Spasticity in children and young people with non-progressive brain disorders: management of spasticity, co-existing motor disorders and their early musculoskeletal complications

Physical therapy (physiotherapy and/or occupational therapy)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Dodd,K.J., Taylor,N.F., Graham,H.K., A randomized clinical trial of strength training in young people with cerebral palsy, Developmental Medicine and Child Neurology, 45, 652-657, 2003 **Ref ID** 75865 **Country/ies where the study was carried out** Australia **Study type** Randomised controlled trial **Aim of the study** To determine whether a home-based strength-training programme could (1) increase the strength of the ankle plantarflexors, knee	**Sample size** Sample size: 21 children and adolescents **Characteristics** Characteristics -Intervention group n=11 GMFCS I: 2 GMFCS II: 2 GMFCS III:7 Sex M/F: 4/7 -Control group n=10 GMFCS I: 5 GMFCS II: 3 GMFCS III: 2 Sex M/F: 6/4 No significant differences between the groups in all the previous or in height and weight or in any of the outcomes of interest **Inclusion criteria** -aged between 8 and 18 years with spastic diplegic CP -able to walk independently, with or without a gait aid, and to be able to	**Interventions** Interventions - 1. Six-week strength training programme -intervention and equipment: Three strengthening exercises designed to target the ankle plantarflexor, knee extensor, and hip extensor muscle groups: a. bilateral heel raises in which the participant stood on the edge of a stable, light-weight portable step (height 20cm) and raised and lowered his or her heels through the full available range b. bilateral half squats in which from a standing position, the participant slowly squatted until knees were flexed to between 30 and 60°. A large inflatable ball (55cm diameter) was placed between the lower back of the	Recruitment: potential participants were identified by one of the authors from the outpatient records of the Hugh Williamson Gait Laboratory at the Royal Children's Hospital, Victoria, Australia Sample size calculation: based on a systematic review of strength training in CP (Dodd et al. 2002). Numbers in each group (n=11) were based on a conservative estimate of effect size of d=1.20, allowed for a significance level of 0.05, and a power of 0.80 (Howell 1987). Effects sizes (d) of greater than 1.2 have been reported for increasing muscle strength and activity in children with CP. Randomisation and allocation concealment: participants were allocated	GMFM D-standing (%) (mean/SD) - -at baseline Experimental: 75.2 (14.4) Control: 74.6 (20.9) -at 18 weeks Experimental: 80.4 (13.2) Control: 80.7 (15.0) NS (p value not reported) GMFM E-walking, running and jumping (%) (mean/SD) - -at baseline Experimental: 52.8 (31.3) Control: 68.3 (30.1) -at 18 weeks Experimental: 58.2 (31.3) Control: 67.8 (28.6) NS (p value not reported) GMFM total (%) (mean/SD) - -at baseline Experimental: 64.2 (27.8) Control: 71.7 (24.9)	**Limitations** Small sample size and calculation based on outcome not relevant to our review. Power analysis revealed that if the effect size were maintained and the sample size increased to n=26 in each group, there was an 80% chance that the comparison for dimension E of the GMFM would have reached statistical significance. One participant in the control group did not complete the 18-week follow-up test due to recent surgery on the lower limbs. **Other information** All of the participants had been involved in active orthopaedic management before participation in this trial. Seventeen of the 21 young people had undergone multilevel orthopaedic surgery a mean of 34 months (range 24–52 months) before the trial commenced. One young person had undergone isolated calf

extensors, and hip extensors and (2) improve physical activity and walking ability in young people with spastic diplegic CP **Study dates** Not stated **Source of funding** Not stated	follow simple commands **Exclusion criteria** -a fixed flexion deformity at the knee, hip greater than 25°, or fixed equinus of more than 10° -current participation in other management strategies such as serial casting, botulinum toxin, or recent orthopaedic surgery (less than 12 months), and -participation in a strength-training programme within the previous three months	participant and the wall to help guide and standardise the exercise; and c. step-ups where the participant stepped onto and off portable steps -setting:unclear, presumably hospital -frequency and duration: the training load was adjusted by adding free weights to a backpack worn by the participant. Once the initial load was determined, participants were instructed to complete three sets of between eight and 10 repetitions of each exercise, three times a week for six weeks. Each exercise session took between 20 and 30 minutes. -who delivered: physiotherapists 2. Normal daily activities: Included school and sport. Participants were also able to attend their normal physiotherapy programme, provided therapy did not include a progressive resistance exercise programme.	randomly to either the strength training or control group using a concealed method. Twenty-two identical pieces of paper were placed in an opaque container, 11 with the words 'experimental group' and 11 with the words 'control group' written on them. In another opaque container, the name of each participant was written on 21 separate pieces of paper. Allocation was achieved by drawing a piece of paper from each container. This process continued until all participants were allocated to a group Outcomes assessed - 1. Dimensions D and E of the Gross Motor Function Measure (GMFM; Russell et al. 1993) When assessed: at baseline, and at 6 and 12 weeks How assessed: participants were asked to attempt each of the items up to three times without using any assistive	-at 18 weeks Experimental: 69.6 (21.4) Control: 74.3 (21.4) Walking speed (m/min) (mean/SD) - -at baseline Experimental: 47.4 (23.3) Control: 49.5 (24.5) -at 18 weeks Experimental: 48.6 (23.3) Control: 51.4 (16.5) Adverse events Total number of events: 3 (apparently all in the experimental group, none reported for the control group) There was no adverse event that led to participants missing a training session. One participant reported pressure on the shoulders from the backpack. As a result, weights were carried in a home-made vest to distribute the load more evenly. Two participants reported mild foot and ankle discomfort during the heel raise exercise. To alleviate this, the physiotherapy	lengthening without multilevel surgery. Three of the younger participants had been managed with botulinum toxin for dynamic equinus on 1–3 occasions. At the time of the trial, all participants were orthopaedically well-aligned with no major equinus deformities. It was expected that the amount of physiotherapy and the level of sport and physical activity the children participated in would not be different between the two groups due to the random allocation procedures Participants were provided with an exercise diary that detailed each exercise and enabled participants to record the weights used and the number of sets and repetitions completed at each exercise session. At the end of the second and fourth week of the exercise programme the physiotherapist visited the participant at home to check the way in which exercises were being performed and to adjust the training load. At the end of the trial the young people in the control group confirmed that they had not participated in a progressive strength-training programme during the trial.

		Typically, physiotherapy for school age children with CP in the state of Victoria is limited to a school consultation of around 45 minutes once or twice a month. **Comparison** Six-week strength training programme + normal daily activities vs. normal daily activities	devices. The best attempt was recorded 2. Self-selected walking speed When assessed: at baseline, and at 6 and 12 weeks How assessed: Participants were given standardised instructions: 'Walk to the end of the walkway at your normal walking speed. This is not a race, don't go fast'. Participants used their normal walking aids if appropriate. The walk was timed over the middle 10 metres of a 14-metre linoleum covered walkway using a stopwatch. A physiotherapist who was blind to group allocation and experienced in assessing movement disorders took all outcome measures. Blinding was maintained until after the final assessment had been completed. 3. Adverse events: Unclear how, when and who measured them	trainer modified the exercise so that ankle dorsiflexion did not exceed the plantigrade position.This modification enabled these participants to continue without incident.	All baseline, six-week, and 18-week measurement sessions were held in the La Trobe University Movement Rehabilitation Laboratory

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Dodd,K.J., Taylor,N.F., Graham,H.K., Strength training can have unexpected effects on the self-concept of children with cerebral palsy, Pediatric Physical Therapy, 16, 99-105, 2004 **Ref ID** 75866 **Country/ies where the study was carried out** Australia **Study type** Randomised controlled trial **Aim of the study** To use a randomised, controlled trial to test the prediction that participation in a home-based progressive resistance strength-training program would increase the self-concept of children with cerebral palsy **Study dates** Not stated **Source of funding**	**Sample size** N = 17 children **Characteristics** Age: 8 to 16 years GMFC (level) I = 6 (35%) II = 4 (24%) III = 7 (41%) No significant differences between both groups in age, height, weight or gender. There was a trend for children assigned to the experimental group to be more physically disabled as measured by the GMFCS (p=0.09) **Inclusion criteria** - spastic diplegic cerebral palsy - ability to walk independently with or without a gait aid - cognitive ability to follow simple commands **Exclusion criteria** - fixed flexion deformity at knee or hip > 25degrees or fixed equines of > 10 degrees - current participation in other management strategies such as serial casting, BoNT or recent orthopaedic surgery - participation in a strength-training program within the previous 3 months	**Interventions** Progressive resistance exercise. Frequency and duration: 3 sets of each exercise 3 times per week for the six weeks of the program Setting: home Who delivered: parents supervised by a physical therapist at first session and followed up on the second and fourth week to ensure compliance **Comparison** Normal daily activities including school and sports. Participants were also able to attend their normal physical therapy program provided that therapy did not include a progressive resistance exercise program	Recruitment - Potential participants were identified by one of the authors from the outpatient records of gait laboratory of a large metropolitan children's hospital.The 17 children recruited for this study comprised most of the 21 participants of a previous RCT examining the effects of strength training for children and adolescents with cerebral palsy on improving muscle strength and physical activity. Sample size calculation - Refer to Dodd 2003 Randomisation and Allocation Concealment - Identical pieces of paper were placed in an opaque container, half with the words experimental group and half with the words control group written on them. In another opaque container, the name of each participant was written on a separate piece of paper. Allocation was	Self perception (Global self-worth) (score 0 to 4) (mean/ -Experimental group (n = 10) Baseline: 3.41 (0.38) 6 Weeks: 3.55 (0.40) 18 Weeks: 3.57 (0.45) -Control group (n = 7) Baseline: 3.27 (0.52) 6 Weeks: 3.21 (0.63) 18 Weeks: 3.41 (n = 6) (0.49) NS at any time period when comparing experimental and control groups	**Limitations** Small sample size and calculation based on outcome not relevant to our review Randomisation was not totally successful as there was a trend for children randomly assigned to the experimental group to be more physically disabled. One participant in the control group did not complete the 18-week follow-up test due to recent surgery on her lower limbs ITT analysis not conducted 3 other participants originally included in the RCT are not included here and it is unclear why **Other information** Retest Reliability of self-perception (Global self-worth) Mean test (SD): 3.28 (0.52) Mean Retest (SD): 3.21 (0.64) ICC (2,1): 0.76 Mean difference: -0.06 (0.42) ICC: interclass correlation coefficient

Supported by a La Trobe University Faculty of Health Sciences Research Grant			achieved by drawing a piece of labelled paper from each container. This process continued until all the children were allocated to a group. <u>Blinding</u> - Single blinding: A physical therapist who was blind to group allocation took all outcome measures. Blinding was maintained until after the final assessment had been completed <u>Outcomes assessed</u> - -Self-perception When measured: At baseline, 6 weeks and at a follow up session held 18 weeks after the initial assessment Who measured: The participants were given standardised instructions for completing the 36-item questionnaire Instrument/test: Self-Perception Profile for Children		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Fowler,E.G., Knutson,L.M., Demuth,S.K., Siebert,K.L., Simms,V.D., Sugi,M.H., Souza,R.B., Karim,R., Azen,S.P., Physical Therapy Clinical Research Network (PTClinResNet), Pediatric endurance and limb strengthening (PEDALS) for children with cerebral palsy using stationary cycling: a randomized controlled trial, Physical Therapy, 90, 367-381, 2010 **Ref ID** 75913 **Country/ies where the study was carried out** USA **Study type** Randomised controlled trial **Aim of the study** To examine the effects of a stationary cycling intervention on muscle strength, locomotor	**Sample size** N=62 children **Characteristics** Age categories/years (n) a. 7 to 11 Cycling group: 20 Control group: 18 b. 12 to 18 Cycling group: 11 Control group: 13 Selective voluntary motor control (n) - a. Fair Cycling group: 17 Control group: 15 b. Good Cycling group: 14 Control group: 16 Mobility (n) - a. GMFCS I Cycling group: 11 Control group: 8 b. GMFCS II Cycling group: 8 Control group: 6 c. GMFCS III Cycling group: 12 Control group: 17	**Interventions** Cycling intervention - Intervention: each 60-minute cycling session was divided into 2 phases: lower extremity strenghtening and cardiorespiratory endurance - Equipment: stationary bycicle designed for rehabilitation. Features included a semirecumbent design with a wide padded seat, trunk support, foot straps and a unique "cyclocentric" lower-limb-loading feature to provide resistance - Setting: community-based pediatric physical therapy clinics - Frequency and duration: 3 times/week, total 30 sessions within a 12-week period - Who delivered: physical therapists, each demonstrated 90% competency for the performance of critical components **Comparison** No cycling intervention (control group)	Recruitment: participants were recruited via flyers and brochures placed in clinics and schools, mailed or posted on disability-related websites. A telephone screening was performed for potential participants who contacted the investigators. Sample size calculation: power analyses determined that a sample size of 58 participants (29 intervention, 29 control) would have 80% power to detect a moderate effect size of 0.7 associated with a 15% strenght improvement. This gain was a conservative estimate based on improved peak knee extensor and flexor moments following an isokinetic knee strenghtening program Randomisation: blocked by age group (7 to 11 years, 12 to 18 years) and selective voluntary motor control ability (good, fair) to minimise effects of maturation and physical impairment.	Thirty-Second Walk Test (30sWT): change from baseline (mean (95% CI)) Cycling group: 1.2 (-3.9 to 6.2) Control group: 3.4 (-1.7 to 8.4) NS GMFM-66: change from baseline (mean (95% CI)) Cycling group: 1.2 (0.5 to 1.8) Control group: 0.5 (-0.2 to 1.3) NS Adverse events (cycling group only) Total number: 24 Complaints of mild pain, soreness or muscle cramping: 17 Observed falls: 6 (no other details reported) Skin rash related to HR sensor: 1	**Limitations** The outcome on which the sample calculation was based is not relevant for our review ITT analysis not conducted Participants with no available outcome data (n=4): during the intervention period 2 participants withdrew for personal reasons and 2 others did not maintain the criteria necessary for inclusion and were withdrawn by the investigators (one child initiated an intensive sports programme and the other child underwent a medical treatment for vision) **Other information** If formal physical therapy had been initiated or discontinued recently, data collection was postponed until 3 months had elapsed. For the duration of the study, participants who were receiving physical therapy were asked to maintain their present regimen

endurance, preferred walking speed and gross motor function in children with spastic diplegic cerebral palsy (CP) **Study dates** Not reported **Source of funding** Grant from the Foundation for Physical Therapy Corporate donations or discounts: Biodex Inc, Freedom Concepts, Helen's Cycles, Santa Monica, National AMBUCS Inc and Sam's Club.	No significant differences at baseline were found for demographic data, participant characteristics or outcomes of interest **Inclusion criteria** -spastic diplegia -aged between 7 and 18 years -ability to follow simple verbal directions -ability to walk independently with or without assistive device, for short distances (GMFCS levels I to III) -good or fair selective voluntary motor control for at least one limb (Good: defined as the ability to isolate both knee and ankle movement out of synergy (knee extension with the hip positioned in flexion; ankle dorsiflexion with the knee positioned in extension). Fair: defined as the ability to isolate knee extension but not ankle dorsiflexion) **Exclusion criteria** -orthopaedic surgery, neurological surgery or baclofen pump implantation within the preceding 12 months -serial casting or new orthotic devices within the preceding 3 months -initiation of oral medications that affect the neuromuscular system (eg, baclofen) within the preceding 3 months -initiation of physical therapy, exercise, sports activity or change in assistive devices for walking within the preceding		Allocation concealment: not reported Outcomes assessed - (Body function and activity levels of the ICFDH) - 1. Thirty-Second Walk Test (30sWT) How assessed: children were asked to walk at their preferred speed. The distance completed in 30 seconds was recorded. Test was performed on a circular path at a nearby track or school gymnasium 2. GMFM-66 How assessed: scores were obtained using section D (standing) and E (walking, running and jumping) Outcomes evaluators were blinded to participants group assignment and had to pass a rigorous standarisation procedure for each outcome measurement protocol by demonstrating 90% competency.		

	3 months -inability or unwillingness to maintain age-appropriate behaviour -serious medical conditions such as cardiac disease, diabetes or uncontrolled seizures -current participation in a fitness program that included a minimun of once-weekly cardiorespiratory endurance exercise -significant hip, knee or ankle joint contractures preventing passive movement of the lower limbs through the pedaling cycle, and -bilateral poor selective voluntary motor control (inability to isolate knee or ankle joint motion out of synergy)		Outcomes were assessed at baseline and following the 12-week intervention period 3. Adverse events Unclear how and who assessed them -		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Lee,J.H., Sung,I.Y., Yoo,J.Y., Therapeutic effects of strengthening exercise on gait function of cerebral palsy, Disability and Rehabilitation, 30, 1439-1444, 2008 **Ref ID** 76046 **Country/ies where the study was carried out** Korea **Study type** Randomised controlled trial **Aim of the study** To assess the effectiveness of strengthening exercises of the lower limbs on improvement of muscle strength and gait function **Study dates** Not stated **Source of funding** Not stated	**Sample size** N = 17 children **Characteristics** Age/years (range): 4 to 12 Diagnosis Diplegia: 9 (53%) Hemiplegia: 8 (47%) There was no significant difference in distribution of age, sex and type of spastic cerebral palsy between the two groups **Inclusion criteria** -spastic diplegic or hemiplegic -ability to ambulate with or without assistive devices or orthosis **Exclusion criteria** -inability to follow commands from therapists -fixed contracture at the knee or hip joint for more than 25 degrees -medical or orthopaedic diseases that prevented exercise -orthopaedic surgery of the lower limb or injection of an antispastic drug	**Interventions** Progressive resistive exercise: targeting the muscle groups of lower limbs. Frequency and duration - 60 minute sessions three times per week for 5 weeks Setting: school Equipment: The intervention consisted of warm up stretching exercise, isotonic, isokinetic and a cool down exercise. For the isotonic exercise, one of three weights, 0.25 kg, 0.45 kg or 0.9 kg, was selected to provide resistance to voluntary muscle contraction in the form of adjustable weight cuffs attached by Velcro straps to the subject. Select weight was determined by the physical therapist depending on the ability of the children Who delivered: physical therapist **Comparison** Conventional physical therapy including NDT, range of motion exercise, and gait training Frequency and duration 5 weeks.	Recruitment - Participants were recruited from an outpatient's clinic. Sample size calculation Not reported Randomisation - Participants were allocated randomly to either the experimental group or control group using concealed methods Allocation concealment - Not clear Outcomes assessed - -Functional tests (GMFMT, GMFMD, GMFME) When measured: at baseline, immediately after completing the program and 6 weeks after completing the program Who measured: all measures taken by the same physical therapist Instrument/test: GMFM -Gait analysis (walking	Walking (speed) (cm/s) (mean/SD) -Experimental group (n = 9) Pre-training: 54.7±30.7 Post training: 74.6±38.7 Follow-up at 6 weeks: 78.2±39.3 -Control group (n = 8) Pre-training : 69.8±43.0 Post training: 68.2±42.9 p<0.05 when compared to control group Follow up at 6 weeks: 67.8±37.2 p<0.05 when compared to control group Optimisation of function (GMFM) GMFM T-total (mean/SD) -Experimental group (n = 9) Pre-training: 86.5±13.3 Post training: 86.9±13.4 Follow up at 6 weeks:87±13.5 -Control group (n = 8) Pre-training : 85.2±13.4 Post training: 85.4±13.5 Follow up at 6 weeks: 85.7±13.3	**Limitations** No blinding of outcomes assessors and not clear who performed gait analysis Small sample size and no calculation Method of randomisation and allocation concealment used not clearly stated **Other information**

			speed) When measured: At baseline, post-training and six week follow-up Who measured: Not clear Instrument/test: Computerised gait analysis was measured using Orthotrack 6.2.4 system. The child was asked to walk independently but was allowed to use an assistive device if necessary	<u>GMFM D-standing (mean/SD)</u> - -Experimental group (n = 9) Pre-training : 73.5±25.7 Post training : 73.7±26.6 p<0.05 when compared to control group Follow up at 6 weeks: 73.8±26.6 -Control group (n = 8) Pre-training: 74.5±23.7 Post training: 74.6±23.7 ; (p<0.05) Follow up at 6 weeks: 75.4±22.7 <u>GMFM E-walking, running and jumping (mean/SD)</u> -Experimental group (n = 9) Pre-training : 61.6±34.1 Post training: 62.7±34.1 p<0.05 when compared to control group Follow up at 6 weeks: 63.0±34.4 -Control group (n = 8) Pre-training : 61.4±33.9 Post training :61.4±33.9 (p<0.05) Follow up at 6 weeks: 61.8±34 (Unless otherwise stated differences between groups	
				were not statistically significant)	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Liao,H.F., Liu,Y.C., Liu,W.Y., Lin,Y.T., Effectiveness of loaded sit-to-stand resistance exercise for children with mild spastic diplegia: a randomized clinical trial, Archives of Physical Medicine and Rehabilitation, 88, 25-31, 2007 **Ref ID** 76060 **Country/ies where the study was carried out** Taiwan **Study type** Randomised controlled trial **Aim of the study** To investigate the effectiveness of the loaded sit-to-stand (STS) exercise on motor activity, muscle strength, and physiologic cost for children with mild spastic diplegia **Study dates** Not reported **Source of funding**	**Sample size** N=20 children **Characteristics** Experimental group Mean age: 85.6±20.8 Sex: 7M/3F GMFCS: 4 level I, 6 level II Control group Mean age: 91.3±17.5 Sex: 5M/5F GMFCS: 6 level I, 4 level II There were no statistically significant differences at baseline regarding socio-demographic, clinical characteristics or outcomes of interest between both groups at baseline **Inclusion criteria** (1) aged between 5 and 12 years old (2) spastic diplegia (3) the GMFCS10 level I or II (4) able to stand up from a chair independently and maintain standing for more than 5 seconds without falling (5) able to follow verbal instructions (6) without obvious limitation in the passive range of motion of lower extremities	**Interventions** - Type of intervention: additional loaded STS exercise at home besides their regular PT - Equipment: Body vests and lead weights were specially made for the loaded STS test and loaded STS exercise. Lead pieces weighed either 1 or 0.5kg. During the loaded STS test or loaded STS exercise, an appropriate amount of weight was put into the pockets of the body vest - Setting: home - Frequency and duration: 3 sets per day, 3 days a week for 6 weeks. - Who delivered: a trainer (unclear their professional affiliation) taught the exercises to the children and their caregivers. Caregivers supervised the children at home **Comparison** - Type of intervention: regular PT only - Setting: unclear - Frequency and duration: 6	Recruitment Before randomisation authors asked the physical therapists, physicians, and special educators of 7 medical centres, teaching hospitals, and schools to help recruit the children with spastic diplegia who met the inclusion criteria Sample size calculation Based on a systematic review of strength training in children with CP (Dodd et al, 2002) authors calculated the sample size to be 9 children per group, 18 in total. The effect size was 1.20 and the power was 80%, with a 1-tailed significance level of 0.05 Randomisation Children were stratified by their GMFCS level (I or II) and age (≥8y or <8y) and then randomly allocated to either the experimental or the control group. Randomised block design Allocation concealment	GMFM goal dimension score (%) (mean/SE) -Actual pre-training Experimental: 76.6 (4.4) Control: 83.1 (3.2) -Actual post-training Experimental:79.8 (4.1) Control:83.5 (2.8) -Adjusted post-training Experimental: 82.7 (0.7) Control: 80.6 (0.7) Mean Square and F values: 21.82 $F_{1, 17}$=4.81 P (1 tailed): 0.02 Gait speed (m/min) (mean/SE) -Actual pre-training Experimental: 56.9 (5.1) Control: 63.8 (3.0) -Actual post-training Experimental: 58.4 (5.0) Control: 62.0 (2.6) -Adjusted post-training Experimental:61.3 (1.7) Control: 59.0 (1.7) Mean Square and F values: 24.56 $F_{1, 17}$=0.87 P (1 tailed): 0.18 (NS)	**Limitations** Sample size calculation was based on an outcome not relevant for our review **Other information** Although the investigators attempted to standardise the frequency and volume of the training, the children did not perform exactly as expected because of other activities. All children of the experimental group had loaded STS exercise at least twice a week, and 3 children exercised more than 3 times a week because the caregivers wanted more than what was asked. Children in both groups decreased or stopped PT services during this study because of the fear of the SARS epidemic in Taiwan. In general, children of the control group received PT more frequently during the study period.

Supported by the National Science Council, Taiwan (grant no. NSC90-2314-B-002-315).	(7) able to attend physical therapy (PT) treatment at least once a week before and during this study while keeping up with regular treatment programs (8) had not received any strength-training program in the past 3 months before the study and (9) parental commitment to allow participation without altering current therapy or activity **Exclusion criteria** (1) have orthopaedic intervention, selective dorsal rhizotomy, or botulinum toxin injection to the lower extremities within 6 months (2) orthopaedic problems or medical conditions that prevented children from participating in the exercises	weeks. - Who delivered: unclear The regular PT programs in both groups included passive range of motion exercises, positioning, balance training, functional training, and neurodevelopment training.	Not reported <u>Outcomes assessed</u> - -Function Instrument/test:Dimension D (13 items) and dimension E (24 items) of the GMFM-88, which measure motor activities in standing, walking, running, jumping, and hopping. Item scores for each goal dimension of GMFM-88 (GMFM goal dimension score) were added together and converted to yield a percentage score for that dimension. The GMFM goal dimension score was derived by averaging the percentage scores for dimension D and E in this study. -Gait speed Instrument/test:Gait speed in meters per minute was calculated using the time it took the child to walk the 10-m distance converted to meters per minute. Before the test, the tester had given the children instruction, such as “I’d like you to walk in the way you would normally do.”		

			The average velocity of 3 separate trials was used as the self-selected speed At the beginning and end of this study, 1 blinded tester who is a physical therapist with paediatric assessment experience (including GMFM-88, gait speed) for 6 years conducted the outcome measures and demographic data collection. The assessments for all the participants were conducted at about the same period of the day, so that all assessments would be performed in the morning for the same child. At the end of a 6-week interval, the same blinded tester conducted outcome measures, including GMFM goal dimension scores and walking speed.		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments

Full citation Unger,M., Faure,M., Frieg,A., Strength training in adolescent learners with cerebral palsy: a randomized controlled trial, Clinical Rehabilitation, 20, 469-477, 2006 **Ref ID** 76312 **Country/ies where the study was carried out** South Africa **Study type** Randomised controlled trial **Aim of the study** To evaluate the impact of an eight-week strength training program targeting multiple muscle groups using basic inexpensive free weights and resistance devices, on gait and perceptions of body image and functional competence **Study dates** Not stated **Source of funding** Not stated	**Sample size** N = 37 adolescents **Characteristics** Age (range): 13 to 18 years Experimental: n=21 Control: n=10 No significant differences between groups for age, height, gender and severity allocation **Inclusion criteria** - aged between 13 and 18 years. - ability to be independently ambulant with or without a walking aid - in good general health - ability to understand instructions in either English or Afrikaans **Exclusion criteria** - history of spasticity-altering surgery such as baclofen pump or selective dorsal rhizotomy, orthopaedic or neurosurgery in the previous 12 months or botulinum toxin infection(s) in the previous six months - history of participation in sports at provincial or international level during the trial period	**Interventions** Progressive resistive exercise during school hours - Setting: unclear - Frequency and duration: 1 to 3 times per week for 8 weeks - Who delivered: programme was designed in consultation with their therapist. A research assistant was given instructions on performance criteria by the researcher and assisted with the implementation and supervision of the exercise programmes **Comparison** No intervention	Recruitment 37 adolescents from a school that caters for children with special needs who met the inclusion criteria Sample size calculation Not reported Randomisation Pretesting was followed by systematic randomisation into either groups with every third name drawn from a hat being allocated to the control group Allocation concealment Not reported Outcomes assessed a. Three dimensional gait analysis (velocity (we will use the term walking speed)) When measured: at baseline and immediately after programme finished (8 weeks) Who measured: research assistants blinded to group allocation both at baseline and post-testing Instrument/test: six-camera video-based motion-capturing system.	Walking speed (mm/s) (mean/SD) - Experimental group (n=24) Pre-training: 1075.6 (235.4) Post-training:1119.3 (232.5) NS Control group (n=13) Pre-training: 1128 (132.0) Post-training: 1171.4 (141.9) NS Self perception of body image (composite score/25) (mean/SD) - Experimental group (n=24) Pre-training: 23.9 (4.1) Post-training: 25.9 (3.4) Control group (n=13) Pre-training: 19.0 (3.2) Post-training: 20.5 (3.3) P = 0.01 (experimental vs. control, but unclear whether this refers to post-training values or to mean difference of change from pre-training) Self perception of functional competence (composite score/25)(mean/SD) - Experimental group (n=24) Pre-training: 19.9 (3.4)	**Limitations** Small sample size and no calculation Baseline characteristics: children in the control group differed significantly from the experimental group from weight (p=0.02) and distribution of involvement (diagnosis) (p=0.03) ITT analysis not conducted 2 adolescents in the experimental group were withdrawn before post testing due to “absenteeism” from the program (criterion not predefined) and one was withdrawn after post-testing and before analysis because of sport participation. 3 adolescents in the control group were after post-testing and before analysis: one because of sport participation, one for incorrect diagnosis (unclear what this meant) and one because participating in a progressive resistance exercise programme Unclear why authors used a 2:1 randomisation **Other information**

			Adolescents instructed walk barefoot at a comfortable speed and without orthotics down and 1-m carpeted walkway. A walking aid was allowed and 3 to 8 trials were recorded. b. Self-perception (body image and functional competence) When measured: at baseline and immediately after programme finished (8 weeks) Who measured: research assistants blinded to group allocation both at baseline and post-testing Instrument/test: self administered questionnaires. Themes relating to body image identified from the physical appearance and attributes subscale of the Piers Harris Children's Self-Concept Scale. Themes for functional competence were decide on in consultation with the school therapy and included activities required by the child for successful functioning in his or her environment. Each statement was qualified using a	Post-training: 21.3 NS Control group (n=13) Pre-training: 19.0 (3.2) Post-training: 21.3 (3.3) NS	

			Likert-type scale in which the numeric values were replaced by descriptive phrases. Adolescents selected the most applicable phrase. Composite scores for each section were calculated and analysed		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments

Full citation Newman,C.J., Kennedy,A., Walsh,M., O'Brien,T., Lynch,B., Hensey,O., A pilot study of delayed versus immediate serial casting after botulinum toxin injection for partially reducible spastic equinus, Journal of Pediatric Orthopedics, 27, 882-885, 2007 **Ref ID** 64814 **Country/ies where the study was carried out** Ireland **Study type** Randomised controlled trial **Aim of the study** To compare delayed versus inmediate casting as an adjunct to botulinum toxin therapy for partially reducible spastic equinus **Study dates** Between August 2004 and March 2006 **Source of funding**	**Sample size** **Characteristics** Total sample size n=12 children Characteristics Age: 3 1/2 to 7 1/2 years Sex: 6 boys, 6 girls Type of CP: -spastic diplegia: 5 -spastic hemiplegia: 7 No significant differences between both groups in baseline measurements (mean age, mean weight and outcomes of interest) **Inclusion criteria** -diagnosis of CP presenting as spastic diplegia or spastic hemiplegia -a true equinus gait pattern with forefoot initial ground contact (excluding apparent equinus due to crotch) -independent walking without assistive devices -triceps surae spasticity -plantar flexion contracture with a decreased slow passive ankle dorsiflexion 0 degree or less with knee extended **Exclusion criteria**	**Interventions** Background interventions Each affected calf was injected with 10 U/kg Desport in 2 divided doses (to the medial and lateral gastrocnemius) Topical application of eutectic mixture of local anaesthetics cream was applied to injection sites 30 minutes before injection All children continued their weekly physical therapy regimen (not described) Comparison 1 Cast immediately after injection (6 children, 8 limbs) Comparison 2 Cast 4 weeks after injection (6 children, 9 limbs) Casts were replaced weekly for 3 weeks, each time in increasing maximal passive dorsiflexion **Comparison**	Recruitment Consecutive sample of children from outpatient clinic Sample size calculation Not performed Randomisation and allocation concealment Block design randomisation sequence where for every 2 children enrolled, 1 would be assigned to each group. Group allocation was concealed until the injection Outcomes assessed Gastrosoleus spasticity and ankle range of motion in the Tardieu scale. Ankle dorsiflexion was measured with a handheld goniometer, with the foot in subtalar neutral, knee extended, child supine. Both a fast (R1) and a slow passive stretch (R2) were applied, assessing the angle at which the spastic catch ocurred and the total passive range of motion (demonstrating a degree of fixed contracture) respectively. The difference	Gastrosoleus spasticity (Modified Tardieu) (degrees) (mean change/SD) a. from before injection to 3 months after casting Immediate: -7.0 (6.7) Delayed: -16.2 (5.4) p=0.007 a. from before injection to 6 months after casting Immediate: 2.9 (9.9) Delayed: -12.1 (6.1) p=0.002 Passive range of motion (degrees) (mean change/SD) a. from before injection to 3 months after casting Immediate: 9.8 (8.1) Delayed: 7.8 (5.2) NS b. from before injection to 6 months after casting Immediate: 6.0 (9.2) Delayed: 6.4 (6.0) NS Adverse effects -Pain	**Limitations** No power calculation performed Outcomes assesor not blinded to group allocation Potential bias introduced by children concurrently receiving non described routine physiotherapy **Other information**

