1.3, 1.9 Group B: 3.3, 2.1, 2.5 The differences between groups were significant at T1 and T2 Mean wrist MAS scores at T0, T1 and T2 Group A: 2.9, 1.7, 2.0 Group B: 2.3, 2.1, 2.6 The differences between groups were significant at T1 and T2 Mean DAS scores at T0, T1 and T2 Group A: 2.1, 1.3, 1.6 Group B: 2.2, 1.7, 216 The differences between groups were significant at T1 and T2
BTX-A + Cointerventions (Constraint induced movement therapy)					
Nasb et al. 2019 **China** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☒	64 patients with the ability to actively extend their wrist joint by 20° and their metacarpophalangeal and interphalangeal joints by ≥10° following stroke, with spasticity MAS of ≥1 for the fingers, wrist, or elbow flexors. 77.8% of the patients were men. Mean age not reported. Mean time since stroke was 4.45 months.	All patients received Botox injections into the biceps brachii, the flexor carpi radialis, flexor carpi ulnaris, flexor digitorum profundus, and flexor digitorum superficialis muscles. Patients were randomized 1:1 to a CIMT group or a control group. The day after injection, patients in the CIMT group began therapy consisting of 1 h/d of training, 6 d/ week plus 1 h for 4 weeks. Patients were asked to wear a mitten for 3 hours per day. Patients in the control group received dose-matched conventional therapy.	**Primary outcomes:** Modified Ashworth Scale (MAS), Fugl-Meyer assessment (FMA), Barthel index (BI)	At 4 weeks, there was significant improvement in MAS scores from baseline for the elbow, wrist and finger for both groups, with no significant difference between groups. At 4 weeks, there was significant improvement in FMA and BI scores from baseline for both groups, with significantly greater improvement in the CIMT group for both outcomes.
Sun et al. 2010 **Taiwan**	CA: ☑ Blinding:	32 patients with severe spasticity (MAS ≥ 3) in elbow, wrist or finger	All patients received 1,000 U Dysport into elbow, wrist and finger flexors + physiotherapy	**Primary outcome:** MAS (elbow, wrist, finger)	*Median baseline MAS, and 4 weeks, 3- and 6-month change scores elbow* CIMT group: 3.2, -2.0, -1.8, -1.1

