CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Rehabilitation and Recovery following Stroke Evidence Tables

Lower Limb Spasticity Following Stroke

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Rehabilitation and Recovery following Stroke Writing Group

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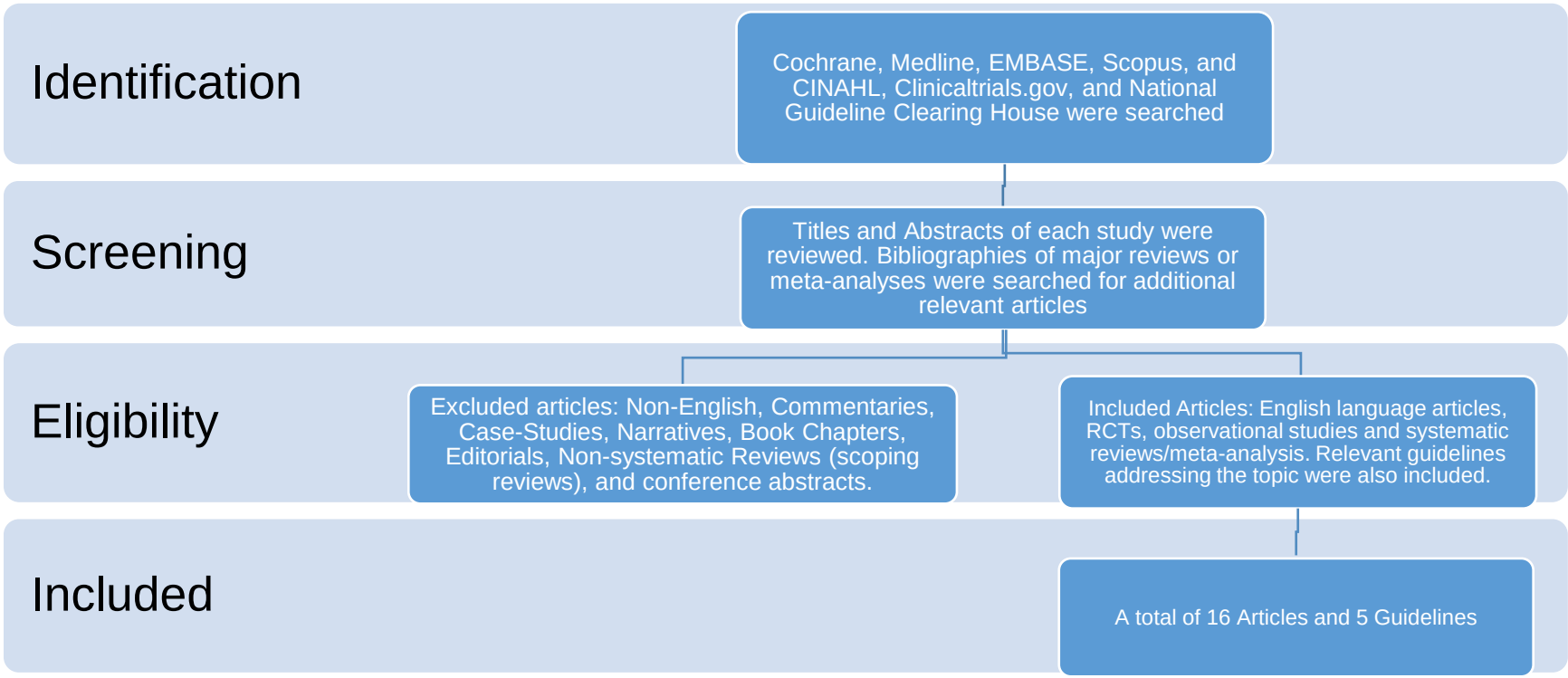
Search Strategy



Cochrane, clinicaltrials.gov, Medline, EMBASE, CINAHL and Scopus were searched using the keywords: Stroke AND (“spasticity” OR “contracture”) AND (“lower extremity” OR “lower limb”) AND (rehabilitation OR therapy OR intervention). Three new sections: shock wave therapy, stretching, and vibration were added for the 2014 update. 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 16 and 5 guidelines were included and were separated into categories designed to answer specific questions.