The first author was supported by grants from the Swiss National Science Foundation , CEREBRAL (Swiss Foundation for Children with Cerebral Palsy)	-having previously undergone orthopaedic surgery		between both angles (R2-R1) was a measure of the degree of dynamic spasticity Who assessed: assessments were undertaken by the principal investigator When assessed: both outcomes were assessed at 3 and at 6 months after casting	Immediate: 3 children complained of pain that required recasting during the first 48 h after having their first cast applied Delayed: 0 P=0.08 (NS) No other procedural complications were recorded	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Aarts,P.B., Jongerius,P.H., Geerdink,Y.A., Van,LimbeekJ, Geurts,A.C., Effectiveness of modified constraint-induced movement therapy in children with unilateral spastic cerebral palsy: A randomized controlled trial, Neurorehabilitation and Neural Repair, 24, 509-518, 2010 **Ref ID** 75716 **Country/ies where the study was carried out** Netherlands **Study type** Randomised controlled trial **Aim of the study** To investigate whether 6 weeks of modified constraint-induced movement therapy (mCIMT) followed by 2 weeks of bimanual task-specific training (mCIMT-BiT) in	**Sample size** N=50 children **Characteristics** a. mCIMT-BiT (n=28) Sex: 14 F/14 M Age: 4.8 (1.3) years GMFCS: 27 GMFCS I/ 1 GMFCS II b. UC group (n=22) Sex: 7 F/14 M Age: 5.1 (1.7) years GMFCS: 21 GMFCS I/ 1 GMFCS II No significant differences between both groups in relation to sociodemographic characteristics or outcomes of interest at baseline **Inclusion criteria** - CP with a unilateral or severely asymmetric, bilateral spastic movement impairment - Aged 2.5 to 8 years - Manual Ability Classification System (MACS) scores I, II or III **Exclusion criteria** - Intellectual disability such that simple tasks could not be understood or executed (ie, developmental age less than 2 years) - Inability to combine the study protocol with the regular school program	**Interventions** Modified constraint-induced movement therapy + bimanual task-specific training (mCIMT-BiT) (n=28) - - Type of intervention, frequency and duration: Functional training during 3-hour afternoon sessions, 3 days per week for 8 weeks (6 weeks of modified constraint-induced movement therapy (mCIMT) followed by 2 weeks of bimanual task-specific training (mCIMT-BiT)) During the first 6 weeks restraint of the unaffected arm and hand was applied. Children were told that they were pirates and that their best arm was injured and had to be kept in a sling. Their affected arm had to be used for all activities, especially to handle a sword. In all these therapy sessions the principles of shaping and repetitive task practice were applied. Immediate feedback on task performance and results was given. During the last 2 weeks the emphasis was on task-specific	Recruitment - Children were recruited from 8 rehabilitation centres. They and their parents were first approached and informed by their treating physiatrist or occupational therapist. A screening was performed by two OT from the recruiting rehabilitation centre Randomisation - Within 48h after inclusion each participant was randomised to either group by throwing a dice with equal probabilities. Sample size calculation - 36 children (18 per group) were required to obtain a power of 90% to detect at least a moderate treatment effect (Cohen's d[20] value>0.5) on the Assisting Hand Assessment (AHA; SD=12.22) and/or ABILHAND-Kids (SD=5.28) using a 2-sided significance level of 0.05. taking into account a maximum attrition rate of 30% (due	AHA (range 0 to 100) - -change from baseline at week 9 CIM-BiT: 6.8 (8.2) U Care: 2.5 (6.3) -change from baseline at week 17 CIM-BiT: 6.4 (5.7) U Care: 1.7 (5.5) COPM-S (range 0 to 10) - -change from baseline at week 9 CIM-BiT: 3.7 (1.6) U Care: 1.4 (1.1) -change from baseline at week 17 CIM-BiT: 3.6 (1.6) U Care: 1.6 (1.3) COPM-P (range 0 to 10) - -change from baseline at week 9 CIM-BiT: 3.5 (1.3) U Care: 1.2 (1.1) -change from baseline at week 17 CIM-BiT: 3.5 (1.3) U Care: 1.3 (1.2) GAS, goal (% children that	**Limitations** Immediately after randomisation 2 children withdrew from the UC group due to family circumstances **Other information** At the end of the study protocol (week 17) the children who had been allocated to the UC group were also offered the opportunity to participate in an mCIMT-BiT group All data handling and analyses were carried out by an independent statistician who was blinded to group allocation

children with unilateral CP improves the spontaneous use of the affected limb in both qualitative and quantitative terms more than usual care (UC) of the same duration **Study dates** Not reported **Source of funding** Johanna Children Fund (JFK; grant number 2007/0199-1100	- Inability to walk independently without a walking aid	exercises in goal directed bimanual play and self-care activities without restraint. These 2 weeks were used to to train individual goals that were set by the parents, using GAS - Setting: Rehabilitation centre and home - Who delivered: OT, PT and parents **Comparison** <u>Usual care (UC) (n=22)</u> - Type of intervention, frequency and duration: Regular rehabilitation programme for 8 weeks: individual OT and or PT twice a week in 0.5- to 1-hour sessions (total time 1.5 hours/week). During each OT or PT child was engaged in exercises to stretch affected arm, to improve its weight bearing capacity and to use affected arm and hand as good assist. In addition parents and teachers were instructed to stimulate the children at least 7.5 hours a week to use affected arm and hand as an assist in daily activities - Setting: Rehabilitation centre, home and school	to the intensity of the program), 52 children needed to be randomised <u>Outcomes assessed</u> All assessments were conducted by the same occupational therapist at the primary rehabilitation centre, who was unaware of the individual study phase of any particular child, blinded for group allocation and not involved in any other aspect of the study. AHA tapes were scored by a certified OT who was blinded for group allocation and test session. All assessments were conducted at week 9 and week 17 a. Assisting Hand Assessment (AHA) When measured: Instrument/test: AHA questionnaire b. Canadian Occupational Performance Measure (perception of current performance (COPM-P) and satisfaction with current performance (COPM-S) Instrument/test: COPM	<u>showed an increase of 2 points or more compared to baseline)</u> -at week 9 CIM-BiT: 82 U Care: 23 -at week 17 CIM-BiT: 86 U Care: 36	

		- Who delivered: OT, PT, parents and teachers	questionnaire. Ratings are on a 10-point scale; scores closer to 10 indicate better performance and increased satisfaction. By means of the COPM training goals were set by the parents c. GAS, goal (% children that showed an increase of 2 points or more compared to baseline) Instrument/test: GAS Scaling. Perceived outcome was scaled from -3 to +2. -3 indicated level lower than the initial performance level, -2 indicated an unchanged level of performance, -1 a level lower than desired outcome, +1 somewhat more improvement than expected and +2 much more improvement than expected Parents scored their children at each measurement		

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation McNee,A.E., Will,E., Lin,J.P., Eve,L.C., Gough,M., Morrissey,M.C., Shortland,A.P., The effect of serial casting on gait in children with cerebral palsy: preliminary results from a crossover trial, Gait and Posture, 25, 463-468, 2007 **Ref ID** 76102 **Country/ies where the study was carried out** UK **Study type** Randomised controlled trial (cross over) **Aim of the study** To evaluate the effect of short term stretch casting on gait in children with spastic cerebral palsy compared to the natural history **Study dates** Not stated **Source of funding** Sports Aiding medical Research for Kids (SPARKS)	**Sample size** N=9 children **Characteristics** - Immediate casting (n=5) Sex: 3M/2F Mean age: 7 years, 3 months Type of CP: 3 diplegia, 1 L hemiplegia, 1 R hemiplegia GMFCS: 3 GMFCS I, 1 GMFCS II, 1 GMFCS III - Delayed casting (n=4) Sex: 1M/3F Mean age: 6 years, 11 months Type of CP: 3 diplegia, 1 R hemiplega GMFCS: 2 GMFCS I, 2 GMFCS II **Inclusion criteria** -spastic CP -mild fixed ankle plantarflexion contractures -clinical recommendation of serial casting to improve ankle dorsiflexion range made previous to study **Exclusion criteria** -BoNT injections in the past 6 months -Previous surgery of the calf musculature	**Interventions** Intervention and comparison Serial casting versus usual care For each group there was a control and a casting period. One group received immediate casting (n=5) and one group received casts after a 3-month period (n=4) Below knee casting was applied by the same physiotherapists for each child. Following each weekly change of cast passive ankle dorsiflexion range was reassessed. Another cast was applied if ankle dorsiflexion range had increased and the target range had not yet been achieved. Casting was ceased if no further gain in range was achieved or if the target amount of dorsiflexion, typically 10 degrees, was achieved Six of the children wore an ankle foot orthosis (AFO) either unilaterally or bilaterally during the day prior to the casting period and all had worn orthoses in the past (unclear the group distribution of these children) **Comparison** See above for details	Recruitment Unclear Sample size calculation Not performed Randomisation and allocation concealment Not reported Outcomes assessed a. Passive ankle dorsiflexion Instrument/test: hand held goniometer b. Walking speed Instrument/test: Three dimensional gait analysis (3DGA). Children walked barefoot at a self-selected speed When measured: both outcomes were measured over the first 5 weeks and over the 12 weeks for both the control period and the casting period	Passive dorsiflexion (knee flexed) (degrees) (mean/SD of the change) a. 0 to 5 week Casting: 7.55 (2.54) Control: -2.45 (2.9) P<0.01 b. 0 to 12 week Casting: 5.3 (4.5) Control: -6.36 (9.6) P=0.01 Passive dorsiflexion (knee extended) (degrees) (degrees) (mean/SD of the change) a. 0 to 5 week Casting: 3 (4.67) Control: -2.55 (3.4) P=0.02 b. 0 to 12 week Casting: -1 (2.8) Control: -2.45 (5.4) NS Walking speed (m/s) (mean/SD of the change) a. 0 to 5 week Casting: 0.04 (0.2) Control: 0.05 (0.2) NS	**Limitations** Small sample size and no calculation performed Unclear who measured the outcomes **Other information** 13 weeks was chosen as the study interval for a crossover trial based on the findings from Corry et al (1998) study that ankle returned to the baseline value at 12 weeks following casting

				b. 0 to 12 week Casting: -0.01 (0.1) Control: 0.02 (0.2) NS	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Katz-Leurer,M., Rotem,H., Keren,O., Meyer,S., The effects of a 'home-based' task-oriented exercise programme on motor and balance performance in children with spastic cerebral palsy and severe traumatic brain injury, Clinical Rehabilitation, 23, 714-724, 2009 **Ref ID** 76012 **Country/ies where the study was carried out** Israel **Study type** Randomised controlled trial **Aim of the study** To evaluate the feasibility and the ability to recruit and retain children with severe traumatic brain injury or cerebral palsy and their families, to a simple home-based exercise programme and to assess the immediate and short	**Sample size** n=20 children **Characteristics** <u>Experimental group (n=10)</u> Mean age: 8.2 (3.8) years Sex: 7 M/3 F Cause of spasticity: 5 TBI/5 CP <u>Control group (n=10)</u> Mean age: 9.2 (2.7) years Sex: 7 M/3 F Cause of spasticity: 5 TBI/5 CP No significant baseline differences between both group regarding socio-demographic and clinical characteristics or relevant outcomes measured **Inclusion criteria** General criteria: -aged 7 to 13 years -able to stand up from a chair independently and maintain standing for more than 5 seconds without falling -without obvious limitation of the passive range of motion of lower extremities Children with post traumatic brain injury (TBI) fulfilled in addition the following criteria:	**Interventions** -Type of intervention and setting: Home-based task oriented exercise. Sit-to-stand and step-up with each leg in forward and sideward directions. They were also instructed to continue with their regular daily activities -Frequency and duration: Three sessions of five 1-minute exercises daily, 5 days/week for 6 weeks -Who delivered: Therapist familiarised child and parent with the exercises at the start of the trial. Children performed exercises at home under parental supervision. Therapist set a day each week to call child and parent to hear and answer any questions and solve any problems that arose during programme **Comparison** Regular daily activities including school and sports for 6 weeks (Note: the control group was offered the programme immediately after the trial period)	<u>Recruitment</u> Children were either outpatients or former patients of a rehabilitation hospital <u>Randomisation and allocation concealment</u> Children were randomised by using a sealed envelope to either group <u>Outcomes assessed</u> -Walking velocity Instrument/test: Unconstrained 10-m walk test. Measurements were made within the mid range of a 14-m long walkway When measured: immediately after programmed finished (at 6 weeks from baseline) Who measured: Unclear -Adverse effects Unclear how and who measured them	<u>Walking velocity (m/s) (mean (SD)</u> a. Initial scores (baseline, t_0) Experimental: 0.96 (0.12) Control: 1.02 (0.19) NS b. Change scores after 6 weeks (t_1 - t_0) Experimental: 0.04 (0.1) Control: 0.01 (0.1) NS <u>Adverse effects</u> None reported	**Limitations** Very small sample size and no calculation performed Unclear who measured the outcomes **Other information** One child in the intervention group did not complete the programme and was lost to follow up before final assessment. His results were incorporated into the final analysis but it is unclear why he did not complete the programme

term effects of such intervention on reducing impairment and improving function **Study dates** Not stated **Source of funding** Not stated	-post severe closed head injury (Glasgow Coma Scale score at admission to ER ≤8 for at least 6 hours) -at least 1 year post trauma -independent ambulation (foot orthoses permitted) Children with cerebral palsy (CP) fulfilled in addition the following criteria: -GMFCS I or II **Exclusion criteria** Unable to fulfil simple instructions				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Novak,I., Cusick,A., Lannin,N., Occupational therapy home programs for cerebral palsy: double-blind, randomized, controlled trial, Pediatrics, 124, e606-e614, 2009 **Ref ID** 76144 **Country/ies where the study was carried out** Australia **Study type** Randomised controlled trial **Aim of the study** To assess the effectiveness of an occupational therapy home program (OTHP), compared with no OTHP, with respect to function and parent satisfaction with child function, participation, goal attainment, and quality of upper limb skill in school-aged children with cerebral palsy.	**Sample size** N=36 children **Characteristics** - Experimental group 1 (8-weeks of OTHP) Mean age: 7.33 (1.09) years Sex: 9M/3F Type of CP: 8 spastic diplegia, 3 spastic hemiplegia, 1 ataxia GMFCS level: g level I, 2 level II, 2 level III, 1 level IV, 1 level V - Experimental group 2 (4-weeks of OTHP) Mean age: 7.17 (2.32) Sex: 8M/4F Type of CP: 1 spastic quadriplegia, 2 spastic diplegia, 6 spastic hemiplegia, 1 dystonia, 2 athetosis GMFCS level: 6 level I, 2 level II, 1 level III, 3 level V - Control group (no OTHP) Mean age: 8.50 (2.27) Sex: 8M/4F Type of CP: 1 spastic quadriplegia, 4 spastic diplegia, 5 spastic hemiplegia, 2 dystonia GMFCS level: 5 level I, 1 level II, 3 level III, 1 level IV, 2 level V No significant differences between the three groups regarding sociodemographic, clinical characteristics or outcomes of interest	**Interventions** An individual OTHP was developed for each child in the OTHP group. Programs focused on the goals set and were based on the following interventions: goal-directed training (24 of 24 programs), parent education (24 of 24), programs), handwriting task training (14 of 24 programs), positive behaviour support (9 of 24 programs), adaptive equipment (9 of 24 programs), recreation/sports therapy (6 of 24 programs), strength training (3 of 24 programs), orthotics (3 of 24 programs), play therapy (3 of 24 programs), and constraint induced movement therapy (1 of 24 programs). Parents determined how frequently and for how long they implemented the OTHP. Both groups implemented the program less than daily but 18 (4-week OTHP) or 17 (8-week OTHP) times per month. Intervention 1 OTHP for 8 weeks Intervention 2 OTHP for 4 weeks	Randomisation and allocation concealment Participants were assigned randomly by an officer at a separate location who was not connected with the study and who had prepared the random assignment schedule and concealed opaque envelopes by using computer-generated random numbers. Participants were assigned randomly to 1 of 3 groups, that is, no OTHP, an OTHP of 4 weeks, or an OTHP of 8 weeks. Participants in the control group had intervention commencement by other study participants concealed from them and commenced an OTHP after the study concluded at 8 weeks Sample size calculation An a priori sample size test of power was performed to identify the probability of detecting clinical effects in the primary outcome measure, the Canadian Occupational Performance	COPM-P (mean difference, 95% CI) - - mean change from baseline at 4 weeks OTHP 4 vs. No OTHP: 1.6 (0.0 to 3.3) p=0.05 OTHP 8 vs. No OTHP: 0.2 (0.1 to 0.3) p=0.01 OTHP 4 vs. OTHP 8: 1.00 (-0.70 to 2.6) NS -mean change from baseline at 8 weeks - OTHP 4 vs. No OTHP: 2.4 (0.7 to 4.2) p=0.01 OTHP 8 vs. No OTHP: 1.4 (0.6 to 2.2) p=0.01 OTHP 4 vs. OTHP 8: 0.7 (-1.2 to 2.6) NS COPM-S (mean, 95% CI) - -mean change from baseline at 4 weeks OTHP 4 vs. No OTHP: 1.6 (0.0 to 3.2) p=0.04 OTHP 8 vs. No OTHP: 0.3 (-0.1 to 0.6) NS	**Limitations** Only 2 participants in the 4-week OTHP group implemented the OTHP for 4 weeks as instructed. **Other information** The mean session length was 15.66 minutes (range: 5– 60 minutes) for the 4-week OTHP and 17.63 minutes (range: 4.28–40 minutes) for the 8-week OTHP. For whole study reporting, the average session length for the 2 groups was calculated as the practical halfway point (16.5 minutes). There was no significant difference in total implementation time between the intervention groups (P=0.49). Most participants (n=9) in the 4-week OTHP group did not discontinue the program after 4 weeks, contrary to instruction, because parents reported that they perceived the program as helpful and they considered it in the best interests of their child to continue. Only 2 participants in the 4-week OTHP group implemented the OTHP for 4 weeks as instructed.

Study dates Between November 2005 and August 2007 **Source of funding** Cerebral Palsy Foundation and the College of Health and Science, University of Western Sydney	**Inclusion criteria** - Diagnosis of cerebral palsy - 4 to 12 years of age - Enrolled in school - Their parents needed to convey a concern about arm use in the screening interview **Exclusion criteria** - Involved in non–OT interventions that focused on developing upper limb use (eg, conductive education) - Receiving OT from another provider, or - The parents stated in the interview that they did not want to carry out OTHP activities	**Comparison** <u>Comparison</u> No OTHP	Measure (COPM), with an α value of 5% and power of 80%, using a minimal clinically important difference of 10%. The analysis accounted for a 20% dropout rate and 20% noncompliance rate. Twelve participants per group were needed to detect clinically worthwhile effects. <u>Outcomes assessed</u> -COPM performance (COPM-P) and COPM satisfaction (COPM-S) scores as adapted for children. The measures ask parents to identify functional problems and to rate the child's performance and their satisfaction with the child's performance on 10-point scales. -Adverse events were to be reported to the treating therapist by the parent via telephone or at an interview. -GAS29 T scores All baseline, 4-week, and	OTHP 4 vs. OTHP 8 0.7 (-1.0 to 2.4) NS~ <u>-mean change from baseline at 8 weeks</u> - OTHP 4 vs. No OTHP: 2.5 (0.8 to 4.3) p=0.01 OTHP 8 vs. No OTHP 1.5 (0.3 to 2.6) p=0.01 OTHP 4 vs. OTHP 8 0.8 (-1.1 to 2.8) NS <u>GAS-T (mean, 95% CI)</u> - <u>-mean change from baseline at 4 weeks</u> - OTHP 4 vs. No OTHP: 22.4 (14.4 to 30.3) p=0.01 OTHP 8 vs. No OTHP: 13.3 (8.6 to 18.0) p=0.01 OTHP 4 vs. OTHP 8: -6.2 (-17.9 to 5.6) <u>-mean change from baseline at 8 weeks</u> - OTHP 4 vs. No OTHP: 37.8 (26.9 to 48.8) p=0.01 OTHP 8 vs. No OTHP: 17.9 (12.4 to 23.4) p=0.01	

			8-week measures were administered by a non-treating occupational therapist who was blinded to study design and group allocation.	OTHP 4 vs. OTHP 8 0.5 (-13.4 to 14.4) NS Adverse events - None reported	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Aarts,P.B., Jongerius,P.H., Geerdink,Y.A., van,Limbeek J., Geurts,A.C., Modified Constraint-Induced Movement Therapy combined with Bimanual Training (mCIMT-BiT) in children with unilateral spastic cerebral palsy: how are improvements in arm-hand use established?, Research in Developmental Disabilities, 32, 271-279, 2011 **Ref ID** 132587 **Country/ies where the study was carried out** The Netherlands **Study type** Randomised controlled trial **Aim of the study** To investigate how the improvements to spontaneous use of an affected upper limb (shown in the trial Aarts et al., 2010) due to	**Sample size** N=50 (52 children were initially randomised, but 2 of those allocated to the Usual Care (UC) group withdrew immediately) **Characteristics** a. mCIMT-BiT (n=28) Sex: 14 F/14 M Age: 4.8 (1.3) years GMFCS: 27 GMFCS I/ 1 GMFCS II Manual Ability Classification system (MACS): I: 9 II: 12 III: 7 Active Wrist Extension (AWE) 1: 11 2: 15 3: 2 b. UC group (n=22) Sex: 8 F/14 M Age: 5.1 (1.7) years GMFCS: 21 GMFCS I/ 1 GMFCS II MACS: I: 7	**Interventions** mCIMT-BiT (n=28) -Type of intervention, frequency and duration: Training to improve the affected arm and hand was given during 3-hour afternoon sessions, three days per week, for eight weeks. Approximately half of the therapy was individual occupational therapy or physical therapy, whereas the rest was in small groups. During the first six weeks, restraint of the unaffected arm and hand was applied, and the affected arm had to be used for all activities. In all sessions, the principles of shaping and repetitive task practice were applied. In the last two weeks, the emphasis was on goal-directed task-specific bimanual training with no restraint. In addition to therapy sessions, the parents were asked to stimulate their child to use the affected arm and hand as much as possible at home, and to register the duration of stimulation on the record form.	Recruitment 52 children were recruited from eight rehabilitation centres. Initially, 28 children were allocated to mCIMT-BiT and 24 to UC; however, 2 children withdrew from the UC arm after allocation due to family circumstances. Randomisation Within 48 hours of inclusion, each child was randomised to mCIMT-BiT or UC by throwing a dice with equal probabilities. Assessment All children underwent a comprehensive upper limb evaluation before the start of the intervention period (week 0), at the end of the intervention period (week 8), and at the end of the study protocol (week 17). After the end of the study protocol, those allocated to the UC group were offered the chance to participate in a mCIMT-BiT group. All assessments were	ROM active wrist extension a. Score at each assessment point (mean ± SD) - Baseline mCIMT-BiT: 127.9 ± 21.2 UC: 117.5 ± 36.7 - Week 9 mCIMT-BiT: 133.8 ± 21.0 UC: 118.9 ± 39.4 - Week 17 mCIMT-BiT: 128.2 ± 22.0 UC: 114.8 ± 38.7 mCIMT-BiT: p = 0.062 UC: p = 0.393 b. Change scores (mean ± SD) - At week 9 compared to baseline mCIMT-BiT: 5.9 ± 13.5 UC: 1.4 ± 17.3 - At week 17 compared to baseline mCIMT-BiT: 0.4 ± 17.5 UC: -2.7 ± 29.1 Mean group difference of change score (95% CI)*: 5.4 (-3.41 - 14.29) Effect size: 0.25	**Limitations** Small sample size (N=50) Power calculation not reported in this paper (however, reported in Aarts et al., 2010, but for another outcome) 2 withdrawals following randomisation **Other information** The authors report that the mCIMT-BiT group received an average of 9 hours per week of therapy, and an additional 3.3 hours of stimulation at home (total stimulation time of 12.3 ± 1.9 hours). The UC group received an average of 1.5 hours per week of therapy and an additional 11.2 hours of stimulation at home or school (total stimulation time of 12.7 ± 2.1 hours).

modified Constraint-Induced Movement Therapy followed by Bimanual Training (cIMT-BiT) were established. **Study dates** Not reported **Source of funding** Grant from the Johanna Children Fund	II: 10 III: 5 AWE: 1: 7 2: 9 3: 6 There were no significant differences between the two arms. **Inclusion criteria** Cerebral palsy with a unilateral or severely asymmetric, bilateral spastic movement impairment Age 2.5 - 8 years MACS scores I, II or III **Exclusion criteria** Intellectual disability such that simple tasks could not be understood or executed (i.e. developmental age below 2 years) Inability to combine the study protocol with the regular school programme Inability to walk independently without a walking aid	-Setting: Rehabilitation centre and home -Who delivered: OT, PT and parents - **Comparison** <u>UC (n=22)</u> -Type of intervention, frequency and duration: Children received a regular rehabilitation programme for eight weeks. This included individual OT or PT given twice a week in 0.5 - 1 hour sessions (total of 1.5 hours per week). Another 7.5 hours per week stimulation of bimanual hand use was given at home or in (pre)school groups, according to predetermined instructions. Parents and teachers were asked to register the duration of specific stimulation on the daily record form. -Setting: Rehabilitation centre, school and home -Who delivered: OT, PT, parents and teachers	performed by one blinded OT. It was not possible to blind either participants or therapists to the treatment allocation, due to the nature of the intervention. <u>Outcomes assessed</u> - The active (aROM) and passive (pROM) range of extension motion at the affected wrist and elbow were measured simultaneously by two therapists, using a standard goniometer. The child was in a seated position, and the aROM was measured first, followed by the pROM. a. Wrist extension Measurements were started with the elbow 90° flexed, the forearm fully pronated and the upper arm alongside the trunk b. Elbow extension Measurements started with the shoulder in 90° anteflexion, the elbow in full flexion with the fingertips on or near the ipsilateral shoulder and the elbow supported by	*corrected for difference at baseline <u>ROM passive wrist extension</u> - <u>a. Score at each assessment point (mean ± SD)</u> - Baseline mCIMT-BiT: 177.7 ± 7.0 UC: 178.2 ± 6.6 - Week 9 mCIMT-BiT: 180.4 ± 7.6 UC: 177.3 ± 10.7 - Week 17 mCIMT-BiT: 179.8 ± 7.9 UC: 176.4 ± 13.2 mCIMT-BiT: p = 0.725 UC: p = 0.623 <u>b. Change scores (mean ± SD)</u> - - At week 9 compared to baseline mCIMT-BiT: 2.7 ± 8.7 UC: -0.9 ± 5.9 - At week 17 compared to baseline mCIMT-BiT: 2.1 ± 6.7 UC: -1.8 ± 8.9	

			the assisting PT. The active movements were demonstrated by the assessing OT, after which the child performed the elbow or wrist extension. The assisting PT maintained the maximally reached joint position, while the OT recorded the aROM joint angle in 5° increments. The PT then moved the joint towards the maximum passive position and the OT recorded pROM joint angle, in 5° increments. Statistical analysis - The two groups were compared with regarded to functional changes between pre and post treatment (week 0 and week 9 respectively) using ANCOVA in which differences at baseline were used as covariates. Cohen's d-values were used to calculate a pre-post intervention effect size, with the following values: small d=0.2, moderate d=0.5, and large d=0.8. Student t-tests were used to	Mean group difference of change score (95% CI)*: 3.5 (-0.82 - 7.76) Effect size: 0.33 *corrected for difference at baseline ROM active elbow extension - a. Score at each assessment point (mean ± SD) - Baseline mCIMT-BiT: 170.2 ± 15.4 UC: 172.1 ± 14.9 - Week 9 mCIMT-BiT: 172.1 ± 10.3 UC: 171.1 ± 14.1 - Week 17 mCIMT-BiT: 173.6 ± 10.4 UC: 170.2 ± 17.6 mCIMT-BiT: p = 0.434 UC: p = 0.611 b. Change scores (mean ± SD) - - At week 9 compared to baseline mCIMT-BiT: 2.0 ± 12.6	

			compare results at week 9 with those at week 17, to see whether the effect remained constant. The statistician was independent and blinded to group allocation.	UC: -0.9 ± 7.5 - At week 17 compared to baseline mCIMT-BiT: 3.4 ± 12.1 UC: -1.8 ± 8.5 Mean group difference of change score (95% CI)*: 2.1 (-2.85 - 6.99) Effect size: 0.17 *corrected for difference at baseline <u>ROM passive elbow extension</u> - <u>a. Score at each assessment point (mean ± SD)</u> - Baseline mCIMT-BiT: 179.8 ± 7.9 UC: 180.9 ± 10.2 - Week 9 mCIMT-BiT: 179.8 ± 7.5 UC: 179.6 ± 11.4 - Week 17 mCIMT-BiT: 180.9 ± 6.4 UC: 178.4 ± 12.5 mCIMT-BiT: p = 0.297 UC: p = 0.397	

				b. Change scores (mean ± SD) - - At week 9 compared to baseline mCIMT-BiT: 0.0 ± 6.2 UC: -1.4 ± 5.2 - At week 17 compared to baseline mCIMT-BiT: 1.1 ± 4.8 UC: -2.5 ± 5.3 Mean group difference of change score (95% CI)*: 1.2 (-2.07 - 4.46) Effect size: 0.15 *corrected for difference at baseline	

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Sakzewski,L., Ziviani,J., Abbott,D.F., Macdonell,R.A., Jackson,G.D., Boyd,R.N., Randomized trial of constraint-induced movement therapy and bimanual training on activity outcomes for children with congenital hemiplegia, Developmental Medicine and Child Neurology, 53, 313-320, 2011 **Ref ID** 158781 **Country/ies where the study was carried out** Australia **Study type** Randomised controlled trial **Aim of the study** To determine if constraint-induced movement therapy (CIMT) is more effective than bimanual training (BIM) in improving upper limb activity outcomes for children with	**Sample size** N = 64 children CIMT n=32 BIM n=32 Results were presented for a total of 62 children at 3 weeks CIMT n = 31 BIM n = 31 Results were presented for a total of 58 children at 26 weeks CIMT n = 28 BIM n = 30 **Characteristics** Age of participants : mean (95% CI) CIMT = 10y, 1m (9y, 1m – 11y) BIM = 10y, 2m (9y, 2m – 11y, 1m) Male CIMT = 17/32 BIM = 16/31 GMFCS n CIMT = Level 1 : 8, Level 2 : 24 BIM = Level 1 : 8, Level 2 : 23 MACS classification n CIMT = Level 1 : 8, Level 2 : 23, Level 3 : 1 BIM = Level 1 : 8, Level 2 : 23, Level 3 : 0 House scale n CIMT Spontaneous use : 3 Active assist : 24 Passive assist : 5	**Interventions** Both interventions were delivered in groups of 9-13 children for 6 hours/day for 10 days (i.e. 60 hours of physical therapy). An intensive day-camp model was chosen and 6 camps were run in community sports facilities in Melbourne and Brisbane, Australia. A circus theme was used to encourage the children's motivation, engagement and participation. Children attending at pairs of camps (one CIMT, one BIM) were grouped by age to ensure activities were tailored to developmental stages. Interventions in both groups used a goal directed, activity based framework. Principles of motor learning (including specific task practice, fostering problem solving (individually and within the group)) were included as well as modifying task and environmental constraints to support goal attainment. Specifically this involved fine motor activities, functional goals identified prior to camp, 2 hour circus training, mealtimes, gross motor upper	Recruitment: potential participants were identified through public and private medical specialists in Queensland and Victoria Australia Sample size calculation: Based on a t-test comparison of changes using a SD of 9 units for both groups, a significance (alpha) level of 0.05 and 80% power, a minimum of 26 children in each group was required (total 52 children) Randomisation and allocation concealment: Children were matched in pairs according to age, sex, side of hemiplegia, and MAUULF scores (function). Once matched the children were randomised to pairs using a computer generated list of random numbers and concealed envelopes opened by non-study personnel. Occupational and physical therapists (who were aware of treatment allocation) measured the outcomes at baseline, 3 and 26 weeks. MUUL and	AHA Mean Difference (95% CI) compared to baseline at 3 weeks CIMT = 3.1 (1.4 to 4.7) BIM = 1.9 (0.2 to 3.6) MD Comparison across groups = 1.2 (-1.2 to 3.5) Mean Difference compared to baseline at 26 weeks CIMT = 1.6 (-0.1 to 3.4) BIM = 2.3 (0.6 to 4.0) MD Comparison across groups = -0.7 (-3.1 to 1.7) MUUL Mean Difference (95% CI) compared to baseline at 3 weeks CIMT = 2.8 (1.2 to 4.3) BIM = 0.9 (-0.6 to 2.5) MD Comparison across groups = 1.8 (-0.3 to 4.0) Mean Difference compared to baseline at 26 weeks CIMT = 4.5 (2.9 to 6.1) BIM = 0.0 (-1.5 to 1.6) MD Comparison across groups = 4.4 (2.2 to 6.7)	**Limitations** Study is adequately powered according to sample size calculation **Other information** Ethics approval : The Children's Hospital Melbourne, La Trobe University, The Royal Children's Hospital and Health Services District Brisbane, University of Queensland Consent Written informed consent was obtained from parents and young people aged 12 years or older and verbal assent from younger participants

congenital hemiplegia **Study dates** Not reported **Source of funding** National Health and Medical Research Council and a Career Development Grant	BIM Spontaneous use : 4 Active assist : 25 Passive assist : 2 **Inclusion criteria** - aged between 5 and 16 years - the ability to follow instructions (determined during a screening assessment and in consultation with caregivers) - predominant spasticity with MAS grades of between 1 and 3 for wrist flexors, forearm pronators, and/or thumb adductors interfering with upper limb function **Exclusion criteria** - predominant dystonia/muscle contracture (MAS>3) - previous upper limb orthopaedic surgery - serial casting or botulinum toxin injections in the upper limb within 6 months of the study intervention starting	limb games and debriefing. For both CIMT and BIM training the focus was on completing all the activities. BIM camps were run immediately before CIMT camps. Tasks undertaken by the BIM training group were modified for the CIMT group to accommodate the unimanual nature of the intervention. Each group received a similar amount of training with similar content delivered in the same environment 1. CIMT n= 32 children Participants wore a tailor made glove on their unimpaired limb. When the glove was removed (for circus activities) fingers of the unimpaired hand were taped together to simulate the glove. Children could use their hand as a support but as the glove was less intrusive than a full arm cast or sling, it was thought to be safer because children could use their hand for safety 2) BIM n= 32 children HABIT strategy was used whereby children were provided with specific instructions on how each	AHA were assessed using videotapes by a trained occupational therapist unaware of treatment allocation. Analysis Intention to treat analysis was performed. Continuous data were compared between groups by fitting a regression model using General Estimating Equations to baseline, 3 week and 26 week results with an interaction term between intervention group and 3-level factor indicating time of measurement. Matching characteristics of age, sex and side of hemiplegia were used as covariates Outcomes assessed 1. Assisting Hand Assessment (AHA) 2. Melbourne Assessment of Unilateral Upper Limb Function (MAUULF)		

		hand should be used before each activity **Comparison** CIMT vs BIM			

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Law,M.C., Darrah,J., Pollock,N., Wilson,B., Russell,D.J., Walter,S.D., Rosenbaum,P., Galuppi,B., Focus on function: a cluster, randomized controlled trial comparing child-versus context-focused intervention for young children with cerebral palsy, Developmental Medicine and Child Neurology, 53, 621-629, 2011 **Ref ID** 158780 **Country/ies where the study was carried out** Canada **Study type** Cluster randomised controlled trial **Aim of the study** To evaluate the efficacy of a child focused intervention compared to a context focused intervention in improving performance of functional tasks and	**Sample size** 91 therapists were trained and randomised to an intervention group 79 therapists treated children in the study Of the children treated : 73/79 children allocated to the child focused intervention, received treatment and a further 2 were lost to follow up 63/67 children allocated to the context focused intervention, received treatment and a further 6 were lost to follow up Results were presented for a total of 128 children Child focused group n = 71 Context focused group n = 57 **Characteristics** Male Child focused group = 50/71 Context focused group = 29/57 Female Child focused group = 21/71 Context focused group = 28/57 p=0.03 using Pearson's chi squared test with Yates' continuity correction GMFCS Child focused group = Level 1 : 24, Level 2 : 11, Level 3 : 11, Level 4 : 8, Level 5 : 17 Context focused group = Level 1 : 13, Level 2 : 12, Level 3 : 10, Level 4 : 13, Level 5 : 9 Age at baseline mean (SD) Child focused group = 3.53 (1.43)	**Interventions** Therapists received 1.5 days' training and ongoing expert consultation throughout the study. A classification of intervention strategies was developed for each intervention approach. Both interventions were delivered over a 6 month period with a frequency of 18-24 sessions. Children returned to their regular therapy between assessments at 6 and 9 months. Parents received general education and information about their child's disability. They also received specified strategies to practice at home that would complement the intervention that their child received from the therapist. 1. Child focused intervention n= 71 children The aim of the intervention was to use a combination of therapeutic strategies to focus on remediation of impairments and to build the children's skills and abilities by practising functional activities. Therapists identified motor, cognitive or sensory	Recruitment: potential participants were identified as children from consenting families under the care of occupational and physical therapists from 19 children's rehabilitation centres in Ontario and Alberta in Canada Sample size calculation: Estimated at 104 children per treatment group to detect a difference of 3 points on the PEDI with a two-sided alpha value of 0.05 and power of 80. This calculation assumed a cluster size (number of children per therapist) of three and an intraclass correlation coefficient (ICC) of 0.1, leading to a variance inflation factor (design effect) associated with therapists of 1.2. Randomisation and allocation concealment: Therapists from 19 children's rehabilitation centres were stratified according to specialty (occupational or physical therapy) and were block randomised by a study coordinator into a	PEDI Functional Skill scale - self-care At Baseline Child focused group = 47.34 (17.00) Context focused group = 46.09 (14.80) At 6 months Child focused group = 51.54 (18.20) Context focused group = 49.05 (14.96) At 9 months Child focused group = 51.88 (18.65) Context focused group = 51.77 (17.75) PEDI Functional Skill scale - mobility At Baseline Child focused group = 49.46 (25.87) Context focused group = 47.64 (22.87) At 6 months Child focused group = 55.02 (26.37) Context focused group = 53.85 (22.34) At 9 months	**Limitations** Unit of analysis error: Therapists were randomised to treatment group. Results are presented by the children in each treatment group. Cluster effects were addressed in the analysis. **Other information** The content of the two interventions differed, as did the person who delivered them

mobility in young children with cerebral palsy **Study dates** September 2006 to April 2009 **Source of funding** National Institutes of Health, USA	Context focused group = 3.92 (1.42) Number of therapy sessions Child focused group = 18.65 (2.94) Context focused group = 17.69 (3.36) Both groups included children who were regularly receiving botulinum toxin type A injections **Inclusion criteria** - aged between 12 months an d 5 years 11 months - diagnosis of cerebral palsy at any level of GMFCS **Exclusion criteria** - planned surgery or medication changes during the 6 month study intervention period that might have affected motor function - starting a botulinum toxin type A regime during the study intervention period	impairments that were due to a functional limitation and provided therapy a) to remediate the impairment and b) to practise specific movements and tasks. Treatment strategies were chosen by the therapist and included - maintaining range of motion and joint alignment by using stretching casting and splinting, strength training, sensorimotor training and stimulation, bilateral isokinematic training, weight bearing through the hands - facilitating normal movement patterns and postural control by physical handling and practice of functional activities 2) Context focused intervention n= 57 children A primary therapist model was used. Each child was assigned to either a physical or occupational therapist who conducted the intervention for that child (consultation was provided by the other therapy specialist)	treatment group. Children from consenting families received the treatment to which their therapist was randomised. Therapists and children and their parents were not blinded to the treatment group. Outcome assessors were blinded to the treatment group Analysis Intention to treat analysis performed and missing values were imputed Change from baseline scores were estimated for 6 and 9 month outcome measures Linear mixed effects models were fitted using time and treatment as fixed effects and participant as a random effect. Covariates were included in the model in the following order: GMFCS, age, sex and therapist specialty. Number of co-interventions was not used as a covariate. Maximum likelihood estimation was used to compare different models. Baseline and 6 month data were used to	Child focused group = 56.72 (26.81) Context focused group = 55.20 (23.81) PEDI Caregiver Assistance scale - self-care At Baseline Child focused group = 37.80 (24.92) Context focused group = 35.56 (22.16) At 6 months Child focused group = 42.31 (26.18) Context focused group = 42.89 (23.51) At 9 months Child focused group = 43.57 (27.22) Context focused group = 42.29 (24.98) PEDI Caregiver Assistance scale - mobility At Baseline Child focused group = 44.75 (29.60) Context focused group = 44.94 (25.55) At 6 months Child focused group = 52.11 (30.75) Context focused group = 51.69 (27.23)	