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
RCT	Patient ☒ Assessor ☑ ITT: ☒	flexors and ≥10° active interphalangeal and metacarpal phalangeal extension and 20° active wrist extension (minimal motor criteria). Mean age was 59 years, 83% were men. Mean time since stroke was 2.9 years.	and occupational therapy (2 hours, 3 times per week for 3 months) starting the day following injections. Patients were randomized to receive modified CIMT with non-affected limb restrained for ≥ 5 hours per day or conventional therapy only.	**Secondary outcomes:** Motor Activity Log (MAL), Action Research Arm Test (ARAT), and patients' global satisfaction Assessments were conducted at 4 weeks and 3 and 6 months after injection	Conventional therapy: 3.2, -1.9, -1.4, -0.4. *Median baseline MAS, and 4 weeks, 3- and 6-month change scores wrist* CIMT group: 2.8, -1.7, -1.7, -1.1 Conventional therapy: 3.0, -1.9, -1.7, -0.4. *Median baseline MAS, and 4 weeks, 3- and 6-month change scores finger* CIMT group: 3.2, -2.3, -2.1, -1.3 Conventional therapy: 3.2, -2.4, -1.6, -0.1 There was significantly greater improvement in elbow, wrist and finger MAS scores at 6 months in the CIMT group ($p = .019$, $p = .019$, and $p < .001$ There were significantly greater improvements in MAL (Amount of Use) and MAL (Quality of Movement) in the CIMT group at 3 and 6 months. There were significantly greater improvements in ARAT scores in the CIMT group at 3 and 6 months.
BTX-A + Cointerventions (Compression sleeve and kinesiotaping)					
Giray et al. 2019 **Turkey** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☑	20 patients, recruited from an outpatient rehabilitation facility with post-stroke spasticity (MAS ≥1 in the elbow, wrist joints, and fingers) and limited upper-limb function and flexed elbow, pronated forearm, flexed wrist, flexed fingers, and thumb-in-palm postures. Mean age was 46.5 years, 70% were men. Time since stroke was >3 months.	All patients received BTX-A injections into the affected muscles. Three days after injection, patients were randomized 1:1 to an intervention group, who wore a lycra sleeve for 8 hours/day plus rehabilitation or a control group that received rehabilitation only. Both groups received therapy for 2 hours/day, 5 days/week for 3 weeks.	**Primary outcome:** Fugl Mayer Assessment (FMA) **Secondary outcomes:** MAS, Motricity Index (MI) Block & Box Test (BBT) and Stroke Impact Scale (SIS) Assessments were conducted at baseline, at 3 weeks and 3 months	There were significant improvements from baseline to end of treatment and follow-up in mean FMA, SIS, and MI (upper limb) scores within both groups, with no significant differences between groups. Overall, there were significant improvements from baseline to end of treatment and follow-up in median MAS (elbow, pronation, wrist, finger and thumb flexion) scores within both groups, with no significant differences between groups. There was no significant in mean BBT within, or between groups over the study period.
BTX-A + Cointerventions (Additional therapy)					
Lannin et al. 2020	CA: ☑	140 patients with moderate to severe	All patients received Botox in any muscle(s) that cross the	**Primary outcomes:** Goal Attainment Scale	At 3 months, there was no significant difference between groups in mean GAS-T scores (43 vs. 41).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Australia **RCT** ***InTENSE trial***	Blinding: Patient ☒ Assessor ☑ ITT: ☑	spasticity after a stroke, >3 months ago, who had completed formal rehabilitation. Mean age was 61 years, 69% were men. Mean time since stroke was 3.3 years.	wrist. Patients were randomized into one of 2 groups. The InTENSE program (up to 3 serial casts applied to place the wrist in maximum extension for 2 weeks, followed by 10 weeks of movement training aimed at decreasing weakness (electrical stimulation and progressive resistance exercises) and improving active movement. There were 4 levels of movement training (level 0–3) to allow training to be individualized for each participant's ability. Participants were encouraged to practice for 60 minutes per day, 7 days a week during the 10 weeks. Patients in the control group received a handout describing stretches and arm and hand exercises.	(GAS), Box and Block Test (BBT) **Secondary outcomes:** Spasticity (Tardieu scale), range of motion (ROM), pain (10 cm VAS, 0-10)	There was no significant difference between groups in mean spasticity scores at baseline (2.0 vs. 1.9) or at 3 months (1.7 vs. 1.5). Mean difference in change scores=0.1 (95% CI −0.3 to 0.4). There was no significant difference between groups in mean wrist extension ROM (degrees) at baseline (35 vs. 38) or at 3 months (47 vs. 44). Mean difference in change scores=5 (95% CI −4 to 13). There was no significant difference between groups in mean pain scores at baseline (1.9 vs. 1.9) or at 3 months (1.0 vs. 1.1). Mean difference in change scores=0.0 (95% CI −0.9 to 0.8).
Devier et al. 2017 **USA** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☒	29 patients with post-stroke upper limb spasticity (MAS ≥3 in the wrist and/or finger), > 6 months since stroke. Mean age was 59 years, 72% were men. Mean time since stroke was 6 years.	All patients received BTX-A injections into 4 required finger and wrist muscles. Patients were eligible for up to 4 additional injections if MAS scores were ≥2, 3 weeks after the last injection. Patients were then randomly assigned to 24 weeks of weekly upper limb rehabilitation (OT/PT) within 2 weeks after injection at the rehabilitation centre + one hour of daily home exercises, or no rehabilitation.	**Primary outcome:** Fugl Mayer Assessment (FMA) **Secondary outcomes:** Modified Ashworth Scale (MAS), Disability Assessment Scale (DAS)	19 patients were reinjected at week 12 and 7 at week 15. At weeks 20 and 27, there was significantly greater improvement in mean total FMA scores in the additional therapy group. There was improvement in DAS and MAS scores in both groups over the study period, with no significant differences between groups.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Demetrios et al. 2014 **Australia** **Prospective study**	NA	59 patients with upper and/or lower limb spasticity (MAS ≥ 2) following stroke, that was interfering with function or causing a clinical problem. Median age was 61 years, 72% were men. Mean time since stroke was 2.5 years.	All participants received individualized BTX-A injections (Botox, Dysport) in their affected limb/s. Patients were assigned to receive a high intensity ambulatory rehabilitation program (≥ 3 sessions, one-hour each for approximately 10 weeks) or usual rehabilitation (≤2 sessions, same duration).	**Primary outcome:** Proportion of participants achieving ≥50% of their goals (using Goal Attainment Scaling: GAS) and GAS T-score change at 12 weeks. **Secondary outcomes:** Modified Ashworth Scale (MAS), Arm activity measure (ArmA) Assessments were conducted at 6, 12 and 24 weeks	40 patients received upper limb injections (21 in high intensity and 19 in usual care groups) and 37 received lower limb injections. 9 patients in each group had both limbs injected. There were no significant differences between groups in the percentage of patients who achieved ≥50% of their goals at 6 (67.9% vs. 64.5%), 12 (75.0% vs. 77.4%) or 24 weeks (78.6% vs. 61.3%). More patients injected in the upper limb achieved their goals in the high intensity therapy group at 24 weeks compared with usual care (median GAS 3 vs. 1, p=0.052). There were no significant differences between groups in median change in GAS-T at 6, 12 or 24 weeks. There was significantly greater improvement in mean change in MAS scores in the high intensity group at 4 weeks (-1.2 vs. -0.6, p<0.05), 12 weeks (-0.8 vs. -0.3, p<0.05), but not at 24 weeks (-0.4 vs. -0.2). There were no significant differences between groups in median change in ARM A (Section A or B) at 6, 12 or 24 weeks.

Intrathecal Baclofen (ITB)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Creamer et al. 2018 **USA** **RCT** ***Spasticity In Stroke–Randomised Study (SISTERS)***	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☑	60 patients recruited from 11 rehabilitation centres in Europe and the US with chronic stroke with spasticity in ≥2 extremities and an Ashworth Scale (AS) score ≥3 in at least two affected muscle groups in the lower extremities. Mean age was 56 years. 70% were men. Mean time since stroke was 4.6 years.	After a run-in period (which varied from 2-25 or 21 days, depending on group assignment), patients were randomized 1:1 to ITB or conventional medical management CMM) with a combination of oral antispastic medications, comprising at least one of oral baclofen, tizanidine, diazepam (or other benzodiazepines), or dantrolene. Both treatment arms received standardized physiotherapy throughout the trial.	**Primary outcome:** Change in AS scores of the lower limb **Secondary outcomes:** Change in AS scores of the upper limb, FIM Outcomes were assessed at baseline, 3 and 6 months.	24 patients in each group completed the trial. The most common oral antispastic medications taken during the randomized period were oral baclofen (mean daily dose, 37.2 mg) and tizanidine (6.3 mg). The mean daily ITB dose increased from 79.0 µg at implantation to 296.6 µg at month 6. The mean AS upper extremity score in both groups at baseline was approximately 2.7. At 6 months, the mean reduction in scores was significantly greater in the ITB group (-0.66 vs. -0.17, p=0.0042). At 6 months, there were no significant differences between groups in the mean improvement in total FIM scores or motor or cognition subscores from baseline. Total adverse events and treatment-emergent serious adverse events occurred more frequently in the ITB group.
Meythaler et al. 2001 **USA** **Crossover RCT**	Screening period: Patient ☑ Assessor ☑ Open-label portion: Patient ☒ Assessor ☒ ITT: ☒	21 patients 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. Mean age was 53 years. Time since stroke was >6 months.	Patients 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. Patients 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.	There was a significant improvement in mean AS scores from baseline to 12 months (3.2 ± 1.1 to 1.8 ±0.09, p<0.0001). There were no significant improvements in mean spasm scores or reflex scores from baseline to 12 months (0.7±1.0 to 0.5, and 2.4 ±0.8 to 1.5, p=ns (12-month result extrapolated from figures) Several mild and transient adverse events were reported.