Published Guidelines

Guideline	Recommendations
Clinical Guidelines for Stroke Management 2017. Melbourne (Australia): National Stroke Foundation. Section 5. Rehabilitation	For stroke survivors with lower limb spasticity, Botulinum Toxin A in addition to rehabilitation therapy may be used to reduce spasticity but is unlikely to improve motor function or walking. (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) 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)
Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, Deruyter F, Eng JJ, Fisher B, Harvey RL, Lang CE, MacKay-Lyons M, Ottenbacher KJ, Pugh S, Reeves MJ, Richards LG, Stiers W, Zorowitz RD; 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**	Recommendations targeting lower limb spasticity: Targeted injection of botulinum toxin into lower limb muscles is recommended to reduce spasticity that interferes with gait function. (A) Recommendations not specific to lower limb spasticity: 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) Postural training and task-oriented therapy may be considered for rehabilitation of ataxia. (A)

Guideline	Recommendations
Intercollegiate Stroke Working Party. *National clinical guideline for stroke,* 5th edition. London: Royal College of Physicians, 2016.	**4.15 Spasticity and contractures** 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. 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. 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. 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. 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. People with stroke should only receive intrathecal baclofen, intraneural phenol or similar interventions in the context of a specialist multidisciplinary spasticity service. 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.
Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with stroke: rehabilitation, prevention and management of complications, and discharge planning. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2010 Jun. 101 p.31	(NB-recommendations not specific to the lower extremity) **4.9.1 Summary of recommendations** **Not recommended** routine resting splinting of the upper limb *Clostridium botulinum* toxin type A **Insufficient evidence** routine functional electrical stimulation robot-mediated passive therapy oral antispasticity agents intrathecal antispasticity agents alcohol neurolysis tibial nerve neurotomy
Management of Stroke Rehabilitation Working Group. VA/DoD clinical practice guideline for the management of stroke	(NB-recommendations not specific to the lower extremity) Use of antispastic positioning, range of motion exercises, stretching, splinting, serial casting or surgical correction for spasticity. **C**

Guideline	Recommendations
rehabilitation. Washington (DC): Veterans Health Administration, Department of Defense; 2010. p. 86-88.	Use of tizanidine (in chronic stroke patients), dantrolene, and oral baclofen for spasticity **B** Avoid drugs with central nervous system effects that may impair recovery **D** Use of botulinum toxin improves spasticity **B** Use of intrathecal baclofen for chronic stroke patients **B** Use of certain neurosurgical procedures **I**

Summary of Spasticity Interventions and Associated Strength of Evidence from Selected Guideline Documents

Intervention	CBPR 2013	SIGN 118 2010*	NSF 2017*	VA/DoD 2010 *	AHA/ASA 2016*	RCP 2016*
Positioning/ROM exercises	Recommended	Not included	Not recommended (routine use of stretch)	C	Recommended [C]	Recommended
Splinting	Not included	A Not recommended	Not recommended	C	Not included	Recommended (only following individualized assessment and with monitoring)
BT-type A	Recommends	Not recommended	Recommended	B	Recommended [A]	Recommended
Phenol/alcohol	Not included	I	Not included	Not included	Not included	Recommended (only in the context of a specialist multidisciplinary service)
Oral agents	Recommends (Tizanidine)	I	Not Included	B (Tizanidine for chronic), oral baclofen)	Recommended (only for generalized spastic dystonia) [A]	Recommended (baclofen, Tizanidine)
Benzodazepines	Not recommended	Not included	Not included	D Not recommended	Not included	Not Included
Electrical stimulation	Not included	I	Recommended	Not included	Recommended (NMES/vibration) [A]	Not Included
Robotic devices	Not included	I	Not included	Not included	Not included	Not Included
Intrathecal agents	Not included	I	Not included	No recommendation for UE	Recommended (only for severe spastic hypertonia) [A]	Not Included
Surgery	Not included	I	Not included	I (spasticity) C (contracture)	Not included	Not Included