		Using COPM, parents identified motor tasks that their children were initiating, trying to modify, or that they were showing an interest in performing but that they were having difficulty in accomplishing. Children were videotaped to record their performance of tasks identified for achieving goals. Task-related, child-related and environmental factors that hindered the child's performance were identified. Therapists analysed the constraints of the observed task performance working with the parents. Treatment focused on modifying identified constraints within the task and/or environment. Wherever feasible, practice of tasks was in the 'natural' environment (e.g. home or preschool). Children were encouraged to use compensatory strategies to achieve functional tasks. Therapists received instruction not to remediate the children's impairments. **Comparison**	fit models which did not include therapist cluster effects because the estimated intraclass correlation for PEDI outcomes were small, indicating a low cluster effect(ranged from 0.08 to 0.13) Outcomes assessed 1. PEDI Functional Skill scale - self-care and mobility and PEDI Caregiver Assistance scale - self-care and mobility When assessed: At baseline, at 6 months and at 9 months How assessed: At all assessments, by independently trained evaluators blinded to treatment allocation 2. GMFM-66 When assessed: At baseline, at 6 months and at 9 months How assessed: At all assessments, by independently trained evaluators blinded to treatment allocation	At 9 months Child focused group = 53.62 (31.54) Context focused group = 50.44 (28.57) GMFM-66 score At Baseline Child focused group = 53.31 (15.80) Context focused group = 52.14 (11.93) At 6 months Child focused group = 55.82 (15.45) Context focused group = 54.26 (11.99) At 9 months Child focused group = 56.84 (15.42) Context focused group = 54.11 (13.73) Right hip abduction - range of motion At Baseline Child focused group = 37.42 (13.08) Context focused group = 38.77 (14.56) At 6 months Child focused group = 38.33 (13.91) Context focused group = 39.31 (12.50)	

		At 6 month assessment: Child focused intervention vs context focused intervention At 9 month assessment: Child focused intervention for 6 months and usual therapy for 3 months vs context focused intervention for 6 months and usual therapy for 3 months	3. Range of motion of hip abduction, popliteal angle and ankle dorsiflexion When assessed: At baseline, at 3 months, at 6 months and at 9 months How assessed: At all assessments, by independently trained evaluators blinded to treatment allocation. The average of 2 consecutive measurements at the joint was used.	At 9 months Child focused group = 41.08 (13.69) Context focused group = 39.78 (11.55) Left hip abduction - range of motion At Baseline Child focused group = 36.61 (12.60) Context focused group = 38.31 (15.55) At 6 months Child focused group = 38.10 (12.50) Context focused group = 39.75 (12.88) At 9 months Child focused group = 40.03 (12.86) Context focused group = 38.61 (12.25) Right hip extension - range of motion At Baseline Child focused group = -0.43 (2.74) Context focused group = -0.35 (1.86) At 6 months Child focused group = -0.12 (0.70) Context focused group =	

				-0.51 (2.58) At 9 months Child focused group = -0.09 (0.66) Context focused group = -0.25 (1.10) Left hip extension - range of motion At Baseline Child focused group = -0.32 (1.69) Context focused group = -0.37 (1.85) At 6 months Child focused group = -0.06 (0.34) Context focused group = -0.68 (3.05) At 9 months Child focused group = -0.16 (0.83) Context focused group = -0.13 (0.79) Right popliteal angle - range of motion At Baseline Child focused group = 24.41 (18.11) Context focused group = 22.35 (17.63) At 6 months Child focused group = 22.55 (16.71)	

				Context focused group = 21.07 (17.13) At 9 months Child focused group = 25.34 (18.20) Context focused group = 25.63 (20.35) Left popliteal angle - range of motion At Baseline Child focused group = 24.80 (17.90) Context focused group = 21.85 (17.19) At 6 months Child focused group = 23.31 (17.94) Context focused group = 19.77 (17.61) At 9 months Child focused group = 26.33 (17.04) Context focused group = 23.66 (20.05) Right ankle dorsiflexion - range of motion At Baseline Child focused group = 14.23 (15.52) Context focused group = 17.88 (23.23) At 6 months	

				Child focused group = 14.53 (14.76) Context focused group = 15.11 (15.43) At 9 months Child focused group = 13.44 (13.47) Context focused group = 12.66 (18.61) Left ankle dorsiflexion - range of motion At Baseline Child focused group = 15.35 (15.72) Context focused group = 18.32 (22.97) At 6 months Child focused group = 13.60 (14.53) Context focused group = 13.92 (16.61) At 9 months Child focused group = 13.37 (12.79) Context focused group = 12.77 (17.50)	

Spasticity in children and young people with non-progressive brain disorders: management of spasticity, co-existing motor disorders and their early musculoskeletal complications

Orthoses

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Developmental Medicine and Child Neurology **Authors** Buckon,C.E., Thomas,S.S., Jakobson-Huston,S., Moor,M., Sussman,M., Aiona,M. **Year of publication** 2004 **Study location** USA **Ref ID** 75791 **Type of study** Randomised controlled study **Aim of study** To determine how three commonly prescribed AFO configurations (HAFO, PLS, SAFO), with varying amounts of ankle motion, influenced proximal joint dynamics, energy expenditure, and functional skill performance in ambulatory children with spastic diplegia.	**Inclusion Criteria** 1) Aged from 4 to 18 years 2) capable of independent ambulation without assistive devices 3) using an AFO at the time of enrollment or with AFO use indicated 4) no orthopedic or neurosurgical intervention in the preceding year **Exclusion Criteria** not stated **Baseline characteristics** Sixteen children with spastic diplegia males: 10, females : 6 Mean age : 8 years 4 months, SD 2 years 4 months Age range : 4 years 4 months to 11 years 6 months 4 children were classified at GMFCS level I 12 were at classified at GMFCS level II. None of the children was	Procedures An ankle mold was made for each child upon initiation into the study by a single orthotist and the original mold was used to fabricate all three AFO configurations. Each AFO was worn daily for 6 to 12 hours and removed at night over a period of 3 months.Each child walked at a self-selected speed along a 7.5 meter walkway. A total of 10 to 20 walking trials were performed in order to obtain five right and five left trials with useful forceplate data. Data from three representative trials for each side were averaged and mean values were used for analysis. Each child's participation in the study lasted 1 year and comprised 4 visits : a baseline assessment after 3m of no AFO wear, and an assessment at the end of each AFO 3 month wearing period.	Outcomes:Kinematic analysis and energy expenditure. BOTMP, GMFM, GMPM and PEDI Baseline assessments were performed barefoot (BF), except for energy expenditure which was performed with shoes on and no AFO. a Mean of this condition differed significantly from mean of BF condition b Mean of HAFO differed significantly from mean of SAFO c Mean of HAFO differed significantly from mean of the PLS Ankle dorsiflexion ($p \leq 0.01$) Initial contact Barefoot = –7.2 (13) HAFO = 5.4 (3.9)a PLS = 4.8 (4.6)a SAFO = 5.0 (4.5)a Peak dorsiflexion stance Barefoot = 5.7 (12.9)	Prospective or retrospective : Prospective Cross-sectional or longitudinal : Cross sectional - group means are presented (not change scores) Design : experimental Randomised : All children randomly assigned to 1 of 3 sequences of AFO use following a 3 month baseline period of no AFO use. Allocation concealment: unclear Similar prognosis at baseline : unclear Blinded subjects : n Blinded therapists : n Blinded assessors : n >85% follow up : y ITT analysis : y Because of the number of variables analyzed using ANOVA, Bonferonni corrections were used to set the level of significance for	Funding : Shriners Hospitals for Children Consent : Informed consent was obtained for each child Ethical approval : Shriners Hospitals for Children and the Institutional Review Board of the Oregon Health Sciences University, Portland

	involved in ongoing PT during their participation	AFO movement details : complete Orthotic Aim : not given AFO ankle angle details : complete toe plate length details :full length materials details : complete alignment details : not given prefab or custom : custom randomised testing order : y acclimatisation time : >4wks	HAFO = 18.6 (8.3)a,b PLS = 14.8 (7.3)a SAFO = 12.5 (5.3)a Peak dorsiflexion time, % Barefoot = 27 (14) HAFO = 46 (5)a,b PLS = 38 (13)a SAFO = 36 (13)a Peak dorsiflexion swing Barefoot = –3.6 (13.9) HAFO = 8.3 (5.5)a PLS = 6.9 (4.6)a SAFO = 7.2 (5.6)a Range Barefoot = 29.7 (14.8) HAFO = 16.5 (5.7)a PLS = 14.6 (4.5)a SAFO = 10.6 (3.8)a Velocity, m/s Barefoot = 1.08 (0.22) HAFO = 0.98 (0.21)b PLS = 1.11 (0.19) SAFO = 1.04 (0.18) Ankle range (p≤0.025) Dorsiflexion knee extension, degrees Barefoot = 8 (5) HAFO = 10 (7) PLS = 8 (6) SAFO = 8 (5) Dorsiflexion knee flexion, degrees Barefoot = 17 (9)	each variable category. Owing to the lack of a significant difference between the right and left lower extremity variables (paired t-tests), the right extremity values were randomly selected for analysis. In the three participants who were braced unilaterally, the braced lower extremity was analyzed. This approach to data analysis was preferred to combining data from both lower extremities into one database, as the latter approach falsely represents the number of participants	

			HAFO = 19 (8) PLS = 18 (9) SAFO = 15 (6) GMFM (p≤0.025) Standing Barefoot = 35.4 (2.7) HAFO = 35.5 (3.0) PLS = 35.6 (3.1) SAFO = 35.8 (2.8) Walking/Running/Jumping Barefoot = 57.1 (12) HAFO = 61.0 (10.9)a PLS = 60.8 (10.3)a SAFO = 60.6 (10.5)a PEDI (p≤0.025) Mobility Functional skills Shoes on/No AFO = 51.2 (2.7) HAFO = 51.9 (2.8) PLS = 52.9 (2.6) SAFO = 52.6 (3.2) Caregiver assistance Shoes on/No AFO = 34.1 (1.4) HAFO = 34.5(1.1) PLS = 34.3 (1.8) SAFO = 34.4(1.3) Percentage of children able to master item (i.e. keep up with peers) Item 31: walk between rooms Shoes on/No AFO = 31		

			HAFO = 25 PLS = 38 SAFO = 44 Item 44: walk more than 150 feet Shoes on/No AFO = 13 HAFO = 0 PLS = 0 SAFO = 13		

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Journal of Pediatric Orthopaedics **Authors** Rethlefsen,S., Kay,R., Dennis,S., Forstein,M., Tolo,V. **Year of publication** 1999 **Study location** USA **Ref ID** 76781 **Type of study** Randomised controlled study **Aim of study** To quantify the effects of fixed and articulated AFOs on gait in children with CP and determine whether one type results in improved mechanics. Secondarily, to determine patient criteria for use of fixed and articulated AFOs	**Inclusion Criteria** 1) No more than 15 degrees hip flexion contractures 2) Popliteal angles of <45 degrees 3) 5 degrees or more dorsiflexion range of motion available with the knee extended 4) Independent ambulation without assistive devices 5) No orthopaedic or neurosurgery in the preceding year **Exclusion Criteria** Not stated **Baseline characteristics** 21 children with diplegia Mean age 9.1 SD 2.2 yrs (range 5.3 - 13.5 yrs) All participants used fixed or articulated AFOs at the time of enrollment or were in need of orthoses.	Intervention : SAFO(fixed) or HAFO (articulated) Control : shoes Procedures 18/21 sparticipants had both a pair of SAFOs (fixed) and a pair of HAFOs (articulated) made from the same mold by the orthotist involved in the project. A pair of SAFOs (fixed) were made for each of the remaining 3 participants who already had HAFOs (articulated) that fit and functioned appropriately. Subjects followed individualised schedules alternating between the 3 footwear conditions (shoes, SAFO, HAFO) every 3 days for 4-6 weeks. The order was determined randomly for each child. The order of gait assessment with the 3 footwear conditions (shoes, SAFO, HAFO) was also randomly determined. Subjects were asked to walk at a self-selected speed making several passes through the laboratory under each footwear condition, with surface EMG electrodes, until 3 clean foot-plate strikes were achieved for both sides.	Outcomes : level walking Ankle dorsiflexion, Initial contact n=42 No AFO (shoes on) = -0.6±6 HAFO = 4±5 SAFO = 3±4 Ankle dorsiflexion,terminal stance n=42 No AFO (shoes on) = 8 ± 8 HAFO = 13 ± 6 SAFO = 8 ± 4 Knee, initial contact (degrees) n=42 No AFO (shoes on) = 27 ± 13 HAFO = 28 ± 12 SAFO = 26 ± 11 Knee, terminal stance (degrees) n=42 No AFO (shoes on) = 12 ± 10 HAFO = 13 ± 10 SAFO = 11 ± 10 Velocity (m/min) n=40 No AFO (shoes on) = 63.2 ± 8.4 HAFO = 64.5 ± 9 SAFO = 63.6 ± 12	Prospective or retrospective : Prospective Cross-sectional or longitudinal : Cross sectional Design : experimental Randomised : random allocation to sequence of tx with FAFO, DAFO or shoes Allocation concealment: No Similar prognosis at baseline : unclear Blinded subjects : No Blinded therapists : No Blinded assessors : No >85% follow up? : Yes ITT analysis : Yes	Funding : United Cerebral Palsy Research and Educational Foundation Ethical approval : not stated Consent : not stated

		AFO movement details : complete Orthotic Aim : ambiguous AFO ankle angle details : unclear toe plate length details :not given materials details : not given alignment details : not given prefab or custom : custom acclimatisation time : alternating 3 days wear for 3 footwear conditions over 4-6 weeks			

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Developmental Medicine and Child Neurology **Authors** Buckon,C.E., Thomas,S.S., Jakobson-Huston,S., Sussman,M., Aiona,M. **Year of publication** 2001 **Study location** **Ref ID** 76476 **Type of study** Randomised controlled study **Aim of study** To examine the effectiveness of the hinged ankle–foot orthosis (HAFO), posterior leaf spring (PLS), and solid ankle–foot orthosis (SAFO), in preventing contracture, improving efficiency of gait, and enhancing performance of functional motor skills in children with spastic hemiplegia	**Inclusion Criteria** 1) Aged from 4 to 18 years 2) capable of independent ambulation without assistive devices 3) using an AFO at the time of enrollment or with AFO use indicated 4) no orthopedic or neurosurgical intervention in the preceding year 5) Diagnosis of hemiplegia **Exclusion Criteria** not stated **Baseline characteristics** 30 children with hemiplegia were recruited Male :21 Female : 9 Left hemiplegia : 16 Right hemiplegia : 14 Mean age : 9y 4m (range =5y3m - 15y3m) At baseline each child was assessed barefoot. Two older children had a history of tendo-achilles lengthening 6-7 years before their participation in the study. One child dropped out of the study after the baseline assessment due to refusal to wear an AFO during the day	Intervention : hinged AFO (with plantarflexion stop), solid AFOs and PLS Control : barefoot or shoes Procedures An ankle mold was made for each child upon initiation intothe study by a single orthotist and the original mold was used to fabricate all three AFO configurations. Each AFO was worn daily for 6 to 12 hours and removed at night over a period of 3 months.Each child walked at a self-selected speed along a 7.5 meter walkway. A total of 10 to 20 walking trials were performed in order to obtain five right and five left trials with useful forceplate data. Data from three representative trials for each side were averaged and mean values were used for analysis. AFO movement details : complete Orthotic Aim : not given AFO ankle angle details : complete toe plate length details :full length materials details : complete alignment details : not given	Outcomes: Passive ankle ROM, gait analysis and energy expenditure. GMFM, GMPM and PEDI All assessments were performed by one of two clinicians with each child's clinician remaining constant throughout the study.Assessments were performed at baseline and at the end of each 3 m period, and therefore consisted of 4 assessments during 1 year Due to the number of variables analyzed using ANOVAs, Bonferonni corrections were used to set a level of significance for each variable category. Significance levels were set as follows: p <0.05 for gait kinetics; p<0.025 for ankle range of motion, GMFM, and PEDI; p <0.017 for ankle and knee kinematics and energy consumption; p <0.0125 for gait parameters, and p<0.007 for the GMPM. Ankle dorsiflexion,°Knee extended Barefoot = 5 (6) HAFO = 7 (5) PLS = 7 (4)	Prospective or retrospective : Prospective Cross-sectional or longitudinal : Cross sectional - group means are presented (not change scores) Design : experimental Randomised : All children randomly assigned to 1 of 3 sequences of AFO use following a 3 month baseline period of no AFO use. . Allocation concealment: unclear Similar prognosis at baseline : unclear Blinded subjects : n Blinded therapists : n Blinded assessors : n >85% follow up : y ITT analysis : y Between group statistical analysis : n	Funding : Shriners Hospitals for Children Consent : Informed consent was obtained for each child Ethical approval : Shriners Hospitals for Children and the Institutional Review Board of the Oregon Health Sciences University, Portland

		prefab or custom : custom randomised testing order : y acclimatisation time : >4wks	SAFO = 6 (4) Ankle dorsiflexion,°Knee flexed Barefoot = 12 (6) HAFO = 14 (6) PLS = 14 (6) SAFO = 13 (4) Ankle dorsiflexion, Initial contact Barefoot = –11 (6) HAFO = 3 (4) PLS = –0.2 (5) SAFO = 2 (4) Ankle dorsiflexion, Peak stance Barefoot = 6 (5) HAFO = 16 (6) PLS = 13 (7) SAFO = 11 (5) Ankle dorsiflexion, Dynamic range Barefoot = 26 (7) HAFO = 16 (4) PLS = 15 (4) SAFO = 11 (3) Group mean (SD) for Velocity (m/s) No AFO (barefoot) = 1.07 (0.22) HAFO = 1.14 (0.16) PLS = 1.18 (0.17) SAFO = 1.11 (0.17)		

			Group mean (SD) for GMFM GMFM dimension Stand No AFO (barefoot) = 37.6 (2) HAFO = 37.9 (1) PLS = 37.8 (1) SAFO = 38.0 (1) GMFM dimension Walk/Run/Jump No AFO (barefoot) = 67.1 (5) HAFO = 68.1 (3) PLS = 68.1 (3) SAFO = 67.6 (4) Group mean (SD) for number of children able to master select PEDI items No AFO (shoes on) = HAFO = PLS = SAFO = PEDI Mobility dimension Functional Skills No AFO (shoes on) = 55.4 (2) HAFO = 56.7 (2) PLS = 56.6 (2) SAFO = 56.8 (2) Indoor/Outdoor Locomotion Distance/Speed Item 31 : moves between rooms – no difficulty No AFO (shoes on) = 24/30 HAFO = 23/30 PLS = 27/30 SAFO = 23/30		

			Item 44 : moves 150 feet or longer – no difficulty No AFO (shoes on) = 8/30 HAFO = 15/30 PLS = 18/30 SAFO = 11/30		

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Gait and Posture **Authors** Sienko,Thomas S., Buckon,C.E., Jakobson-Huston,S., Sussman,M.D., Aiona,M.D. **Year of publication** 2002 **Study location** USA **Ref ID** 98325 **Type of study** Randomised controlled study **Aim of study** To determine whether different AFO configurations have a detrimental effect on both funtion and kinematics during stair locomotion in children with spastic hemiplegia	**Inclusion Criteria** Patients recruited from larger study of children with cerebral palsy. Inclusion criteria were 1) 4 - 18 years of age 2) no ankle or foot surgery 1 year prior to enrollment 3) independent ambulation 4) Require AFO useas indicated by a physician **Exclusion Criteria** Not stated **Baseline characteristics** 19 children with hemiplegia were included in the analysis. They were able to ascend and descend the stairs reciprocally during the barefoot assessment with or without the use of a handrail. Mean Age : 9±3 yrs (range : 6-15 years) Mean height : 138.7 cm (range : 122-173cm) Mean weight : 34.7kg (range 19-75kg)	Intervention : SAFO, HAFO, PLS with child's own shoes (for each evaluation and with attempt made to keep the shoes constant throughout the study) AFO movement details :incomplete Orthotic Aim : incomplete AFO ankle angle details : not given toe plate length details : not given materials details : not given alignment details : not given prefab or custom : custom randomised testing order : yes acclimatisation time : 3 months for each condition Control : barefoot Comparisons relevant to this review : 1) Barefoot vs SAFO 2) SAFO vs HAFO 3) SAFO vs PLS Procedure Each child participated in the study for a year. After 3 months of no AFO wear children then followed 3 months of SAFO, HAFO and PLS wear according to a	Gait parameters : Velocity = the amount of time required for the limb to move the distance from stair one to stair three with an average of three trials from each limb used in the analysis. Between group statistical analysis : yes - ANOVA, significance set at p=0.025 for gait parameters Velocity ascent (time for distance stair 1 to stair 3) 1) Barefoot vs SAFO Barefoot = 0.280 ± 0.06 SAFO = 0.270 ± 0.07 P= No significant difference (reported) 2) SAFO vs HAFO SAFO = 0.270 ± 0.07 HAFO = 0.281 ± 0.07 P= No significant difference (reported) 3) SAFO vs PLS SAFO = 0.270 ± 0.07 PLS = 0.304 ± 0.07 P= No significant difference (reported) Velocity descent (time for distance stair 3 to stair 1) 1) Barefoot vs SAFO Barefoot = 0.259 ± 0.06 SAFO = 0.296 ± 0.10	Prospective or retrospective Prospective Cross-sectional or longitudinal Cross sectional Design : Experimental Randomised : random allocation to order of treatment with SAFO, HAFO or PLS Allocation concealment : no details Similar prognosis at baseline : unclear Blinded subjects : no Blinded therapists : no Blinded assessors : no >85% follow up? : yes ITT analysis : yes	Funding : Shriners Hospitals for Children Consent : Participants gave written consent Ethical approval : Institutional Review Board

		randomised treatment order. Assessments were performed at the end of each condition's period. Each child reciprocally ascended and descended 4 stairs (rise = 15.2cm, run = 24.1cm, slope = 32 degrees) which were smaller and less steep than those found in the community (slope = 36.8 degrees) Stair ascent cycle = foot contact (involved or uninvolved) on stair one to foot contact with the same foot on stair three. Stair descent cycle = foot contact (involved or uninvolved) on stair three to foot contact with the same foot on stair one. The average of three trials for both the involved and uninvolved limbs were used for the analysis of stair ascent and descent.	P= No significant difference (reported) 2) SAFO vs HAFO SAFO = 0.296 ± 0.10 HAFO = 0.280 ± 0.08 P= No significant difference (reported) 3) SAFO vs PLS SAFO = 0.296 ± 0.10 PLS = 0.323 ± 0.11 P= No significant difference (reported) Kinematic data for stair locomotion : No relevant kinematic data (in stance and swing) Functional impact of AFO configurations on stair locomotion assessed by structured interviews with parents, using stair specific outomes from PEDI % of children capable of performing (defn keeping up with peers) Item 54 (walks up entire flight without difficulty) and Item 59 (walks down entire flight without difficulty). Between group statistical analysis : yes - Cochran Q-test, significance set at p<0.05 Ascent PEDI Item 54 (keeps		

			up with peers) 1) Barefoot vs SAFO Barefoot = 6/19 SAFO = 9/19 P= No significant difference (reported) 2) SAFO vs HAFO SAFO = 9/19 HAFO = 12/19 P= No significant difference (reported) 3) SAFO vs PLS SAFO = 9/19 PLS = 8/19 P= No significant difference (reported) Descent PEDI Item 59 (keeps up with peers) 1) Barefoot vs SAFO Barefoot = 5/19 SAFO = 7/19 P= No significant difference (reported) 2) SAFO vs HAFO SAFO = 7/19 HAFO = 10/19 P= No significant difference (reported) 3) SAFO vs PLS SAFO = 7/19 PLS = 6/19 P= No significant difference (reported)		

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Gait and Posture **Authors** Radtka,S.A., Skinner,S.R., Johanson,M.E. **Year of publication** 2005 **Study location** USA **Ref ID** 98326 **Type of study** **Aim of study** To compare the effects of solid and hinged ankle foot orthoses on the gait of children with s[astic diplegic cerebral palsy who ambulate with excessive ankle plantar flexion during stance	**Inclusion Criteria** Patients recruited from regular outpatients clinical for children with cerebral palsy. Inclusion criteria were each child 1) ankle dorsiflexion to 0 degrees in weightbearing during static standing 2) excessive ankle plantarflexion of 5 degrees or more during stance in gait 3) passive ankle dorsiflexion of 5 degrees with knee extended 4) passive hip extension to -10 degrees or less as measured by the Thomas test 5) passive hamstring length of 50 degrees or more as measured by a straight leg raise 6) mild spasticity of the triceps surae, hamstring and quadriceps or a score of 1 (Ashworth) mild resistance at the end range of passive motion. **Exclusion Criteria** Not stated **Baseline characteristics** 12 children with diplegia who ambulate with excessive ankle plantar flexion during stance Mean age 7.5 SD 3.83 yrs (range 4-16 yrs) None of the subjects had ever undergone Achilles tendon or	Intervention : Solid and hinged AFO (with shoes) AFO movement details : clear Orthotic Aim : complete AFO ankle angle details : complete toe plate length details : full length materials details : complete alignment details : not given prefab or custom : custom randomised testing order : y acclimatisation time : 1 month Control : barefoot Comparisons relevant to this review : 1) Barefoot vs SAFO 2) SAFO vs HAFO Procedures : Each child wore no orthoses for an initial 2 wks baseline period, solid or hinged AFOs for 1 month, no orthoses for 2 wks, and solid or hinged AFOs AFO for 1 mth. The order was randomly assigned. Children were asked to walk on a 10m walkway at a self-selected speed without being informed of the position of footplates and with active surface electrode pairs on lower limbs and footswitches	Outcomes : EMG, 3 dimensional motion analysis and temporal-distance characteristics, knee and ankle sagittal joint moments and powers during the stance phase Outcomes were assessed at the end of the initial 2 week period with no orthoses for a baseline measurement, the 1 month period wearing solid AFOs and the 1 month period wearing hinged AFOs (NB not at the end of the second 2 week period with no orthoses) Group means with standard deviations were calculated for outcomes. ANOVA with repeated measures was used to examaine the barefoot and AFO configurations on these coutomes at an alpha level of 0.05. For signicicant ANOVA tests, three post-hoc pairwise comparisons (SAFO vs HAFO, No AFO vs SAFO and No AFO vs HAFO) were conducted using Tukey's Honestly Significant Difference Test to determine significant differences at an alpha level of 0.05. Temporal-distance gait	Prospective or retrospective : Prospective Cross-sectional or longitudinal : Cross sectional Design : Experimental Randomised : random allocation to order of treatment with SAFO or HAFO Allocation concealment : n Similar prognosis at baseline : n Blinded subjects : n Blinded therapists : n Blinded assessors : n >85% follow up : y ITT analysis : y	Funding : Shriners Hospitals for Children Consent : Parents or participants aged over 12 gave written consent Ethical approval : Institutional Review Board, University of California

	gastrocnemius lengthening surgical procedures in the past or any other orthopaedic surgery during preceding year. 10 subjects ambulated without assistive devices. 9 subjects wore rigid AFO and 3 subjects used hinged AFO for at least 1 year prior to participation.	alone the entire plantar surface of both feet for the barefoot baseline test and on the shoes for tests with both orthoses. 2 trials with 4 -6 gait cycles per condition were averaged for each subject.	characteristics : Velocity (cm/sec) 1) Barefoot vs SAFO Barefoot = 90.62 ± 23.02 SAFO = 94.70 ± 22.07 P = No significant difference (reported) 2) SAFO vs HAFO SAFO = 94.70 ± 22.07 HAFO = 99.63 ± 20.53 P = No significant difference (reported) Ankle dorsi/plantarflexion at initial contact - post hoc analysis 1) Barefoot vs SAFO Barefoot = -8.14 ± 5.46 SAFO = 7.09 ± 5.06 P < 0.05 (reported) 2) SAFO vs HAFO SAFO = 7.09 ± 5.06 HAFO = 5.37 ± 7.00 P = No significant difference (reported) Ankle dorsi/plantarflexion at terminal stance - post hoc analysis 1) Barefoot vs SAFO Barefoot = -1.30 ± 6.59 SAFO = 11.50 ± 4.28 P < 0.05 (reported) 2) SAFO vs HAFO SAFO = 11.50 ± 4.28		
			HAFO = 16.13 ± 6.17 P < 0.05 (reported)		

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical American Journal of Physical Medicine and Rehabilitation **Authors** Carlson,W.E., Vaughan,C.L., Damiano,D.L., Abel,M.F. **Year of publication** 1997 **Study location** USA **Ref ID** 76482 **Type of study** Randomised controlled study **Aim of study** To compare the effects of a fixed AO, a SMO and a no brace condition, but including shoes	**Inclusion Criteria** Patients recruited from regular outpatients clinical for children with cerebral palsy. Inclusion criteria were each child 1) had to be ambulatory 2) have no fixed joint contractures requiring surgery 3) had to exhibit a dynamic equinus or crouch gait 4) have no varus or valgus hindfoot instability **Exclusion Criteria** Not stated **Baseline characteristics** 11 children with diplegia and spastic equinus rigid hindfoot Mean age 6.9y Age range 4-11yrs Males n=6, Females n=5 9 children had no history of surgery, 2 children had a history of adductor and tendo-achilles lengthening on both sides 9 children were independent walkers, 1 child was an independent walker with AFOs and one ambulated aroundthe house with a walker Prior bracing : 5 children had had AFOs, 5 children had had AFOs and SMOs and one child had previously had SMOs only	Intervention : rigid AFO, SMO with no plantar flexion stop Control : shoes only AFO movement details : clear Orthotic Aim : complete AFO ankle angle details : not given toe plate length details : not given materials details : not given alignment details : not given prefab or custom : not given randomised testing order : y acclimatisation time : one month Procedures : Subjects were bought a pair of shoes at the start of the protocol and were required to wear them during the 4 months of the experiment and throughout the gait studies. Each subject made 4 difference visits to the gait lab with visits spaced one month apart. Month 1 : after wearing no brace for one month a baseline test of walking with shoes but no orthosis was performed Month 2 : the child wore an AFO or SMO (as randomised) inside the shoes for one month	Outcomes : Temporal-distance, kinematic and kinetic parameters were assessed using data averaged from three walking trials for each or the right and left sides. There were no statisitically significant differences between the left and right sides (from preliminary data) therefore the two sides were averaged for each patient before making comparisons among the baseline, AFO and SMO conditions. Velocity (m/s) - group mean SAFO = 1.00 ± 0.19 SMO = 1.00 ± 0.20 P= No significant difference (reported) Ankle dorsiflexion angle at foot strike (degrees) - group mean SAFO = 10.0 ± 6.0 SMO = 3.3 ± 7.0 P < 0.05 (reported)	Prospective or retrospective : Prospective Cross-sectional or longitudinal:Cross sectional Design : experimental Randomised : random allocation to order of treatment with SAFO or SMO Follow up length : 4 months Allocation concealment: No Similar prognosis at baseline : unclear Blinded subjects : No Blinded therapists : Unclear Blinded assessors : unclear >85% follow up? : Yes ITT analysis : Yes	Funding : supported in part by a grant NIH HD30134 from the US Public Health Service and grant H133P10006 from the US Dept of Education Ethical approval : Approved by the authors institution's Human' Subjects Committee Consent : All subjects (or their families) signed a consent form

	In most cases clinic notes indicated that there was only mild involvement of both sides and all children were considered to be community ambulators	and returned for testing Month 3 : after wearing no brace for one month a 2nd baseline test of walking with shoes but no orthosis was performed Month 4 : the child wore an AFO or SMO (as randomised) inside the shoes for one month and returned for testing Subjects walked at their freely selected speed during each gait testing session where they were asked to perform between 10-20 walking trials (usually) before the desired minimum of 3 clean strikes for each foot were obtained on force plates. The subjects had no difficulty in performing this amount of walking Temporal-distance, kinematic and kinetic parameters were assessed using data averaged from three walking trials for each or the right and left sides.			

