Objective: To investigate whether nonsurgical treatment can reduce muscle contractures in individuals with neurologic disorders. The primary outcome measure was muscle contractures measured as joint mobility or passive stiffness.

Data Sources: Embase, MEDLINE, Cumulative Index to Nursing and Allied Health, and Physiotherapy Evidence Database in June-July 2019 and again in July 2020.

Study Selection: The search resulted in 8020 records, which were screened by 2 authors based on our patient, intervention, comparison, outcome criteria. We included controlled trials of nonsurgical interventions administered to treat muscle contractures in individuals with neurologic disorders.

Data Extraction: Authors, participant characteristics, intervention details, and joint mobility/passive stiffness before and after intervention were extracted. We assessed trials for risk of bias using the Downs and Black checklist. We conducted meta-analyses investigating the short-term effect on joint mobility using a random-effects model with the pooled effect from randomized controlled trials (RCTs) as the primary outcome. The minimal clinically important effect was set at 5°.

Data Synthesis: A total of 70 trials (57 RCTs) were eligible for inclusion. Stretch had a pooled effect of 3° (95% CI, 1-4°; prediction interval (PI) = 0 to 7°; I² = 66%; \( P < 0.001 \)), and robot-assisted rehabilitation had an effect of 1° (95% CI, 969 to 97; PI = 0 to 9; I² = 73%; \( P = 0.03 \)). We found no effect of shockwave therapy (\( P = 0.56 \)), physical activity (\( P = 0.27 \)), electrical stimulation (\( P = 0.11 \)), or botulinum toxin (\( P = 0.13 \)). Although trials were generally of moderate to high quality according to the Downs and Black checklist, only 18 of the 70 trials used objective measures.

List of abbreviations: BTX, botulinum toxin; CCT, controlled clinical trial; PROM, passive range of motion; PICO, patient, intervention, comparison, outcome; PI, prediction interval; RCT, randomized controlled trial.

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Muscle contractures are a common complication of neurologic disorders such as stroke, spinal cord injury, multiple sclerosis, and cerebral palsy. The prevalence has been reported to range from 36%-60%. Muscle contractures represent a unique muscle adaptation characterized by increased passive stiffness of the muscle and limited mobility of the joint with little or no active force production. Muscle contractures lead to joints fixated in abnormal positions and limited use of the affected limbs. Furthermore, muscle contractures can cause considerable pain, strength loss, and muscle atrophy.

To restore the mobility of affected joints, surgical procedures such as various forms of tendon lengthening and intramuscular aponeurotic recession are used. These procedures may increase the range of motion for some time, but because they rarely have lasting effects, other effective treatment approaches should be considered also. A variety of other treatment options currently exists. A few of these have previously been reviewed (stretching and shockwave therapy), but a systematic evaluation of the effectiveness of all the available nonsurgical treatment options in a single review has so far not been conducted. A critical and comprehensive evaluation of the effect of all treatment options in one single study may help clinicians to obtain a better overview of the field. It may also help to clarify where the existing knowledge needs to be strengthened by further research and point to new therapy options.

Therefore, the aim of this systematic review was to provide an overview of the evidence supporting the use of current nonsurgical treatment options for reduction of muscle contractures in individuals with neurologic disorders. We included randomized controlled trials (RCTs) and controlled clinical trials (CCTs) of nonsurgical interventions administered with the aim to treat muscle contractures in individuals with neurologic disorders. We decided to include not only RCTs but also CCTs because we wanted to review all available treatment options. The primary outcome measure was muscle contractures measured as either joint mobility or passive stiffness.

Methods

Study design

We conducted this systematic review with meta-analyses of RCTs and CCTs using a protocol based upon Cochrane Collaboration recommendations and reported it according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.
PICO criteria by the 2 review authors (C.S., J.L.). Through subjective judgment, the reviewers doing the data extraction decided whether the intervention was administered to treat muscle contractures. Disagreements were solved by discussion and, when necessary, arbitrated by a third review author (J.B.N.) deciding whether to include or exclude the disputed.

Data synthesis

C.S. extracted short-term joint mobility data (up to 1wk after intervention). Preferably, change scores and SDs were extracted. If change scores were not available, post-intervention scores were used instead. Change scores/post-intervention scores and SDs were not available for all trials. In trials where this information was not available, we contacted the corresponding author of the article in an attempt to retrieve the information. Several trials investigated the effect of the intervention on multiple joints and/or both sides. In these cases, we used data from a single joint on the right side of the body. In prioritized order, we chose to use data from the ankle joint, the elbow joint, the knee joint, or the wrist joint. This order was based on our experience of where muscle contractures are frequent and severe and in accordance with literature on muscle contracture prevalence in different neurologic disorders.1-3

We identified 6 types of interventions with multiple trials: stretch, shockwave therapy, physical activity, botulinum toxin (BTX) treatment, electrical stimulation, and robot-assisted rehabilitation interventions. Based on the recommendations by Valentine et al,14 we conducted individual meta-analyses for these 6 intervention types. Because very few trials used passive stiffness as an outcome measure, the meta-analyses were performed based on PROM results. The primary outcome measure was set as the pooled PROM from RCTs. For all intervention types, we conducted sensitivity analyses to examine the effects of randomization on joint mobility. Similarly to Harvey et al,11 we did not consider a treatment effect of <5% PROM as clinically important. Because we considered the included trials to have varying effect sizes, all meta-analyses were performed using a random-effects model. In accordance with the Cochrane Handbook for Systematic Reviews of Intervention,13 we reported the effects using mean differences in the meta-analysis in cases where the outcome was reported using comparable measures. In 1 case with robot-assisted rehabilitation, the outcome was not measured using comparable methods. Here, we reported the effect of the intervention using standardized mean differences in the meta-analysis. In forest plots, randomized and non-randomized trials are presented separately. Subgroup analyses were used to explore possible differences between types of stretch. In studies with several relevant experimental groups (2 types of stretch protocols), we combined the experimental groups in to 1 single group.13 Prediction intervals were calculated in accordance with the method described by Borenstein.15 Meta-analyses were conducted using Review Manager 5.3.8