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

Evidence Tables

Botulinum Toxin-Type A (BTX-A)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Rosales et al. 2016 **Philippines** **Meta-analysis**	N/A	6 RCTs including persons with stroke (n=4) and other non-progressive brain lesions (n=2), with onset <3 months previous.	Intervention comparisons included BTX-A treatment versus placebo (n=5), or versus no intervention (n=1). 3 trials targeted upper limb spasticity, and 3 trials targeted lower limb spasticity.	**Primary Outcomes:** Hypertonicity of most affected joint 4-12 weeks after treatment	Hypertonicity (n=3): SMD=-0.76, 95% CI -1.66 to 0.13, p=0.009. No separate analyses of upper vs. lower-limb were conducted.
Tao et al. 2015 **China** **RCT**	CA: ☒ Blinding: Assessor ☒ Patient ☒ ITT: ☒	23 participants within 30d of stroke onset (experimental: 24.2d; control: 23.2d)	Participants were randomly assigned to receive 200 units of BTX-A in the gastrocnemius and the posterior tibial muscle, or placebo injection in addition to rehabilitation	**Primary Outcomes:** Fugl-Meyer assessment (FMA); modified Ashworth Scale (MAS); Modified Barthel Index (MBI), step length; cadence; gait speed; 6-minute walking distance (6MWT). Assessments were carried out at baseline (week 0), 4, and 8 weeks after the injections.	The gait analysis, FMA, and MBI results were significantly improved in both groups (p<0.05). The FMA and the MBI scores by week 8 were significantly better in the treatment groups) than those in the CG (all p<0.05). The step length, cadence, speed and the 6MWT of the TG were significantly greater than those of the CG (all p<0.05). At week 8, the MAS scores in the TG were significantly lower than those in the CG (p<0.05).
Santamato et al. 2013a **Italy** **Pre-Post**	N/A	71 patients with post-stroke spasticity (MAS=2, ankle flexors); mean time since stroke 28.8±12.9 months.	Subjects received intramuscular injections of onabotulinum toxin A (BoNT-A) NT 201 in the soleus, and medial and lateral gastrocnemius with a maximum dose of 180 U (range 25-100 U per muscle).	**Primary Outcomes:** Modified Ashworth Scale (MAS), Spasm Frequency Scale (SFS) Outcomes were assessed at baseline, 30 days and 90 days after treatment.	A reduction was noted at 30 days and 90 days in MAS (p<0.001 for both) and SFS (p<0.001 for both).
Santamato et al. 2013b **Italy**	N/A	25 subjects with upper and lower limb spasticity (AS≥2, Disability Assessment Scale [DAS] ≥2, ankle flexors) with	Subjects received one set of injections of onabotulinum toxin A (BoNT-A) NT 201, in the lower limbs. A dosage of	**Primary Outcomes:** Modified Ashworth Scale (MAS), Disability Assessment Scale (DAS)	A significant reduction in spasticity was noted for both MAS and DAS at 30 days (p<0.001 for both) and 90 days (p<0.001 for both) after treatment.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Pre-Post		mean time since stroke 32.4±8.3 months.	maximum 340 U (range 250-340 U per muscle) was administered.	Outcomes were assessed at baseline, 30 days and 90 days after treatment.	
Dunne et al. 2012 **Australia** **RCT with open-label extension**	CA: ☑ Blinding: Assessor ☑ Patient☑ ITT: ☑	85 stroke patients (≥ 6 weeks post stroke), with lower extremity hypertonia (AS≥2)	Subjects received a single injection of 200 U Botox (n=28), 300 U Botox (n=28) or saline injections to the tibialis posterior, soleus and flexor digitorum longus or medial gastrocnemius.	**Primary Outcomes:** Adverse event incidence, Modified Ashworth Scale (MAS) (ankle Plantar flexors) **Secondary Outcomes:** Self-reported spasm frequency, physician rated hypertonia (7- point Likert scale). Assessments were conducted at baseline (on 2 occasions) and at 4, 8, and 12 weeks post injection	Data from the 2 Botox groups were not different and combined. Adverse events (serious): experimental group n=6, placebo group n=3. Improvement in AS≥1 at 12 weeks BT-A group vs. placebo: 16/54 vs. 5/29, p=0.22 Reduction in leg spasms at 12 weeks: BT-A group vs. placebo: 22/26 vs. 4/19, p=0.01 Improvement in Physician rating of hypertonia of ≥1 at 12 weeks BT-A group vs. placebo: 29/54 vs. 8/29, p=0.04 Improvement in pain (≥20%) at 12 weeks BT-A group vs. placebo: 8/14 vs. 1/8, p=0.02 Increase in ankle dorsiflexion (≥15%) at 12 weeks BT-A group vs. placebo: 8/54 vs. 1/29, p=0.03 Dropouts: n=5 (all experimental group)
Foley et al. 2010 **Canada** **Systematic review and meta-analysis**	N/A	8 trials (5 RCTs, 3 uncontrolled trials, 228 subjects) that examined the use of BT-A for the treatment of spastic equinovarus deformity. Subjects in all trials could ambulate with/without a device and with/without assistance for at least 5 metres Mean of median interval from stroke to entry into study was > 6 months if all trials.	Comparisons of a single injection of BT-A vs. placebo or before and after single injection. Doses varied from 190 to 400 U of Botox and 500 to 2,000 U of Dysport	**Primary Outcomes:** Gait speed Outcome was assessed at baseline and from 4 weeks to 5 months	Gait speed: SMD= 0.193±0.081, 95% CI 0.033 to 0.353, p<0.018