Centrally Acting Oral Agents

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Güntürk et al. 2022 **Turkey** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☒ ITT: ☑	29 patients with spastic hemiparesis (MAS grades 2-4) associated with chronic stroke. Median age was 52 years, 69% were men. Median time since stroke was 21 months.	Patients were randomized to receive treatment with BTX-A (total dose 100-300 U) or oral baclofen (total dose 3-80 mg daily). Patients in both groups received a physical therapy and rehabilitation program during the 6-week study period (60 minutes/day, 5x/week)	**Primary outcome:** MAS **Secondary outcomes:** Pain (10 cm VAS), Barthel Index (BI), Brunnstrom motor staging (upper extremity, hand) Assessments were conducted at baseline and at 6 weeks.	Median elbow, wrist and finger MAS scores improved significantly at 6 weeks, with no significant differences between groups. Median wrist and finger MAS scores in both groups decreased from 3 to 2, while median elbow MAS scores decreased from 3 to 2 in the BTX-A group and from 2.5 to 2 in the baclofen group. There was no significant improvement in median Brunnstrom motor staging scores in the upper extremity within, or between groups. The median hand score was significantly higher in the BTX-A group at 6 weeks (from 3 to 4), with no change in the baclofen group (median score of 3 at baseline). There was significant improvement in median VAS pain scores in both groups with no significant difference between groups. There was no significant improvement in median BI scores within, or between groups at 6 weeks.
Yazdchi et al. 2013 **Iran** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☒	68 patients with post-stroke spasticity (MAS ≥2) of the upper limb. Mean age was 66 years, 57% were men. Time since stroke onset was >3 months.	Patients were randomized 1:1 to receive BTX-A (Dysport, max dose 1,000 U) vs. oral tizanidine (TZD), maximum dose of 24 mg/day for 12 weeks.	**Primary outcomes:** MAS, ARAT Assessments were conducted at baseline, 12 and 24 weeks.	There was significantly greater reduction in mean MAS scores for the elbow and wrist joints over the study period in the BTX-A group. BTX-A: Elbow joint 3.32 (baseline), 2.17 (12 weeks), 1.79 (24 weeks) TZD: 2.79 (baseline), 2.67 (12 weeks), 2.32 (24 weeks) BTX-A: Wrist joint 3.13 (baseline), 2.2 (12 weeks), 1.56 (24 weeks) TZD: 2.77 (baseline), 2.65 (12 weeks), 2.31 (24 weeks) There was significantly greater reduction in mean ARAT scores over the study period in the BTX-A group.

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					BTX-A: 1.79 (baseline), 5.64 (12 weeks), 10.79 (24 weeks) TZD: 11.02 (baseline), 11.08 (12 weeks), 11.35 (24 weeks). 13 patients discontinued TZD when the dosage reached 24 mg, due to sedation and dizziness. No adverse events were reported in BTX-A group.
Simpson et al. 2009 **USA** **RCT**	CA: ☑ Blinding: Patient ☑ Assessor ☑ ITT: ☑	60 patients with stroke (n=49) or traumatic brain injury (n=11) of at least 3 months duration with a MAS score of ≥3 of the wrist flexors and difficulty with dressing or hygiene. Mean age was approximately 52 years, 55% were men.	Patients were randomized to receive BTX-A + oral placebo (average of 400 U, n=20); tizanidine (maximum dose of 36 mg/day, n=21) + oral placebo or placebo injection + oral placebo (n=19). 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. Study duration was 22-24 weeks.	**Primary Outcome:** Modified Ashworth Scale (MAS) wrist **Secondary Outcome:** Disability Assessment Scale, Assessments were conducted at baseline, 3, 6,12 and 18 weeks	Mean change from baseline to week 3 in MAS scores: BTX-A: -1.55 ± 1.2; tizanidine: -0.25 ± 0.64; placebo: -0.67 ± 0.91, p<0.001 (BTX-A was more effective compared with other 2 groups). The differences persisted at week 6, but by weeks 18 and 22 there appeared to be no differences between the groups. Results from inferential statistics not reported, The choice of the Principal Therapeutic Target (PTT) on the DAS was dressing (32.2%), hygiene (28.8%), cosmesis (23.7%) and pain (10.2%), with the remainder being combinations of these categories. There was a non-significant trend to a greater reduction in PTT at week 6 in the BTX-A group (BTX-A: -1.13; TZD: -0.47; placebo: -0.67; p = 0.20). The cosmesis domain of the DAS improved at week 6 in the BTX-A group as compared with TZD and placebo (BTX-A: -1.00, TZD: + 0.12; placebo: -0.16), p=0.003). There were no group differences in other domains of the DAS. Early terminations: BTX-A-A group: 6; tizanidine group: 8; placebo: 5 Number of adverse events: BTX-A group: 8; tizanidine group n=15; placebo group: n=10
Gelber et al. 2001	NA	47 patients, recruited from 4 centres at least 6 months post stroke with	All patients received a maximum daily dose of tizanidine 36 mg/day, titrated	**Primary Outcomes:** Modified Ashworth Scale (MAS), elbow, wrist,	32 patients completed the study. There was a significant decrease in mean UE MAS