We assessed trials for risk of bias using the Downs and Black checklist. Subsequently, C.S. and J.L. scored the remaining trials independently. The maximum score attainable using the Downs and Black checklist is 33 points. The quality of included trials was ranked as high if the total score was >75% of the maximum, moderate if 60%-74% of the maximum, and low if <60% of the maximum.17,18 In question 20 we focused on whether the primary outcome measure was objective. We defined an objective measure as a measure not easily influenced by the rater. All torque-controlled goniometric measures were defined as objective, whereas noncontrolled goniometric were not. As we were interested in whether joint mobility was measured objectively and by use of blinded assessors to not introduce bias, we focused in particular on question numbers 15 and 20.

Ethics and registration

This study did not require ethical approval. The systematic review protocol was prospectively registered in the PROSPERO international prospective register of systematic reviews under registration number CRD42019140424.

Results

Study selection

The review process is explained in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram (fig 1). We excluded 243 full-text articles because the trials...
| Study          | Participants                                      | Intervention | Intervention details                                                                 | n (Experimental Group) | n (Control Group) | Primary Outcome                                                                                   |
|---------------|---------------------------------------------------|--------------|----------------------------------------------------------------------------------------|------------------------|-------------------|---------------------------------------------------------------------------------------------------|
| Stretch       | Elderly persons with cognitive and functional impairment | Bed positioning | Bed positioning for 40 min, 4 × /wk for 8 wk                                            | 12                     | 12                | PROM of knee extension measured using a goniometer                                                 |
| Fox et al     | Children with CP                                  | Orthosis     | Foot orthosis for 1 y                                                                   | 13                     | 11                | PROM of ankle DF measured using a single digital inclinometer attached to a torque wrench        |
| Copley et al  | Adults with acquired brain injury                 | Splinting    | Individualized, thermoplastic resting mitt splint for 3 mo                              | 6                      | 4                 | Wrist and finger PROM measured using a goniometer                                                  |
| DeMeyer et al | Adults with stroke                                | Casting/orthosis | Bivalve cast group wore custom fiberglass cast. PRAFO group wore off-the-shelf AFO. Wearing schedule of 8-12 h every night for ~4 wk. | 19                     | 13                | Ankle DF PROM measured using a standardized torque application                                    |
| Beckerman et al | Adults with stroke                                | Orthosis     | AFO for 15 wk                                                                         | 16                     | 14                | PROM of ankle joint measured using a goniometer                                                   |
| Harvey et al  | Adults with stroke/SCI/TBI                        | Splinting    | Experimental thumbs splinted into abduction. 8 h per night for 12 wk                   | 29 thumbs             | 29 thumbs         | PROM of palmar measured using a standardized torque measure                                        |
| Kerem et al   | Adults with CP                                    | Splinting    | Johnstone pressure splints. 5 d/wk for 3 mo                                          | 17                     | 17                | PROM of the lower extremity measured using a goniometer                                           |
| Harvey et al  | Adults with SCI                                   | Passive movements  | Passive ankle for 10 min in the morning and 10 min in the evening, 5 d/wk for 6 mo   | 20                     | 20                | PROM of ankle DF measured through application of standardized torque                              |
| Theis et al   | Children with CP                                  | Passive stretch | 15 min (60-s repetitions) of ankle DF stretch 4 d/wk for 6 wk                         | 7                      | 6                 | Passive stiffness of triceps surae                                                               |
| Harvey et al  | Adults with SCI                                   | Passive stretch | Passive hamstring stretch for 30 min/d, 5 d/wk for 4 wk                                | 14                     | 11                | Hamstring muscle extensibility measured using a torque-controlled measure                         |
| Cheng et al   | Children with CP                                  | Repetitive passive movements  | Knee repetitive passive movement intervention, 3/wk for 8 wk                           | 18                     | 18                | PROM of knee joint measured using an electric goniometer                                           |
| Lannin et al  | Adults with stroke                                | Splinting    | Static, palmar resting mitt splint on a daily basis, for max 12 h/night for 4 wk    | 18                     | 11                | PROM of wrist extension measured using a torque-controlled measure                               |
| Basaran et al | Adults with stroke                                | Splinting    | Static volar or dorsal splints for 5 wk                                                | Volar 13              | 12                | PROM of wrist extension measured using a goniometer                                               |
| Moseley       | Children and adults with TBI                      | Casting      | Below-knee cast for 7 d                                                               | Volar 13              | 9                 | PROM of the ankle joint measured using a torque-controlled measure                               |
| Pradines et al | Adults with chronic hemiparesis                  | Passive and active stretch                  | Guided self-rehabilitation Contract program, consisting of daily self-stretch exercises for 1 y | 12                     | 11                | Maximal extensibility (XVI of the Tardieu Scale) of several muscles (PROM) measured with a goniometer |
| Reference | Intervention Details | Participant Group | Notes |
|-----------|----------------------|-------------------|-------|
| Lee et al. | Posterior talocrural glide | Adults with stroke | DF of the ankle joint for 10 glides of 5 sets/d, 5 d/wk for 4 wk |
| Harvey et al. | Splinting | Adults with tetraplegia | One thump of each participant was splinted each night for 3 mo |
| Hill | Casting | Children and adults with brain injury | Casting for 1 mo |
| Lannin et al. | Splinting | Adults with stroke | Hand splints positioning wrist in 0-10° extension (neutral splint group) or 45° wrist extension (extension splint group) at night for 4 wk |
| Smedes et al. | Manual mobilization | Adults with stroke | 10-min manual mobilization of the wrist 2 d/wk for 6 wk |
| Horsley et al. | Passive stretch | Adults with stroke | 30 min of self-assisted stretch of the wrist and finger flexors, 5 d/wk for 4 wk |
| An and Jo | Splinting | Adults with stroke | Talocrural mobilization 3 sessions/wk for 5 wk. Each session consisted of 6 sets of 10 repetitions. |
| Smedes et al. | Manual mobilization | Adults with stroke | Neutral splint 20 Extension splint 21 |
| Electrical stimulation | FES | Children with CP | 8-wk FES intervention, FES used at least 1 h/d 6 d/wk |
| Pool et al. | FES | Children with CP | FES device, which dorsiflexes the ankle during the swing phase of gait for at least 4 h/d, 6 d/wk for 8 wk |
| Sabut et al. | FES | Adults with stroke | FES for 20-30 minutes to the TA muscle of the paretic limb 5 d/wk for 12 wk |
| Bakaniene et al. | Transcutaneous electrical nerve stimulation/Mollii suit | Children with CP | Electrical stimulation through the Mollii suit for 1 h/d, 3/wk for 3 wk |
| Malhotra et al. | NMES | Adults with stroke | 30 min sessions of NMES to the wrist and finger extensors at least 2 times/d, 5 d/wk for 6 wk |
| Nakipoglu Yuzer et al. | FES | Adults with stroke | FES for 30 min/d, 5 d/wk for a total of 20 sessions per patient |
| Leung et al. | Electrical stimulation | Adults with TBI | The intervention group received 30-min tilt table standing with electrical stimulation to the ankle dorsiflexor muscles 5 d/wk and ankle splinting 12 h/d, at least 5 d/wk. Control group only received tilt table standing for 30 min, 3 times/wk. |
| Sabut et al. | FES | Adults with stroke | FES of the TA muscle for 30 min, 5 d/wk for 12 wk |