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Neurorehabilitation **Authors** Elliott,C.M., Reid,S.L., Alderson,J.A., Elliott,B.C. **Year of publication** 2011 **Study location** Australia **Ref ID** 132638 **Type of study** Randomised controlled study **Aim of study** To investigate the effects of lycra arm splint wear on goal attainment and three dimensional kinematics of the upper limb and trunk in children with cerebral palsy (CP)	**Inclusion Criteria** Children diagnosed with hypertonic CP **Exclusion Criteria** Not reported **Baseline characteristics** n=16 Age / years (mean±SD, range): 11.5±2.2, 8 - 15 Sex (n) Male: 8 Female: 8 3 children had quadriplegia and 13 had hemiplegia Hypertonic responses (n): - Spastic: 10 - Dystonic: 5 - Rigid: 1 Functional ability of the affected upper limb ranged from 27 - 85 on the Melbourne Assessment of Unilateral Upper Limb Function. No significant difference was identified between the two groups in Melbourne assessment score, maximum elbow extension, and maximum supination. No children had Botulinum	Randomisation - The study used a randomised parallel group trial with waiting list control design. Participants were randomised to two groups. Group 1 completed a splint-wearing regime combined with goal directed training for three months. Group 2 completed goal directed training only, therefore acting as a control population. Subsequently, group 2 then completed the splint-wearing regime combined with goal directed training for three months. Intervention: - The intervention consisted of three months of lycra arm splint wear, combined with goal directed training. The Second Skin lycra splints were individually custom designed, and consist of sections of lycra stitched or under tension with a specific direction of pull. The arm splint extends from the wrist to the axilla, and is designed to promote better hand and arm function by	GAS-T scores at 3 months Group 1 Mean change ± SD = 53 ± 5.0 Group 2 Mean change ± SD = 35 ± 6.8 The authors note that a change score ≥50 represented the expected change in goal attainment over the 3 month period.	Prospective or retrospective: prospective Cross-sectional or longitudinal: longitudinal Design: experimental Randomised: method of randomisation not reported Allocation concealment: unclear Similar prognosis at baseline: yes - no significant difference in Melbourne Assessment Blinded subjects: no Blinded therapists: unclear Blinded assessors: unclear, also not reported who measured RoM. >85% follow up: yes ITT analysis: yes	Further details of methodology can be found in an excluded study, Elliott et al. 2011, which did not report any outcomes relevant to the review, but describes methodology in more detail. Funding: All splints were provided by Second Skin, but the company had no involvement in study design, data collection, analysis or interpretation, or preparation of the manuscript. Consent: Written informed consent was attained from each participating family Ethical approval: From University of Western Australia

	Neurotoxin-A or lycra splinting within previous two years.	addressing postural and tonal issues impacting on the elbow, by addressing either pronation-flexion or supination-extension. The pronation-flexion splint is designed for children whose functional performance is limited by strong elbow extension and supination. The supination-extension splint is designed for those whose performance is limited by strong elbow flexion and pronation. - The participants wore their arm splints during school hours, approximately 6 hours per day, 5 days per week. The goal directed training consisted of active practice of task-specific activities related to the child's functional goals. Active practice was incorporated into the child's daily routine taking approximately 25 minutes to complete. <u>Assessment</u> - The children were assessed at baseline and then at 3 months. All baseline assessments were completed with the splint off. The three months condition was performed wearing the splint,			

		following three months of the splinting intervention. <u>Data analysis</u> - To determine the effect of the splint on variables, repeated measures ANOVAs were conducted to analyse differences between the splinting conditions for the entire cohort of participants. Each independent variable had four levels (k=4). The assumptions of normality, homogeneity of variance and sphericity were met for all variables. A medium effect size of 0.5 was used to establish functional differences between changes over time that were shown to be significantly different.			

Spasticity in children and young people with non-progressive brain disorders: management of spasticity, co-existing motor disorders and their early musculoskeletal complications

Oral drugs

Bibliographic details	Number of Participant Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Authors Scheinberg,A., Hall,K., Lam,L.T., O'Flaherty,S. **Year of publication** 2006 **Study location** Australia **Ref ID** 56461 **Type of study** Randomised controlled study **Aim of study** To assess: -the effectiveness of baclofen in reducing spasticity and improving passive function in children with cerebral palsy (CP) and	**Inclusion Criteria** Convenience sample drawn from a physical disability clinic at a tertiary paediatric hospital Age: 1 to 15 years CP and clinically significant spasticity defined as: increased tone or spasms, causing pain, reported difficulty with cares or impaired movement Children with dystonia as additional motor disorder also included **Exclusion Criteria** Children already taking oral anti-spasticity medication Epileptic seizure within the previous month **Baseline characteristics** **Intervention Group**	**Intervention** Group A: 13 weeks of oral baclofen followed by a 2-week non-treatment (washout) period and then 13 weeks of oral placebo Dose: -children aged < 8 years at enrolment: starting with 2.5 mg daily, increased weekly over a 7-week period to 10 mg three times a day and then continued at that dose for the next 5 weeks -children aged 8 or >8 years at enrolment: starting with 5 mg daily, increased weekly over a 9-week period to 20 mg three times a day and then continued at that dose for the next 3 weeks At the end of each 12-week period the drug (either baclofen or placebo) was tapered over 6 days **Comparison 1**	**Outcome 1** Modified Tardieu scores (MTS) score (mean, 95% CI) baseline: 20.9 (15.7 to 26.2) placebo: 27.1 (21.0 to 33.3) baclofen: 25.6 (19.4 to 25.8) change: -4.4 (-10.8 to 2.0) -Significance of different effects treatment: F (1,10)=0.9 ; p=0.36 period: F (1,10)=0.0 ; p=0.96 carry-over: F (1,10)=0.1 ; p=0.72 **Outcome 2** Goal Attainment Scaling (GAS) T score (mean, 95% CI) baseline: 35.0 placebo: 44.7 (39.3 to 50.0) baclofen: 51.3 (47.4 to 55.1) change: 6.6 (1.0 to 12.3) -Significance of different effects treatment: F (1,13)=4.5 ; p=0.05 period: F (1,13)=1.0 ; p=0.34 carry-over: F (1,13)=0.3 ; p=0.57 **Outcome 3** Paediatric Evaluation of Disability Inventory (PEDI) (mean, 95% CI)	Limitations Allocation concealment : unclear. but carried out by the hospital pharmacy Participants blinded to intervention : yes Carers blinded to intervention : yes Investigators blinded to intervention : yes Number of participants not completing treatment : none Number of participants with no available outcome data : none Selective outcome reporting : none Any other limitations : small sample size Indirectness Population : None Intervention : None	**Funding** The Children's Hospital at Wetsmead Small Grants Scheme **Other information** The same researcher explained study procedures to all children and carers, recorded demographic data, administered the parent questionnaire and assisted with measurements of MTS. An experienced paediatric physiotherapist undertook all other assessments including the MTS, GAS and PEDI. Assessments were performed at baseline and at the end of each 12-week period,

clinically significant spasticity -parent/carer reported side effects and whether they would choose the drug to be continued	(this is the total sample) 15 children -age range: 4 to 12 (mean: 7.4 years) -type of CP (n children): Spastic quadriplegia: 11 Spastic/dystonic quadriplegia: 4 GMFC IV: 10 GMFC V: 5 Mean weight: 17.2 kg (4.3) Intervention group: Group A (n=8) Comparison group: Group B (n=7) Specific sociodemographic and clinical characteristics other than study outcomes not reported separately for each group Baseline clinical outcomes not compared between groups -	Group B: 13 weeks of oral placebo followed by a 2-week non-treatment (washout) period and then 13 weeks of oral baclofen	a. Self care baseline: 15.2 (6.5 to 23.8) placebo: 20.5 (9.8 to 31.3) baclofen: 19.1 (8.8 to 29.4) change:-1.5 (-3.5 to 0.6) -Significance of different effects treatment: F (1,13)=1.7 ; p=0.21 period: F (1,13)=1.7 ; p=0.21 carry-over: F (1,13)=0.1 ; p=0.78 b. Mobility baseline: 17.5 (7.3 to 27.8) placebo: 18.7 (8.1 to 29.4) baclofen: 17.3 (6.9 to 27.7) change: -1.5 (-3.1 to 0.2) -Significance of different effects treatment: F (1,13)=3.6 ; p=0.08 period: F (1,13)=2.4 ; p=0.14 carry-over: F (1,13)=0.6 ; p=0.45 c. Social function baseline: 31.8 (18.0 to 45.6) placebo: 32.9 (19.3 to 46.5) baclofen: 32.7 (19.8 to 45.6) change: -0.2 (-3.0 to 2.6) -Significance of different effects treatment: F (1,13)=0.0 ; p=0.96 period:F (1,13)=1.4 ; p=0.27 carry-over: F (1,13)=0.0 ; p=0.95 Outcome 4 Parental satisfaction with the medication effect Placebo treatment 4 parents would continue with placebo 10 parents would not continue with placebo	Comparison : None Outcomes assessed : None	prior to tapering of the drug Both groups were followed up for an equal length of time Study had an appropriate length of follow up (GDG confirmed) and a precise definition of outcome A valid and reliable method was used to determine outcome The comparison groups recived the same care apart from the interventions studied **Selective outcome reporting** - **Sample size** This was a pilot study The sample size estimation was based on a single measure of the GAS, as according to authors there is a lack of quantifiable information in the literature of the assessments measures used in this study. It was assumed that baclofen had a large

			Baclofen treatment 6 parents would continue with baclofen 8 parents would discontinue baclofen treatment 1 parent was unsure. Outcome 5 Positive effects reported by parents during treatment periods Placebo treatment better sleeping (2), being more vocal (1), being more relaxed/settled (3) and less drooling were reported. Baclofen treatment period better sleeping (3), being more vocal (1), being easier to dress (1) and fewer spasms (1) were reported		treatment effect of 0.8 standard deviations when compared with placebo using a simple pair-comparison scenario. it was further assumed that there was negiglible carry-over as well as time period effects that potentially impacted on the analyisis of a cross-over study. A sample size of 14 would be sufficient to provide the study with 80% power to detect a tru difference, should one exist, using a significance level of 5%.

Bibliographic details	Number of Participant Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Authors Milla,P.J., Jackson,A.D. **Year of publication** 1977 **Study location** UK **Ref ID** 56476 **Type of study** Randomised controlled study **Aim of study** To assess the effects of baclofen in comparison with placebo on the disability due to pyramidal spasticity in children suffering from cerebral palsy (CP)	**Inclusion Criteria** Children aged 2 to 16 years, suffering from spasticity due to CP **Exclusion Criteria** Epilepsy, muscle hypotonia, severe psychiatric disturbance, renal or hepatic insufficiency, being treated with tricyclic or phenothiazine psychotropic drugs **Baseline characteristics** (total sample) 20 children attending either a hospital treatment centre as outpatients or local special shools for the physically handicapped -age range: 2 to 16 years -9 boys, 11 girls -type of CP (n children): Diplegic: 5 Hemiplegic: 7 Quadriplegic: 8 3 also exhibited athetosis -Ashworth scale (n children):	**Intervention** Oral baclofen 4-week treatment (inmediately followed by 4-week placebo treatment) First 2 weeks for dose adjustment in order to find optimal therapeutic level for each patient. This dose was then continued for the remaining 2 weeks. Initial dose: 10 mg daily in divided doses, increased in 3 increments over a period of 9 days, to maximun daily dosage of 60 mg (children over the age of 8 years) or 30 to 40 mg (children 2 to 7 years) Patients' routine physiotherapy continued unchanged throughout trial **Comparison 1** Placebo 4-week treatment (inmediately followed by 4-week baclofen treatment) First 2 weeks for dose adjustment in order to find optimal therapeutic level for each patient. This dose was then continued for the remaining 2 weeks. Initial dose: 10 mg daily in divided doses, increased in 3 increments over a period of 9 days, to maximun daily dosage of 60 mg (children over the age of 8 years) or 30 to 40 mg (children 2 to 7	**Outcome 1** Severity of spasticity (Ashworth Scale) after 28 days treatment (n of children) a. no increase in tone baclofen: 2 placebo: 0 b. slight increase in tone baclofen: 9 placebo: 3 c. more marked increase in tone baclofen: 8 placebo: 9 d. considerable increase in tone baclofen: 1 placebo: 8 e. affected parts rigid baclofen: 0 placebo: 0 14 children showed improvement whilst taking baclofen, whereas only 2 improved on placebo. 5/14 children who improved on baclofen did so by more than one category in the Ashworth Scale. The 2 children who improved on placebo did so by only one category 1/3 children with athetosis showed improvement whilst taking 60 mg/day and no improvement whilst receiving placebo Analysis of results by age groups did not show any statistically significant difference between younger (2 to 7 year olds) and older patients (7 to 16 year olds) **Outcome 2** Other clinical evaluation a. Extrapyramidal signs: recorded but not reported b. Cerebellar symptoms: no patients exhibited them c. Clonus: no patients exhibited it	Limitations Allocation concealment : unclear, but "random allocation" stated Participants blinded to intervention : yes Carers blinded to intervention : yes Investigators blinded to intervention : yes Number of participants not completing treatment : none Number of participants with no available outcome data : none Selective outcome reporting : unclear Any other limitations : none Indirectness Population : None Intervention : None Comparison : None Outcomes assessed : None	**Funding** Supplies of baclofen made available by CIBA Laboratories, Horsham, West Sussex. Other details unclear. **Other information** Patients assessed at the start of trial and subsequently at intervals of 7 days during the trial period by the same physician at the same time of the day. At the end of each treatment period the clinician, physiotherapist and the parent or nurse made independent overall evaluations of the patients' progress Both groups were followed up for an equal length of time Study did not have an appropriate length of follow-up or a precise definition of outcome. Unclear whether a valid and reliable method was used to determine outcome Unclear whether

	No increase in tone: 0 Slight increase in tone: 2 More marked increase in tone: 9 Considerable increase in tone: 9 Affected parts rigid: 0 **Intervention Group** -	years) Patients' routine physiotherapy continued unchanged throughout trial	d. Tendon reflexes: changes reported as "insignificant" **Outcome 3** Disabilities due to spasticity a. walking ability b. scissoring c. impairment of passive an active limb movements d.degree of self help e. manual dexterity These outcomes were only reported for the period when children were taking baclofen but not for placebo, therefore they are non-comparative and not included		investigators were kept blind to participants' exposure to the intervention or to other important confounding and prognostic factors **Selective outcome reporting** - **Sample size** No calculation reported

Bibliographic details	Number of Participant Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Authors Mathew,A., Mathew,M.C., Thomas,M., Antonisamy,B 2005a. **Year of publication** 2005 **Study location** India **Ref ID** 56486 **Type of study** Randomised controlled study **Aim of study** To compare the effects of two dose sizes of diazepam and placebo given in a single bedtime dose	**Inclusion Criteria** All children with spastic CP below 12 years of age and weighting 15kg or less including those with co-morbid factors such as dysmorphic features or visual or hearing impairments. **Exclusion Criteria** Children who were in distress due to painful spasms were given diazepam and excluded. Children needing immediate medical attention due to acute illness were also excluded Children with hyptonic or extrapyramidal CP **Baseline characteristics** There were no significant differences among the three treatment groups (Total N = 180) for : Age up to 5 years Half dose diazepam group = 52/60 Full dose diazepam group = 57/60 Placebo group = 54/60 Sex (no of girls)	**Intervention** Sachets of diazepam prepared by the pharmacy (to be taken in a half or full dose) **Comparison 1** Sachets of placebo prepared by the pharmacy	**Outcome 1** 1) Mean change in muscle relaxation (modified Ashworth scale) Half dose diazepam group = 8.53 Full dose diazepam group = 13.32 Placebo group = 0.53 p<0.001 2) Adverse effects : Drowsiness No daytime drowsiness was reported for any child **Outcome 2** - **Outcome 3** -	Limitations Allocation concealment : computer generated in pharmacy Participants blinded to intervention : yes Carers blinded to intervention : yes Investigators blinded to intervention : yes Number of participants not completing treatment : 7/180 Number of participants with no available outcome data : 7/180 Selective outcome reporting : study powered for range of movement outcomes although mean change in muscle relaxation also reported. Outcomes for the well being of the child found in the full dose and placebo groups are reported in a separate publication above Any other limitations : standard deviations	**Funding** not stated **Other information** Informed consent: Yes Ethical approval :Research and Ethics committee of the Christian Medical College Hospital. Vellore Sample size calculation: based on clinical use of the drug over 6 months prior to trial. A total of 180 children (n=60 in each group) with 90% power (beta = 10%) and a two-tailed 2% significance level (alpha = 2%) would be required to detect a 10 degree change in the angle of flextion at ankle between the placebo and diazepam groups **Selective outcome reporting** - **Sample size** -

	Half dose diazepam group = 38/60 Full dose diazepam group = 36/60 Placebo group = 37/60 Socioeconomic status (High/Upper /Middle/Low) Half dose diazepam group = 3/6/14/37 Full dose diazepam group = 2/12/16/30 Placebo group = 5/9/18/28 Type of cerebral palsy (diplegia, hemiplegia, triplegia, double hemiplegia, quadriplegia) Half dose diazepam group = 15/10/3/2/30 Full dose diazepam group = 17/8/5/0/30 Placebo group = 7/8/4/5/36 Weight <5kgs Half dose diazepam group = 4/60 Full dose diazepam group = 4/60 Placebo group = 7/60 Height (51 to 70cm/71 to 90cm/91 to 110cm/110-130cm) Half dose diazepam			are not given Indirectness Population : none Intervention : none Comparison : none Outcomes assessed : none	

	group = 19/27/10/4 Full dose diazepam group = 26/29/5/0 Placebo group = 27/21/11/1 Each child was seen in outpatients department once every 7 to 10 days. At each visit drug compliance was reviewed and assessments for muscle relaxation, motor function and well being of the child were carried out. The caregiver was taught the passive stretching exercises for the child and advised to administer the bedtime medications. Results were obtained 15 to 20 days after therapy started. **Intervention Group** Half dose diazepam group n=60 children under 8.5kg given 0.5mg daily at bedtime children over 8.5kg given 1mg daily at bedtime				

	Full dose diazepam group n=60 children under 8.5kg given 1mg daily at bedtime children over 8.5kg given 2mg daily at bedtime				

Bibliographic details	Number of Participant Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Authors Mathew,A., Mathew,M.C. 2005b **Year of publication** 2005 **Study location** India **Ref ID** 56488 **Type of study** Randomised controlled study **Aim of study**	**Inclusion Criteria** Serially recruited children with spastic CP who attended the outpatients department of a developmental paediatrics unit and who weighed under 15kgs **Exclusion Criteria** Child had received muscle relaxants Child weighed over 15kgs **Baseline characteristics** 120 recruited children were randomised into two groups of 60 participants. At baseline there was no significant difference between the two groups for the following characteristics: Age up to 5 years Diazepam group = 57/60 Placebo group = 54/60 Sex (no of girls) Diazepam group = 24/60 Placebo group = 23/60 Socioeconomic status (High/Upper	**Intervention** Packets of diazepam prepared by the Pharmacy Department. Single dose of diazepam given to children at bedtime, but size of dose given is not stated. **Comparison 1** Packets of placebo, identical in appearance to the diazepam packets prepared by the Pharmacy Department. Single dose of placebo given to children at bedtime.	**Outcome 1** All outcomes were assessed at the first visit and reviewed in all children after 15-20 days of receiving either diazepam or placebo. 1) Disposition of the child during activities of daily living: Detailed enquiries to ascertain and score the well-being of the child during the daily activities like feeding, bathing, playing, exercising and sleeping were made. The disposition of the child during the activity was graded from 0-5 on a scale with aa spectrum ranging from usually pleasant and happy to unhappy, persistently fretful and disturbed. Mean change in score from baseline Diazepam group = 6.31 SD±1.94 n=59 Placebo group = 0.38 SD± 0.62 n=55 2) Burden of caring for the child on the family: The burden of caring for the child on the family was found out from the information given by the mother or chief care-giver. The frequency of occurrence of the difficulties described below was the index of scoring the child on a scale from 0-7 i) Attention demand on caregiver due to inconsolable daytime crying spells ii) Disturbed sleep for caregiver due to frequent waking at night iii) Extended time requirement for feeding due to crying during meal-times iv) Caregiver's pesence required to carrry/comfort fretting child in waking hours v) Physical therapy stressful due to crying when limbs are moved Mean change in score from baseline Diazepam group = 7.75 SD±1.98 n=59 Placebo group = 0.44 SD± 0.66 n=55	Limitations Allocation concealment : computer randomisation Participants blinded to intervention : yes Carers blinded to intervention : yes Investigators blinded to intervention : yes Number of participants not completing treatment : 6 (1 from treatment group and 5 from placebo group) Number of participants with no available outcome data : 6 Selective outcome reporting : unclear Any other limitations : Outcomes are reported clearly but are not validated tools. No aim of the study or sample size calculation are reported, therefore it is difficult to tell whether there has been selective	**Funding** Not stated **Other information** Ethical approval : Research and Ethics Committee of the Christian Medical College and Hospital, Vellore Informed consent : Yes Sample size : not given **Selective outcome reporting** - **Sample size** -

	/Middle/Low) Diazepam group = 2/12/16/30 Placebo group = 5/9/18/28 Grade of cerebral palsy according to functional limitation of physical activity (Mild/Moderate/Severe) Diazepam group = 0/16/44 Placebo group =1/13/46 Type of cerebral palsy (diplegia, hemiplegia, triplegia, double hemiplegia, quadruplegia) Diazepam group = 17/8/5/0/30 Placebo group = 7/8/4/5/36 All mothers or caregivers were shown different passive movements (stretching programme) that could be easily carried out regularly at home from the 5th day of starting the drug trial. **Intervention Group** n=60		3) Child's behavioural profile: The frequency of undesirable behaviour given below during the time of clinical examination was observed and graded by the investigator as rarely =0, occasionally = 1, some of the time = 2, most of the time = 3, continuously = 4 vi) irritability vii) crying for reasons other than for vegetative needs viii) non-compliance ix) resistance to movement of limbs x) wanting to be carried xi) disinterest xii) drowsiness Mean change in score from baseline Diazepam group = 8.17 SD±2.14 n=59 Placebo group = 0.82 SD± 1.07 n=55 4) Adverse effects : no episodes of daytime drowsiness reported in either group **Outcome 2** - **Outcome 3** -	reporting of outcomes Indirectness Population : None Intervention : None Comparison : None Outcomes assessed : None	

Bibliographic details	Number of Participant Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Authors Joynt,R.L., Leonard,J.A.,Jr. **Year of publication** 1980 **Study location** USA **Ref ID** 56533 **Type of study** Randomised controlled study **Aim of study** To evaluate the physiological activity, safety and side-effects of dantrolene sodium suspension in children	**Inclusion Criteria** Children with cerebral palsy from a pediatric rehabilitation clinic Able to participate in the study Spasticity interfering with function Neurologically and psychologically stable at the time they entered the study **Exclusion Criteria** Unclear **Baseline characteristics** 20 children -Total sample characteristics (not broken down by group in study): a. sex: 8 girls, 12 boys b. age rage: 4 to 15 years c. diagnoses: Spastic diplegia: 7 spastic quadriplegia: 7 spastic hemiplegia: 5 spastic parapegia: 1 Etiology in the patient with paraparesis was undetermined: this child	**Intervention** Dantrolene sodium was administered for a total time of 6 weeks It was provided in a 5mg/cc suspension and was administered by a calibrated dropper or measuring cup, as appropriate. Following initial evaluation at visit l, treatment was begun with a drug dosage of 4mg/kg/day and was increased gradually during the next three weeks to an optimum level, 12mg/kg/day being the approximate maximum The children were re-evaluated after three weeks (visit 2) and dosage was adjusted to an optimum level depending on the results of the history and physical examination at that time, and was then maintained at this level until visit 3 (six weeks after initiating treatment) The drug was then discontinued and the children were tested again three weeks later (visit 4) Other medications were not altered during the treatment period. Concomitant medications included mephobarbital, phenobarbital, phenytoin, antibiotics, decongestants, vitamins, imipramine and (in one patient) diazepam	**Outcome 1** <u>Strength of voluntary plantar flexion</u> . (Positive numbers = increase; negative numbers = decrease. Strength measured in foot/pounds of torque generated by plantar flexion againts a foot-plate) a. after 6 weeks -dantrolene: < -0.2 (8); -0.2 (0); > -0.2 (0) -placebo: < -0.2 (1); -0.2 (1); > -0.2 (5) p=0.003 b. after 9 weeks -dantrolene: < -0.8 (6); -0.8 (0); > -0.8 (3) -placebo: < -0.8 (1); -0.8 (0); > -0.8 (4) NS **Outcome 2** <u>Spasms (number of children)</u> - a. after 3 weeks -dantrolene: improved: 3 no change: 8 -placebo: improved: 0 no change: 9 p=0.089 It is reported that spasms were not subsequently reduced in the intervention group but no more figures are provided. Spasms were rated by the severity of muscle contractions that were produced in other areas during the range-of-motion examination of a joint of one of the extremities. Mild spasms (rated 1) would include motion at another joint, such as knee flexion or extension occurring while the ankle was	Limitations Allocation concealment : pharmacy controlled Participants blinded to intervention : yes Carers blinded to intervention : yes Investigators blinded to intervention : yes Number of participants not completing treatment : 2 one from each group of total n=21 patients Number of participants with no available outcome data : 1 from placebo group Selective outcome reporting : yes Any other limitations : small sample size Indirectness Population : None Intervention : None Comparison : None Outcomes assessed : Unvalidated measures used	**Funding** Eaton Laboratories and the Norwich Pharmacal Company provided the drug and also financial assistance **Other information** - **Selective outcome reporting** Yes, as 61 variables were studied including 36 timed variables for testing function and mobility of extremities Besides some the outcomes reported were measured during the three assessment visits but only results from one or two of those visits were reported **Sample size** Small sample size, no calculation performed

	presented at nine years with progressive spastic paraparesis, not strictly cerebral palsy in the usual sense At baseline intervention and comparison group were statistically similar, except that those in the intervention group were "somewhat" stronger **Intervention Group** n=11	**Comparison 1** Placebo (no other details reported) Other medications were not altered during the treatment period. Concomitant medications included mephobarbital, phenobarbital, phenytoin, antibiotics, decongestants, vitamins, imipramine and (in one patient) diazepam	being examined. Severe spasms (rated 3) were, for example, a mass flexion pattern of the trunk and arms occurring while a leg was being examined. The scores for a given result from each extremity were totalled to produce the final score assigned to that particular examination. **Outcome 3** <u>-Unscrewing medium-sized barrels (time in secs)</u> - (Positive numbers = improved negative numbers = worsened) a. after 6 weeks - dantrolene: < -0.3 (4); -0.3 (1); > -0.3 (5) -placebo: < -0.3 (5); -0.3 (0); > -0.3 (4) NS b. after 9 weeks -dantrolene: < -0.15 (5); -0.15 (0); > -0.15 (6) -placebo: < -0.15 (5); -0.15 (0); > -0.15 (4) NS -<u>Left arm vertical alignment of buttons (elbow flexion-extension, time in secs)</u> - (Positive numbers = improved negative numbers = worsened) a. after 6 weeks -dantrolene: < 0 (7); 0 (0); > 0 (3) -placebo: < 0 (2); 0 (1); > 0 (6) p= 0.051 b. after 9 weeks -dantrolene: < -0.095 (6); -0.095 (0); > -0.095 (5) -placebo: < -0.095 (4); -0.095 (0); > -0.095 (5) NS <u>-Unbuttoning medium-sized buttons (time in secs)</u> - (Positive numbers = improved negative numbers = worsened) a. after 6 weeks		

			-dantrolene: < 0.3 (7); 0.3 (0); > 0.3 (2) -placebo: < 0.3 (2); 0.3 (0); > 0.3 (7) p=0.028 b. after 9 weeks -dantrolene: < 0.2 (5); 0.2 (0); > 0.2 (6) -placebo: < 0.2 (3); 0.2 (0); > 0.2 (6) NS <u>-Buttoning small-sized buttons (time in secs)</u> - (Positive numbers = improved negative numbers = worsened) a. after 6 weeks -dantrolene: < 0 (4); 0 (2); > 0 (4) -placebo: < 0 (0); 0 (4); > 0 (5) p=0.054 b. after 9 weeks -dantrolene: < 0 (2); 0 (4); > 0 (5) -placebo: < 0 (1); 0 (5); > 0 (3) NS		

Bibliographic details	Number of Participant Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Authors Denhoff,E., Feldman,S., Smith,M.G., Litchman,H., Holden,W. **Year of publication** 1975 **Study location** USA **Ref ID** 56537 **Type of study** Some other intervention type **Aim of study** To evaluate the effects of dantrolene sodium in children with spastic cerebral palsy	**Inclusion Criteria** Unclear (apart from children with cerebral palsy) **Exclusion Criteria** Unclear **Baseline characteristics** Total: 28 children Sex: 16 boys, 12 girls Age range: 18 months to 12 years (mean 7 years) Types of cerebral palsy: -spastic quadriplegia: 15 -spastic hemiplegia: 7 -spastic diplegia: 4 -mixed spasticity and athetosis: 1 -mixed spasticity and rigidity: 1 Degrees of severity: -mild: 14 -moderate: 5 -severe: 9 21 of the children were participating in the Meeting Street School's daily service program for multi-handicapped children; the other	**Intervention** Dantrolene sodium ('Dantrium') administered orally in suspension form containing 25mg per 4ml for six weeks each group with a washout period of two weeks in between. Drug dosage was begun at 1mg/kg q.i.d. (4mg/kg/24hrs) and was increased by 1mg/kg at weekly intervals up to a maximum dose of 3mg/kg/dose (12mg/kg/24hrs) at the beginning of the third week of treatment. This dosage was then continued for the remaining three weeks of the drug-treatment period. <u>Note:</u> At least two weeks prior to the beginning of the study, 3 children had their diazepam discontinued. During the study, 8 children were maintained on various drugs: one each on diphenylhydantoin, phensuximide, phenobarbital and promethazine and two each on primidone and methylphenidate **Comparison 1**	**Outcome 1** Measurements in all areas were made before treatment began, at the end of each treatment period and during the 'washout' period. Additional evaluations of motor performance, activities of daily living and general behaviour were made at two points within each treatment period. Only treatment difference scores were reported, but not raw data for individual measurements 1) Neurological measurements Included: muscle strength, spasticity, tendon jerk reflexes and clonus in both upper and lower extremities Measured by: paediatric neurologist Unit of measurement: an objective system of clinical evaluation was used (unclear which one) and values were assigned to the evaluations in a standardised manner 2) Orthopaedic measurements Included: active and passive range of motion in the major joints (shoulder, elbow, hip, knee) Measured by: orthopaedist Unit of measurement: degrees of movement 3) Motor performance Included the time, distance and/or errors in: leg-spread over a barrel crawling or walking on a plank precision of foot placement forward and lateral reaching on a table stacking blocks rotation of a wheel, calibrated in degrees, which measures range of motion in the shoulder	Limitations Allocation concealment : unclear Participants blinded to intervention : yes Carers blinded to intervention : yes Investigators blinded to intervention : yes Number of participants not completing treatment : 0 Number of participants with no available outcome data : 9 Selective outcome reporting : yes (orthopaedic data could not be converted from raw scores to treatment change and treatment difference scores-according to authors-therefore not reported) Any other limitations : validity of instruments used to measure most of the outomes is unclear	**Funding** Grant from Eaton Laboratories, Division of Morton-Nonvich Products Inc., Nonvich, New York. **Other information** Informed consent? : unclear Ethical approval? : unclear Sample size calculation? : no **Selective outcome reporting** - **Sample size** -

	seven had attended the school previously, and came back at regular intervals for evaluation. **Intervention Group** -	An identical volume of placebo was administered during the non-drug treatment period	Measured by: physical therapist 4) Measurements by program staff (Only in 21 children attending Meeting Street School) Activities of daily living included: co-ordination of movement in dressing and eating control of limbs in spontaneous play stamina for daily activities freedom of movementfacilitation of therapy ‘body anxiety’ in space (fear of change of position) Behavioural ratings included: attention and distractibility activity level and emotionality’ (e.g. irritability, temper tantrums, intolerance of frustration, fearfulness, crying episodes) Unit of measurement: a five-point scale of activities of daily living and behavioural functioning (no other details provided) 5) Parental measurements Activities of daily living and behavioural functioning as previous but excluding the measurement of ‘body anxiety’ Unit of measurement: a five-point scale of activities of daily living and behavioural functioning (no other details provided) In calculating scores for parental and staff evaluations, ratings obtained during the later parts of the treatment periods were weighted more heavily, on the assumption that heavier dosages at those times should have more significance attached to them **Outcome 2** 6) Paediatric evaluations Clinical determination (assume it means history taking and physical examination but unclear) Measured by: paediatrician regularly during the study Laboratory determinations included:complete blood counts urinalysis biochemical tests (creatinine and creatinine phosphokinase	Indirectness Population : none Intervention : none Comparison : none Outcomes assessed : some measurements were grouped under an "umbrella" outcome category which is not directly applicable to clinical practice. For example neurological measurement grouped together muscle strength and spasticity which are not necessarily clinically related. Activities of daily living and behaviour rating were also grouped under one single outcome without any clinical rationale supporting this decision	

			levels) 7) Adverse effects during formal study period Noted in 23 of the 28 children, but generally transient and disappeared within a week Included: irritability, lethargy, drowsiness and general malaise. Irritability was reported more often during placebo periods than during drug periods 16 children showed adverse effects during dantrolene periods and 7 during placebo periods ($p < 0.03$) 8) Adverse effects after formal study period Four of the nine children in whom the drug was continued after the completion of the formal study developed or had exacerbations of seizures. One nine-year-old boy who had been treated with dantrolene during the first treatment period showed laboratory evidence of elevated serum levels of liver enzyme two months after last receiving medication. His SCOT was 90 units (normal 11 to 52). A further determination 10 days later was 116 units. At no time did he show clinical signs or symptoms of hepatitis. **Outcome 3** Number of children showing changes in functioning between dantrolene and placebo (ΔD – ΔP) Changes a. Neurological Marked: ΔD (4); ΔP (0) Moderate: ΔD (2); ΔP (2) Marginal: ΔD (7); ΔP (2) Total changes: ΔD (13); ΔP (4) No changes: 11 P<0.04 b. Motor Marked: ΔD (0); ΔP (2) Moderate: ΔD (5); ΔP (4) Marginal: ΔD (5); ΔP (2)		

			Total changes: ΔD (10); ΔP (8) No changes: 8 P= N.S c. Staff Marked: ΔD (4); ΔP (0) Moderate: ΔD (4); ΔP (0) Marginal: ΔD (3); ΔP (2) Total changes: ΔD (11); ΔP (2) No changes: 9 P<0.02 d. Parents Marked: ΔD (5); ΔP (1) Moderate: ΔD (4); ΔP (2) Marginal: ΔD (3); ΔP (0) Total changes: ΔD (12); ΔP (3) No changes: 13 P<0.03 <u>Notes:</u> Significance levels were determined by the binomial distribution. Changes: Marked treatment-difference score (3) indicated a 3-point spread or larger between scores in drug and placebo periods. For example, during drug period a child may have shown marked change compared with baseline period (+ 3) but no measurable change during placebo period (0). Treatment difference score of 3 between periods. Again, a child may have shown moderate changes during drug period compared with baseline (+ 2) but showed poorer functioning during placebo period (-1), also giving a marked (+ 3) treatment-difference score		

Bibliographic details	Number of Participant Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Authors Haslam,R.H., Walcher,J.R., Lietman,P.S., Kallman,C.H., Mellits,E.D. **Year of publication** 1974 **Study location** USA **Ref ID** 58561 **Type of study** Randomised controlled study **Aim of study** To investigate the potential of dantrolene as a therapeutic agent in children with spasticity	**Inclusion Criteria** Children with upper neuron signs admitted to the John F kennedy Institute. Spasticity was defined as "an initial resistance to an extremity of passive movement, followed by a sudden giving way - the claspknife phenomenon" **Exclusion Criteria** No details given **Baseline characteristics** Age range 1.5 to 17 years (mean 6.5 years) IQ range : 10 to 80 (mean 45) Sex : 18/26 Some children took anticonvulsants, however, all muscle relaxant drugs were discontinued for at least 2 weeks before the beginning of the study **Intervention Group** -	**Intervention** On the day of admission a neurological examination, laboratory evaluation, urinalysis, serum GOT, serum GPT, alkaline phosphatase, bilirubin, calcium, phosphorus, serum urea nitrogen, creatinine and serum electrolytes were performed. On the second day the participant started their pre-assigned intervention for 14 days. There was a 10 day wash out period between interventions and the second treatmennt period was 15 days. Dantrolene was given orally before meals, four times a day in a flavoured suspension containing a concentration of 5mg/ml. Dosages began at 1mg/kg and were increased to a maximum of 3mg/kg or 12/mg/kg/day **Comparison 1** A placebo (indistinguishable from the drug) was given orally before meals, four times a day in a flavoured suspension.	**Outcome 1** Examinations took place on days 4, 8, 11 and 15 of each treatment period as well as two evaluations performed in the washout phase. Neurological assessment made by one of two alternating examiners. Spasticity was graded on a scale according to severity of clonus, passive movement, spontaneous movement, tone, reflexes and scissoring. This was then revised to a quantitative score 1) Scissoring mean improvement score : (none = 1, minimal = 2, moderate = 3, marked = 4) during dantrolene treatment mean improvement score signifcantly different from baseline : <0.01 during placebo treatment mean improvement score did not signifcantly differ from baseline : >0.05 Mean difference in improvement score between dantrolene and placebo groups = 0.381 p>0.05 2) Muscle tone mean improvement score (range subnormal or hypotonia = 1 to marked increase or hypertonia = 8) during dantrolene treatment mean improvement score signifcantly different from baseline : <0.005 during placebo treatment mean improvement score did not signifcantly differ from baseline : >0.05 Mean difference in improvement score between dantrolene and placebo groups = 0.609 p<0.05 **Outcome 2** - **Outcome 3** -	Limitations Allocation concealment : Adequate Participants blinded to intervention : Yes Carers blinded to intervention : Yes Investigators blinded to intervention : Yes Number of participants not completing treatment : 3/26 Number of participants with no available outcome data : 3/26 Selective outcome reporting : Yes, "self help skils" outcome data are not reported though referred to Any other limitations : Investigators tried to account for unwillingess of children to co=-operate by developing a spasticity scale. This did not lend itself to statistical analysis and another scoring system was used. The	**Funding** Not stated. Acknowledgement given to Eaton Laboratories for its support, however no further details are provided **Other information** Informed consent? : not stated Ethical approval? : not stated Sample size calsulation?: not stated **Selective outcome reporting** - **Sample size** -

				authors believe that the effect of dantrolene was underestimated because of the range of different children seen in their group and because of insufficiently sentitive scales being used. Indirectness Population : none Intervention : none Comparison : none Outcomes assessed : Muscle tone outcome measurement is not Ashworth or modified Ashworth scale.	