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USA **Single group intervention study**		moderate spasticity (MAS scores of 2 or 3 in major muscle groups) with functional limitations or pain. Mean age was 61 years, 57% were men. Mean chronicity of stroke was 30 months.	in 2 mg increments. The drug was tapered off after 16 weeks.	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) Outcomes were assessed at baseline and weeks 16 and 18.	score from baseline (9.03) to week 16 (6.47). At week 18 (off-meds) MAS was 7.46. There were no significant decreases in muscle strength using any of the BMRC sub scales. There were no significant improvements 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. There was no significant decrease in the frequency of pain, but there was a decrease in the intensity of pain at week 16 (1.6 ± 0.20 to 1.4 ± 0.23, p=0.038). There was significant improvement in disability assessed by the physician ay week 16 (2.5 ± 0.12 to 1.9 ± 0.19, p<0.0001). There was no significant improvement in BI scores at week 16 (80.2 ± 2.7 to 81.1 ± 2.9, p=ns) 89% of subjects reported at least 1 adverse event. 28% of subjects discontinued the study due to an adverse event.
Medici et al. 1989 **Uruguay** **RCT**	CA: ☒ Blinding: Patient ☑ Assessor ☒ ITT: ☒	30 patients with moderate or severe post-stroke spasticity. Mean age was 50 years, 80% were men. Mean time since stroke onset was 3.5 years.	Patients were randomized 1:1 to receive maximum doses of 20 mg tizanidine (TZD) or 50 mg baclofen, provided in 3 daily doses for 12 months.	**Primary outcomes:** Symptoms associated with spasticity: muscle tone (Ashworth scale), muscle spasms (score 0 to 4), clonus (score 0 to 2), (decreased) muscle strength (0-5) **Secondary outcomes:** Disability (Pedersen scale), patients' self-assessment of disability, physician's global assessment of clinical changes	25 patients completed the study. At 12 months, there was significant improvement in muscle tone in patients in both groups (13/15 TZD group and 11/14 baclofen group). The difference in proportions between groups was not significant. At 12 months, 5/8 patients in the TZD group reported improvement in spasms vs. 5/6 patients in the baclofen group. There were no significant within, or between-group differences. At 12 months, 5/7 patients in the TZD group reported improvement in clonus vs. 4/5 patients in the baclofen group. There were no significant within, or between-group differences.

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					At 12 months, 8/15 patients in the TZD group reported improvement in muscle strength vs. 3/14 patients in the baclofen group. There were no significant within, or between-group differences. At 12 months, 6/15 patients in the TZD group reported improvement in the upper extremity portion of the Pedersen Scale vs. 6/14 patients in the baclofen group. Patients in both groups reported significant improvement in their self-assessment of disability due to spasticity, with no significant difference between groups. Patients in both groups improved significantly according to the physician's global assessment of clinical changes, with no significant difference between groups. No patients in the TZD group discontinued the medications vs. 3 in the baclofen group.
Bes et al. 1988 **France** **RCT**	CA: ☒ Blinding: Patient ☑ Assessor ☒ ITT: ☒	105 patients (89 with stroke, 16 with brain injury) with spasticity interfering with daily function. Mean age was 51 years, 73% were men. Mean time since stroke was 21 months.	Patients were randomized to receive a maximum dose of 24 mg tizanidine (TZD, n=51) or 30 mg diazepam (n=54) per day for 8 weeks.	**Primary outcomes (upper):** Duration of contraction in the stretch reflex of the forearm flexors, angle of contracture, biceps muscle strength, investigators' assessment of patients' clinical response to treatment	15 patients on diazepam and 6 patients on TZD discontinued treatment early due to side-effects. At 8 weeks, patients in both tizanidine and diazepam reduced the duration of contractions in the forearm flexors and increased the angle at which contraction occurred, but there were no significant differences between the groups. There was improvement in the strength of the forearm flexors in both groups (35.5% TZD and 33.4% diazepam). There was improvement in the investigators' assessment of patients' clinical response to treatment (48.9% in the TZD vs. 50.0% in the diazepam group).

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					Drowsiness and fatigue were the most commonly reported adverse events in both groups.

Extracorporeal Shockwave Therapy (ESWT)

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Cabanas-Valdés et al. 2020 **Spain** **Systematic review & meta-analysis**	The mean PEDro score was 7.25 points (range 3–9)	16 RCTs, including 764 participants who had sustained an ischemic or hemorrhagic stroke and had residual hemiparesis and spasticity. Most studies included persons in the chronic stage of stroke. Mean age ranged from 47 to 69 years, 34% were women.	Trials examined the effect of extracorporeal shockwave therapy (ESWT) vs. sham therapy (n=2), or ESWT + conventional therapy vs. conventional physiotherapy.	**Primary Outcomes:** Upper limb spasticity and function, pain Outcomes were assessed in the very short-term (immediately to 24 hours), short-term (from 24hours to 3 weeks), medium-term (from f4 to 12 weeks) and long term (>12weeks)	ESWT vs. sham therapy was associated with a significant reduction in MAS scores compared with therapy alone (SMD=-0.28, 95% CI -0.54 to -0.03). ESWT plus conventional physiotherapy was associated with a significant reduction in MAS scores compared with therapy alone (SMD=-0.94, 95% CI -1.25 to -0.63). ESWT plus conventional physiotherapy was associated with a significant improvement in FMA scores compared with therapy alone (SMD=0.95, 95% CI 0.61 to 1.29). ESWT plus conventional physiotherapy was associated with a significant reduction in pain scores compared with therapy alone (SMD=-1.63, 95% CI -2.05 to -1.22). The effects for all outcomes were significant when assessed in the very short term, short term, medium term and long term.
Li et al. 2016 **China** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☒	60 patients with stable spasticity in the wrist and hand (≥1+ MAS). The duration of spasticity was approximately 60 months. Mean age was approximately 56 years, 68% were men.	Patients were randomized 1:1:1 to receive one session of radial ESWT (rESWT) per week for 3 consecutive weeks (group A) vs. a single session of rESWT (group B); vs. one session of sham rESWT per week for 3 consecutive weeks (group C).	**Primary outcomes:** Modified Ashworth Scale (MAS) of the hand and wrist, **Secondary outcomes:** Fugl-Meyer Assessment (FMA) of hand function and wrist control	There was significant improvement in mean MAS scores for both hand and wrist in the active rESWT groups from baseline to 16 weeks, with no significant improvement in the sham group. At 16 weeks, the mean MAS scores for both hand and wrist were significantly better in group A vs. group B, as were the scores of group A vs. group C. There was no significant difference in mean MAS scores for group B vs. group C.