PROM of ankle joint measured using a digital goniometer
Extensibility of the flexor pollicis longus muscle measured with a standardized torque application
PROM of casted joints measured using a goniometer
Muscle extensibility measured using a standardized torque measure
PROM of wrist extension measured using a goniometer
PROM of wrist extension measured using a torque-controlled measure
DF PROM measured using a dynamometer
PROM of ankle DF measured using a goniometer
PROM of ankle DF measured using a goniometer
PROM in the ankle joint measured using a goniometer
PROM of ankle and knee joint measured using a goniometer
PROM at slow stretch
Passive stiffness at slow stretch
PROM of wrist extension measured using a goniometer
PROM of ankle DF measured with a torque-controlled measure
PROM of the ankle joint

(continued on next page)
| Study | Participants | Intervention | Intervention details | n (Experimental Group) | n (Control Group) | Primary Outcome |
|-------|--------------|--------------|----------------------|------------------------|-------------------|-----------------|
| Beaulieu et al<sup>49</sup> | Adults with stroke | Repetitive peripheral magnetic stimulation | Single session of repetitive peripheral magnetic stimulation | 9 | 9 | PROM of ankle DF |
| Shockwave therapy | Manganotti and Amelio<sup>50</sup> | Adults with stroke | ESWT | As single session of ESWT | 20 | 20 | PROM of the wrist measured using a digital goniometer |
| Lee et al<sup>51</sup> | Adults with stroke | ESWT | A single session of ESWT | 10 | 10 | PROM of the ankle joint measured using a goniometer |
| Wang et al<sup>52</sup> | Children with CP | ESWT | 1 ESWT session per wk for 3 mo. | 34 | 33 | PROM of the ankle joint measured using a goniometer |
| Gonkova et al<sup>53</sup> | Children with CP | ESWT | A single session of ESWT | 25 | 25 | PROM of ankle joint |
| Moon et al<sup>54</sup> | Adults with stroke | ESWT | 3 sessions of ESWT, 1 session/wk for 3 wk | 30 | 30 | PROM of the ankle measured using a goniometer |
| Vidal et al<sup>55</sup> | Adults with CP | ESWT | Group 1 received ESWT in the spastic muscle, group 2 received radial ESWT in the spastic muscle and in the antagonistic muscle. 3 sessions, 1-wk intervals. | Group 1 = 14 muscles | Group 2 = 13 muscles | 13 | 13 | PROM of lower limbs measured using a goniometer |
| BTX | Love et al<sup>56</sup> | Children with CP | Botox | 1 session of Botox into gastrocsoleus and where clinically indicated also into tibialis posterior | 12 | 12 | PROM of ankle joints measured using a goniometer |
| | Hawamdeh et al<sup>57</sup> | Children with CP | Botox | 3 successive Botox injections at intervals of 3-4 mo | 40 | 40 | PROM of ankle DF measured using a protractor goniometer |
| | Rameckers et al<sup>58</sup> | Children with congenital spastic hemiplegia | Botox | 1 session of Botox injections | 10 | 10 | PROM of wrist and elbow extension measured with a Mie goniometer |
| | Meythaler et al<sup>59</sup> | Adults with stroke | Botox | Botox with therapy or placebo injections with therapy. 12-wk intervention. Two Botox injections at 6-mo intervals | 21 | 21 | PROM of elbow and wrist joint measured monthly using a goniometer |
| | Tedroff et al<sup>60</sup> | Children with CP | Botox | Botox injections at baseline and at wk 4 | 56 | 58 | PROM of multiple joints measured using a goniometer |
| | Koman et al<sup>61</sup> | Children with CP | Botox | Control group received 12 wk of conventional rehabilitation, intervention group received 12 wk of rehabilitation plus Botox injections | 41 | 24 | PROM of multiple joints measured using a Lafayette goniometer |
| | Schasfoort et al<sup>62</sup> | Children with CP | Botox | Botox administered after baseline measurements | 20 | 20 | Ankle joint PROM measured using goniometer |
| | El-Etribi et al<sup>63</sup> | Children with CP | Botox | | | | |
| **Physical activity** | **Participants** | **Intervention** | **Details** | **Outcome** | **Method** |
|----------------------|-----------------|------------------|-------------|-------------|------------|
| Horsley et al.64      | Adults with stroke | Upper limb training | Active repetitive motor training by using the SMART Arm device for up to 1 h/d, 5 d/wk for 5 wk | 25 | PROM of multiple joints measured using a digital goniometer and a torque-controlled measure |
| Scholtes et al.65     | Children with CP | Resistance training | 12-wk program of functional PRE training, 3 times/wk for 60 min | 24 | PROM of the multiple joints measured using a goniometer |
| Schmid et al.66       | Adults with stroke | Yoga | Therapeutic yoga sessions were delivered in group sessions for 1 h, 2 times/wk for 8 wk | 37 | PROM of hamstrings muscles measured using a goniometer |
| Rydwik et al.67      | Adults with stroke | Exercise program | Exercise program including active and passive range of motion of the ankle with a portable device (Stimulo), 3 times/wk for 30 min, over a 6-wk period | 9 | PROM of ankle joint measured using a goniometer |