Bibliographic details	Number of Participant Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Authors McKinley,I., Hyde,E., Gordon,N. **Year of publication** 1980 **Study location** UK **Ref ID** 58566 **Type of study** Randomised controlled study **Aim of study** To conduct a crossover double blind RCT to assess the effects of baclofen on everyday activities.	**Inclusion Criteria** Children with spasticity attending a day school for physically handicapped children **Exclusion Criteria** Not stated **Baseline characteristics** Of 20 included children, All children had a degree of spasticity, but six had a mixed cerebral palsy : 5 had choreoathetosis and 3 had ataxia. There was an even sex distribution, the age range was 7-16 years. Half of the children were believed to be within the range of average intelligence, but three were severely mentally handicapped. Two children had a history of epilepsy and were on regular anticonvulsants. No other children received medication throughout the trial. **Intervention Group** -	**Intervention** Tablets were given at specified times by the school nurse or by parents in response to weekly written instructions. The dosage of baclofen given in three divided doses in each period was 0.5mg/kg, 1mg/kg, 2mg/kg, and 1mg/kg each for one week. No child exceeded 60mg/kg/day. There was a two week wash out period between treatment periods. **Comparison 1** Tablets were given at specified times by the school nurse or by parents in response to weekly written instructions. No further details are stated	**Outcome 1** In addition to the 9-weekly standard examination and test, weekly reports of behaviour, recorded by parent, teachers and therapists were obtained. Children were examined at the same time at the end of each week by the investagators, where possible by the same investigator each week. 1) Muscle tone : Reduced muscle tone or better movement measured on the Ashworth scale baclofen period : 14/19 placebo period : 5/19 unchanged throughout n=1 (p=0.064) 2) Gait assessment baclofen period : 8/12 placebo period : 4/12 unchanged throughout n=8 (p = NS) 3) Side effects The parents of 9 children reported side effects baclofen period : 8 - In 4 of these children reduction of dose relieved side effects placebo period : 1 Overall, side effects reported were drowsiness (5), sickness (2), dizziness (2), nocturnal enuresis (2), absence states, query epliptiform (2) slurred speech (2) and weakness (1) Therapists and teachers reported drowsiness in 12 children during the trial : all were taking baclofen at the time (p<0.001) and had shown reduced tone or improved movement 4) Would wish their child to continue on active treatment (if parents' guess correct)? 1/20 parents	Limitations : Allocation concealment : unclear, not specified Participants blinded to intervention : yes Carers blinded to intervention : yes Investigators blinded to intervention : yes Number of participants not completing treatment : 2/20 Number of participants with no available outcome data : 2/20 although most data available Selective outcome reporting : Any other limitations : Indirectness : Population : None Intervention : None Comparison : None Outcomes : None	**Funding** not stated **Other information** Informed consent? : Yes Ethical approval? : Local ethical committee Sample size calculation : No **Selective outcome reporting** - **Sample size** -

			Outcome 2 - **Outcome 3** -		

Bibliographic details	Number of Participant Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment

Authors Rice,J., Waugh,M.C. **Year of publication** 2009 **Study location** **Ref ID** 59380 **Type of study** **Aim of study** To evaluate the effect of high-dose trihexyphenidyl on change in overall dystonia severity, with secondary outcomes assessed of change in upper limb function and achievement of individualized goals	**Inclusion Criteria** Children aged between 2 and 18 years with predominant dystonic cerebral palsy, verified by one of the study physicians. Not treated with trihexyphenidyl or another anticholinergic medication in the previous 3 months and use of other treatments such as oral baclofen or intrathecal baclofen at a stable dose for 3 months and unlikely to be altered **Exclusion Criteria** Planned change in therapy program over the duration of the study (6 months). Surgical or medical interventions such as orthopaedic surgery or botulinum toxin injections scheduled during the study or in the 6 months prior to study entry **Baseline characteristics** 16 children Median age: 7.9 years (range 2-17 years) Sex: 10 males and 6 females	**Intervention** Trihexyphenidyl for 12 weeks. Dose escalation according to the following schedule: Week 1 0.2 mg/kg/d in 3 divided doses Week 2 0.5 mg/kg/d in 3 divided dose Week 3 1.0 mg/kg/d in 3 divided doses Week 4 1.5 mg/kg/d in 3 divided doses Week 5 2.0 mg/kg/d in 3 divided doses Week 6 2.5 mg/kg/d in 3 divided doses Week 7-12 2.5 mg/kg/d in 3 divided doses Week 13-16 Washout Adjustments were made to the dose of medication in a stepwise manner if any significant symptoms or side effects related to the medication were encountered Washout period: 4 weeks **Comparison 1** Placebo for 12 weeks Placebo was matched in colour, odour and taste to the active medication Same dose escalation as in medication Washout period: 4 weeks	**Outcome 1** Assessments were performed at baseline, 12, and 28 weeks after commencement. Method: videotaping the child in his or her usual sitting or standing position and recording resting and active limb movements over several minutes in each body region in a standardized fashion. Recorded activities included those listed as target areas for functional change as well as the protocol for the Quality of Upper Extremity Skills Test. This video was coded to allow subsequent random order of scoring Who measured: A blinded occupational therapist trained in the use of the Barry-Albright Dystonia scale (BAD) At the baseline visit, a physician member of the research team performed a comprehensive medical assessment including review of abnormal muscle tone and distribution. Instruments: The Barry-Albright Dystonia scale <u>BAD (mean score, 95% CI)</u> Baseline: 18.4 (15.5 to 21.2) Placebo: 16.9 (13.4 to 20.4) Triehxy: 18.3 (14.8 to 21.8) Change: 0.9 (-2.2 to 3.9) <u>Analysis of effects</u> Treatment: F (1, 12) =0.2, p=0.67 Carry: F (1, 12) = 1.7, p=0.22 Order: F (1, 12) =0.3, p=0.57 **Outcome 2** Assessments were performed at baseline, 12, and 28 weeks after commencement 1. Assessment of upper limb function Method: videotaping the child in his or her usual sitting or standing position and recording resting and active limb	Randomisation and allocation concealment: After recruitment, children were randomly assigned using a randomization table generated by the hospital pharmacy to initial treatment with either placebo medication or active medication (trihexyphenidyl). Balanced randomization was performed by the hospital pharmacist, who also kept these codes concealed until data collection was complete. Active medication was constituted in a concentration of 10 mg/mL. Both medications were matched in color (green), odor (aniseed), and taste (bitter). Medication A was the phase 1 treatment and	**Funding** Unclear **Other information** Informed consent A legal guardian gave written informed consent before entry into the study Ethical approval Study was approved by the Ethics Committee of the Children's Hospital at Westmead Instruments used: According to the authors reliability, validity, and responsiveness have been demonstrated for the Quality of Upper Extremity Skills Test and the Canadian Occupational Performance Measure **Selective outcome reporting** No **Sample size** Sample size is small but the study was designed as a pilot study and as such a power calculation was not performed Authors estimated

	Type of cerebral palsy according to the Gross Motor Function Classification System: 2 children: Level III (13%) 3 children: Level IV (19%) 11 children: Level V (69%) 11 children (69%) had associated spasticity **Intervention Group**		movements over several minutes in each body region in a standardized fashion. Recorded activities included those listed as target areas for functional change as well as the protocol for the Quality of Upper Extremity Skills Test. This video was coded to allow subsequent random order of scoring Who measured: A blinded occupational therapist trained in the use of the Quality of Upper Extremity Skills Test Instrument: Quality of Upper Extremity Skills Test (QUEST) <u>QUEST (mean score, 95% CI)</u> Baseline: 15.3 (–0.1 to 30.7) Placebo: 15.1 (2.8 to 27.4) Trihexy: 13.5 (1.4 to 25.5) Change: –1.6 (–6.3 to 3.1) <u>Analysis of effects</u> Treatment: F (1, 12) =0.9, p=0.37 Carry: F (1, 12) =1.4, p=0.25 Order: F (1, 12) =0.2, P= 0.90 2. Other functional goals Instruments, methods and who measured: Families completed the Canadian Occupational Performance Measure (COPM) with an experienced occupational therapist. A change score of 2 or more is considered clinically significant. The assessment then directed the family and occupational therapist to identify up to 5 functional goals for the Goal Attainment Scale to measure change Participants and their caregivers selected a total of 80 goals, averaging 5 goals per participant. The goals covered the following areas: mobility and posture, dressing, feeding, toileting and play skills, including the use of switching for communication. Goal Attainment Scale (GAS) scores were converted to a normalized T-score, with the baseline score set at 20	medication B, the phase 2 treatment. The bottles were identical apart from the labels A and B. Participants blinded to intervention: Yes Carers blinded to intervention: Yes Researchers blinded to intervention: Yes Indirectness: Population: some. Only 11/16 children had associated spasticity Intervention: none Comparison: none Outcomes: some? Canadian Occupational Performance Measure - Is this used in the UK?	that within the scope of the study it was feasible to recruit 15-20 participants into the trial However it is unclear why if a total of 55 children were invited to participate only the first 16 children who were subsequently seen and met entry criteria were recruited into the study

			GAS Mean Score (95% CI) Baseline: 20.0 Placebo: 33.3 (27.4 to 39.1) Trihexy: 39.3 (31.8 to 46.8) Change: 6.8 (-3.7 to17.5) Analysis of effects Treatment: F (1, 11) = 1.7, p=0.22 Carry: F (1, 11) = 0.0, p=0.89 Order: F (1, 11) = 10.2, p= 0.009 COPM (Satisfaction) (95% CI) Baseline: 2.3 (1.8 to 2.7) Placebo: 3.8 (2.8 to 4.8) Trihexy: 4.7 (3.5 to 5.9) Change: 0.7 (-0.3 to 1.8) Analysis of effects Treatment: F (1, 10) = 1.5, p=0.24 Carry: F (1, 10) = 0.6, p=0.45 Order: F (1, 10) =1.1, p= 0.31 COPM (Performance) (95% CI) Baseline: 2.6 (2.2 to 3.0) Placebo: 3.8 (3.0 to 4.7) Trihexy: 4.4 (3.6 to 5.3) Change: 0.8 (-0.5 to 2.0) Analysis of effects Treatment: F (1, 12) =2.2, p=0.17 Carry: F (1, 12) =0.1, p=0.72 Order: F (1, 12) =4.7, p=0.05 **Outcome 3** Adverse effects How measured: the child's guardian was contacted weekly by telephone to review any problems encountered during the trial, and adverse effects were recorded systematically on the results proforma Who measured: unclear, but one of the rehabilitation physicians		

			was available 24 hours a day to manage medication adverse effects Adverse effects symptoms occurred in all children during the active medication phase and included: agitation (distressed without reason or other odd behaviour) constipation dry mouth poor sleep One child developed multiple adverse effects related to trihexyphenidyl (including dry mouth, confusion, agitation, inability to sleep, tachycardia, hallucinations, and urinary incontinence), requiring brief admission to hospital after the initial dose and had to withdraw from the trial The second child withdrew after 8 weeks due to a family crisis unrelated to medication dosing Peak doses ranged from 0.05 to 2.60 mg/kg/d. The maximum dose achieved on active medication was 70 mg/d Symptoms while on placebo were recorded in 6/16 (38%) of children Overall perception of the medication trial and overall satisfaction with the study Families completed questionnaires at the end of phases 1 and 2 Despite the frequency of side effects, most parents or carers (81%) indicated that they were satisfied with their child's participation in the study, indicating that even if their child did not respond to the medication this in itself was useful information for them. Some parents and carers indicated altruistically that their participation in the study may assist other children with the treatments.		

Spasticity in children and young people with non-progressive brain disorders: management of spasticity, co-existing motor disorders and their early musculoskeletal complications

Botulinum toxin

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Ackman,J.D., Russman,B.S., Thomas,S.S., Buckon,C.E., Sussman,M.D., Masso,P., Sanders,J., D'Astous,J., Aiona,M.D., Shriners Hospitals,B.T.X. **Year of publication** 2005 **Country** USA **Ref ID** 64332 **Design** Randomised controlled study **Aim of study** A multicentre randomised placebo controlled trial to investigate the single and cumulative effectiveness (three repeated treatments) of BoNT, casting and the combination of BoNT and casting to reduce dynamic equinus during gait in children with spastic CP.	**Inclusion Criteria** Diagnosis of spastic hemiplegia or diplegia, aged between 3 and 10 years, independent ambulators without assistive devices, ambulate in functional equinus (toe-toe or toe-heel pattern), neutral ankle position with full knee extension **Exclusion Criteria** Previous orthopaedic surgery to tendo-achilles or subtalar joint, no BoNT injections in previous 6 months, hip or knee flexion contractures greater than 10°. **Baseline Characteristics** 39 children with cerebral palsy were included (Results for 12 children receiving BoNT alone not reported here) Number of participants Placebo + cast = 14 BoNT + cast = 13 Mean age (months) Placebo + cast = 68	**BoNT treatment** BoNT A type : Not specified Dilution : 100U/cm^3 Maximum total dose : Not stated Dosage and Muscle Selection : 4U/body weight for each gastrocnemius muscle. Injections were performed by the physician-investigator at each hospital and made into the medial and lateral gastrocnemius muscles using a 23-27 guage needle Sedation and pain management : choices were at the discretion of the physician Placebo injections : No details provided but given with similar methods to BoNT	Appropriate randomisation method : Yes Allocation concealment adequate : Yes Groups comparable at baseline : Yes Participants blinded to treatment allocation : Yes Caregivers blinded to treatment allocation : Yes Length of follow up similar for each group : Yes No of participants not completing treatment (by group) : Casting alone = 1, BoNT + casting = 1 Outcome assessment methods valid : Yes Investigators blinded to treatment allocation : Yes	Primary outcome measures included: Gait analysis (velocity, stride length and ankle kinematics of ankle dorsiflexion at initial contact (DFIC) and peak dorsiflexion in swing (PDFSw)) using a Vicon motion system Secondary outcome measures included : triceps surae spasticity (Ashworth and Tardieu), passive and active dorsiflexion, ankle dorsiflexion and plantarflexion strength and ankle power generation Outcomes were measured at baseline, 3months, 6 months, 7.5 months, and 12 months <u>Ashworth score at ankle – mean change 3 months (read from graph)</u> Placebo + cast = -0.5 p ≤0.02 (reported)(estimated final score 2.1±0.8) BoNT + cast = -0.2 p = no SD (reported)(estimated final score 2.4±0.5) <u>Ashworth score at ankle – mean change 6 months (read from graph)</u>	Unrestricted educational grant from Allergan Inc Consent: All parents signed an informed consent form approved by each Institutional Review Board Ethical approval : Research Integrity Office at Oregon Health and Sciences University

	BoNT + cast = 72 Mean age of all 39 participants =70 months Age range of all 39 participants = 3 to 9 years Age range (months) Placebo + cast = 36-108 BoNT + cast = 41-99 Number with hemiplegia Placebo + cast = 10 BoNT + cast = 8 Number with diplegia Placebo + cast = 4 BoNT + cast = 5 Males Placebo + cast = 6 BoNT + cast = 6 GMFCS level I Placebo + cast = 14 BoNT + cast = 12 GMFCS level II Placebo + cast = 0 BoNT + cast = 1 Ashworth score at ankle (read from graph) Placebo + cast = 2.6±1.0 BoNT + cast = 2.6±0.9 Active dorsiflexion at ankle – (as reported, read from graph) Placebo + cast = -12°±14	Injections were given following evaluation at baseline, 3 months and 6 months (ie three treatments) **Therapy treatment** At each treatment visit children received a cast which remained on for 3weeks. Casts were applied by the same physical therapist, physician or casting technician during each visit. The child was positioned prone with the knee flexed to 90° . The foot was placed in a subtalar neutral with the ankle in 0 to 5 of dorsiflexion. The bottom of the cast was flattened and a cast shoe was provided to allow walking during the 3 weekd of cast wear. After cast removal children were instructed to wear their AFOs (solid ankle, posterior leaf spring or articulated) during the day and night with removal of the AFO for 2-4 hrs during the evening.	Limitations : Serious, no analysis or results across groups provided, results estimated from graphs Imprecision : Insufficient recruitment of participants reduced power of study to identify statistically significant differences between treatment groups Other considerations : Study terminated early due to recruitment difficulties. Approximately 90 children met the inclusion criteria, although only 39 children agreed to participate. A higher than 50% refusal rate by parents with children who could be included, primarily because parents did not want their children to receive a placebo when they could receive BoNT, at no cost and without a rigorous follow up schedule.	Placebo + cast = 0.4 p ≤0.02 (reported)(estimated final score 2.2±0.7) BoNT + cast = 0.4 p = no SD (reported)(estimated final score 2.2±0.6) <u>Active dorsiflexion at ankle – mean change at 3 months (read from graph)</u> - Placebo + cast = 1° p = no SD (reported)(estimated final score -11°±20) BoNT + cast = 3° p = no SD (reported)(estimated final score -15°±20) <u>Active dorsiflexion at ankle – mean change at 6 months (read from graph)</u> - Placebo + cast = 4° p = no SD (reported)(estimated final score -8°±13) BoNT + cast = 7° p = no SD (reported)(estimated final score -11°±14) <u>Velocity (m/s) mean change 3 months (read from graph)</u> - Placebo + cast = -0.05, p = no SD (reported) (estimated final score 0.8±0.2) BoNT + cast = 0.15 p = no SD (reported) (estimated final score 1.05±0.15)	

	BoNT + cast = -18°±16 Velocity (read from graph) Placebo + cast = 0.85±0.25 BoNT + cast = 0.9±0.25	New casts were applied following evaluation at baseline, 3 months and 6 months (ie three treatments) **Comparisons** Placebo injection and casting vs BoNT injection and casting	Power analysis Initial : 25 children/group would give a 90% probability of detecting at least a 5° change in ankle kinematics, 0.15m/s change in velocity and a 0.10m change in stride length Post-hoc : With 13 children/ group, the power to detect a 5° change in ankle kinematics was reduced to 66%, whereas the power to detect a change in velocity of 0.15m/s and stride length of 0.10m was reduced to 55% Block design randomisation for every three children enrolled at each centre, randomly allocating one child to each treatment group. Children were also randomised by diagnostic group to ensure even distribution of children with hemiplegia and diplegia within each treatment group.	<u>Velocity mean change 6 months (as reported, read from graph)</u> - Placebo + cast = 0.05 p = no SD (reported) (estimated final score 0.9±0.25) BoNT + cast = 0.1 p = no SD (reported) (estimated final score 1.0±0.15) <u>Adverse Effects</u> - Placebo + cast = none reported BoNT + cast = one child fell more often immediately after treatment, although this resolved within 1 to 2 weeks. There were no pressure sores or injuries associated with the casts or their removal in either group and no casts were removed early.	

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Hoare BJ, Wallen MA, Imms C, Villanueva E, Rawicki HB, Carey L. Botulinum toxin A as an adjunct to treatment in the management of the upper limb in children with spastic cerebral palsy (UPDATE). Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.: CD003469. DOI: 10.1002/14651858.CD003469.pub4. **Year of publication** 2010 **Country** Australia **Ref ID** **Design** Cochrane Review **Aim of study** To assess the effectiveness of injections of BoNT-A or BoNT-A and occupational therapy in the treatment of the upper limb in children with CP.	**Inclusion Criteria** All randomised controlled trials (RCTs) comparing BoNT-A injection or BoNT-A injection and occupational therapy in the upper limb(s) with other types of treatment (including no treatment or placebo) in children with CP. **Exclusion Criteria** Within the seven individual RCTs relevant here, the most common reasons for exclusion were if children had received BoNT treatment to the upper limb in the previous 6 -12 months, if they had had previous surgery on the affected limb, if they had fixed contractures or if parents were unwilling to give up other upper limb interventions during treatment eg splints or casts. **Baseline Characteristics** Ten RCTs were included in the entire systematic review - Boyd 2004, Corry 1997, Fehlings 2000, Greaves 2004, Karamura 2007, Koman 2007, Lowe 2006, Russo 2007, Speth 2005, Wallen 2007. Seven RCTs were included in	**BoNT treatment** All RCTs used Botox administered in multilevel injections in one session. The majority of RCTs used a standard dilution of 100U Botox /1.0ml saline. However, Speth 2005, used low concentration of 50U Botox /1.0ml saline and Lowe 2006 used a high concentration of 200U Botox /1ml saline. Maximum doses ranged from 220U to 410U. Doses were also expressed in U/kg for the different muscles that were injected. Six RCTs used electrical stimulation to locate the muscle (two additionally used EMG - Greaves 2004, Lowe 2006) and one used anatomical knowledge and palpation (Fehlings 2000). Four trials used	Two reviewers independently reviewed titles and abstracts of articles retrieved using the aforementioned search strategy. Trials that clearly failed tomeet the inclusion criteria were not reviewed further. Those that could not be excluded were retrieved and reviewed in full-text by the two reviewers. In all instances, differences of opinion were resolved by discussion. Those thatmet criteria were retrieved and reviewed in detail. Quality of trials: Two reviewers independently assessed the methodological quality of the included trials using the PEDro scale with discrepancies resolved by discussion. A point is given for each of the following (maximum score = 10): random	Optimisation of movement Modified Ashworth scale - shoulder adductors One RCT included Greaves 2004 4 Months Greaves 2004: log(Odds Ratio) : -1.609, SE :0.894, Odds Ratio : 0.20 [0.03, 1.15] Modified Ashworth scale - elbow flexors Two RCTs included Russo 2007, Wallen 2007 3 Months Russo 2007 : log(Odds Ratio) : -2.62 SE :0.722 Odds Ratio : 0.07 [0.02, 0.30] Wallen 2007 : log(Odds Ratio) : -1.102 SE :0.686 Odds Ratio : 0.33 [0.09, 1.27] Meta analysis : Odds Ratio (Fixed, 95% CI) 0.16 [0.06, 0.43] 6 Months Russo 2007 : log(Odds Ratio) : -2.296 SE :0.694 Odds Ratio : 0.10 [0.03, 0.39] Wallen 2007 : log(Odds Ratio) :0.06 SE :0.69 Odds Ratio : 1.06 [0.27, 4.11] Meta analysis : Odds Ratio (Fixed, 95% CI) 0.33 [0.13, 0.86] Modified Tardieu scale - elbow flexors (change from baseline R2-R1) One RCT included Greaves 2004 4 Months Greaves 2004 : BoNT and OT group n= 9, Mean : -24.44 SD : 33.95 OT group n= 9, Mean : -3.89 SD : 41.23 Mean difference :-20.55 [-55.44,	Details of funding for the review are not stated

	the one comparison that was relevant to this guideline - Boyd 2004, Fehlings 2000, Greaves 2004, Lowe 2006, Russo 2007, Speth 2005, Wallen 2007. 259 children aged between 1y 11m and 16 were included in total. 6/7 of these RCTs included children with hemiplegia, although 39% of the children included in one study had quadriplegia and 15% had triplegia (Wallen 2007). Five studies included children with upper limb spasticity of Ashworth greater than or equal to level 2 (Fehlings 2000, Greaves 2004, Lowe 2006, Russo 2007, Wallen 2007), one study included children with upper limb spasticity of Ashworth of level 1 (Boyd 2004) and it is unclear for Speth 2005. .	general anaesthesia during the procedure (Boyd 2004, Fehlings 2000, Russo 2007, Speth 2005), one used general anaesthesia or sedation (Greaves 2004), one used sedation and analgesia (Lowe 2006) and one used sedation and local anaesthesia (Wallen 2007). **Therapy treatment** Boyd 2004 An upper limb training program was provided for one hour once a week for 6 weeks by an occupational therapist blinded to group allocation. The program utilised principles of motor skills learning, occupational performance and goal attainment. Children were also encouraged to undertake 30minutes of daily training at home for at least six days per week for 12 weeks. No casts or splints were used. Fehlings 2000	allocation; allocation concealment; prognostic similarity at baseline; subject blinding; therapist blinding; assessor blinding; greater than 85% follow up of one key outcome; intention to treat analysis; between group statistical comparison of at least one key outcome, and reporting of point estimates and measures of variability of at least one key outcome. PEDro quality ratings ranged from 6/10 to 10/10. The Cochrane team sought data from the authors of the seven trials included in their review. The data sought was the mean change from baseline values (and standard deviations) for the experimental and controls groups for entry into RevMan. This is the best although time consuming method to solve missing data	14.34] Elbow extension PROM (change from baseline) Two RCTs included Fehlings 2000, Wallen 2007 3 Months Fehlings 2000 : BoNT and OT group n= 14, Mean : 5.46 SD : 11.74 OT group n= 15 Mean : 3 SD : 12.83 Mean difference : 2.46 [-6.48, 11.40] Wallen 2007 : BoNT and OT group n= 20 Mean : 1.3 SD : 6.3 OT group n= 16, Mean : 1.5 SD : 3.6 Mean difference : -0.20 [-3.48, 3.08] Meta analysis : Mean Difference (IV, Random, 95% CI) 0.11 [-2.96, 3.19] 6 Months Fehlings 2000 : BoNT and OT group n= 14, Mean : 2.84 SD : 6.69 OT group n= 15, Mean : 0.79 SD : 9.32 Mean difference : 2.05 [-3.83, 7.93] Wallen 2007 : BoNT and OT group n= 20, Mean : -0.5 SD : 5.8 OT group n= 17, Mean : 0.6 SD : 6.1 Mean difference : -0.20 [-3.48, 3.08] Meta analysis : Mean Difference (IV, Random, 95% CI) -0.15 [-3.38, 3.07] Modified Ashworth scale - pronators Two RCTs included Greaves 2004, Wallen 2007 3 Months Wallen 2007 : log(Odds Ratio) : 0.459 SE :0.637 Odds Ratio : 1.58 [0.45, 5.52] 4 Months Greaves 2004 : log(Odds Ratio) : -2.003 SE : 1.005 Odds Ratio : 0.13	

		Community based occupational therapy at a minimum frequency of one session every two weeks. An occupational therapy manual with guidelines was developed for the study and sent to participating occupational therapists. The guidelines incorporated activities for upper extremity strengthening and the development of skills for daily living. Greaves 2004 Individualised occupational therapy twice weekly, one hour sessions for 6 weeks (Total number of sessions: Treatment Group = 11.8 (0.4), Control Group = 11.5 (0.5). Therapy provided by non-blinded study occupational therapist and community occupational therapists.	issues. The authors classified the measures using the ICF (WHO 2001) according to the domains they assessed (acknowledging that some of the measures include items that assess change across multiple domains of the ICF (for example the COPM). Relevant outcomes for this guideline are: Body functions and body structures (changes in physiological systems or in anatomical structures). Difficulties in this domain are referred to as impairments. • Spasticity (Tardieu scale or modified Tardieu scale (MTS)) • Muscle tone (Ashworth scale, modified Ashworth scale (MAS)) • Active range of motion (AROM) • Passive range of	[0.02, 0.97] 6 Months Wallen 2007 : log(Odds Ratio) : 0.404 SE : 0.977 Odds Ratio : 1.50 [0.22, 10.16] Supination AROM (change from baseline) One RCT included Speth 2005 3 Months Speth 2005 : BoNT and OT group n= 10, Mean : 9.3 SD : 15.11 OT group n= 10, Mean : 25.6 SD : 22.32 Mean difference : -16.30 [-33.01, 0.41] 6 months Speth 2005 : BoNT and OT group n= 10, Mean : 13.3 SD : 28.91 OT group n= 10, Mean : 21.7 SD : 35.43 Mean difference : - -8.40 [-36.74, 19.94] Forearm supination PROM (change from baseline) Two RCTs included Fehlings 2000, Wallen 2007 3 Months Fehlings 2000: BoNT and OT group n= 14, Mean : 5.15 SD : 8.1 OT group n= 15, Mean : 1.67 SD : 6.28 Mean difference : 3.48 [-1.82, 8.78] Wallen 2007: BoNT and OT group n= 20, Mean : 2.5 SD : 9.5 OT group n= 16, Mean : -1.6 SD : 16.1 Mean difference : - 4.10 [-4.82,	