Robotics

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Veerbeek et al. 2017 **Netherlands** **Systematic review & meta-analysis**	Median PEDro score was 6.	34 RCTs including 1,362 participants with upper limb impairment following stroke. Mean age ranged from 43 to 76 years. Sex distribution was not reported.	Trials compared robot treatment vs. nonrobotic treatment. Treatment was provided most frequently from 20-60 minutes/day, 3-5 x/week for 2-12 weeks. The most commonly used robotic devices were the MIME robot, the BiManuTrack, the NeReBo, the MIT MANUS, and the InMotion Shoulder Elbow Robot.	**Spasticity outcomes:** Modified Ashworth Scale (MAS)	Muscle tone in the paretic arm, assessed using MAS was significantly improved following treatment in the control group (SMD=0.24, 95% CI 0.04 to 0.44; 3 RCTs, n= 429 persons). Robotic treatment was not associated with significant improvement in pooled muscle tone scores (SMD −0.16, 95% CI −0.55 to 0.23; 4 RCTs, n= 107 persons) for the elbow flexors or the wrist flexors (SMD=0.28, 95% CI −0.91 to 1.46; 3 RCTs, n=54 persons) for the wrist flexors.
Lee et al. 2016 **Korea** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☒ ITT: ☒	58 patients with upper limb spasticity (MAS >1) following stroke admitted to an inpatient rehabilitation unit. Mean age was 51 years, 66% of persons who completed the trial were men. Mean time since stroke was 41 days.	In addition to conventional therapy, patients were randomized to receive robot-assisted therapy with the Neuro-X upper limb training robot or no robot therapy. Training was provided for 30 min, 2x/d, 5x/wk, for 2wks.	**Primary Outcomes:** Modified Ashworth Scale (MAS) of the elbow flexor and shoulder adductor **Secondary outcomes:** Manual Muscle Test (MMT); Manual Function Test (MFT); Brunnstrom Stage (BBS); Modified Barthel Index (MBI). All measures were evaluated at baseline and post-intervention.	There were significant improvements after treatment in MAS scores in both groups, with no significant differences between groups. Mean difference (SD) from baseline (Elbow flexor): –0.41±0.50 (robot) vs. –0.23±0.43 (control) Mean difference (SD) from baseline (shoulder adductor): –0.36±0.49 (robot) vs. –0.23±0.43 (control) There were significant improvements in both groups on all the secondary outcomes from baseline to end of treatment with no significant differences in mean change from baseline scores between groups. 22 patients in each group completed the trial.
Taveggia et al. 2016 **Italy** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☒	54 patients aged 18-80 years admitted from 3 rehabilitation units with self-reported functional impairments of their upper extremities following stroke. Mean age was 71 years, 57% were women. Mean time	Patients were randomized to receive a passive mobilization of the upper limb through the robotic device ARMEO Spring + conventional therapy or traditional passive mobilization of the limb. Treatment was provided for 6 consecutive weeks (5 days/week) in both groups.	**Primary Outcomes:** Functional Independence Measure (FIM), Motricity Index (MI). **Secondary Outcomes:** Modified Ashworth Scale (MAS), pain (VAS).	There was significant improvement in both groups in mean MAS scores from baseline to end of treatment and baseline to end of follow-up, with no significant difference between groups in the mean change score at end of treatment or follow-up. There was significant improvement in both groups in mean VAS pain scores from baseline to end of treatment and baseline to end of follow-up, with no significant difference between groups in the mean

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		since stroke ranged from 0.5 to 12 months.		Outcomes were evaluated at baseline, after the intervention and at 6wk post intervention.	change score at end of treatment. There was significantly greater improvement in the robot group at the end of follow-up.
Masiero et al. 2014 **Italy** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☑	34 patients admitted to a stroke unit with upper limb impairment. Mean age was 65 years, 59% were men. Mean time since stroke was 9 days.	Patients were randomized to receive standard therapy (65% of exercise time) associated with robotic (NeReBot) training (35% of exercise time) or standard therapy only. All participants received total daily rehabilitation for 120 minutes, 5 days per week, for 5 weeks.	**Primary Outcomes:** Modified Ashworth Scale (MAS), Medical Research Council (MRC), Fugl-Meyer Assessment (FMA-UE), Functional Independence Measure (FIM), Box and Blocks Test (BBT), dexterity, Frenchay Arm Test (FAT). All assessments were performed at baseline, at the end of therapy time, at 3 months and at 7 months after entry.	There were no significant between-group differences in median MRC, FMA-UE, FIM, BBT, FAT or MAS from baseline to follow-up. Median baseline MAS scores in the robot and control groups were 0 and 0, respectively. At 7 months the median scores were 0 and 0.5.

Neuromuscular Electrical Stimulation (NMES)

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Qian et al. 2017 **Hong Kong** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☑	24 participants with upper limb motor deficits following stroke. Mean55 in the NMES group and 65 years in the control group, 63% were men. Mean time since stroke ranged from 14 to 148 days.	Participants were randomized to receive either upper limb motor training using an EMG-driven NMES robotic arm, or traditional therapy. Each participant received a total of 20 sessions with the robot, at an intensity of 5 sessions/wk, 1session/d, within 1mo.	**Primary Outcomes:** Fugl Meyer Assessment (FMA-UE), Action Research Arm Test (ARAT), Modified Ashworth Scale (MAS), Functional Independence Measure (FIM). Outcomes were assessed at pre-, post-intervention and at 3 mo	There were significant differences between the groups in the pre-post and pre-3mo changes in FMA-UE scores (total score, shoulder/elbow, and wrist/hand scores) with significantly greater improvement in the NMES group. There was significant greater improvement in the mean MAS scores in the elbow, wrist and finger from baseline to follow-up in the robot group. Mean MAS scores increased significantly from baseline to end of treatment and to end of follow-up in the control group.