| Baik et al.68        | Children with CP | Horseback riding | Therapeutic horseback riding 60 min/d, 2 d/wk for 12 wk. Daily program consisted of 10 min of warm-up, 40 min of workout, and 10 min of cooldown. | 8 | PROM of hip joint measured using a goniometer |
| Lorentzen et al.69   | Adults with CP | Treadmill training | 30-min daily uphill gait training for 6 wk on a treadmill | 12 | Passive stiffness of the ankle joint quantified using a stationary and hand-held dynamometer. The hand-held dynamometer also to assess the PROM of the ankle joint. |
| Kirk et al.70        | Adults with CP | Resistance training | Resistance training, 3 times/wk for 12 wk | 12 | Passive stiffness of ankle plantar flexors measured using a stationary dynamometer |
| An and Won71         | Adults with stroke | MWM and WBE | 30 min of MWM or WBE 3 times/wk for 5 wk | MWM 12 | PROM of the ankle joint using a isokinetic dynamometer |
| Teixeira-Machado and DeSantana72 | Children with CP | Dance | 24 one-h sessions twice a wk for 3 m | WBE 8 | PROM of multiple joint measured using a goniometer |
| Hemachitara et al.73 | Children with CP | Horse riding | 1 session of horse riding using a horse riding simulator | 12 | PROM of hip abduction measured using a goniometer |
| Robot-assisted rehabilitation | Mirbagheri et al.74 | Adults with SCI | Robotic-assisted step training | Three 1-h robotic-assisted step training sessions/wk for 4 wk | 23 | Intrinsic ankle stiffness measured as using torque/unit change in ankle position |
| Robot-assisted rehabilitation | Waldman et al.75 | Adults with stroke | Stretch and active movements | A portable rehabilitation robot with controlled passive stretching and active movement training capabilities. 18 sessions, 3 times/wk for 6 wk | 12 | Ankle DF PROM measured using the robotic device |
| Robot-assisted locomotor training | Mirbagheri et al.76 | Adults with SCI | Robot-assisted locomotor training LOKOMAT | LOKOMAT training 3 d/wk for 4 wk | 23 | Intrinsic dynamic stiffness of the ankle joint |
| Franceschini et al.77 | Adults with stroke | Upper limb rehabilitation | Upper limb robot-assisted rehabilitation; 30 sessions, 5 d/wk for 6 wk | 25 | PROM of shoulder and elbow joint | (continued on next page)
### Table 1 (continued)

| Study | Participants | Intervention | Intervention details | n (Experimental Group) | n (Control Group) | Primary Outcome |
|-------|---------------|--------------|----------------------|------------------------|-------------------|-----------------|
| Sale et al\(^7\) | Adults with stroke | Robot-assisted therapy | Thirty 45-min sessions, 5 d/wk for 6 wk, using the robotic system that supported arm movements | 26 | 27 | PROM of the shoulder and elbow joint |
| Rayegani et al\(^9\) | Adults with SCI | Passive cycling | Motorized cycle that passively moved legs for 20 min, 3 times/wk for 2 mo | 35 | 29 | PROM of multiple joints measured using a goniometer |
| Xu et al\(^8\) | Adults with stroke | MT combined with neuromuscular electrical stimulation | MT group received 30 min of MT training. Control group performed the same training but with nonreflecting side of the mirror. MT + NMES group combined MT with 30 min NMES. | MT 23 | MT + NMES 23 | PROM of ankle joint DF assessed using a goniometer |
| Lorentzen et al\(^1\) | Adults with TBI | Neural tension technique | 1 session of neural tension technique treatment | 10 | 10 | Passive knee stiffness measured using the Neurokinetics RA1 Rigidity Analyzer |
| Mathew et al\(^2\) | Children with CP | Antispastic medication | Participants received A (placebo), B (0.5/1.0mg diazepam), or C (1.0/2.0mg diazepam) for 15-20 d | 60 | 60 | PROM of ankle joint measured using a goniometer |
| Velasco et al\(^3\) | Children with CP | Physical therapy based on head movements and serious games | 10 sessions of gaming using the ENLAZA interface | 5 | 5 | Cervical PROM |
| Wayne et al\(^4\) | Adults with stroke | Acupuncture | Traditional Chinese acupuncture, twice a wk for 10 wk | 16 | 17 | PROM of each major upper extremity joint |
| Cheng et al\(^5\) | Children with CP | Whole body vibration | 8-wk whole body vibration intervention | 16 | 16 | PROM of knee joint measured using an electrogoniometer |
| Fosdahl et al\(^6\) | Children with CP | Stretching and PRE | 16 wk of 3 weekly sessions of stretching and resistance training | 17 | 20 | Passive popliteal angle registered as maximum passive extension of the knee measured using a goniometer |
| Takeuchi et al\(^7\) | Adults with cerebrovascular disease | HI-LPNR and stretching | Participants were randomized to 1 session of HI-LPNR, stretching, a combination, or a control group | HI-LPNR 10 | Stretching 10 combination 10 | PROM of ankle DF and passive resistive joint torque of ankle DF |
| Ghannadi et al\(^8\) | Dry needling | 1 session of dry needling | 12 | 12 | PROM of dorsiflexors measured using a goniometer |