		Intervention used goal setting, general training, goal directed training and a home program. Dynamic and static splinting were used. Treatment group received 1.4 (SD 2.3) extra sessions of occupational therapy compared with 0.5 (SD1.1) in the control group between the end of intervention and six week follow-up. Lowe 2006 Occupational therapy from the same occupational therapist. Frequency and intensity not reported. Treatment, driven by the family, included a suite of intervention offered by the therapist including functional training, strengthening, splinting, casting and motor learning. Individualised family goals with	motion (PROM) Activity (execution of a task or action by an individual). Difficulties in these areas are referred to as activity limitations. • Individual goal identification, rating and scaling (Canadian Occupational Performance Measure (COPM), Goal Attainment Scaling (GAS)). • Activities of Daily Living Skills (Pediatric Evaluation ofDisability Inventory (PEDI). Participation (involvement in a life situation). Difficulties in these areas are referred to as participation restrictions. • None identified in the studies reviewed. Outcomes independent of ICF domains	13.02] Meta analysis : Mean Difference (IV, Random, 95% CI) 3.64 [-0.92, 8.20] 6 Months Fehlings 2000 : BoNT and OT group n= 14, Mean : 3 SD : 12.08 OT group n= 15, Mean : 0.64 SD : 6.62 Mean difference : 2.36 [-4.80, 9.52] Wallen 2007 : BoNT and OT group n= 20, Mean : -0.3 SD : 15.5 OT group n= 17, Mean : 0.6 SD : 10 Mean difference : -0.90 [-9.19, 7.39] Meta analysis : Mean Difference (IV, Random, 95% CI) 0.97 [-4.45, 6.39] Modified Ashworth scale - wrist flexors Three RCTs included Greaves 2004, Russo 2007, Wallen 2007 3 Months Russo 2004 : log(Odds Ratio) : -4.781 SE : 1.057 Odds Ratio : 0.01 [0.00, 0.07] Wallen 2007 : log(Odds Ratio) : -1.35 SE : 0.67 Odds Ratio : 0.26 [0.07, 0.96] Meta analysis : Odds Ratio (Fixed, 95% CI) 0.10 [0.03, 0.29] 4 Months Greaves 2004 : log(Odds Ratio) : -1.026 SE : 0.842 Odds Ratio : 0.36 [0.07, 1.87] 6 Months Russo 2007 : log(Odds Ratio) : -3.095 SE : 0.747 Odds Ratio : 0.05 [0.01, 0.20]	

		mutually agreed levels of attainment were used to guide treatment. Individualised home programmes were developed with the family to implement in goal-relevant contexts of home or school/pre-school. Russo 2007 Weekly occupational therapy sessions for 4weeks.The focus of each therapy sessionwas on upper extremity weightbearing, balls skills, fine motor strengthening (through the use of resistive putty-based activities) and bilateral functional activities (which included activities assisting finger agility and dexterity). Speth 2005	Health related quality of life and self perceived competence • Child Health Questionnaire (CHQ). • Pediatric Quality of Life (PedsQL).	Wallen 2007 : log(Odds Ratio) : -0.57 SE : 0.62 Odds Ratio : 0.57 [0.17, 1.91] Meta analysis : Odds Ratio (Fixed, 95% CI) 0.20 [0.08, 0.51] Modified Tardieu scale - wrist flexors (change from baseline R2-R1) Two RCTs included Greaves 2004, Wallen 2007 3 Months Wallen 2007: BoNT and OT group n= 20 Mean : -27.75 SD : 17.43 OT group n= 16 Mean : -5.94 SD : 18.46 Mean difference : -21.81 [-33.65, -9.97] 4 Months Greaves 2004: BoNT and OT group n= 10 Mean : -12.78 SD : 28.73 OT group n= 10 Mean : -2.22 SD : 15.63 Mean difference : -10.56 [-30.83, 9.71] 6 Months Wallen 2007: BoNT and OT group n= 20 Mean : -10.25 SD : 30.02 OT group n= 17 Mean : -12.06 SD : 28.29 Mean difference : 1.81 [-17.00, 20.62] Wrist extension AROM (change from baseline) One RCT included Speth 2005 Three months Speth 2005 : BoNT and OT group	

		30 minutes physiotherapy and 30 minutes occupational therapy three times a week for 6 months. A treatment protocol including strength and coordination and task specific training was made for each level of hand function impairment (Zancolli grade). This was tailored to the individual child based on individual goal setting and clinical reasoning. All children wore a night splint. During the day children with Zancolli IIB wore a cock-up splint almost all day. Children with less impairment used a wrist cockup splint or web-space splint only during specific activities		n=10, Mean : 35.4, SD : 30.48 OT group n=10 Mean : 20.7 SD : 20.08 Mean difference : 14.70 [-7.92, 37.32] Six months Speth 2005 : BoNT and OT group n=10, Mean : 34.2, SD : 30.19 OT group n=10, Mean :18.6, SD : 18.54 Mean difference : 15.60 [-6.36, 37.56] Wrist extension PROM (change from baseline) One RCT included Fehlings 2000 Three months Fehlings 2000 : BoNT and OT group n=14, Mean : 4.58, SD : 11.92 OT group n=15 Mean : 1.27 SD : 9.91 Mean difference : 3.31 [-4.70, 11.32] Six months Fehlings 2000 : BoNT and OT group n=14, Mean : 2, SD : 15.02 OT group n=15, Mean :2.07, SD : 11.49 Mean difference : -0.07 [-9.85, 9.71] Palmar thumb abduction PROM (change from baseline) One RCT included Fehlings 2000 Three months Fehlings 2000 :BoNT and OT group n=14, Mean : 1.46, SD :	

		Wallen 2007 One week after baseline assessment children received 1 hour a week of occupational therapy for 12 weeks. Therapy was provided by the children's usual occupational therapist or at the The Children's Hospital at Westmead. Therapy programs were individualised and included techniques to improve impairment (e.g. stretching, casting, splinting) and enhancing activities (e.g. motor training, environmental modification and practice of specific goal activities). **Comparisons**		8.52 OT group n=15 Mean : -0.6 SD : 10.01 Mean difference : 2.06 [-4.69, 8.81] Six months Fehlings 2000 : BoNT and OT group n=14, Mean : 2.77, SD : 8.12 OT group n=15, Mean : 1.21, SD : 6.96 Mean difference : 1.56 [-3.96, 7.08] Optimisation of Function - Goal Attainment Scaling (change from baseline) – Parent Five RCTs included Boyd 2004, Greaves 2004, Lowe 2006, Russo 2007, Wallen 2007 Three months Boyd 2004 : BoNT and OT group n=15, Mean : 15.4 SD : 7.61 OT group n=15, Mean : 13.34 SD : 13.68 Mean difference : 2.06 [-5.86, 9.98] Lowe 2006 : BoNT and OT group n=21, Mean : 19.55 SD : 11.06 OT group n=2, Mean : 10.21 SD : 7.95 Mean difference : 9.34 [3.51, 15.17] Russo 2007 : BoNT and OT group n=21, Mean : 21.93 SD :	

		Comparisons reviewed were : 1) BoNT-A vs placebo or no treatment 2) BoNT-A and therapy vs therapy only 3) BoNT-A and therapy vs BoNT only 4) BoNT-A and therapy vs placebo or no treatment 5) BoNT-A only vs therapy only 6) High dose BoNT-A vs Low dose BoNT-A Comparison 2 was the only comparison prioritised by the GDG		13.95 OT group n=22, Mean : 8.91 SD : 10.1 Mean difference : 13.02 [5.71, 20.33] Wallen 2007: BoNT and OT group n=20, Mean : 30.8 SD : 12.33 OT group n=17, Mean : 22.18 SD : 10.62 Mean difference : 8.62 [1.22, 16.02] Meta analysis : Mean Difference (IV, Random, 95% CI) 8.52 [4.42, 12.62] Four months : Greaves 2004 : BoNT and OT group n=10, Mean : 35.95 SD : 9.31 OT group n=10, Mean : 26.74 SD :9.29 Mean Difference (IV, Random, 95% CI) 9.21 [1.06, 17.36] Six months Lowe 2006 : BoNT and OT group n=21 Mean : 24.28 SD : 10.32 OT group n=21 Mean : 15.13 SD : 8.04 Mean difference : 9.15 [3.55, 14.75] Russo 2007 : BoNT and OT group n=21 Mean : 20.4 SD : 17.81 OT group n=22 Mean : 16.58 SD : 15.26 Mean difference : 3.82 [-6.11, 13.75] Wallen 2007 : BoNT and OT group n=20, Mean : 31.5 SD :13.35	

				OT group n=17, Mean : 31.35 SD : 11.09 Mean difference : 0.15 [-7.73, 8.03] Meta analysis : Mean Difference (IV, Random, 95% CI) 5.04 [-0.75, 10.83] <u>COPM Performance (change from baseline)</u> Four RCTs included Boyd 2004, Greaves 2004, Lowe 2006, Wallen 2007 Three months <u>Boyd 2004</u> : BoNT and OT group n=15, Mean : 4.44 SD : 1.42 OT group n=15, Mean : 4.09 SD : 2.45 Mean difference : 0.35 [-1.08, 1.78] <u>Lowe 2006</u> : BoNT and OT group n=21, Mean : 1.99 SD : 1.12 OT group n=21, Mean : 1.14 SD : 1.13 Mean difference : 0.85 [0.17, 1.53] <u>Wallen 2007</u> : BoNT and OT group n=20, Mean : 2.9 SD : 1.8 OT group n=17, Mean : 2.1 SD :1.7 Mean difference : 0.80 [-0.33, 1.93] Meta analysis : Mean Difference (IV, Random, 95% CI) 0.77 [0.23, 1.31] Four months <u>Greaves 2004</u> : BoNT and OT	

				group n= 10, Mean : 2.32 SD : 1.19 OT group n=10, Mean : 1.72 SD : 1.68 Mean Difference (IV, Random, 95% CI) 0.60 [-0.68, 1.88] Six months Lowe 2006 BoNT and OT group n=21, Mean : 2.56 SD :1.16 OT group n=21, Mean : 2.31 SD : 1.6 Mean difference : 0.25 [-0.60, 1.10] Wallen 2007 : BoNT and OT group n=20, Mean : 3.4 SD : 2.0 OT group n=17, Mean : 2.7 SD : 1.8 Mean difference : 0.70 [-0.52, 1.92] Meta analysis : Mean Difference (IV, Random, 95% CI) 0.40 [-0.30, 1.09] PEDI scaled score – Functional Skills (change from baseline) Three RCTs included Boyd 2004, Fehlings 2000, Wallen 2007 Three months Boyd 2004 : BoNT and OT group n=15, Mean : 6.14 SD : 9.7 OT group n=15, Mean : 8.43 SD : 17.31 Mean difference : -2.29 [-12.33, 7.75] Fehlings 2000 : BoNT and	

				OT group n=14, Mean : 2.78 SD : 3.72 OT group n=15, Mean : 1.09 SD : 4.07 Mean difference : 1.69 [-1.15, 4.53] Wallen 2007 : BoNT and OT group n=20, Mean : 3.0 SD : 3.9 OT group n= 17, Mean : 3.4 SD : 5.3 Mean difference : -0.40 [-3.44, 2.64] Meta analysis : Mean Difference (IV, Random, 95% CI) 0.60 [-1.44, 2.63] Six months Fehlings 2000 : BoNT and OT group n=14, Mean : 5.5 SD : 4.54 OT group n=15, Mean : 3.3 SD : 6.05 Mean difference : 2.20 [-1.68, 6.08] Wallen 2007 : BoNT and OT group n=20, Mean : 3.9 SD : 3.3 OT group n= 17, Mean : 4.0 SD :7.9 Mean difference : -0.10 [-4.12, 3.92] Meta analysis : Mean Difference (IV, Random, 95% CI) 1.09 [-1.70, 3.88] PEDI scaled score – Caregiver assistance (change from baseline) One RCT included Wallen	

				2007 Three months Wallen 2007 : BoNT and OT group n=20, Mean : 2.1 SD : 11.2 OT group n=17, Mean : 8.4 SD :14.3 Mean difference : -6.30 [-14.68, 2.08] Six months Wallen 2007 : BoNT and OT group n=20, Mean : 2.1 SD : 11.2 OT group n=17, Mean : 8.4 SD :14.3 Mean difference : -6.30 [-14.68, 2.08] Quality of life Three RCTs included Boyd 2004, Fehlings 2000, Wallen 2007 CHQ –physical functioning 3 months Boyd 2004 : BoNT and OT group n=15, Mean : 1.86 SD : 23.71 OT group n=15, Mean : -6.24 SD : not reported Mean difference : not estimable Wallen 2007 : BoNT and OT group n=20, Mean : 2.12 SD : OT group n=17, Mean : SD : Mean difference (95% CI):	

				Russo 2007 : BoNT and OT group n=21, Mean : 2.12 SD : 21.04 OT group n=22, Mean : 5.56 SD : 23.76 Mean difference (95% CI): -3.44 (-16.84 to 9.96) 6 months Wallen 2007 : BoNT and OT group n=20, Mean : SD : OT group n=17, Mean : SD : Mean difference (95% CI): Russo 2007 : BoNT and OT group n=21, Mean : 3.70 SD : 28.30 OT group n=22, Mean : 1.26 SD : 24.66 Mean difference (95% CI): 2.44 (-13.46 to 18.34) CHQ – role emotional 3 months Boyd 2004 : BoNT and OT group n=15, Mean : 9.6 SD : 23.121 OT group n=15, Mean : 0.74 SD : 39.41 Mean difference (95% CI): 8.86 (-14 to 31.98) Wallen 2007 : BoNT and OT group n=20, Mean : SD : OT group n=17, Mean : SD : Mean difference (95%	

				CI): Russo 2007 : BoNT and OT group n=21, Mean : 1.06 SD : 36.34 OT group n=22, Mean : 3.16 SD : 27.92 Mean difference (95% CI): -2.12 (-21.90 to 17.66) 6 months Wallen 2007 : BoNT and OT group n=20, Mean : SD : OT group n=17, Mean : SD : Mean difference (95% CI): Russo 2007 : BoNT and OT group n=21, Mean :3.18 SD : 36.54 OT group n=22, 1. Mean : -1.06 SD : 33.68 Mean difference (95% CI): 4.24 (-16.79 to 25.27) CHQ – role physical 3 months Boyd 2004 : BoNT and OT group n=15, Mean : 3.1 SD : 30.63 OT group n=15, Mean : -11.6SD : 52.14 Mean difference (95% CI): 14.70 (-15.90 to 45.30) Wallen 2007 : BoNT and OT group n=20, Mean : SD :	

				OT group n=17, Mean : SD : Mean difference (95% CI): Russo 2007 : BoNT and OT group n=21, Mean : 5.00 SD : 14.41 OT group n=22, Mean : 3.18 SD : 31.89 Mean difference (95% CI): 1.82 (-12.86 to 16.50) 6 months Wallen 2007 : BoNT and OT group n=20, Mean : SD : OT group n=17, Mean : SD : Mean difference (95% CI): Russo 2007 : BoNT and OT group n=21, Mean : 5.00 SD : 37.89 OT group n=22, Mean : 4.76 SD : 35.80 Mean difference (95% CI): 0.24 (-21.78 to 22.26) Adverse Effects Boyd 2004 : No major adverse events reported. Three children were noted to have decreased extension of the index finger that impaired the pinch grip tasks at 3 week	

				follow-up (n=2 BoNT-A group and n=1 control group). These were resolved by 6 weeks. Fehlings 2000 : Weak grasp (n=1 Tx group) lasting 2 weeks. Greaves 2005 : No adverse events Lowe 2006 : There were 31 adverse events reported by 15 participants and no between-group difference. No events were considered related to BoNT-A by the South Eastern Sydney Area Health Service review panel. Russo 2007 : There were 29 adverse events reported by 20 participants over six months. Control group - 5 reported serious adverse events (2 hospital admissions for seizures in 1 child with epilepsy, 3 hospital admissions for medical reasons in another) . Intervention group - One significant	

				adverse event reported in a child with epilepsy (admission to hospital after a seizure). Other minor adverse events included; feeling unwell after the anaesthetic (n=4); excessive weakness in the injected limb (n=5) which was prolonged in 2 children; headache (n=2); flu like symptom (n=1) for one day; fainting episodes (n=1) on a hot day; anxiety (n=1) and depression (n=1) in an adolescents with past histories; alopecia (n=1) and fatigue (n=1). Speth 2005 : No adverse events Wallen 2007 : Adverse events for each group were as follows; BoNT-A/OT group - (Frequency n = 5) including nausea and vomiting 3 days post-injection, unsettled a few days after	

				injection, vomiting post nitrous oxide, flu symptoms 2 weeks post-injection, sick and coughing 2-3 weeks postinjection) OT group - (Frequency n = 4) including illness at 1 week, illness at 2 weeks post baseline, ill at 2 week appointment, sick with rash at 2-4 weeks post baseline)	

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Kanovsky,P., Bares,M., Severa,S., Richardson,A., Dysport Paediatric Limb Spasticity Study Group. **Year of publication** 2009 **Country** European multicentre study **Ref ID** 64662 **Design** Randomised controlled study **Aim of study** To compare the long term efficacy and tolerability of two dosage regimens of BoNT-A (repeat treatments once every 4 months vs once yearly) in children with CP and lower limb spasticity.	**Inclusion Criteria** Children aged 1 to 8 years with a clinical diagnosis of diplegic cerebral palsy were recruited by 18 European centres. Participants had to be able to walk with or without a walking aid or orthosis, have the potential to benefit from injections of BoNT-A to the gastrocnemius (judged by investigator) and be able to achieve 10° passive dorasl dorsiflexion. **Exclusion Criteria** Children were excluded if: 1) the investigator perceived a clinical need for surgery to the affected limbs within 2 years 2) they were judged to need multilevel injections of BoNT-A 3) they had a significant foot deformity (the inability to obtain calcaneum neutral position during measurement of maximum passive ankle dorsiflextion for which the muscle was stretched passively to give maximum dorsiflextion with the knee in full extension) 4) they had had previous surgery on the affected muscle	**BoNT treatment** BoNT type : Dysport Dilution : not detailed Maximum total dose : For children > 33kg 1000U/treatment cycle Dosage and Muscle Selection : 30 LD_{50}U/kg of body weight BoNT-A was divided equally between both limbs. The gastrocnemius muscle was injected in two locations : the junction of the proximal quarter and the distal three-quarters of the gastrocnemius. Ijection volume at each site = 0.5mL (total injection volume = 2.0mL) Location of injection site : Palpation of the femoral and calcaneal insertions Sedation and pain management : Midazolam and topical anaesthetic cream given <u>Four monthly group</u>	Appropriate randomisation method : Yes Allocation concealment adequate : Yes Groups comparable at baseline : Yes Participants blinded to treatment allocation : No Caregivers blinded to treatment allocation : Yes Length of follow up similar for each group : 28 months, yes No of participants not completing treatment (by group) : Four monthly group = 19, yearly group= 18 Outcome assessment methods valid : Yes Investigators blinded to treatment allocation : Yes	<u>GMFM Overall score -</u> Median change from baseline at month 28 Four monthly group = 8.6 Yearly group = 5.9 p=NS <u>GMFM Goal total score -</u> Median change from baseline at month 28 Four monthly group = 12.3 Yearly group = 9 p=NS <u>Adverse events</u> <u>All adverse events</u> Four monthly group = 89/110 (81%) Yearly group = 88/104 (85%) p=NS <u>Pain</u> Four monthly group = 19/110 (17%) Yearly group = 22/104 (21%) p=NS <u>Infection</u> Four monthly group = 17/110 (15%) Yearly group = 18/104 (17%) p=NS <u>Weakness</u> Four monthly group = 15/110 (14%) Yearly group = 15/104 (14%) p=NS <u>Cough increased</u> Four monthly group = 15/110 (14%) Yearly group = 11/104 (11%) p=NS	No details given. First 3 authors stated a conflict of interest as they were in receipt of research funds from Ipsen Ltd UK (manufactures Dysport). The fourth named author was an employee of Ipsen Ltd UK Ethical Approval : Local ethics committee or institutional review boards at different centres Consent : Parents/guardians gave written consent before the study

	5)they had any known sensitivity to BoNT-A 6) they had a generalise disorder of muscle activity 7) aminoglycoside antibiotics or spectinomycin were being used 8) they were unwilling or unable to comply with the protocol 9) they had received BoNT-A treatment during the 9 months previous to study entry except for participants of two previous studies who could enter provided any treatment benefit had disappeared completely and any adverse events considered possibly or probably related to study medication had resolved **Baseline Characteristics** 214 children were included (Czech Republic =69, France =1, Italy =3, Poland =98, Slovak Republic = 17, Spain =24 and UK = 2). 4 monthly group = 110 yearly group = 104 Overall 83% of children completed the study. Key demographics described as "well balanced". Any significant differences are not reported	Children had 7 sessions (at baseline and then 4monthly up to years) Yearly group Children had 3 sessions (at baseline , 1 year and two years) **Therapy treatment** Physiotherapy, n(%) 4 monthly group = Continued during study 80 (73), Stopped before study 23 (21) Yearly group = Continued during study 67 (64), Stopped before study 36 (35) **Comparisons** Four monthly BoNT-A treatment vs Yearly BoNT-A treatment		Surgical intervention Four monthly group = 12/110 (11%) Yearly group = 13/104 (13%) p=NS Fever Four monthly group = 13/110 (12%) Yearly group = 9/104 (9%) p=NS Convulsions Four monthly group = 6/110 (5%) Yearly group = 14/104 (13%) p=0.044 Development of fixed contractures Four monthly group = 10/110 (9%) Yearly group = 7/104 (7%) Time to develop fixed contractures Hazard Ratio = 0.734 95%CI [0.28 to 1.94] p=0.533 Referral for surgery to correct fixed contractures Four monthly group = 8/110 (7%) Yearly group = 4/104 (4%) Time to referral for surgery Hazard Ratio = 0.381 95%CI [0.10 to 1.45] p=0.381 Neutralising antibodies One patient in each group had antibodies at baseline. 5 patients (2%) in total developed neautralising antibodies over the 2 year study period.	

	Age Mean (SD) 4 monthly group = 3years 8 months (1y 6m) yearly group = 4 years 4 months (1y 6m) Age Range 4 monthly group = 1-8 years yearly group = 2-8 years Sex (female) n 4 monthly group = 71 yearly group = 57 Race White(%) 4 monthly group = 110 (100) yearly group = 104 (100) Maximum Passive Ankle Dorsiflexion, median (range) 4 monthly group = Better leg 15.00° (10.00 - 33.00), Worse leg 11.67° (9.67 - 24.00) yearly group = Better leg 15.33° (10.00 - 32.67), Worse leg 11.67° (10.00 - 22.33) GMFM median (range) 4 monthly group = 75.9 (16.8 - 98.6) yearly group = 77.9 (10.0 - 100.0) Use of aids and orthoses n(%) 4 monthly group = 48 (44) yearly group = 44 (42)			Four monthly group = 4 patients developed Yearly group = 1 patient developed In four patients the levels of antibodies were low or low-intermediate In one patient the levels of antibodies were high	

	Other medications for CP n(%) 4 monthly group = Continued during study 16(15), Stopped before study 13(12) yearly group = Continued during study 13(13), Stopped before study 22(21) Age at diagnosis mean (SD) 4 monthly group = 13.2 months (10.4) yearly group = 15.4 months (12.8) Neutralising antibodies 2 of all patients had antibodies at baseline Epilepsy, epileptic syndrome, partial epilepsy or febrile convulsions at baseline 4 monthly group = 4 patients yearly group = 10 patients				

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Kay,R.M., Rethlefsen,S.A., Fern-Buneo,A., Wren,T.A.L., Skaggs,D.L. **Year of publication** 2004 **Country** USA **Ref ID** 64668 **Design** Randomised controlled study **Aim of study** The main objective was to determine whether better outcomes are achieved when BoNT-A is added to the casting regimen in the management of children with cerebral palsy who have plantar flexion or equinus contractures as well as dynamic spasticity.	**Inclusion Criteria** Inclusion criteria were : 1) a diagnosis of cerebral palsy with associated spastic diplegia, hemiplegia or quadriplegia 2) an age of four years or more 3) a plantar flexion or equinus contracture associated with a decreased range of passive dorsiflexion of ≤0º with the knee extended 4) an ability to walk independently with or without assistive devices 5) no history of orthopaedic surgery or selective doral rhizotomy in the preceding twelve months. **Exclusion Criteria** Children with a "mixed cerebral palsy", ataxia or athetosis were excluded from the study **Baseline Characteristics** Number of participants Casting only : 12 (20 limbs) Casting +BoNT : 11 (16 limbs) Age Casting only : 7.3 ± 3.3 Casting +BoNT : 6.9 ± 2.8 p=0.9020 Female Casting only : 6 Casting +BoNT :5	**BoNT treatment** BoNT type : Botox Dilution : Not stated Maximum total dose : 400U per subject Dosage and Muscle Selection : 8U/body weight into the affected gastrocnemius muscle or muscles. Injections were performed by the physician-investigator and were also made bilaterally into the soleus in one subject and into the medial hamstrings of two others. Location of injection site : Not stated Sedation and pain management : Details not provided **Therapy treatment** Serial casting for equinus contracture was performed on all children by the same experienced physiotherapist and aide. Short leg fibreglass walking casts were applied and changed every 2 weeks until ≥5° of dorsiflexion was reached with the knee extended. Csts were	Appropriate randomisation method : Yes, random number generator Allocation concealment adequate : Yes Groups comparable at baseline : Yes Participants blinded to treatment allocation : Unclear Caregivers blinded to treatment allocation : Unclear Length of follow up similar for each group : Yes No of participants not completing treatment (by group) : Casting alone =2, BoNT + casting = 1 Outcome assessment methods valid : Yes Investigators blinded to treatment allocation : No Limitations : serious, unclear or lack of blinding Other considerations : none	The outcome measures included : - duration of casting required for contracture resolution - differences in passive dorsiflexion, spasticity and peak dorsiflexion during the stance and swing phases for each limb. - Plantar flexor spasticity - Gross Motor Function Measure scores (dimensions C, D and E) Outcomes were assessed at baseline, 3, 6, 9 and 12 months (6, 9 and 12 months results reported in graphs) <u>Plantar flexor spasticity, modified Ashworth grade at 3 months, change from baseline</u> Casting alone : -1.1 ± 1.2 Casting and BoNT : -0.9 ± 1.0 Mean difference =0.20 [-0.52 to 0.92] p = 0.59 <u>Plantar flexor spasticity, modified Ashworth grade at 6 months, change from baseline (read from graph)</u> Casting alone : -1.2 ± 1.3 Casting and BoNT : -0.26 ± 1.14 Mean difference = 1.46 [0.66 to 2.26] p = 0.0003 <u>GMFM (C, D and E) % score at 3 months, change from baseline</u> Casting alone : -1.3 ± 5.1 Casting and BoNT : 2.5 ± 7.5 Mean difference = 3.80 [-0.50 to 8.10] p = 0.08	Funding: One or more of the authors received grants or outside funding from Allergan Incorporated in support of their research or preparation of this manuscript. Consent: Informed consent was obtained from the parents or guardians of children enrolled in this study Ethical Approval: The institutional review board

	p=1.0 Walking ability Casting only : Aided = 3, Independent = 9 Casting +BoNT : Aided = 2, Independent = 9 p=1.0 Type of cerebral palsy Casting only : Hemiplegia = 4, Diplegia = 7, Quadriplegia = 1 Casting +BoNT : Hemiplegia = 5, Diplegia = 6, Quadriplegia = 0 p=0.6802 Physical therapy (number of days/year) Casting only : 22.1 ± 27.6 Casting +BoNT : 28.4 ± 36.6 p=0.7742 Physical therapy (total number of hours) Casting only : 16.7 ± 21.3 Casting +BoNT : 19.5 ± 28.6 p = 0.914 Previous multilevel orthopaedic surgery Casting only : 2 children Casting +BoNT : 1 child Each child's surgery had been performed over four years previously	applied with the ankle in neutral supination-pronation and in maximum passive dorsiflexion. Csts were lined with stockinette and Websril and polycushion was applied over osseous prominences. Support for the longitudinal arch was incorporated into the cast, and an extension was added for support under the hindfoot(when the ankle was plantar flexed) or the forefoot (when the ankle was dosrilexed) to allow the patient to walk without hyperextension or excessive flexion of the knee. Cst shoes were used during walking. Hemiplegic children were cast on the affected side only. Dipleig and quadriplegic children were managed with bilateral casting (except one child with asymptomatic diplegia who was manged with		<u>GMFM (C, D and E) % score at 6 months, change from baseline (read from graph)</u> Casting alone : 1.83 ± 3.17 Casting and BoNT : 2.84 ± 3.33 Mean difference = 1.01 [-1.13 to 3.15] p = 0.36	

		unilateral csting for a unilateral contracture). After casting, the children were given new bivalved fibreglass splints, positioned in maximum passive dorsiflexion for nightime use. The children were provided with AFOs (type decided by treating physian and physical therapist, all orthoses from same certified orthotist) for daytime wear upon completion of serial casting. Other therapy Subjects who received physical therapy continued their regular regiment throughout the course of the study. The treating physical therapists completed a treatment log for each subject. Parent-reported compliance with brace wear was also recorded for each child.			
		Comparisons Serial casting alone vs BoNT and serial casting			

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Kwon,J.Y., Hwang,J.H., Kim,J.S. **Year of publication** 2010 **Country** South Korea **Ref ID** 64711 **Design** Randomised controlled study **Aim of study** To compare the clinical outcomes of two different injection techniques, one guided by electrical stimulation and the other by ultrasound, for botulinum toxin A injection into calf muscles for the treatment of spastic equinus in children with cerebal palsy	**Inclusion Criteria** 1) diagnosis of cerebral palsy 2) ambulation with or without devices or assistance 3) spastic equinus gait 4) Gross Motor Function Classification System level up to level III **Exclusion Criteria** 1) age >7 years~ 2) previous serial casting or botulinum toxin A treatment within 6 months before enrollment 3) previous lower limb surgery 4) failure to attend for follow-up assessment at 3 months **Baseline Characteristics** The Final cohort comprised of 30 children Number of patients Ultrasound group = 14 Electrical stimulation group = 16 Age (mean ± SD, months) Ultrasound group = 49.3 ± 19.4 Electrical stimulation group = 45.9 ± 18.3 Gender (Male:Female ratio) Ultrasound group = 8:6 Electrical stimulation group = 6:10	**BoNT treatment** Every participant received 4 U/kg of Botox (Allergan, Irvine, CA) per gastrocnemius Dilution used was 100 units per 5 ml of 0.9% saline Botox was injected into the gastrocnemius at 4-6 points in total, with 2-3 points each on the medial and lateral heads **Therapy treatment** <u>Ultrasound-guided group</u> Ultrasonography carried out using the Sonoace ultrasound system (Medison Co., Ltd.) using a 7.5 MHz linear transducer <u>Electrical stimulation-guided group</u> Electrical stimulation was performed by the nerve stimulation of an EMG machine (Viking IV, Nicolet, Germany) Stimulating current:	Study was a pseudo-randmised, prospective controlled trial Following informed consent, all children with cerebral palsy who met the inclusion criteria at an out-patient clinic of St. Vincent's Hospital, Suwon, South Korea, between March 2007 and June 2008, were recruited Participants were enrolled in separate categories according to their level under the Gross Motor Function Classification System and then alternately assigned to one of the two groups, as the parents/guardians had no particular preference All children were sedated by oral chloral hydrate and/or intravenous midazolam and lidocaine cream was applied at injection site 1 hour	Modified Ashworth scale [median (interquartile range)] - <u>With knee extended</u> Ultrasound group: - Baseline = 3(3–3) - at 3 months = 3(2–3); P < 0.05 Electrical stimulation group: - Baseline = 3(3–3) - at 3 months = 3(2–3); P > 0.05 <u>With knee flexed</u> Ultrasound group: - Baseline = 2(2–3) - at 3 months = 2(2–2); P < 0.05 Electrical stimulation group: - Baseline = 2(2–3) - at 3 months = 1(2–2); P > 0.05 Modified Tardieu scale (mean ± SD) - <u>R1 with knee extended</u> Ultrasound group: - Baseline = −17.1 ± 10.7 - at 3 months = −6.7 ± 14.3; P < 0.05 Electrical stimulation group: - Baseline = −16.8 ± 12.2 - at 3 months = −11.4 ± 11.9; P > 0.05 <u>R2 with knee extended</u> Ultrasound group: - Baseline = 6.7 ± 17.0 - at 3 months = 14.6 ± 13.4; P < 0.05 Electrical stimulation group: - Baseline = 11.6 ± 12.9; - at 3 months = 13.4 ± 15.5; P > 0.05	None reported

	Weight (mean ± SD, kg) Ultrasound group = 16.6 ± 6.3 Electrical stimulation group = 15.7 ± 4.1 Legs injected (n) Ultrasound group = 23 Electrical stimulation group = 24 Orthosis Ultrasound group = 1/13 Electrical stimulation group = 1/15	5-10mA Duration: 0.1 msec **Comparisons** Ultrasound-guided Botox injection compared to electrical stimulation-guided injection	before procedure Standard injection sites were identified using anatomic landmarks Details reported in the paper	<u>R1 with knee flexed</u> Ultrasound group: - Baseline = 3.0 ± 10.5 - at 3 months = 9.0 ± 13.8; P > 0.05 Electrical stimulation group: - Baseline = 2.6 ± 10.5 - at 3 months = 6.9 ± 17.0; P > 0.05 <u>R2 with knee flexed</u> Ultrasound group: - Baseline = 26.3 ± 16.0 - at 3 months = 29.6 ± 13.7; P > 0.05 Electrical stimulation group: - Baseline = 27.1 ± 10.9 - at 3 months = 28.6 ± 14.1; P > 0.05 Speed of gait (Physician's Rating sacle) [median (interquartile range)] Ultrasound group: - Baseline = 0(0–1) - at 3 months = 1(0–1); P > 0.05 Electrical stimulation group: - Baseline = 0(0–1) - at 3 months = 0(0–1); P > 0.05	

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Olesch,C.A., Greaves,S., Imms,C., Reid,S.M., Graham,H.K. **Year of publication** 2010 **Country** Australia **Ref ID** 64828 **Design** Randomised controlled study **Aim of study** A randomised controlled trial of repeat injections of Botulinum toxin-A in the upper extremity of young children with cerebral palsy. This study evaluated the effectiveness of repeated injections of botulinum toxin A (BoNT-A in the hemiplegic upper limb in children with cerebral palsy combined with occupational therapy (OT) compared to OT alone, regarding goal achievement, occupational performance and quality of movement.	**Inclusion Criteria** Children aged 18m to 5 years who had a diagnosis of congenital CP hemiplegia with spasticity affecting upper arm activity but who did not have fixed contractures. Consecutive recruitment of children attending an outpatient CP clinic at a tertiary referral centre **Exclusion Criteria** 1) Children who had undergone upper limb surgery or had upper limb BoNT A injections within the previous 6 months 2) Those whose caregivers were unwilling to cease other upper-limb interventions (such as splinting and casting) during the trial **Baseline Characteristics** Nineteen boys and 3 girls participated. There was no evidence of differences between the groups in : number of boys (treatment group=9, control group=10), mean age (treatment=3.7 years, control=3.7 years), side of hemiplegia (right side: treatment=6, control=7), baseline Peabody score (standardized score: treatment=503.6, control=502.6).	**BoNT treatment** BoNT-A Type : Botox Dilution : 10U/0.1mL Maximum total dose : Dependant on child's bodyweight Dosage and Muscle Selection : 0.5U/kg dose for adductor pollicis, flexor pollicis longus and flexor digitorum superficialis. 1U/kg for flexor digitorum profundus, flexor carpi radialis, fexor carpi ulnaris and pronator teres. 2U/kg for the biceps brachii Muscle selection by assessment made by an occupational therapist and a physician. Same muscles were targeted at each injection cycle Muscle Localisation : Muscle stimulation Type of Anaesthesia : Short general anaesthesia (sevoflurane) Intervention occurred	Randomisation : Analyses of between-group differences were undertaken using independent samples t-tests with alpha set at 0.05 Two children did not complete the trial. Allocation to group was concealed from researchers. Occupational therapists were not blinded to group allocation Outcomes were rated by assessor blind to group allocation. PEDro Quality Assessment Good	Primary outcomes included the Canadian Occupational Performance Measure (COPM), Goal Attainment Scale, (GAS) measured at baseline and 4 monthly intervals to 12 months. Secondary outcomes included the Peabody Developmental Fine Motor Scale (Peabody), Quality of Upper Extremity Skills Test (QUEST) and measures of spasticity. Reduction of Spasticity <u>Modified Tardieu scale - elbow flexors (across group comparison of scores)</u> Four months (cycle 1) BoNT and OT group n= 11 Mean : 43.0 SD : 45.7 OT group n=11 Mean : 77.3 SD : 39.3 Mean difference : -34.30 [-70.67, 2.07] Eight months (cycle 2) BoNT and OT group n= 11 Mean : 54.5 SD : 44.1 OT group n=11 Mean : 90.5 SD : 40.3 Mean difference : -36.00 [-71.30, -0.70] Twelve months (cycle 3) BoNT and OT group n= 11 Mean : 34.5 SD : 48.0 OT group n=11 Mean : 77.3 SD : 56.2 Mean difference : -42.80 [-86.48, 0.88]	Not reported