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				follow-up.	NMES differences between groups in the pre-post and pre-3mo changes in the MAS for elbow and wrist (all p<0.05); only the change in MAS for finger at pre-3mo was significantly different between the groups (p<0.001). There was no significant difference between the groups in mean ARAT and FIM score changes.
Miyasaka et al. 2016 **Japan** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☒ ITT: ☒	30 patients admitted to hospital following first-ever stroke with upper limb paresis. Mean age was 65 years in the robot only group and 57 years in the robot + NMES group. 70% were men. Mean time since stroke was 66 days.	Patients were randomized 1:1 to an experimental group that received robot training with NMES or a control group that received robot training only. Training was performed 1h/d 5x/d for 2wk.	**Primary Outcomes:** Active Range of Motion (ROM), Fugl Meyer Assessment (FMA-UE) total score, FMA-shoulder/ elbow. Outcomes were assessed before and after the intervention.	Only the experimental group demonstrated a significant improvement on ROM for shoulder flexion and shoulder abduction (p<0.01). There were significant differences between the groups in mean active ROM (p<0.05). Within-group differences revealed that both groups improved on the FMA-shoulder/elbow measure at post intervention (p<0.01), and on the FMA-UE total score (experimental group: p<0.01; control group: p<0.05). No significant between-group differences were groups on the FMA-UE.
Stein et al. 2015 **Brazil** **Systematic review & meta-analysis**	Adequate randomization was described in 27 trials, adequate concealed allocation was described in 8 trials. Outcome assessors were blinded in 19 trials. A description of losses and exclusions was provided in 25 trials and intention-	29 RCTs including 940 participants with upper or lower limb spasticity following stroke. Mean age ranged from 45 to 74 years. Time since stroke was not reported.	Trials compared the use of NMES with or without cointerventions with a control condition. Control conditions included conventional therapy and sham NMES, among others.	**Primary Outcomes:** Modified Ashworth Scale (MAS) of the wrist and elbow **Secondary Outcomes:** Range of motion (ROM) for upper extremity (wrist and elbow).	NMES was not associated with significant improvement in wrist spasticity (MAS MD=0.12, 95% CI -0.41 to 0.64; 6 RCTs). Only 1 RCT included participants in the acute/subacute stage of stroke recovery, with the remainder evaluating stroke patients in the chronic stage. NMES was not associated with significant improvement in elbow spasticity (MAS MD=-0.39, 95% CI -0.89 to 0.11, 4 RCTs). All RCTs were in chronic stroke participants. NMES was not associated with significant improvement wrist ROM (MD=0.46, 95% CI -2.28 to 3.21, 4 RCTs). Only 1 RCT included participants in the acute/subacute stage of stroke recovery, with the remainder evaluating stroke patients in the chronic stage. NMES was associated with significant improvement

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	to-treat analysis was performed in 7 trials.				wrist ROM (MD=4.57, 95% CI 0.57 to 8.57, 3 RCTs). All RCTs were in chronic stroke participants.
Cui et al. 2015 **China** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☑	45 patients admitted to a single centre with hemiplegia following stroke. Mean age was approximately 62 years, 67% were men. Mean time since stroke was approximately 13 weeks.	Participants were randomized to one of three groups: (1) 12hr-NMES group which received 12 hours of NMES and conventional rehabilitation, (2) 30min-NMES group which received 30min of NMES and conventional rehabilitation, or (3) control group which received conventional rehabilitation. Electrical stimulation treatment was provided for 12hr or 30min session/d respectively, 6d/wk for 4wk.	**Primary Outcomes:** Modified Ashworth Scale (MAS), Fugl Meyer Assessment-proximal (shoulder/elbow) (FMA-p), Fugl Meyer Assessment-distal (wrist/hand) (FMA-d), Action Research Arm Test (ARAT). Outcomes were assessed at pre-, post-intervention and at 8 wk follow-up.	There were no significant within-group or between-group differences in mean MAS scores in the wrist or elbow at 4 or 8 weeks. *Elbow* 12-hr NMES, 30-minute group and control group scores Baseline: 1.40 vs. 1.53 vs.1.53 Post treatment: 1.5 vs. 1.67 vs. 1.80 Follow-up: 1.67 vs. 1.69 vs. 1.71 *Wrist* 12-hr NMES, 30-minute group and control group scores Baseline: 1.40 vs. 1.73 vs.1.53 Post treatment: 1.36 vs. 1.67 vs. 1.80 Follow-up: 1.67 vs. 1.69 vs. 1.57 All groups demonstrated within-group improvements at 4 and 8wk on the FMA-p, FMA-d and the ARAT (all $p<0.05$). Significant improvements in the FMA-d were found in the 12h-NMES group compared with the NMES group at 4 and 8wk ($p=0.007$; $p=0.003$). Significant improvements in the FMA-p were obtained in the 12h-NMES group compared with the control group at 4 and 8wk ($p=0.01$; $p=0.000$).
Shimodozono et al. 2014 **Japan** **RCT**	CA: ☑ Blinding: Patient ☑ Assessor ☒ ITT: ☑	27 patients admitted to an inpatient rehabilitation unit following stroke with onset 3-13 weeks, with severe arm impairment. Mean age was 61 years, 74% were men. Mean time since stroke was approximately 6.5 weeks.	Patients were randomized 1:1:1 to the repetitive facilitative exercise (RFE)-under-surface neuromuscular electrical stimulation (NMES) group was given 100-150 repetitions of standardized movements of shoulder, elbow, wrist joints of their	**Primary Outcomes:** Fugl Meyer Assessment (FMA-UE), Active Range of Motion (ROM). Outcomes were assessed at baseline and at post intervention.	All groups demonstrated a significant improvement in ROM elbow extension over the study period ($p=0.034$). The RFE-NMES group demonstrated a significantly greater improvement on the ROM of the elbow compared to the control group ($p=0.003$) but not compared not to the RFE group.