Abbreviations: AFO, ankle-foot orthosis; CP, cerebral palsy; DF, dorsiflexion; ESWT, extracorporeal shock wave therapy; FES, functional electrical stimulation; HI-LPNR, high-intensity pulse irradiation with linear polarized near-infrared rays; MT, mirror therapy; MWM, mobilization with movement; NMES, neuromuscular electrical stimulation; PRE, progressive resistance exercise; SCI, spinal cord injury; TA, tibialis anterior; TBI, traumatic brain injury; WBE, weight-bearing exercise.
| Study | Reporting Validity | External Validity: Bias | Internal Validity: Confounding | Power | Total | Percentage | Quality |
|-------|-------------------|-------------------------|-----------------------------|-------|-------|-----------|---------|
| Stretch |                  |                         |                            |       |       |           |         |
| Fox et al | 10 | 3 | 5 | 5 | 3 | 26 | 79 | High |
| Maas et al | 11 | 3 | 6 | 6 | 3 | 29 | 88 | High |
| Copley et al | 10 | 3 | 4 | 5 | 1 | 23 | 70 | Moderate |
| DeMeyer et al | 10 | 3 | 5 | 5 | 3 | 26 | 79 | High |
| Beckerman et al | 7 | 3 | 3 | 5 | 3 | 21 | 64 | Moderate |
| Harvey et al | 11 | 3 | 6 | 6 | 5 | 31 | 94 | High |
| Kerem et al | 10 | 0 | 4 | 3 | 3 | 20 | 61 | Moderate |
| Harvey et al | 10 | 3 | 6 | 3 | 4 | 26 | 79 | High |
| Theis et al | 8 | 1 | 5 | 3 | 2 | 19 | 58 | Low |
| Harvey et al | 10 | 2 | 5 | 6 | 3 | 26 | 79 | High |
| Cheng et al | 10 | 0 | 3 | 4 | 3 | 20 | 61 | Moderate |
| Lannin et al | 6 | 1 | 3 | 5 | 3 | 17 | 52 | Low |
| Basaran et al | 10 | 1 | 5 | 5 | 3 | 24 | 73 | Moderate |
| Moseley | 9 | 1 | 4 | 5 | 2 | 21 | 64 | Moderate |
| Pradines et al | 10 | 1 | 5 | 5 | 3 | 24 | 73 | Moderate |
| Lee et al | 9 | 0 | 3 | 5 | 3 | 20 | 61 | Moderate |
| Harvey et al | 11 | 2 | 5 | 4 | 3 | 25 | 76 | High |
| Hill | 6 | 1 | 3 | 4 | 3 | 17 | 52 | Low |
| Lannin et al | 9 | 0 | 6 | 5 | 3 | 23 | 70 | Moderate |
| Smedes et al | 10 | 2 | 3 | 2 | 3 | 19 | 58 | Low |
| Horsley et al | 11 | 2 | 6 | 6 | 3 | 28 | 85 | High |
| An and Jo | 9 | 1 | 3 | 5 | 3 | 21 | 64 | Moderate |
| Averages | 10 | 2 | 5 | 5 | 3 | 23 | 71 | Moderate |
| Electrical stimulation |       |                         |                            |       |       |           |         |
| Pool et al | 9 | 0 | 3 | 3 | 3 | 18 | 55 | Low |
| Pool et al | 9 | 1 | 4 | 6 | 3 | 23 | 70 | Moderate |
| Sabut et al | 10 | 3 | 3 | 5 | 4 | 25 | 76 | High |
| Bakuaniene et al | 9 | 0 | 4 | 2 | 2 | 17 | 52 | Low |
| Malhotra et al | 9 | 2 | 5 | 5 | 5 | 26 | 79 | High |
| Nakipoglu Yuzer et al | 9 | 0 | 4 | 4 | 3 | 20 | 61 | Moderate |
| Leung et al | 10 | 1 | 5 | 5 | 3 | 24 | 73 | Moderate |
| Sabut et al | 9 | 3 | 5 | 4 | 3 | 24 | 73 | Moderate |
| Beaulieu et al | 10 | 0 | 6 | 5 | 2 | 23 | 70 | Moderate |
| Averages | 9 | 1 | 4 | 4 | 3 | 22 | 67 | Moderate |
| Shockwave therapy |       |                         |                            |       |       |           |         |
| Manganioti and Amelio | 11 | 2 | 5 | 3 | 3 | 24 | 73 | Moderate |
| Lee et al | 10 | 3 | 6 | 6 | 2 | 27 | 82 | High |
| Wang et al | 11 | 3 | 4 | 3 | 5 | 26 | 79 | High |
| Gonkova et al | 6 | 1 | 4 | 1 | 4 | 16 | 48 | Low |
| Moon et al | 10 | 0 | 4 | 4 | 4 | 22 | 67 | Moderate |
| Vidal et al | 5 | 0 | 4 | 3 | 3 | 15 | 45 | Low |
| Averages | 9 | 2 | 5 | 3 | 4 | 22 | 66 | Moderate |
| Botox |       |                         |                            |       |       |           |         |
| Love et al | 10 | 3 | 4 | 5 | 4 | 26 | 79 | High |
| Hawamdeh et al | 10 | 2 | 4 | 5 | 4 | 25 | 76 | High |
| Rameckers et al | 9 | 0 | 4 | 5 | 2 | 20 | 61 | Moderate |
| Meythaler et al | 8 | 0 | 6 | 4 | 4 | 22 | 67 | Moderate |
| Tedroff et al | 11 | 1 | 5 | 4 | 2 | 23 | 70 | Moderate |
| Koman et al | 6 | 0 | 4 | 3 | 5 | 18 | 55 | Low |
| Schasfoort et al | 10 | 1 | 5 | 2 | 5 | 23 | 70 | Moderate |
| El-Etribi et al | 8 | 0 | 2 | 3 | 3 | 16 | 48 | Low |
| Averages | 9 | 1 | 4 | 4 | 4 | 22 | 66 | Moderate |