	All children were in GMFCS levels I or II. Age Twenty-four children aged 18 months to 5 years were recruited (mean age=3.7 years [SD=0.9]).	in three 16-week cycles and included BTX-A injections followed by twice weekly OT for 6 weeks. **Therapy treatment** A generic protocol for the OT intervention was individualised for each child. Therapy was based upon a goal directed approach – interview with parent to establish goal, task analysis to identify factors hindering or supporting the child's achievement of this goal. Targeted activities to support goal achievement were practised in therapy, and the home based programme used practicing of tasks related to the child's everyday life to support goal achievement. Amount of practice to be undertaken was individualised and adherence to the home programme was not recorded.		<u>Modified Tardieu scale - forearm pronators (across group comparison of scores)</u> Four months (cycle 1) BoNT and OT group n= 11 Mean : 48.5 SD : 37.2 OT group n=11 Mean : 75.5 SD : 31.7 Mean difference : -27.00 [-55.88, 1.88] Eight months (cycle 2) BoNT and OT group n= 11 Mean : 39.5 SD : 40.6 OT group n=11 Mean : 77.3 SD : 22.8 Mean difference : -37.80 [-65.32, -10.28] Twelve months (cycle 3) BoNT and OT group n= 11 Mean : 22.7 SD : 33.2 OT group n=11 Mean : 72.7 SD : 28.7 Mean difference : -50.00 [-75.93, -24.07] <u>Modified Tardieu scale - wrist flexors (across group comparison of scores)</u> Four months (cycle 1) BoNT and OT group n= 11 Mean : 11.0 SD : 17.4 OT group n=11 Mean : 29.5 SD : 27.6 Mean difference : -18.50 [-37.78, 0.78] Eight months (cycle 2) BoNT and OT group n= 11	

		All children received a twice weekly OT programme for 6 weeks after BoNT injection (or at a comparable time point for the OT only group). The initial 2 weeks of each programme was delivered the study therapist, then for the remaining 4 weeks by either the child's community therapist or by the study therapist Both groups returned to their usual therapy regimens until each 16 wk cycle was completed. **Comparisons** BoNT + OT vs OT alone		Mean : 7.3 SD : 9.3 OT group n=11 Mean : 25.0 SD : 30.7 Mean difference : -17.70 [-36.66, 1.26] Twelve months (cycle 3) BoNT and OT group n= 11 Mean : 3.2 SD : 7.2 OT group n=11 Mean : 24.1 SD : 28.5 Mean difference : -20.90 [-38.27, -3.53] <u>QUEST scores (across group comparison of scores)</u> Total score Four months (cycle 1) BoNT and OT group n= 11 Mean : 76.3 SD : 13.2 OT group n=11 Mean : 70.8 SD : 12.8 Mean difference : 5.50 [-5.37, 16.37] Eight months (cycle 2) BoNT and OT group n= 11 Mean : 76.9 SD : 10.4 OT group n=11 Mean : 69.3 SD : 13.4 Mean difference : 7.60 [-2.42, 17.62] Twelve months (cycle 3) BoNT and OT group n= 11 Mean : 79.6 SD : 8.0 OT group n=11 Mean : 72.9 SD : 11.5 Mean difference : 6.70 [-1.58,	

				14.98] <u>COPM Performance (change from baseline)</u> Four months (cycle 1) BoNT and OT group n= 11 Mean : 2.4 SD :1.0 OT group n=11 Mean :1.7 SD : 1.4 Mean difference :0.70 [-0.32, 1.72] Eight months (cycle 2) BoNT and OT group n= 11 Mean : 2.7 SD : 0.9 OT group n=11 Mean : 1.8 SD : 1.0 Mean difference :0.90 [0.10, 1.70] Twelve months (cycle 3) BoNT and OT group n= 11 Mean : 3.0 SD : 1.3 OT group n=11 Mean : 1.6 SD : 1.2 Mean difference :1.40 [0.35, 2.45] Over whole year (includes goals for entire year) BoNT and OT group n= 11 Mean : 2.5 SD : 1 OT group n=11 Mean : 1.7 SD : 0.6 Mean difference :0.80 [0.11, 1.49] Author reports -0.80 [-0.15, 0.0] <u>Goal Attainment Scale T score</u> Four months (cycle 1) BoNT and OT group n= 11 Mean : 54.1 SD : 9.8 OT group n=11	

				Mean :48.1 SD : 10.1 Mean difference :6.00 [-2.32, 14.32] Eight months (cycle 2) BoNT and OT group n=11 Mean : 55.0 SD : 4.3 OT group n=11 Mean : 47.3 SD : 11.6 Mean difference :7.70 [0.39, 15.01] Twelve months (cycle 3) BoNT and OT group n=11 Mean : 54.9 SD : 9.5 OT group n=11 Mean : 50.0 SD : 7.1 Mean difference : 4.90 [-2.11, 11.91] Over whole year BoNT and OT group n=11 Mean : Incorrect data SD : 6.6 OT group n=11 Mean : 48.8 SD : 8.6 Mean difference : Not estimable <u>Adverse Events</u> Three self resolving adverse events were reported in BoNT/OT group. One child had a maculopapular rash (immunological test to consider if response to BoNT inconclusive).Child continued with treatment without further adverse events. One child developed weakness in index finger after BoNT administration into adductor	

				pollicis. This spontaneously resolved and the child continued with treatment without further adverse events. One child developed prolonged weakness in the finger flexors and thereafter the child did not receive any further BoNT injections at this site, but completed the study with respect to other muscle groups.	

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Reddishough,D.S., King,J.A., Coleman,G.J., Fosang,A., McCoy,A.T., Thomason,P., Graham,H.K. **Year of publication** 2002 **Country** Australia **Ref ID** 64882 **Design** Randomised controlled study **Aim of study** To compare functional outcome in young children with cerebral palsy when given BoNT treatment with a physiotherapy programme and when given a physiotherapy programme alone in a randomized, cross over trial and to particularly determine what changes might persist at 6 months following injection.	**Inclusion Criteria** Children with spastic diplegia or mild-to-moderate spastic quadriplegia without fixed myostatic contractures, who required active treatment of dynamic contractures in the lower limb that were interfering with function. The following were indication for treatment of spasticity : a) at the hip - children with adductor "scissoring" and difficulties with sitting, standing, toileting and dressing b) at the knee - children with hamstring spasticity causing difficulties in standing or long sitting, loss of knee extension in standing and a walking pattern charaterised by a "crouch gait" c) at the ankle/foot - spasticity of gastrosoleus, the tibialis and peroneal muscles, causing equinus, equinovarus, and equinovalgoid postural problems. These problems manifested as difficulties in achieving a plantigrade position in standing and walking, frequent falls, orthotic intolerance and footwear problems	**BoNT treatment** BoNT type : Not stated Dilution : Not stated Maximum total dose : max at any one muscle site - 20U, max in any one large muscle group - 120U, max for a first injection - 300U Dosage and Muscle Selection : Dose range was 8-20U/kg body weight, distributed between a minimum of 2 and a maximum of 6 muscle groups. Mean total dose 13.5U/kg body weight. Target muscles were identified by examination and discussion among parents, therapists and an orthopaedic surgeon. The number of injection sites per muscle varied accoring to the number of muscles to be injected and the total dose available according to the child's weight. Location of injection site : Manual	Appropriate randomisation method : Yes Allocation concealment adequate : Unclear Groups comparable at baseline : Yes for GMFCS levels, no other details given Participants blinded to treatment allocation : No Caregivers blinded to treatment allocation : Unclear Length of follow up similar for each group : Yes (6months) although unclear how many assessments made from which children at 3 months or at the mid point of the control treatment period No of participants not completing treatment = 12 : Group 1 = not given , Group 2 = not given Outcome assessment methods valid : Yes Investigators blinded to treatment allocation : Yes	Outcomes assessed at baseline, 3 and 6 months for the BoNT treatment period. The protocol stipulated that assessments would only be made at baseline and 6 months during the control period (to improve compliance), however, this was later changed to include an assessment at the mid point of the control period. 19 children had five assessments in total and 30 children had four assessments. Modifed Ashworth scores were taken for right and left calves and hip adductors at 3month/mid-point in control period and 6 months. Only results where a significant difference between treatment periods were reported. MAS Left calf mean change 6 months Therapy alone phase = 0.43± 0.81 (n=35) BoNT and therapy phase = -0.09± 0.78 (n=35) P<0.05 MAS Left adductor mean change 6 months Therapy alone phase = 1± 0.76 (n=8) BoNT and therapy phase = -0.63± 1.06 (n=8) P<0.05 MAS Total score mean change 3 months Therapy alone phase = 1.38 ± 1.30	Support from the Royal Children's Hospital Research Institute, the Murdoch Children's Research Institute (Theme Grant), the Financial MarketsFoundation for Children and the Hugh DT Willinamson Foundation. Ethical approval and parental consent were obtained. No further details given

	Children were recruited from CP clinics at the Royal Children's Hospital, Victoria. **Exclusion Criteria** 1) hemiplegia (as more appropriately examined using gait analysis, rather than GMFM) 2) severe spastic quadriplegia 3) had undergone orthopaedic surgery to the lower limb within the 12 months prior to study entry 4) had had either BoNT therapy of inhibitory plasters applied within 6 monthe of the start date of the project 5) were having tone reducing interventions eg ITB for gnerealised spasticity 6) were receiving controversial therapies **Baseline Characteristics** 61 children were recruited. 12 did not continue - 7 required surgery during the study period and 5 were unble to continue with the assessment protocol. 49 children were in the final cohort Males = 24 Age range = 22 - 80 months Mean age = 4 yrs 1 month Group 1 GMFCS levels (n=22) I = 3, II = 6, III = 9, IV = 4 Group 2 GMFCS levels (n=27)	methods of muscle identification. Commonly, there were two injection sites per muscle for adductor/hamstrings and four injection sites for the gastrocnemius muscle. The most common injection site was the hamstrings (44 right and 42 left). Calves - 35 right and 36 left. Adductors - 8 children had injections in each adductor muscle Sedation and pain management : Short general anaesthesia **Therapy treatment** Physiotherapy programme consisted of advice and treatment aimed at improving function and mobility and the provision of appropriate orthotics and walking aids. Approaches included programmes based upon the principles of neurodevelopmental treatment, conductive education, and hydrotherapy. These	Matching of pairs of children according to GMFCS level and age and then randomisation to treatment group Limitations : Other considerations : No wash out period details given (ie presumed that BoNT effects have stopped at 6 months)	(n=18) BoNT and therapy phase = -1.13 ± 0.83 (n=18) GMFM Total score mean change 3 months Therapy alone phase = 4.03± 7.05 (n=19) BoNT and therapy phase = 2.70±4.62 (n=19) GMFM Total score mean change 6 months Therapy alone phase = 3.44±6.79 (n=49) BoNT and therapy phase = 3.60±7.44 (n=49) GMFM Total score with aids mean change 3 months Therapy alone phase = 2.80±14.40 (n=7) BoNT and therapy phase = 6.52±4.95 (n=7) GMFM Total score with aids mean change 6 months Therapy alone phase = 11.13±11.18 (n=24) BoNT and therapy phase = 3.94±11.60 (n=24) Adverse effects Parents were asked whether their child experienced some form of complication or side effect from the	

	I = 4, II = 5, III = 11, IV = 7	were delivered in individual or group settings. Children receiving controversial therapies were excluded from the study. Mean number or physiotherapy sessions during the study period Therapy alone phase = 20.9 BoNT and therapy phase = 27.8 **Comparisons** Physiotherapy alone vs BoNT and physiotherapy In the first 6 month treatment period, Group 1 received BoNT injections within 3 weeks of their baseline assessment and physiotherapy programme whilst Group 2 received physiotherapy alone. At the end of the first 6 month treatment period, children in Group 2 received BoNT injections and physiotherapy		BoNT injection. 4 of 21 parents at 3months and 6 of 23 parents at 6 months agreed that their child had experienced a complication/side effect. Those reported were some level of incontinence, (n=4), short term muscle weakness (n=4) and less specific complaints of the child being “out of sorts” and “a little sick and sore” (n=2). Pain Parents were asked whether their child experienced any pain in their legs following injection. 7 of 23 parents at 3months and 4 of 23 parents at 6 months recalled their child having experienced pain Acceptability and tolerability Parental perception was assessed with a short questionnaire which specifically addressed the effects of BoNT treatment at 3 and 6 months after injection. A chi-squared analysis of the results to the question asking whether the parent felt that the BoNT injection had been of benefit to the child demonstrated significantly more positive responses at both 3 and 6 months post-injection ($\chi2 = 12.0$, $p<0.05$ and $\chi2 =7.16$, $p<0.05$ respectively). Of those parents who considered BoNT beneficial for their child, 36 of 47 parents at 3months and 35 of 43 parents at 6 months rated the	

		programme and Group 1 received physiotherapy alone		benefit as good, very good or excellent. At 3 months post-injection, of 33 parents who noticed a benefit with BoNT treatment, 26 reported the maximum benefit occurring within 6 weeks of the injection. The remainder (7 parents) reported the maximum benefit occurring 6-12 weeks post-injection. At 6 months post-injection, of 35 parents who noticed a benefit with BoNT treatment, 23 reported the maximum benefit occurring within 1-2months of the injection, 5 reporting maximum benefit at 2 to 3 months and the remainder (7 parents) reporting the maximum benefit occurring 3 to 6 months post-injection.	

Study details	Participants	Interventions	Methods	Outcomes	Comments
Authors Xu,K., Yan,T., Mai,J. **Year of publication** 2009 **Country** China **Ref ID** 65079 **Design** Randomised controlled study **Aim of study** To compare the efficacy of botulinum toxin A injection skills guided by electrical stimulation and that guided by palpation, and to learn whether botulinum toxin A injection improved gait or not, as a means of treating the spasticity of the ankle plantar flexors in ambulant Chinese children with cerebral palsy	**Inclusion Criteria** Children aged 24-120 months with spastic hemiplegic and mild diplegic cerebral palsy; ankle plantar flexors ≥ grade 2 on the modified Ashworth Scale; ability to walk independently; informed consent and compliance with study instructions **Exclusion Criteria** Orthopaedic surgery to the lower limb within 12 months; other lower limb muscles ≥ grade 2 on the modified Ashworth Scale; use of spasticity-reducing interventions e.g. baclofen, dantrium, artane; failure to meet visit schedule **Baseline Characteristics** The Final cohort comprised of 65 children Number of patients Electrical stimulation group = 23 Palpation group = 22 Age (mean ± SD, months) Electrical stimulation group = 55 ± 11.5 Palpation group = 59.4 ± 22.7 Gender (Male:Female ratio) Electrical stimulation group = 16:7	**BoNT treatment** Botulinum toxin A diluted in preservative-free, sterile saline to a concentration 100 U/mL The dosages were 3-10 U/kg, limited to no more than 12 U/kg The maximum dose of botulinum toxin A at any one site was 10 U The number of injection sites ranged from 6-8 in the one ankle planatar flexors **Therapy treatment** <u>Physiotherapy</u> Each session lasted 60 to 90 minutes, five days a week for two weeks <u>Electrical stimulation</u> Pulse duration: 0.1 to 0.5 ms Frequencies: 0.66 Hz to 1.00 Hz Amplitude: maximum of 10 mA <u>Palpation</u> Spastic ankle plantar	Ambulant children with cerebral palsy aged 24 to 120 months who met inclusion criteria at Guangzhou Children's Hospital, China, between June 2004 and August 2007, were recruited to the trial Demographic characteristics, spasticity of ankle plantar flexors and functional performance were obtained All participants received physiotherapy three days after botulinum injection In the electrical stimulation group, the motor point in the ankle plantar flexors of the spastic limb were located using a set of electrodes For the palpation group, the spastic ankle flexors were stretched to increase muscle tone and the	Change of outcome data at three months (i.e. month 3 value − baseline value) (mean ± SD) <u>Electrical stimulation group</u> Passive range of movement, degrees = 20.5 ± 5.2 Modified Ashworth scale = −1.9 ± 0.3 Gross Motor Function measure, D and E dimensions = 18.9 ± 4.0 Walking velocity, m/s = 0.15 ± 0.06 <u>Palpation group</u> Passive range of movement, degrees = 16.2 ± 5.1 Modified Ashworth scale = −1.4 ± 0.5 Gross Motor Function measure, D and E dimensions = 11.3 ± 1.8 Walking velocity, m/s = 0.08 ± 0.04	None reported

	Palpation group = 15:7 Weight (mean ± SD, kg) Electrical stimulation group = 9.8 ± 1.5 Palpation group = 9.7 ± 1.6 Spastic limb right Electrical stimulation group = 18/23 (56%) Palpation group = 17/22 (55%) Spastic limb left Electrical stimulation group = 14/23 (44%) Palpation group = 14/22 (45%) Passive range of movement (mean ± SD, degrees) Electrical stimulation group = −8.8 ± 6.3 Palpation group = −7.6 ± 6.0 Modified Ashworth Scale (mean ± SD) Electrical stimulation group = 2.8 ± 0.5 Palpation group = 2.7 ± 0.6 Gross Motor Function Measure (mean ± SD, D and E dimensions) Electrical stimulation group = 55.8 ± 9.3 Palpation group = 54.5 ± 10.9	flexors stretched to increase muscle tone, with child in prone position **Comparisons** Botulinum toxin A injection guided by electrical stimulation plus physiotherapy compared to botulinum toxin A injection guided by palpation plus physiotherapy	bulging area of the spastic muscle was located by palpation where the injection was applied Details reported in the paper		

	Walking velocity (mean ± SD, m/s) Electrical stimulation group = 0.6 ± 0.1 Palpation group = 0.6 ± 0.2 Botulinum toxin A injection sites (mean ± SD) Electrical stimulation group = 7.6 ± 0.7 Palpation group = 7.8 ± 0.8 Botulinum toxin A injection dosage (mean ± SD, U/kg) Electrical stimulation group = 5.7 ± 1.8 Palpation group = 5.8 ± 1.4 Botulinum toxin A injection dosage (mean ± SD, U/site) Electrical stimulation group = 7.0 ± 0.8 Palpation group = 6.9 ± 1.2				

Spasticity in children and young people with non-progressive brain disorders: management of spasticity, co-existing motor disorders and their early musculoskeletal complications

Intrathecal baclofen

Bibliographic details	Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality Assessment	Reviewer comment
Authors Krach,L.E., Kriel,R.L., Gilmartin,R.C., Swift,D.M., Storrs,B.B., Abbott,R., Ward,J.D., Bloom,K.K., Brooks,W.H., Madsen,J.R., McLaughlin,J.F., Nadell,J.M. **Year of publication** 2004 **Country of study** USA **Aim of Study** To assess whether reduction in muscle tone by CITB affects the progression of hip subluxation in persons with CP **Ref ID** 56510 **Type of study** Prospective case series (follow-up of Gilmartin 2000)	**Inclusion Criteria** Patients who had a CITB pump implanted in the previous study and also had radiographic evaluation of their hips before and after a year of treatment with CITB and a baseline and 12-month post initiation of therapy comparison **Exclusion Criteria** Failure to respond to the bolus dose of intrathecal baclofen, pregnancy during the year after the pump implantation, infection of the pump or catheter or lack of comparison radiographic information **Participant characteristics** Total: 33 patients Total number of children: 28 < 8 years: 11 8 to 18 years: 17 Cerebral palsy groups(number of patients, including adults) CP 1 and 2 (walks without device; walks with assistive device): 9 (18 hips)	**Intervention** Continuous intrathecal infusion of baclofen (CITB) via the programmable infusion pump Medtronic SynchroMed Infusion System. Two baclofen injection concentrations were available: 500 µg/mL and 2000 µg/mL Maximum refill interval was 90 days. The pump reservoir was refilled every 1 to 3 months as needed **Comparison** N.A **Background treatment** Oral baclofen was stopped prior to study participation unless discontinuation presented a hazard to the patient which happened in 2 cases. In these 2 patients the dose was held constant during phase 1 but it is unclear what happened with them during phase 2	Progression of hip subluxation Measured when: 12 months after pump was implanted Measured by: unclear Instrument/test: radiographic evaluation of hips Unit of measurement: migration percentage (it is a measure of the amount of the ossified femoral head which is uncovered by ossified acetabular roof) Results <u>Absolute migration percentage by age category (%) (mean ± SD):</u> Age category < 8 years Number of hips: 22 Baseline: 27.1 ± 19.7 12-month: 27.2 ± 20.9 Change from baseline: 0.0 ± 8.4 P<0.05 Age category 8 to 18 years	Outcomes assessors / investigators blinded to intervention : unclear because it is not reported who assessed the outcomes, but it is stated that the pharmaceutical company that produces the SynchroMed Infusion System provided some support for data collection and analysis including assisting with statistical analysis Number of participants not completing treatment: 11 of the 44 patients who received pumps were excluded for the following reasons: 2 developed an infection in the pump pocket 1 wanted to become pregnant and withdrew from study 4 had orthopaedic surgery during the study period 3 did not have data on migration % at 12 months and 1 at baseline Number of participants with	**Funding** Medtronic, Inc. (Minneapolis, Minnesota) supplied SynchroMed TM Implantable Pumps and Lioresal Intrathecal TM for the duration of the study and provided some support for data collection and analysis , including assisting with statistical analysis **Other information**

	CP 3 (crawling with hands and knees on wheelchair): 6 (12 hips) CP 4 (May commando crawl or roll): 12 (24 hips) CP 5 (Totally dependent for activities of daily living, no independent motor activity): 6 (12 hips)		Number of hips: 34 Baseline: 23.8 ± 20.2 12-month: 25.0 ± 17.2 Change from baseline: 1.2 ± 12.8 P<0.05 <u>Absolute migration percentage by CP classification (%) (mean ± SD):</u> (this outcome includes adult patients) CP 1 and 2 Number of hips: 18 Baseline: 22.7 ± 18.8 12-month: 19.7 ± 10.3 Change from baseline: -3.0 ± 14.9 P<0.05 CP 3 Number of hips: 12 Baseline: 23.6 ± 8.4 12-month: 27.1 ± 13.2 Change from baseline: 3.5 ± 8.9 N.S CP 4 Number of hips: 24 Baseline: 19.9 ± 18.3 12-month: 23.4 ± 16.9 Change from baseline: 3.5 ± 11.6 N.S CP 5 Number of hips: 12	no available outcome data: none Selective outcome reporting: no Sample size: small, no power calculation performed Indirectness Population: 5 adults included Intervention: None Comparison: N.A Outcomes assessed: none	

			Baseline: 34.8 ± 31.3 12-month: 36.3 ± 32.6 Change from baseline: 1.4 ± 7.3 N.S <u>Change of 5% or more in migration percentage by CP classification (number of patients and %)</u> (Worse=increased ≥5%; better= decreased ≤5%; unchanged=changes within 5% of more) (this outcome includes adult patients) CP 1 and 2 Number of hips: 18 Worse: 4 (22.2) Unchanged: 12 (66.7) Better: 2 (11.1) CP 3 Number of hips: 12 Worse: 5 (41.7) Unchanged: 6 (50.0) Better: 1 (8.3) CP 4 Number of hips: 24 Worse: 9 (37.5) Unchanged: 11 (45.8) Better: 4 (16.6) CP 5 Number of hips: 12 Worse: 4 (33.3) Unchanged: 7 (58.3)		
			Better: 1 (8.3)		

Bibliographic details	Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality Assessment	Reviewer comment
Authors Awaad,Y., Tayem,H., Munoz,S., Ham,S., Michon,A.M., Awaad,R. **Year of publication** 2003 **Country of study** USA **Aim of Study** To describe the outcomes of a series of patients with CP who received intrathecal baclofen to reduce spasticity **Ref ID** 58588 **Type of study** Prospective case series	**Inclusion Criteria** Phase 1 (testing) A diagnosis of CP At least 4 years of age Weight more than 30 pounds Have severe spasticity in lower extremities (defined as an average Ashworth Scale score of at least 3) Patients also had to undergo a trial of oral antispasmodic agents for at least 6 months prior to be considered for CITB Phase 2 (CITB) A positive response to testing (defined as a 1-point reduction in the average Ashworth scores in the lower extremities) Agreement from the family to have the pump implanted Patients considered “appropriate” candidates for the therapy (no other details provided) **Exclusion Criteria** Phase 1 (testing) Severe contractures	**Intervention** Phase 1 (testing) Bolus of intrathecal baclofen 50 µg into the lumbar region (no other details provided) Phase 2 (CITB) CITB delivered via a programmable pump After the pump was implanted the patients received individualised rehabilitation, including physical and occupational therapies, speech therapy and gait training. Patients had on average, 2 to 3 visits per week for rehabilitation **Comparison** Phase 1 (testing) N.A Phase 2 (CITB) N.A **Background treatment** Phase 1 (testing) Unclear Phase 2 (CITB) Rehabilitation programmes based on individual needs, including physical and occupational therapies, speech therapy and gait training. Patients had on average 2 to 3 visits/weeks for rehabilitation	Phase 1 (testing) Spasticity Measured when: every 2 hours after the injection (unclear how many times) Measured by: physical and occupational therapists Instrument/test: Ashworth scale Unit of measurement: Ashworth scores for seven lower-extremity muscle groups (hip adductors, abductors, and flexors; knee flexors and extensors; and ankle dorsiflexors and plantarflexors) and four upper extremity muscle groups (wrist and elbow flexors and extensors) were averaged for one combined score Results: (n=28, all children) (Mean, SD) Before trial: 3.19 (0.56) After trial: 1.34 (0.50) Change: -1.85 (0.51) P<0.001 Adverse effects were not reported for testing	Phase 1 (testing) Outcomes assessors blinded to intervention : no Number of participants not completing treatment: All patients completed testing but only 39 proceeded to have pumps implanted. The following reasons explain why 10 did not: 3 patients elected to use oral medications 2 had “family issues” 1 child’s body size was too small 1 child died unrelated to the baclofen trial 1 child underwent spinal fusion 1 child had “medical issues” and 1 family decided not to undergo implant at time of study (unclear why) Number of participants with no available outcome data: 6 patients did not have baseline PEDI scores and were not included in the data analysis (and apparently they did not receive a pump) Selective outcome reporting: Adverse effects were not reported for testing, unclear	**Funding** not stated **Other information** Phase 1 (testing) Sample size: small, no power calculation performed Indirectness Population: none, adult patients included but subgroup analysis performed Intervention: None Comparison: N.A Outcomes assessed: Ashworth scores for lower-extremity muscle groups and upper extremity muscle groups were averaged for one combined score which is both methodologically and clinically incorrect and should be reported as score for individual muscles instead Phase 2 (CITB) Sample size: small, no power calculation performed Indirectness Population: none, adult patients included but subgroup analysis performed Intervention: None Comparison: N.A Outcomes assessed: Ashworth scores for lower-extremity

	Phase 2 (CITB) - None stated **Participant characteristics** Phase 1 (testing) Total: 55 patients Sex: 19 females and 36 males Age: between 4 and 32 years (mean age 13.09y, SD 7.49) PEDI functional skills mobility scores: mean 25.39 SD (20.18) Phase 2 (CITB) Total: 39 patients Sex: 12 females and 27 males Age: between 4 and 32 years (mean age 13.69y, SD 7.43) PEDI functional skills mobility scores: mean 25.44 SD (20.41)		Phase 2 (CITB) Spasticity Measured when: 12 months after pump implantation Measured by: physician, nurse and/or physical therapist Instrument/test: Ashworth scale Unit of measurement: Ashworth scores for seven lower-extremity muscle groups (hip adductors, abductors, and flexors; knee flexors and extensors; and ankle dorsiflexors and plantarflexors) and four upper extremity muscle groups (wrist and elbow flexors and extensors) were averaged for one combined score Results: Ashworth score at 12 months and change as compared to baseline (mean, SD) (children only) Ashworth score: 1.76 (0.64) Change: -1.49 (0.69) P<0.001 Adverse effects Measured when: unclear, presumably at postoperative follow-up assessments (1, 6,	whether it is because there were not any Phase 2 (CITB) Outcomes assessors blinded to intervention : no Number of participants not completing treatment: 2 patients had their pump removed, one because of a change of behaviour owing to an increased in seizure activity and another one owing to pocket infection Number of participants with no available outcome data: 10/39 patients lacked follow-up data: 2 were followed at other facilities, 6 did not have follow-up PEDI scores and 2 patients had their pump removed (see above) Selective outcome reporting: no	muscle groups and upper extremity muscle groups were averaged for one combined score which is both methodologically and clinically incorrect and should be reported as score for individual muscles instead 28 of the 39 patients who had the pump implanted were children, but it is unclear what were the ages of the patients who did not have available follow up data to begin with, or the age of those who were lost to follow up at different assessment times, therefore it is not possible to tell exactly how many children were included in the sample whose outcomes are reported here. This is a serious limitation of the study

			12, 18 and 24 months) Measured by: unclear, presumably physician, nurse and/or physical therapist Instrument/test: unclear Results: Total number of adverse effects: 35 Total number of patients involved: unclear Nausea: 4 Constipation: 6 Increased in seizure frequency: 2 (unclear if this includes the patient in which the pump had to be stopped after 5 months because of a change of behaviour owing to an increased in seizure activity) New-onset seizures: 2 Increased oral secretions: 2 Sleepiness: 2 Urinary retention: 2 Total number of patients who required their pump to be explanted: 4 (unclear whether any of these patients were children) Reasons: Meningitis: 1 Infection: 2 (1 was a “pocket infection”, unclear about the other one) Lack of effect-no clinical		

			improvement: 1 (unclear if the latter the same patient in which the pump had to be stopped after 5 months because of a change of behaviour owing to an increased in seizure activity)		

Bibliographic details	Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality Assessment	Reviewer comment

Authors Gilmartin,R., Bruce,D., Storrs,B.B., Abbott,R., Krach,L., Ward,J., Bloom,K., Brooks,W.H., Johnson,D.L., Madsen,J.R., McLaughlin,J.F., Nadell,J. **Year of publication** 2000 **Country of study** USA **Aim of Study** to asses the efficacy of continuous intrathecal infusion of baclofen (CITB) in patients with spastic cerebral palsy (CP) **Ref ID** 58683 **Type of study** Phase 1: Double-blind cross-over RCT (placebo-controlled) Phase 2: Prospective case series	**Inclusion Criteria** Phase 1 (testing): Patients with congenital CP or who had acquired spastic CP before 2 years of age, with moderate to severe spasticity (as indicated by an Ashworth score of 3 or more in the four lower extremity measurements: hip abductors, knee flexors, knee extensors and foot dorsiflexors) and with/without a mild degree of atethosis or dystonia. Patients had to be 3 years or older and with sufficient body mass to accommodate and implantable pump Phase 2 (CITB): a positive response to testing, defined as a reduction in 1 point in the average Ashworth Scale score for all 8 lower-extremity sites maintained over two successive measurements between 1 and 8 hours after the bolus dose (either 50, 75 or 100 µg of intrathecal baclofen) was delivered **Exclusion Criteria** None stated for phase 1 Phase 2: positive response to placebo or no reduction of 1 point in the average Ashworth Scale score in the lower extremities after administering	**Intervention** Phase 1 (testing): 50 µg of Lioresal Intrathecal (baclofen injection), one single dose. If no positive response the patient was given an additional open-label 75-µg bolus injection. If no positive response to the previous a 100 -µg bolus injection was delivered open-label 24 hours later. Patients were assigned to a baclofen-placebo or placebo-baclofen sequence with a 48-hour washout period between injections Baclofen/placebo were delivered by lumbar puncture, percutaneous spinal catheter or implanted port with spinal catheter Phase 2 (CITB): Continuous intrathecal infusion of baclofen (CITB) via the programmable infusion pump Medtronic SynchroMed Infusion System. Two baclofen injection concentrations were available: 500 µg/mL and 2000 µg/mL Maximum refill interval was 90 days. The pump reservoir was refilled every 1 to 3 months as needed **Comparison**	Phase 1 (testing): Spasticity Measured when: 4 hours after the bolus was delivered Measured by: unclear, but the same evaluator throughout the trial for any given patient Instrument/test: Ashworth scale Unit of measurement: Ashworth scores bilaterally assessed in 4 lower-extremity muscle groups ((hip abductors, knee flexors and extensors; and foot dorsiflexors) and also in the upper extremities (unclear which muscles) Results: Lower extremities (at 4 hours and after single dose 50µg) (mean, SD; SE; range) (n=51) Baclofen: 2.14 (0.85); 0.12 (1.00 to 4.75) Placebo: 3.11 (0.69);0.14 (1.75 to 5.00) p<0.001 Lower extremities (after open label dose 75µg) (mean, SD; SE; range) (n=10) Baclofen: 2.04 (0.67); 0.21 (1.37 to 3.50)	Phase 1 (testing): Randomisation and blinding: methods unclear Allocation concealment: unclear Participants blinded to intervention : yes Carers blinded to intervention : yes Investigators blinded to intervention : yes Number of participants not completing treatment: All patients completed treatment with at least one single dose of 50 µg of baclofen but 7 did not proceed to have the pump implanted for the following reasons: 3 patients had a positive response to placebo, 2 did not have a positive response to the 50-µg baclofen dose and withdrew before getting a higher dose (unclear why), 1 patient developed meningitis and 1 patient had an adverse event of nausea, vomiting, elevated blood count, nystagmus and agitation (the investigator noted that this patient had intercurrent	**Funding** supported in part by Medtronic, Inc **Other information** Phase 1 (testing): Sample size: small, no power calculation performed Indirectness Population: adult patients included and no subgroup analysis performed Intervention: None Comparison: placebo not used for testing in UK clinical practice Outcomes assessed: None Ashworth scores for lower-extremity muscle groups and upper extremity muscle groups were averaged in both cases which is both methodologically and clinically incorrect and should be reported as score for individual muscles instead Phase 2 (CITB): Sample size: small, no power calculation performed Indirectness Population: Unclear as specific characteristic of patients included in this phase were not reported Intervention: None