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			affected arm with concurrent low amplitude NMES for each corresponding musculature vs. the RFE-only group, which received the same exercise regimen, without NMES vs. a control group which received a conventional rehabilitation programme without NMES. All experimental groups were provided for 4 weeks, 40 minutes per day, for 5 days per week.		There was no statistically significant difference between groups over the study period regarding of ROM on shoulder flexion and wrist dorsiflexion. There were statistically significant differences between groups across the study period for the FMA-UE (p=0.014). The RFE-NMES group demonstrated a significantly greater improvement on the FMA-UE compared to the control group (p=0.003) but not to do RFE group.
Malhotra et al. 2013 **UK** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☑	90 patients admitted to an acute stroke unit, with no useful hand function. Median age was 74 years, 49% were men. Median time since stroke was 3 weeks.	Participants were randomized to receive surface NMES plus physiotherapy (PT) or PT only. Duration: 30 min (2-3x/d), 5d/week for 6 weeks NMES & 45 min/session PT.	**Primary Outcomes:** Pain (5-point verbal rating pain scale), spasticity (EMG muscle activity during passive extension of the wrist), contractures (passive ROM stiffness at slow stretch at the wrist), Assessments were conducted at baseline assessment, 6, 12, 24 and 36 weeks after recruitment.	At the end of the intervention the mean pain score was unchanged in the NMES group but had increased in the control group (0.5 vs. 1.1, mean difference in change =0.6, 95% CI 0.05 to 1.15), but the difference was no longer significant at the end of follow-up (0.4 vs. 1.0, mean difference in change 0.6, 95% CI −0.04 to 1.24). There were no significant differences in mean scores or mean change scores between groups at any of the assessment points for contracture or spasticity. At the end of treatment 23 patients had died.

Somatosensory Stimulation

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Alashram et al. 2019 **Italy** **Systematic review and meta-analysis**	Trials were at high of unclear risk of bias for CA (4 trials), blinding (n=5) and incomplete outcome data reporting (n=4).	8 RCTs including 268 persons with upper-limb hemiparesis following stroke. Mean age ranged from 49.5 to 68.6 years, 28.7% were women. Mean time since stroke was < 6 months (n=1), >12 months (n=6) and was not stated in one trial.	Trials compared focal muscle vibration (FMV) +/- conventional physiotherapy vs. physiotherapy or placebo. Treatment was provided 2-5 x/week, for 1-8 weeks.	**Primary Outcome:** Modified Ashworth Scale (MAS)	No pooled data analysis was conducted. MAS scores were reduced significantly following FMV treatment compared with the control group in 5 trials. Effect sizes, when reported, ranged from 0.10 to 0.52.
Cai et al. 2017 **Australia** **Systematic review & meta-analysis**	All trials were at unclear risk of bias for CA and blinding of patients. Risk of bias was low in 9 trials for randomization; risk of bias was low in 3 trials for blinding of outcome assessors.	22 RCTs (1425 subjects), of which 7 evaluated upper extremity outcomes following stroke. Of these, 4 RCTs evaluated spasticity, and 4 RCTs evaluated motor function (1 RCT evaluated both). Of these, 3 did not report on the time post stroke, 1 evaluated the participants in the acute phase of stroke recovery, and 3 corresponded to the sub-acute phase of stroke.	Interventions for the 7 RCTs evaluating upper limb recovery included: electroacupuncture combined with rehabilitation versus rehabilitation only (n=6), and electroacupuncture combined with rehabilitation and baclofen versus rehabilitation with baclofen (n=1).	**Primary Outcomes:** Modified Ashworth Scale (MAS). **Secondary Outcomes:** Fugl Meyer Assessment (FMA), adverse events.	Electroacupuncture was associated with a significant reduction in mean MAS (SMD=-0.57, 95% CI -0.84 to -0.29, 4 RCTs), but did not improve motor function (FMA SMD=13.32, 95% CI -6.53 to 33.17, I4 RCTs). Adverse events: No reporting.
Calabro et al. 2017 **Italy** **RCT**	CA: ☒ Blinding: Patient ☒ Assessor ☑ ITT: ☑	20 patients with first ever left hemisphere stroke with impairment and spasticity of the upper limb. Mean age was 66 years, 45% were men. Mean time since stroke was 5.5 months.	Participants I were randomized 1:1 to receive Armeo-Power robotic training coupled with focal muscle vibration therapy (experimental group) or Armeo-Power training only (control group). Therapy was provided for one hour/ 5 days/week for 8 weeks (40 sessions in total).	**Primary Outcomes:** Reduction in MAS score >1 (responder) **Secondary Outcomes:** Fugl Meyer Assessment (FMA), Functional Independence Measure (FIM)-6 items Outcomes were assessed	10/10 patients in the experimental group were responders vs. 3/10 in the control group. Mean MAS scores were decreased significantly from baseline to end of treatment and from baseline to end of follow-up in the experimental group without significant corresponding decreases in the control group. The differences between groups were significant at both assessment points (p<0.001 for both).

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				at baseline, end of treatment and at one-month follow-up.	There was significantly greater improvement in FMA and FIM scores in the experimental group at the end of treatment and at follow-up.