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Kaji et al. 2010 **Japan** **RCT**	CA: ☑ Blinding: Assessor ☑ Patient ☑ ITT: ☑	120 patients from 19 medical institutions with lower limb spasticity (MAS>3 ankle flexors) following stroke > 6 months previously	Subjects were randomized to receive a single treatment of 300 U Botox or placebo. 75 U was injected per muscle group Sites included: gastrocnemius, soleus and tibialis posterior	**Primary Outcomes:** MAS **Secondary Outcomes:** Gait pattern scale assessed using a -1 to 9-point scale, based on 3 parameters over 10m (initial foot contact, foot contact at midstance and gait assisting devices), gait speed. Clinical Global Impression scale (CGI) scored from -5 to 5. Outcomes were assessed at baseline, weeks 1,4,6,8 and 12.	Mean ±sd Δ from baseline at 12 weeks for subjects in experimental and control groups MAS: -0.56±0.69 vs. -0.40±0.58, p=0.240 (p<0.05 at weeks 4 and 8) Gait pattern scale: 0.55±1.26 vs. 0.58±1.57, p=0.775 Gait speed (sec over 10 m): -10.14±26.93 vs. -8.53±24.71, p=0.585 CGI (investigator): 0.81±1.30 vs. 0.52±1.27, p=0.166 CGI (patient): 0.49±1.53 vs. 0.49±2.18, p=0.409 Dropouts: experimental group n=6, control group n=1 Adverse events (serious): experimental group n=9%, control group n=2%