(continued on next page)
did not fulfill our PICO criteria (211); because the full text was not available (12), not accessible (14), or was a duplicate (3); or because the primary data/summary statistics was not presented (3). The remaining 70 articles were included in this systematic review. Of the 70 articles included in the review, 57 were RCTs (see fig 1).

Of the included trials, there were 22 trials (19 RCTs) on stretch interventions, 6 trials (2 RCTs) on shockwave interventions, 8 trials (7 RCTs) on BTX interventions, 9 trials (5 RCTs) on electrical stimulation interventions, 10 trials (8 RCTs) on physical activity interventions, and 5 trials (5 RCTs) on robot-assisted interventions. We performed meta-analyses for all of these intervention types. Additionally, we found 10 trials investigating other interventions. These trials are described in the section “Other interventions.”

### Study characteristics

Table 1 depicts the characteristics of the included studies, including information about the intervention, the number of participants, and the measure of muscle contractures.

### Evidence quality

Table 2 summarizes the quality assessments performed based on the Downs and Black checklist. Data are presented as the subtotal scores, the total score, and the quality ranking of all trials. Furthermore, the average score for the different intervention types are presented. For detailed scoring of each individual article, we refer to the supplemental table S2 (available online only at http://www.archives-pmr.org/).

For stretch interventions, 8 trials were of high quality, 11 trials of moderate quality, and 3 trials of low quality. For electrical stimulation interventions, 2 trials were of high quality, 5 trials of moderate quality, and 2 trials of low quality. For shockwave interventions, 2 trials were of high quality, 2 trials of moderate quality, and 2 trials of low quality. For BTX interventions, 2 trials were of high quality, 4 trials of moderate quality, and 2 trials of low quality. For physical activity interventions, 2 trials were of high quality, 6 trials of moderate quality, and 2 trials of low quality. For robot-assisted interventions, 3 trials were of high quality, 1 trial of moderate quality, and 1 trial of low quality (table 3).
Table 3 depicts the results of question numbers 15 and 20 of the Downs and Black checklist. Question number 15 concerns assessor blinding; question number 20 concerns whether joint mobility was measured objectively. The assessor was blinded in 39 trials and not blinded in 25 trials. We were unable to determine whether the assessor was blinded in 6 trials. We rated the primary outcome measure as objective in 18 trials and not objective in 50 trials. In 2 trials, we were unable to determine if the primary outcome measure was measured objectively. In 19 trials, joint mobility was measured using neither assessor blinding nor an objective measure. In 4 of the trials where we were unable to determine the use of assessor blinding, joint mobility was measured using a nonobjective measure.

**Effect of stretch on joint mobility (fig 2, fig 3)**

Short-term effect is defined as effects measured up to 1 week after the end of the intervention. Of the 22 trials investigating...
the short-term effect of stretch on joint mobility,\textsuperscript{19-40} we were able to obtain pre/post (± SD) measurements of PROM from 19 studies.\textsuperscript{19-22,24-26,28-35,37-40} Three of these trials\textsuperscript{22,31,37} compared 2 types of stretch interventions with a control situation. For these trials, we combined the experimental groups into 1 single group. The short-term effect of stretch intervention on joint mobility was investigated by pooling data from 17 RCTs with available data. Stretch had a pooled effect of 3\textsuperscript{2} (95% CI, 1-4; prediction interval (PI) = -2 to 7; $I^2 = 66$; $P < .001$). To explore differences in types of stretch, we explored the use of subgroup analysis. Here, we divided RCT studies in a casting/splinting subgroup and a stretching subgroup (including passive stretching protocols, self-stretching protocols, etc) (see fig 3). The effect of casting/splinting was 2\textsuperscript{2} (95% CI, 0-5) and the effect of stretching was 3\textsuperscript{2} (95% CI, 1-5).