Non-invasive Brain Stimulation

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
rTMS					
Wang et al. 2022 **China** **Systematic review & meta-analysis**	The risk of bias was assessed as low for most of the domains, with the high risk for blinding in most trials.	18 RCTs, representing 14 unique studies including 236 persons with post stroke spasticity. Mean age ranged from 49 to 80 years. Time since stroke was not reported.	Trials compared non-invasive brain stimulation interventions including rTMS (n=11) or tDCS (n=7) with sham stimulation +/- co-interventions.	**Primary outcome:** Modified Ashworth Scale	rTMS was associated with a significant reduction in mean MAS scores compared with the control condition (MD= −0.40, 95% CI −0.56 to −0.25). Low-frequency rTMS was associated with the greatest effect (MD = −0.51, 95% CI −0.78 to −0.24). tDCS was associated with a significant reduction in mean MAS scores compared with the control condition (MD=−0.65, 95% CI −1.07 to −0.22). Anodal stimulation was associated with the greatest effect (MD = −0.74, 95% CI −1.35 to −0.13).
McIntyre et al. 2017 **Canada** **Systematic review & meta-analysis**	PEDro scores for the 2 RCTs were 8 and 9.	10 studies (2 RCTs) including 273 participants with chronic post stroke spasticity of the upper limb. Mean age ranging from 55.0 to 64.6 years, 66% were men. Mean stroke duration ranged from 6 months to 10 years.	In the 2 RCTs, trials compared TMS + conventional rehabilitation vs. sham stimulation; and rTMS + conventional rehabilitation + botulinum toxin vs. rTMS without botulinum toxin. In the remaining noncontrolled trials, persons received contralesional or bihemispheric +/- conventional rehabilitation, +/- additional medication (levodopa or botulinum toxin). On average, the total number of minutes of rTMS applied ranged from 400 to 480 minutes over 2 weeks,	**Primary Outcome:** Modified Ashworth Scale (MAS) for elbow, wrist, and finger. Outcomes were assessed at baseline and following intervention	Using data from 2 uncontrolled studies, rTMS treatment was associated with significant improvement in spasticity of the elbow flexors (SMD=0.53, 95% CI 0.046-1.02). Using data from 2 uncontrolled studies, rTMS treatment was associated with significant improvement in spasticity of the elbow flexors (SMD=0.53, 95% CI 0.046-1.02). rTMS treatment was not associated with significant improvement in spasticity using data from 2 RCTs (SMD=0.34, 95% CI -0.30 to 0.99). Using data from 5 uncontrolled studies rTMS treatment was associated with significant improvement in spasticity of the finger flexors (SMD=0.54, 95% CI 0.4-0.74).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			and the pulse count ranged from 100 to 2400 per session.		
tDCS					
Alashram et al. 2023 **Jordan** **Systematic review**	Risk of bias scores ranged from 3/6 to 5/6	7 RCTs, including 320 participants, with post stroke spasticity. Mean age was 60 years, 69% were men. Time since stroke was <6 months in 4 trials, > 6 months in one trial and 2-9 months in 2 trials.	Trials compared treatment with tDCS intervention +/- co-intervention(s) vs. sham stimulation +/- cointerventions. The number of sessions ranged from 5-20 (10-30 minutes each).	**Primary Outcomes:** Modified Ashworth Scale (MAS) and H-reflex	5 RCTs combined the tDCS intervention and other traditional interventions. There were significant reductions in mean MAS scores following tDCS. 2 RCTs delivered tDCS intervention alone. There was no significant reduction in mean MAS scores following tDCS.
Huang et al. 2022 **China** **Systematic review & meta-analysis**	Risk of bias was generally low (or uncertain)	13 RCTs, including 924 participants, with post stroke spasticity. Mean age ranged from 45 to 68 years. Mean time since stroke ranged from 42 days to 34 months.	Trials compared treatment with tDCS +/- other treatments (e.g., conventional rehabilitation) vs. sham treatment +/- other treatments.	**Primary Outcome:** Modified Ashworth Scale (MAS)	tDCS combined with other therapies was associated with significantly greater improvement in mean MAS scores of the upper limb including the shoulder, wrist and elbow (SMD=-0.83, 95% CI -1.25 to -0.40; 12 RCTs) In subgroup analyses, effect sizes were greater for patients <60 years, subacute/chronic stroke, anodal stimulation, >20 minutes of stimulation and current intensity of 0.7 mA.
Mazzoleni et al. 2017 **Italy** **RCT**	CA: ☒ Blinding: Patient ☑ Assessor ☒ ITT: ☒	24 stroke patients with upper limb hemiparesis, within 9 to 60 days from stroke onset. Mean age was 73 years, 29% were men.	Patients were randomly assigned to the experimental (EG) or control group (CG). All participants performed wrist robot-assisted training a) in conjunction with tDCS (real stimulation for patients in EG) or b) without tDCS (sham stimulation for patients in CG). Each patient was asked to perform 5 sessions/wk, each session lasted 30 minutes, for 6 weeks of goal-directed planar reaching tasks.	**Primary Outcomes**: Fugl Meyer Assessment (FMA-UE), Modified Ashworth Scale (MAS), Motricity Index (MI), Box and Blocks Test (BBT). Outcomes were assessed before and after therapy.	There were significant improvements in both groups on the FMA-UE, FMA-wrist, MI, and BBT after the intervention ($p<0.05$ all). There as no significant improvement in mean MAS-wrist scores in either group. There were no significant between group differences for any the outcome measures after the intervention.

Abbreviations

ARAT: Action Research Arm test	CA: Concealed Allocation
CI: Confidence Interval	IQR: Interquartile Range
ITT: Intention to treat	MAS: Modified Ashworth Scale
MD: Mean Difference	N/A: Not Applicable; not assessed
NMES: Neuromuscular electrical stimulation	OR: Odds Ratio
RCT: Randomized Controlled Trial	RFE: Repetitive facilitative exercise
rTMS: repetitive transcranial magnetic stimulation	SMD: standardized mean difference
tDCS: transcranial direct current stimulation	VAS: Visual analogue scale

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