Intrathecal Baclofen (ITB)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Meythaler et al. 2001 **USA** **Randomized crossover followed by open-label follow-up**	Screening period: assessor ☑ patient ☑ Open-label portion: assessor ☒ patient ☒ ITT: ☒	21 subjects with disabling and painful intractable hypertonia (AS score of at least 3 in one affected extremity or an average spasm score of at least 2 in the affected extremities on the day of screening) following stroke of at least 6 months duration, and failure to respond to oral antispasticity medications.	Subjects were randomized to receive a screening bolus trial of either 50 µg baclofen or saline placebo. 17 subjects responded to the active drug and were then implanted with a continuous-infusion pump and continued to receive treatment for up to a year. Subjects were initiated to continued treatment at 100 µg/day with dose	**Primary Outcome:** Ashworth Scale (AS) (average of hip abduction, knee flexion, knee extension, ankle dorsiflexion) **Secondary Outcomes:** 5-point Penn Spasm Frequency Scale, 6-point reflex scale (patella, Achilles) At 1 year, data from 13 subjects were available.	Mean (± sd) scores at baseline and 12 months AS: 3.7 ± 1.0 to 1.8 ±1.1, p<0.0001. Spasm score: 1.2±1.3 to 0.6±1.0, p=ns Reflex Score: 2.4 ±1.3 to 1.0±1.3, <0.0001 3 subjects who were wheelchair dependent at the start of treatment progressed to independent ambulation with assistive devices. Adverse events: Several mild and transient adverse events were reported.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			increases up to an average of 268 ± 175 µg/day.		

Physical Therapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Kluding et al. 2008 **RCT** **USA**	CA: ☑ Blinding: Assessor ☒ ITT: ☒	16 subjects with hemiparesis persisting from 6 months to 5 years following stroke with less than 8° of passive ankle dorsiflexion ROM on the hemiparetic side.	Subjects were randomized to receive 8 sessions lasting 30 minutes each over 4 weeks of either functional task practice (FP) combined with ankle joint mobilizations or functional task practice only.	**Primary Outcomes:** Ankle ROM, ankle kinematics during sit-to-stand (STS) and gait, and lower-extremity weight-bearing symmetry during STS and static standing, Rivermead Mobility Index (RMI) Outcome measures were assessed before and after treatment.	Mean ±sd change scores for subjects in the mobilization + FP and FP groups Dorsiflexion passive ROM (deg): 5.7 ±3.1 vs. 0.2±2.6, p<0.01 Total active ROM (deg): 17.3±6.5 vs. 2.3±7.6, p<0.05 Peak dorsiflexion: STS (deg):-1.88±4.72 vs. 1.42±3.93, p=ns Peak dorsiflexion: gait (deg): 0.38±3.44 vs. 2.58±8.14, p=ns Peak weight bearing difference during STS (deg): -0.79±4.9 vs. -14.9±15.0, p<0.05 STS time (sec); -0.82±0.91 vs. 0.17±0.77, p<0.05 RMI: 0.75±0.71 vs. 0.63±1.1, p<0.05 Dropouts: n=1 (control group) Adverse events: None related to intervention

Shock Wave Therapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Santamato et al.	N/A	23 subjects with	Subjects received one	**Primary Outcomes:**	For those with Heckmatt grades I, II, and III, MAS

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
2014 **Italy** **Pre-Post**		unilateral spastic equinus foot (MAS range 1-4) 24.9±11.9 months post stroke.	extracorporeal shock wave therapy session applied with the EvoTron RFL0300; 1,500 pulses were applied at an intensity of 0.10 mJ/mm^2. Targeted muscles included gastrocnemius and soleus.	Modified Ashworth Scale (MAS), stratified by Heckmatt grade (muscle echo intensity) Patients were evaluated immediately after treatment and at 30 days post treatment.	scores were significantly reduced immediately after treatment ($p<0.001$) and at 30 days post treatment ($p<0.001$). For those with a Heckmatt grade of IV, MAS scores did not improve ($p>0.05$).
Moon et al. 2013 **Korea** **Pre-Post**	N/A	30 patients with ankle plantar flexor spasticity (MAS >1), on average 80.5±46.5 months post stroke.	Subjects received one session per week for 3 weeks of extracorporeal shock wave therapy. Targeted muscles included the musculo-tendinous junction of the medial and lateral gastrocnemius muscles.	**Primary Outcomes:** Modified Ashworth Scale (MAS), clonus score Patients were evaluated immediately, at 1 week and 4 weeks after treatment.	MAS scores showed significant decreases immediately after treatment ($p=0.002$), one week ($p=0.02$); however, effects were not maintained at four weeks post treatment. Improvements in clonus score were non-significant at both follow-up time points ($p>0.05$ for both).