**Fig 2** Forest plot showing the mean difference with 95% CI for short-term effects of stretch on joint mobility.

| Study or Subgroup | Intervention | Mean Difference (95% CI) | Year |
|-------------------|--------------|-------------------------|------|
|                   |              | IV, Random, 95% CI (Degrees) |      |
| 1.1 Randomized studies |              |                          |      |
| Mosesley 1997     | -1.9         | 10.2, 9                  | 1997 |
| Fox 2000          | -4           | 17, 12                   | 2000 |
| Harvey 2003       | 4            | 5.003892, 16             | 2003 |
| Larren 2003       | 0.3          | 10.4, 20                 | 2003 |
| Harvey 2006       | 0.3          | 14.7, 18                 | 2006 |
| Horsey 2007       | 1.1          | 16.9, 21                 | 2007 |
| Harvey 2007       | 2            | 5.26, 4.4                | 2007 |
| Larren 2007       | 2.3          | 4, 20                    | 2007 |
| Basaran 2012      | 5.8          | 26, 13                   | 2012 |
| Copley 2013       | 5.3          | 28, 16                   | 2013 |
| Cheng 2014        | 1.8          | 6.7, 9                   | 2014 |
| Maas 2014         | -2.1         | 31, 34                   | 2014 |
| Delmeyer 2015     | 9.5          | 36, 13                   | 2015 |
| An 2017           | 6.6          | 4, 20                    | 2017 |
| Lee 2017          | 3            | 4, 20                    | 2017 |
| Pradines 2019     | 3.3          | 5, 20                    | 2019 |

**Fig 3** Forest plot with subgroups showing the mean difference with 95% CI for short-term effects of stretch on joint mobility. Stretching includes interventions such as passive stretching and self-stretching protocols.
Effect of shockwave therapy on joint mobility (fig 4)

Of the 6 included trials investigating the effect of shockwave therapy on joint mobility,50-55 we were able to obtain pre/post (±SD) measurements of PROM from 5 studies.50-54,59 However, only 1 of these studies was an RCT.51 The single RCT study had a short-term effect of 2° (95% CI, −5 to 10°; P = .56).

Effect of physical activity on joint mobility (fig 5)

Of the 10 trials investigating the effect of physical activity,64-73 we obtained pre/post (±SD) measurements of PROM from 9 studies.54-72 The short-term effect of physical activity on joint mobility was investigated by pooling data from 7 RCTs with available data. Physical activity had a pooled effect of 3° (95% CI, −2 to 8°; PI = −15 to 20°; I² = 87%; P = .28).

Effect of BTX on joint mobility (fig 6)

Of the 8 included trials investigating the effect of BTX on joint mobility,58-65 we were able to obtain pre/post (±SD) measurements of PROM from 6 studies.59-63 The short-term effect of BTX on joint mobility was investigated by pooling data from 5 RCTs with available data. BTX had a pooled effect of 4° (95% CI, −1 to 8°; PI = −13 to 20°; I² = 85%; P = .13).

Effect of electrical stimulation on joint mobility (fig 7)

Of the 9 included trials investigating the effect of electrical stimulation on joint mobility,56-63 we were able to obtain pre/post (±SD) measurements of PROM from 8 studies.61-69 The short-term effect of electrical stimulation on joint mobility was investigated by pooling data from 5 RCTs with available data. Electrical stimulation had a pooled effect of 3° (95% CI, −1 to 6°; PI = −8 to 13°; I² = 78%; P = .11).

Effect of robot-assisted rehabilitation on joint mobility (fig 8)

Of the 5 included trials investigating the effect of robot-assisted rehabilitation on joint mobility,74-78 we were able to obtain pre/post (±SD) measurements of PROM from 3 studies.75-77 The short-term effect of robot-assisted rehabilitation on joint mobility was investigated by pooling data from 5 RCTs with available data. Robot-assisted rehabilitation had a pooled effect of 1 (95% CI, −0 to 2; PI = −8 to 9; I² = 73%; P = .03).
Effect of other interventions on joint mobility

Of the 70 included trials, 10 were not of the abovementioned intervention types. Rayegani et al found significant improvements in hip and ankle PROM after a 2-month passive cycling intervention in individuals with spinal cord injury. Xu et al investigated the effect of 4 weeks of mirror therapy or mirror therapy plus neuromuscular electrical stimulation. Compared with a control group, they found a significant effect of both interventions on ankle dorsiflexion PROM. Mathew et al investigated the effect of the antispasticity drug diazepam in children with cerebral palsy. After 15-20 days of intervention, they found a significant increase in PROM in the group receiving a large dose of diazepam but not in groups receiving placebo treatment or low-dose treatment. Wayne et al investigated the effect of up to 20 sessions of traditional Chinese acupuncture in adults with chronic hemiparesis after stroke. After treatment, they found significant increases in some but not all PROM measures in the acupuncture group compared with the control group. Ghannadi et al investigated the effect of dry needling in adults with stroke and found significant improvements of dorsiflexion PROM after treatment compared with the control group. Trials investigating the effect of neural tension technique, serious games, whole body vibration, stretch combined with resistance training, and high-intensity pulse irradiation with near-infrared rays found no significant effects on joint mobility.

Sensitivity analysis

Table 4 depicts the results of the sensitivity analyses. In the sensitivity analyses, we examined the effect of randomization.

Discussion

In this systematic review, we aimed to determine whether the existing literature supports that nonsurgical treatment options can reduce muscle contractures in individuals with neurologic disorders. Through our systematic search, we found 70 trials (57 RCTs) eligible for inclusion; 22 trials (19 RCTs) on stretch interventions, 6 trials (2 RCTs) on shock-wave interventions, 8 trials (7 RCTs) on BTX interventions, 9 trials (5 RCTs) on electrical stimulation interventions, 10 trials (8 RCTs) on physical activity interventions and 5 trials (5 RCTs) on robot-assisted interventions. Additionally, there were 10 single trials on other intervention types. Through meta-analysis and quality assessment, we did not find...
convincing evidence supporting the use of any nonsurgical treatment option.