Vibration

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Huang et al. 2017 **China** **Systematic review**	N/A	9 trials (266 subjects) evaluating whole body vibration on spasticity among people with central nervous system disorders. Only 4 trials were conduced in a stroke population.	6 studies involved a comparison group that performed the same exercises as the whole-body vibration group but without the vibration stimuli or with sham vibrations. 3 studies incorporated a control group that was involved in other activities (e.g. routine treatment, strength training).	**Primary Outcomes:** Spasticity	The evidence found in the stroke population is inconsistent. Overall, there is no strong evidence that the added whole-body vibration can confer additional effects on reducing spasticity post-stroke.
Liao et al. 2015 **China**	CA: ☑ Blinding:	84 participants with chronic stroke	Participants received either high intensity whole body vibration, or	**Primary Outcomes** Muscle strength (knee extension and flexion)	There was no significant Group x Time interaction found for any of the outcomes.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
RCT	Assessor ☒ Patient ☑ ITT: ☑		low-intensity whole body vibration, or sham vibration (control group), 3x/wk, for a total of 30 sessions.	**Secondary Outcomes:** Spasticity (Modified Ashworth scale), balance (Mini balance evaluation systems test), walking endurance (6-minute walk test), functional mobility (Timed up and go test), Balance self efficacy (activities-specific balance confidence scale), participation in daily activities (Frenchay activities index), perception environmental barriers (Craig Hospital Inventory of environmental Factors), Quality of life (Short form 12 health survey). Outcomes were evaluated before and after the intervention.	
Pang et al. 2013 **Hong Kong** **RCT**	CA: ☑ Blinding: Assessor ☒ Patient ☑ ITT: ☒	82 chronic stroke patients (treatment= 4.6±3.5 years, control= 5.3±4.2 years post stroke).	Patients were randomized into two groups: 1) exercise training with whole body vibration (WBV) stimulation for a maximum of 15 minutes, 3 days per week for 8 weeks, 2) control group received the same exercises without WBV.	**Primary Outcome:** MAS Participants were evaluated at baseline, immediately after the 8-week training period and 1-month follow-up.	Knee spasticity decreased in the treatment group (p=0.005) but not the control group (p=0.465); however, ankle MAS scores did not change significantly over time in either group (p>0.05).
Tankisheva et al. 2014 **Belgium** **RCT**	CA: ☑ Blinding: Assessor ☒ Patient ☑ ITT: ☒	15 chronic stroke patients (treatment= 7.71±8.6 years, control= 5.28±3.6 years post stroke).	Patients were randomized into two groups: 1) exercise training (static and dynamic squats) with whole body vibration (WBV) stimulation at	**Primary Outcome:** Modified Ashworth Scale (MAS) Patients were evaluated at baseline, upon completion of the 6-week protocol and at a	No significant differences were noted between the two groups on MAS upon completion of the protocol or at 6-week follow-up (p>0.05 for both).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			frequencies of 35Hz and 40Hz, lasting 30-60 sec, with 5 to 17 repetitions per exercise 3 times weekly for 6 weeks, 2) control group continued usual activities and did not receive a training program.	6-week follow-up.	

Abbreviations

AS = Ashworth Scale	CA = Concealed Allocation
ITT = Intention to Treat	MAS = Modified Ashworth Scale
N/A = Not Applicable	RCT= Randomized Controlled Trial
ROM = Range of Motion	

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