Similarly to Harvey et al.,11 we do not consider a treatment effect of <5° PROM as clinically important. From the only available RCT on shockwave therapy, we found a nonsignificant effect of 2°. By including the 4 available nonrandomized studies, there was a significant effect of 12° (CI, 4–21°) (see fig 4 and table 4). Based on the Downs and Black checklist, 1 trial was of low quality, 2 were of medium quality, and 2 were of high quality. Perhaps more importantly, 2 of the 5 trials used neither assessor blinding nor an objective measure of joint mobility, thus introducing a large possibility of bias. The trial reporting the largest short-term effect (30°)50 did not use assessor blinding, an objective measure of joint mobility, or randomization. Four of the 5 trials measured PROM of the ankle joint, 1 measured PROM of the wrist. Four studies used a single session of shockwave therapy, and 1 study used 3 sessions of shockwave therapy. Because of limited data, we were not able to investigate the long-term effect of shockwave treatment through meta-analysis. However, 4 trials did indeed report possible sustained effects at follow-up intervals. Gonkova et al.53 found an immediate significant effect of 14° after shockwave treatment; after 4 weeks the effect was 11° and still significant compared with baseline. Moon et al.54 found a significant 30° effect of the shockwave intervention; at the 4-week follow-up the effect was 20°, and at the 12-week follow-up the effect was 10°. They found significant differences between baseline and measurements immediately after and 4 weeks after intervention. They did not find a statistical difference between baseline and 12-week follow-up measurements. Gama et al.55 found an immediate nonsignificant effect of 3°; at the 4-week follow-up this difference was 4° and still nonsignificant compared with baseline. Lee et al.51 found an immediate nonsignificant difference in joint mobility of 2.33° between the control group and the shockwave group; at the 4-week follow-up this difference was 3.55° and still nonsignificant. Because all indications concerning the effect of shockwave therapy are based on only a few trials of limited quality, we encourage cautious interpretations of the results.

From RCTs on stretch and robot-assisted rehabilitation interventions, we found small, clinically nonimportant effects on joint mobility. The estimated effect of stretch interventions was 3° PROM (CI, 1–4°). This finding is roughly consistent with that of the most recent systematic Cochrane review on the effect of stretch interventions on joint mobility in individuals with neurologic disorders by Harvey et al.14 Harvey14 found no short-term effect of stretch (mean difference = 2° (95% CI, 0–3°)). The estimated effect of robot-assisted rehabilitation interventions was 1° PROM (95% CI, 0–2°). We did not find significant effects from RCTs on physical activity (P = .27), electrical stimulation (P = .11), or BTX interventions (P = .13) on joint mobility.

An important finding of this review was the lack of objective measures of muscle contractures found in many trials. Only 18 of the 70 included trials used objective measures of muscle contractures such as passive stiffness or torque-controlled goniometric measurements; most of these were trials investigating the effect of stretch. The remaining 52 trials measured PROM using primarily standard, non–torque-controlled goniometric measurements. Furthermore, these nonobjective measures were used in 23 trials without convincing use of assessor blinding, thus introducing a large possibility of bias. In future research in this field, we strongly advocate the use of objective, instrumented measures such as passive stiffness (eg, measured using the portable stiffness assessment device90) or torque-controlled goniometric measurements.

Study limitations

As with all systematic review studies, there is a possibility of retrieval bias—the fact that potentially eligible trials might have been missed. To minimize retrieval bias we chose to use a broad search string, which we tested by its ability to identify already known eligible trials. This strategy resulted in a large amount of identified trials, but we hope that it minimized the amount of missed trials. We are aware of the fact that the inclusion of nonrandomized studies introduces a possibility for bias. To address this issue we based conclusions primarily on meta-analyses performed on RCTs only and performed sensitivity analyses investigating the effect of randomization. In the data extraction process, the reviewers doing the data extraction used subjective judgment to determine if the intervention was administered to treat muscle contractures. We acknowledge that doing this without objective and clear criteria is problematic but believe that this was the best
possible solution. In the meta-analyses, we combined data from studies on different joints using absolute PROM measures. Although range of motion does differ between joints, we decided to maintain the use of an absolute outcome measure to ensure easy transferability and interpretation in a clinical setting. In all included trials, the severity of contractures at baseline may affect the effect of the intervention. Unfortunately, we were not able to quantify the severity of contractures at baseline because the included trials used different measurement tools, investigated different joints, etc. Similarly, past treatment history is likely to influence the effect of the intervention. Because only a very limited number of studies included information on treatment history, we were not able to include this information. This is therefore a limitation to the study. A possibility of bias is also introduced because 2 of the authors (J.L., J.B.N.) of this review were also authors of included trials. We addressed this possibility of bias by not letting authors extract data from trials in which they had been involved. Despite the fact that all trials were screened by 2 authors and arbitrated by a third review author in case of unsolvable disagreement, we acknowledge the possibility of selection bias in systematic reviews such as this.

Conclusions

The central findings of this systematic review are that effective, nonsurgical treatment of muscle contractures is yet to be convincingly achieved and that there is a need for the use of objective measures of muscle contractures. Future research in this field should focus on the use of an objective measure of muscle contractures, thereby increasing the validity of the trials. We believe that the implementation of such objective measures would advance the continued search for effective, nonsurgical treatment of muscle contractures in individuals with neurologic disorders.

Supplier

a. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Corresponding author

Christian Svane, MSc, Department of Neuroscience, University of Copenhagen, Blegdamsvej 3, 2200 Copenhagen N, Denmark. E-mail address: christian.svane@sund.ku.dk.

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