	100 µg of baclofen **Participant characteristics** Phase 1 (testing): Total: 51 patients Sex: 22 females and 29 males Age: between 4 and 31.3 years (mean age 10y 3mo, median 11y 2mo) Cerebral palsy type: 12 spastic diplegia 4 spastic paraplegia 35 spastic quadriplegia Phase 2 (CITB): Total: 44 of the previous patients, specific characteristics not reported	Phase 1 (testing): 50 µg of 0.9% preservative-free sodium chloride injection Phase 2 (CITB): N.A **Background treatment** Phase 1 (testing): Oral baclofen was stopped prior to study participation unless discontinuation presented a hazard to the patient which happened in 2 cases. In these 2 patients the dose was held constant during phase 1 Phase 2 (CITB): 2 patients received oral baclofen after pump implantation; in one the oral baclofen was discontinued 1 month post implantation, and the second patient withdrew from the study after 4 months (unclear whether these were the same patients who also received oral baclofen during phase 1)	Baseline: 3.31 (0.60);0.19 (2.00 to 4.00) p<0.001 Lower extremities (after open label dose 100µg) (mean, SD; SE; range) (n=2) Baclofen: 1.81 (0.62); 0.44 (1.37 to 2.25) Baseline: 3.44 (0.62);0.43 (3.00 to 3.87) Upper extremities (at 4 hours and after single dose 50µg) (mean, SD; range) (n=51) Baclofen: 1.92 (0.80); (1.0 to 4.4) Baseline: 2.21 (0.80); (1.0 to 4.5) p<0.001 Adverse effects Measured when: during the 3-day inpatient procedure Measured by: unclear Instrument/test: unclear Results: Total number of adverse effects: 29 (7 during placebo) Total number of patients affected: 18 (4 during placebo) 1 patient developed meningitis (withdrew from	gastroenteritis) Number of participants with no available outcome data: none Selective outcome reporting: results for placebo not reported for the upper extremities Phase 2 (CITB): Outcomes assessors blinded to intervention : N.A Number of participants not completing treatment: 7 patients withdrew after pump implantation for the following reasons: 2 developed and infection in the pump pocket, 2 had “family issues”, 1 wanted to become pregnant and, 2 died (1 as passenger in a motor vehicle accident and 1 of respiratory failure due to pneumonia) Number of participants with no available outcome data: Lower limbs Ashworth scores: 2 patients at 6 months, 4 patients at 12 months, 11 patients at 24 months Upper limbs Ashworth scores: 3 patients at 6 months, 4 patients at 12 months, 12 patients at 24 months	Comparison: N.A Outcomes assessed: Ashworth scores for lower-extremity muscle groups and upper extremity muscle groups were averaged in both cases which is both methodologically and clinically incorrect and should be reported as score for individual muscles instead

			study) 1 patient developed nausea, vomiting, elevated blood count, nystagmus and agitation. The investigator noted that the child had intercurrent gastroenteritis (withdrew from study) Nausea, vomiting and drowsiness were common effects reported during baclofen, but unclear how many children involved in each of them <u>Phase 2 (CITB-pump):</u> Spasticity (n=44) Measured when: within 2 weeks of implantation, monthly for 6 months and then at 3-month intervals Measured by: unclear Instrument/test: Ashworth scale Unit of measurement: Ashworth scores bilaterally assessed in 4 lower-extremity muscle groups ((hip abductors, knee flexors and extensors; and foot dorsiflexors) and also in the upper extremities (unclear which muscles)	Selective outcome reporting: no	

			Results: Lower extremities (mean, SD; range) -at 24 months after implantation(n=33): 2.21 (0.75); (1.0 to 3.5) -at 12 months after implantation(n=40): 2.15 (0.60); (1.1 to 3.3) -at 6 months after implantation(n=42): 2.33 (0.64); (1.0 to 3.8) -Baseline (n=44): 3.64 (0.57); (3.0 to 5.0) Upper extremities (mean, SD; range) -at 24 months after implantation(n=32): 1.72 (0.69); (1.0 to 3.1) -at 12 months after implantation(n=40): 1.73 (0.66); (1.0 to 4.1) -at 6 months after implantation(n=41): 1.80 (0.72); (1.0 to 3.8) -Baseline (n=44): 2.54 (0.98); (1.0 to 4.5) Adverse effects Measured when: unclear, presumably during the 10 routine visits required by protocol in the first year post-implantation Measured by: unclear		

			Instrument/test: unclear Results: Total number of device related events: 59 Total number of patients involved: 30 39 were procedure related and 20 system related (“procedure” related occurred in the first 60 days after implantation and were not directly attributable to device, and “system” after 60 days and the other way round) Procedure related (number of events): Pocket seroma: 7 Pocket infection: 5 Catheter dislodged: 3 CSF leak: 3 Other: 20 System related: Catheter break: 2 Catheter dislodge: 2 Back pain at catheter site: 2 Other: 14 Total number of baclofen related events: 65 Total number of patients involved: unclear		

			Most common baclofen related events (number of events): Hypotonia: 16 Seizure: 15 Headache: 9 Total number of patients requiring pump explantation: 3 (unclear whether any of these patients were children) Reasons: the 3 because of infections of the pump pocket: 1 had a second pump re-implanted to complete study and the other 2 withdrew from study)		

Bibliographic details	Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality Assessment	Reviewer comment
Authors Hoving,M.A., van Raak,E.P., Spincemaille,G.H., Palmans,L.J., Sleypen,F.A., Vles,J.S., Dutch Study Group on Child Spasticity. **Year of publication** 2007 **Country of study** The Netherlands **Aim of Study** (1) to select children eligible for CITB treatment (2) to assess the effective ITB bolus dose; and (3) to evaluate effects, side effects, complications, and procedures **Ref ID** 58704 **Type of study** Double-blind cross over RCT (placebo-controlled)	**Inclusion Criteria** 1. Age between 4 and 16 years 2. Spastic diplegia or tetraplegia as part of cerebral palsy 3. Insufficient response to oral spasticity-reducing medication 4. In a mixed cerebral palsy syndrome, spasticity is the most prominent sign 5. Spasticity results in a decrease in the quality of life of the child and/or its caregivers 6. Sufficient motivation for study participation including availability for follow-up 7. Magnetic resonance imaging of the brain rules out progressive diseases 8. Minimal weight of 20kg (valid until 1 January 2004) 9. Wheelchair bound without ability to creep or sit unsupported (valid until 1 January 2004) 10. Child is able to understand and carry out instructions (valid until 1 January 2004) (Note: From January 2002 to December 2003 many children who wished to participate were not included because they did not meet the weight, mobility, and/or cognition criteria. Authors therefore	**Intervention** After admission, the neurosurgeon inserted under general anaesthesia an external lumbar catheter (Perifix 300 Mini Set; B Braun, Melsungen, Germany) Postoperatively and during the test days, the children stayed on the paediatric medium care unit, where vital signs were monitored. The morning after catheter insertion, the first study medication bolus was administered intrathecally via the catheter During the first two test days the bolus randomly contained baclofen 25µg or placebo. On each of the subsequent six test days the bolus contained baclofen 50 µg or placebo, then baclofen 75 µg or placebo, and, finally, baclofen 100 µg or placebo. In a given two-day treatment period, patients received baclofen and placebo in random order. **Comparison** Placebo (unclear what it consisted of) 14 children preventively received one to four doses of cefazoline perioperatively	Spasticity Measured when: every day before bolus administration (baseline) and 2, 4, and 6 hours afterward Measured by: an experienced paediatric physiotherapist. For each child scores were always rated by the same physiotherapist Instrument/test: Ashworth scale Unit of measurement: Ashworth scores bilaterally assessed in seven lower-extremity muscle groups. Before catheter insertion, authors selected the hip, knee, and ankle-related muscle group with highest tone on both sides, in total identifying six muscle groups per child (hip adductors, flexors, and extensors; knee flexors and extensors; and ankle plantarflexors and dorsiflexors) Results: <u>Baclofen (n=17):</u> The Ashworth scores, assessed 2, 4, and 6 hours after administration of the effective ITB dose, significantly decreased in	Randomisation and blinding: An independent statistician generated the randomization lists, permitting a balanced distribution of study medication sequences within the same child as well as between the children. The pharmacist prepared and numbered the study medication in accordance with these randomization lists Allocation concealment: unclear Participants blinded to intervention : yes Carers blinded to intervention : yes Investigators blinded to intervention : yes Number of participants not completing treatment : none Number of participants with no available outcome data: 15 One boy who responded to ITB 20µg had two separate test treatments. During the first day of the first test treatment he experienced apathy and, in an upright position, nausea	**Funding** Main sponsor: the Research Fund of the University Hospital Maastricht. In addition: grant from Medtronic Inc., Heerlen, the Netherlands. Medtronic Inc **Other information** Sample size: small, but the fact that this is a cross over trail increase the power. No calculation was performed based on the outcomes assessed in this report Indirectness Population: None Intervention: None Comparison: placebo not used for testing in UK clinical practice Outcomes assessed: None

	decided to widen the eligibility criteria by omitting inclusion criteria 8, 9, and 10 from January 2004) **Exclusion Criteria** 1. Hypersensitivity to baclofen 2. Contraindications for general anaesthesia 3. Insufficient general health 4. Intractable epileptic seizures 5. Infection of the lumbar skin 6. Systemic infection **Participant characteristics** 38, 23 males and 15 females, were referred as possible candidates for the Dutch national ITB study. The main reasons for referral were 'having pain' and problems with 'ease of care'. Total: 17 children Sex: 9 females and 8 males Age: between 7 and 16 years (mean age 13y 2mo [SD 2y 9mo]) Weight: (range 17 to 84 kg) Cerebral palsy type: 12 spastic, 5 spastic/dyskinetic, 3 diplegia, 14 tetraplegia GMFCS level: III (1), IV (2), V (14) Most children had one or more	On the day that a positive clinical response was observed, the test treatment ended and the study medication code was broken. Only if this positive clinical response was observed on the first test day did the child and caregivers have the opportunity to experience the results of the second test day before the test treatment was ended. We offered this opportunity because the decision on pump implantation should be well based. Having noticed a positive clinical response on the first test day, children and parents might have a need for confirmation by observing a lack of effect on the second test day. If the code break proved that the child had responded to baclofen, they were considered eligible for further treatment with CITB. If after eight test days no positive clinical effect had been observed, the child was not eligible for pump implantation Clinical effect defined as positive only if the following two criteria were met:	comparison with baseline for all muscle groups (0.001≤p≤0.040), except for the left hip flexors 2 hours after ITB administration (p=0.080) <u>Placebo (n=17):</u> Did not change significantly in any muscle group at any test moment (0.083≤p≤1.000). In the three children who had two placebo days, the results of the first placebo day were used Ease of care Measured when: Each VAS was rated once before the test treatment started (baseline) and at the end of each test day, reviewing the observations of that day. During VAS rating, the children and parents did not know the Ashworth scores for that day Measured by: Depending on both the ability to understand the test and to draw a vertical line, the VAS was rated by the child or by a parent Instrument/test: Visual Analogue Scale (VAS) for individually formulated problems	and vomiting. His vital signs were normal. The test treatment was broken off because his condition impeded the observation of effects and side effects. During a second admission, authors decided to do an open label test treatment administering ITB 20µg by lumbar puncture. This resulted in a positive clinical response and slight lethargy as a side effect. Authors decided to exclude the test results from statistical analyses because the test treatment had not been carried out double-blinded. 14 of the 17 children were bed-bound because they had symptoms of lowered CSF pressure. Consequently, certain individually formulated problems could not be evaluated during the test treatment Selective outcome reporting: actual results for the Ashworth scores in individual muscles not reported	

	of the following associated problems: speech problem, drooling, constipation, urological problem, sleeping disorder, visual impairment, epilepsy, bronchopulmonary problem and auditory problem	(1) a satisfying improvement in the individual treatment goals as experienced by the child and/or the caregivers; and (2) at least a one-point reduction on the Ashworth scale compared with the baseline score of that specific day, in at least three of the six individually selected muscle groups. This one-point reduction had to last for two successive measurements on the same day. **Background treatment** 7 children still used oral baclofen and they continued this use during the test	Unit of measurement: Straight 10cm horizontal line with anchor points of 'very dissatisfied' (score 0) and 'very satisfied' (score 10) Results: <u>Baclofen (n=14): </u>(mean, SD) Baseline: 2.3 (1.4) After baclofen: 7.4 (2.2) Difference: 5.1 (2.1) P=0.001 <u>Placebo (n=13): </u>(mean, SD) Baseline: 2.4 (1.4) After baclofen: 3.3 (2.0) Difference: 0.9 (1.7) P=0.093 Pain Measured when: Each VAS was rated once before the test treatment started (baseline) and at the end of each test day, reviewing the observations of that day. During VAS rating, the children and parents did not know the Ashworth scores for that day Measured by: Depending on both the ability to understand the test and to draw a vertical line, the VAS was rated by the child or by a parent		

			Instrument/test: Visual Analogue Scale (VAS) for individually formulated problems Unit of measurement: Straight 10cm horizontal line with anchor points of 'no pain' (score 0) and 'unbearable pain' (score 10) Results: Baclofen (n=11): (mean, SD) Baseline: 3.2 (2.0) After baclofen: 6.5 (3.1) Difference: 3.3 (2.9) P=0.010 Placebo (n=10): (mean, SD) Baseline: 3.2 (2.1) After baclofen: 4.3 (2.6) Difference: 1.1 (3.5) P=0.262 Adverse effects Measured when: twice every test day, before bolus administration and at the end of the test day, reviewing the observations of that day Measured by: caregivers Instrument/test: caregivers' notes on		

			standardised forms, which included time of occurrence Results: <u>Baclofen (n=17):</u> Total number of adverse effects: 9 Total number of children affected: 8 7 children became slightly lethargic, including a child who also experienced transient excessive hypotonia One child: excessive perspiration of hands and feet Total number of complications: 19 Total number of children affected: 16 14 children presented one or more symptoms that could fit in with the diagnosis of lowered CSF pressure (included lethargy, decreased appetite, dry mouth, dizziness, perspiration, pallor, nausea, vomiting, and headache). The last four symptoms appeared or increased only in an upright position. None of these symptoms were observed in 3 children in		

			whom the neurosurgeon had tunnelled the catheter subcutaneously for a few centimetres In 3 children, CSF leaked from the catheter connection. In one of these, the catheter connection was defective, so a new catheter had to be inserted; in the other two, reconnection of the cap solved the problem. One child had radicular pain in his right leg postoperatively. The pain was completely resolved by retracting the catheter for 5cm Another child first had abdominal cramps due to constipation, developing gastroenteritis later on. At that time, more children on the ward had gastroenteritis. Overall, none of the children required respiratory support or admission to intensive care. None of the children developed meningitis.		

			Placebo (n=17): None reported Other individually formulated problems In individual cases, improvements were noted concerning transfers, voiding, startle responses, operating the electric wheelchair, and arm function. One boy underwent the test treatment because of deteriorating gait in spite of multilevel treatment with botulinum toxin. He saw his goals fulfilled: with ITB 50µg the pain in his hamstrings disappeared and walking took less energy		

Bibliographic details	Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality Assessment	Reviewer comment
Authors Hoving,M.A., van Raak,E.P., Spincemaille,G.H., Palmans,L.J., Becher,J.G., Vles,J.S., Dutch Study Group on Child Spasticity. **Year of publication** 2009 **Country of study** The Netherlands **Aim of Study** To study the efficacy of continuous infusion of intrathecal baclofen (CITB) in the treatment of children with problems caused by intractable spastic cerebral palsy **Ref ID** 58706 **Type of study** Double-blind before randomisation Open-label after randomisation Parallel RCT	**Inclusion Criteria** 1. Age between 4 and 16 years 2. Spastic diplegia or tetraplegia as part of cerebral palsy 3. Insufficient response to oral spasticity-reducing medication 4. In a mixed cerebral palsy syndrome, spasticity is the most prominent sign 5. Spasticity results in a decrease in the quality of life of the child and/or its caregivers 6. Sufficient motivation for study participation including availability for follow-up 7. Magnetic resonance imaging of the brain rules out progressive diseases 8. Minimal weight of 20kg (valid until 1 January 2004) 9. Wheelchair bound without ability to creep or sit unsupported (valid until 1 January 2004) 10. Child is able to understand and carry out instructions (valid until 1 January 2004) (Note: From January 2002 to December 2003 many children who wished to participate were not included because they did not meet the weight, mobility, and/or cognition criteria. Authors therefore	**Intervention** Programmable Synchromed infusion pump (no other details provided on the specific model) (Medtronic Inc., Minneapolis, MN) after 1 month Children also received "standard treatment" described by the authors as "any physiotherapy, speech therapy and occupational therapy". No other details were provided **Comparison** "Standard treatment" only **Background treatment** 3 children in the CITB group and 4 in the control group used oral baclofen. The children in the CITB group gradually discontinued this use, all during the first 10 post operative days	<u>Primary outcomes</u> Individually formulated problems Measured when: at 6 months after pump implantation/standard treatment initiation Measured by: Depending on both the ability to understand the test and to draw a vertical line, the VAS was rated by the child or by a parent Instrument/test: Visual Analogue Scale (VAS) for individually formulated problems Unit of measurement: average of 3 individually formulated VAS scores per child Results (6-month-change scores) (Mean, SD) CITB group (n=9) 4.0 (1.7) Control group (n=8) -0.2 (1.3) P=0.001 Ease of care Measured when: at 6 months after pump implantation/standard treatment Measured by: Depending on both the ability to understand	Randomisation, blinding and allocation concealment: an independent statistician generated the allocation schedule with an unpredictable sequence of assignments. The investigator who enrolled the children had no entry into this list and was at the time of each enrolment not aware of next assignment in the sequence. For assignment the investigator called the independent statistician who consulted the allocation list Participants blinded to intervention : no Carers blinded to intervention : no Investigators blinded to intervention: yes but only before randomisation. The main investigator was present during all admissions and follow-up visits of the children Number of participants not completing treatment: None Number of participants with no available outcome data: None	**Funding** Grants from the Research Fund of the University Hospital Maastricht. Grant from Medtronic Inc., Heerlen, the Netherlands. **Other information** Sample size: small. Power calculation was based on the results of a study about children with spastic CP who were treated with selective dorsal rhizotomy. In this study caregiver assistance scale scores for PEDI self care domain at baseline and 12-mont follow-up were compared. After 12 months PEDI scores had significantly improved with 4.44 points (SD 1.32). Authors assumed that in this study the children would have not reached maximum improvement after 6 months yet and therefore set the clinically significant difference worth to detect in this study at three points with an estimated SD of 1.82. With a significance level of 0.005 and a power of 90% the number of patients needed per group was 8. allowing for a drop out of 10% a maximum of 18 children would be included.

	decided to widen the eligibility criteria by omitting inclusion criteria 8, 9, and 10 from January 2004) **Exclusion Criteria** 1. Hypersensitivity to baclofen 2. Contraindications for general anaesthesia 3. Insufficient general health 4. Intractable epileptic seizures 5. Infection of the lumbar skin 6. Systemic infection **Participant characteristics** Total: 17 children Sex: 9 females and 8 males Age: between 7 and 16 years (mean age 13y 2mo [SD 2y 8mo]) ITB patients Total: 9 children Sex: 4 females and 5 males Age: mean age 13y 9mo [SD 2y 3mo]) Cerebral palsy type: 7 spastic, 2 spastic/dyskinetic, 1 diplegia, 8 tetraplegia GMFCS level: III (0), IV (1), V (8) Control group (“standard treatment”) Total: 8 children Sex: 5 females and 3 males Age: mean age 12y 4mo [SD 3y 2mo]) Cerebral palsy type: 5 spastic, 3 spastic/dyskinetic, 2 diplegia,		the test and to draw a vertical line, the VAS was rated by the child or by a parent Instrument/test: Visual Analogue Scale (VAS) for individually formulated problems Unit of measurement: VAS scores Results (6-month-change scores) (Mean, SD) CITB group (n=9) 3.9 (2.2) Control group (n=7) 0.1 (1.6) P= 0.008 Pain Measured when: at 6 months after pump implantation/standard treatment Measured by: Depending on both the ability to understand the test and to draw a vertical line, the VAS was rated by the child or by a parent Instrument/test: Visual Analogue Scale (VAS) for individually formulated problems Unit of measurement: VAS scores Straight 10cm	Selective outcome reporting: Yes. Actual scores of the Ashworth scale were not reported because there were “too many data” according to the authors	Baseline characteristics: There were no apparent significant differences between both groups, although figures were not reported Indirectness Population: None Intervention: None Comparison: unclear as not described in detail. Outcomes assessed: None Other limitations: it is unclear whether the standard treatment that both groups received was exactly the same, or even whether there were any variations within groups [STUDY 2009a]

	6 tetraplegia GMFCS level: III (1), IV (1), V (6)		horizontal line with anchor points of 'no pain' (score 0) and 'unbearable pain' (score 10) Results (6-month-change scores) (Mean, SD) CITB group (n=6) 4.2 (2.9) Control group (n=6) -1.3 (2.4) P= 0.016 Movement and function (activities and participation in the ICF-International Classification of Disability and Health) Measured when: at 6 months after pump implantation/standard treatment Measured by: unclear Instrument/test: Dutch version of the Paediatric Evaluation of Disability Inventory (PEDI)-PEDI caregiver assistance scale Unit of measurement: PEDI scores Results (6-month-change scores) (median, range): CITB group (n=9) 0.0 (-11.7 to 4.1) Control group (n=8) 0.0 (-16.0 to 16.0)		

			p=0.720 <u>Secondary outcomes</u> Spasticity Measured when: at 6 months after pump implantation/standard treatment Measured by: an experienced paediatric physiotherapist. For each child scores were always rated by the same physiotherapist Instrument/test: Ashworth scale Unit of measurement: Ashworth scores bilaterally assessed in 7 lower-extremity muscle groups (hip adductors, flexors and extensors; knee flexors and extensors; and ankle plantarflexors and dorsiflexors) and 4 upper extremity muscle groups (elbow and wrist flexors and extensors). Scores of the total 22 muscles separately analysed Results (6-month-change scores): The 6-month-change score between both groups significantly differed in		

			favour of the CITB group for the left hip adductors (p=0.0025), both hip flexors (p=right=0.022; left=0.043) and the right wrist flexors (p=0.038) Movement and function (activities and participation in the ICF-International Classification of Disability and Health)Measured when: at 6 months after pump implantation/standard treatment Measured by: unclear Instrument/test: Dutch version of Gross Motor Function Measure (both the GMFM-66 and the GMFM-88 versions) Dutch version of the Paediatric Evaluation of Disability Inventory (PEDI)-functional skills scale Unit of measurement: scores of previous tests (GMFM-88: 4-point ordinal scale; GMFM-66: interval scaling) Results (6-month-change scores):		

			GMFM-66 overall (Mean, SD) CITB group (n=7) 1.2 (2.3) Control group (n=5) -1.6 (3.0) P=0.028 GMFM-88 lying and rolling (median, range): CITB group (n=7) 3.9 (-12.0 to 10.0) Control group (n=5) 0.0 (-10.0 to 0.0) P=0.512 GMFM-88 sitting (median, range): CITB group (n=7) 3.3 (0.0 to 10.0) Control group (n=5) 0.0 (-7.0 to 7.0) P=0.085 GMFM-88 goal dimensions (median, range): CITB group (n=5) 3.0 (2.0 to 10.0) Control group (n=4) 1.3 (-6.0 to 6.0) p=0.140 PEDI functional skills(median, range): CITB group (n=9) 0.0 (-7.4 to 5.7) Control group (n=8) 0.0(-5.4 to 2.1) P=0.720		

			Quality of Life Measured when: at 6 months after pump implantation/standard treatment Measured by: unclear Instrument/test: Dutch version of the Child-Health Questionnaire-Parent Form (CHQ-PF50) Unit of measurement: scores of CHQ-PF50, each domain is scaled from 0 to 100 with higher scores reflecting a better HRQL. Physical and psychosocial summary scores calculated using normative data from North American children Results (6-month-change scores) (Mean, SD) physical summary CITB group (n=8) 2.1 (10.3) Control group (n=8) -7.5 (6.9) P= 0.074		

			psychosocial summary CITB group (n=8) 3.4 (7.9) Control group (n=8) -5.7 (8.8) P= 0.027 This study did not assess adverse effects		

Bibliographic details	Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality Assessment	Reviewer comment
Authors Motta,F., Stignani,C., Antonello,C.E. **Year of publication** 2008 **Country of study** Italy **Aim of Study** to evaluate, with the use of functional scales, the effect of ITB on generalized dystonia in 19 patients affected by cerebral palsy (CP) and with severe degree of impairments **Ref ID** 58774 **Type of study** Prospective case series	**Inclusion Criteria** Children affected by CP and with severe degree of impairment **Exclusion Criteria** Not stated **Participant characteristics** Total: 19 children Sex: 6 females, 13 males Age at implant: between 2 years 5 months and 16 years 6 months (mean age 8.49 years, SD 3.2) Type of CP: 13 (70%): spastic dystonic tetraplegia with severe generalised dystonia 6 (30%): dystonic tetraplegia All patients suffered form severe limitations to all areas of motor function, even when using aids. They were unable to stay seated or to keep their head steady and the needed assistance with everyday activities. None showed painful retractions before pump implant	**Intervention** Continuous intrathecal baclofen therapy via programmable pump Initially the pump was placed subcutaneously (5 children) whereas from the 3rd year of the study the pump was positioned more deeply in the abdomen between the external oblique muscle and abdominal rectus (14 children) 9 children were implanted the 10-ml SyncroMed pump, 1 with the 18-ml SyncroMed pump and the remaining 10 with the 20-ml SyncroMed pump **Comparison** N.A **Background treatment** None reported	Dystonia Measured when: pre-implant and at 3, 6 and 12 months post-implant Measured by: same team of 2 rehabilitation therapists and same orthopaedic physician Instrument/test: Barry-Albright scale (BAD) and Burke-Fahn-Marsden scale (BFM)-standard video recording was used for assessment Unit of measurement: BAD and BFM scores, both from 0 to 4. A low score equates with less severe dystonias in both scales Results: <u>Overall BAD scores (mean, SD)</u> at 12 months: 17.79 ± 3.3 baseline: 23.84 ± 4.11 P<0.001 (Individual BAD scores not reported for each region, only p values for change) Eyes: <0.05 Mouth: <0.01 Neck: <0.001 Upper limb dx: <0.001 Upper limb sx: <0.001 Trunk: <0.001	Outcomes assessors blinded to intervention: no Number of participants not completing treatment: none Number of participants with no available outcome data : unclear , none apparently Selective outcome reporting: Individual BAD and BFM scores not reported for each body region, only p values for change Dystonia assessed at 3, 6 and 12 months post-implant but outcomes reported only for the 12 month follow up	**Funding** none of the authors received financial support **Other information** Sample size: small, no calculation performed Indirectness Population: 30% may not have had spasticity Intervention: none Comparison: N.A Outcomes assessed: none

			Lower limb dx: <0.01 Lower limb sx: <0.01 <u>Overall BFM scores-movement components (mean, SD)</u> at 12 months: 77.60 ± 20.56 baseline: 98.57 ± 13.07 P<0.001 <u>BFM scores- movement components</u> (actual scores not reported for each region, only p values for change) Eyes: NS Mouth: <0.05 Language-Swallowing: NS Neck: <0.05 Upper limb dx: <0.05 Upper limb sx: <0.05 Trunk: <0.001 Lower limb dx: <0.001 Lower limb sx: <0.001 <u>BFM scores-degree of disability</u> None of the patients showed any change regarding everyday activities Movement and function Measured when: at each follow up (unclear how was analysed) Measured by: patient or caregiver if patient unable to communicate		

			Instrument/test: non-validated questionnaire Results (number of children): Dystonia Improved: 18 Unchanged: 1 Worsened: 0 Hygiene Improved: 12 Unchanged; 6 Worsened: 0 Dressing Improved: 18 Unchanged: 1 Worsened: 0 Feeding Improved: 10 Unchanged: 8 Worsened: 1 Sleeping Improved: 10 Unchanged: 8 Worsened: 1 Pain Improved: 10 Unchanged: 8 Worsened: 1 Acceptability and tolerability Measured when: at each follow up (unclear how was analysed)		

			Measured by: patient or caregiver if patient unable to communicate Instrument/test: non-validated questionnaire Results: Satisfied with the implant: 15 Would do it again: 14 Not totally satisfied: 3 Uncertain whether to do it again: 3 Dissatisfied: 1 Would not do it again: 1 (chose to explant pump 4 years after implant) Adverse effects and complications Measured when: unclear, presumably at 3, 6 and 12 months post-implant Measured by: unclear, presumably same team of 2 rehabilitation therapists and same orthopaedic physician Instrument/test: unclear Results: (only major complications were considered, defined as those that needed medical		

			assistance to be resolved) 1 complication related to catheter breakage and infection, solved by catheter replacement CSF leakage (considered as minor): 4 patients, generally solved spontaneously		

Bibliographic details	Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality Assessment	Reviewer comment
Authors Senaran,H., Shah,S.A., Presedo,A., Dabney,K.W., Glutting,J.W., Miller,F. **Year of publication** 2007 **Country of study** Turkey **Aim of Study** To test the hypothesis that intrathecal baclofen has an effect on the incidence of scoliosis, the rate of curve progression and the magnitude of pelvic obliquity **Ref ID** 58828 **Type of study** Case-control	**Inclusion Criteria** ITB patients: Patients with spastic cerebral palsy who were treated with ITB, had spine radiographs at time of pump implantation and subsequently developed or had progression of scoliosis after ITB which was documented by radiographs at follow-up Controls: Age, gender and GMFCS score-matched patients who did not have ITB **Exclusion Criteria** ITB patients: Having a posterior spinal fusion before or simultaneously with pump implantation developing a sagittal plane deformity whilst on ITB, not having adequate spine radiographs at pump implantation Controls: not stated **Participant characteristics** <u>ITB patients</u> Total number of patients: 2 age at pump implantation (years. Mean, range) 11.8, 5 to 18 sex: 14 female, 12 male GMFCS (number of patients) GMFCS 4: 2, GMFCS 5: 24	**Intervention** Programmable ITB pump (Synchromed EL or II, Medtronic Inc., Minneapolis, MN) **Comparison** No ITB pump, other interventions not reported either **Background treatment** None reported	Rate of curve progression Measured when: - ITB patients: at time of pump implantation and at minimum 2 years follow-up - Controls: at time of diagnosis of scoliosis and at minimum 2 years follow-up Measured by: unclear Instrument/test: standard posteroanterior and lateral radiographs of the spine taken with patient sitting erect, those who could not sit independently were positioned in special adaptative seat with straps to allow them to sit erect, but no attempts to correct the scoliosis were made Unit of measurement: Cobb angle in thoracic, thoracolumbar, lumbar and double major curves Results: (mean, SD) <u>ITB patients (n=26)</u> Curve at follow-up (degrees): 65.19 (24.74) Age at follow-up (years): 14.77 (3.37) Curve at baseline (degrees):	Outcomes assessors blinded to intervention: unclear, possibly not as nothing was reported on the characteristics of the outcomes assessors Number of participants with no available outcome data: no Selective outcome reporting: no Sample size: no calculation performed Baseline characteristics: not statistically compared Other limitations: In case-control studies, data are not available to calculate the incidence rate of the disease being studied. This is the reason why this outcome is not reported here Unclear whether the ITB patients were also quadriplegic Indirectness Population: none Intervention: none Comparison: none Outcomes assessed: none	**Funding** Authors stated that no funds were received in support of this study **Other information**

	follow-up time (years. Mean, range): 2.9, 2 to 7 <u>controls</u> Total number of patients: 25 (all quadriplegic) age at diagnosis of scoliosis (years. Mean, SD, range) 11.6, 3.5, 5 to 18 sex: 10 female, 15 male GMFCS (number of patients) GMFCS 4: 3, GMFCS 5: 22 follow-up time (years. Mean, range): 4.0, 2 to 11		24.08 (15.97) Age at baseline (years): 11.84 (3.66) <u>Controls (n=25)</u> Curve at follow-up (degrees): 73.00 (21.81) Age at follow-up (years): 15.64 (3.75) Curve at baseline (degrees): 28.16 (17.53) Age at baseline (years): 11.60 (3.51) P value comparing both groups: 0.181		

Bibliographic details	Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality Assessment	Reviewer comment
Authors Shilt,J.S., Lai,L.P., Cabrera,M.N., Frino,J., Smith,B.P. **Year of publication** 2008 **Country of study** USA **Aim of Study** To examine the effect of intrathecal baclofen (ITB) treatment on the progression of scoliosis in patients with cerebral palsy (CP) **Ref ID** 58834 **Type of study** Case-control	**Inclusion Criteria** <u>ITB patients:</u> Patients with CP who received ITB treatment in the multidisciplinary paediatric spasticity clinic at the School of Medicine aged between 3 and 18 years diagnosis of spastic CP failed oral spasticity management completed positive ITB bolus study, denoted by a 1 grade improvement in the Ashworth scale and had no prior spinal fusion or a concomitant spinal fusion and ITB pump implantation <u>Controls:</u> Patients with CP, chosen from the multidisciplinary spasticity clinic database, which includes all patients with spasticity at the School of Medicine. For each ITB patient a control patient was matched by age (± 12 months), sex, topographical involvement (i.e. diagnosis of diplegia or quadriplegia) and an initial Cobb angle within 10 degrees. In cases where multiple cases were identified, one was randomly chosen. No matched controls were	**Intervention** ITB programmable infusion pump, technical details not reported One surgeon performed the implantation of ITB pumps and catheter in all patients. The catheter was placed percutaneously through the interspinous ligament in the lumbar spine. The catheter was connected to the pump through a subcutaneous tunnel around the torso. The pump was located anteriorly in a subfacsial pocket created in the potential space under the rectus fascia. **Comparison** No ITB pump, but other interventions not reported either **Background treatment** None reported	Progression of scoliosis Measured when: - ITB patients: initial angle measured before or within the immediate postoperative period after pump insertion and final angle at most recent follow-up - Controls: unclear, but all had serial radiographs, one initial and at least one at follow-up Measured by: unclear Instrument/test: - ITB patients: posteroanterior radiographs of the spine taken with patient in seated position when possible. If unsupported sitting not possible, then a supine radiograph was used. (36/104 films were obtained in the supine position. All but 7 of these were from historically obtained control patients - Controls: chest or spine radiographs taken with patient in supine or prone position Unit of measurement: Cobb angle degrees of the primary curve of scoliosis in the coronal plane Results: <u>Initial Cobb angle</u> (degrees: mean, SD, range)	Outcomes assessors blinded to intervention: unclear, possibly not as nothing was reported on the characteristics of the outcomes assessors Number of participants with no available outcome data: 2 patients for whom a control could not be found were excluded from comparison analysis Selective outcome reporting: none	**Funding** 3 of the authors received financial support by a grant from Medtronic, Inc (Minneapolis, Minn) **Other information** Sample size: the sample size was calculated assuming a type 1 error of 0.005 and a type 2 error of 0.10. the difference before and after ITB pump insertion identified in a previous study was 7.3 degrees per year, was used as the expected difference between patients with an without ITB in this study. The SD was assumed to be twice the median difference (14.6). The sample size needed to identify the expected difference was 42 in each group. To increase power to identify differences between ITB and control groups additional patients were included in the study Baseline characteristics: there were no significant differences in population characteristics (age, sex, type of CP), follow-up time and outcome measures at baseline (Cobb angle) Indirectness:

	matched for more than one ITB patient. Similar to the ITB patients 2 measurements were used among the control patients: 1 initial measurement at the age of match and 1 final measurement at the last follow-up in the database **Exclusion Criteria** None stated **Participant characteristics** ITB patients Total number of patients: 50 Age (years. Mean, SD, range) 9.8 (3.7), 3.6 to 16.7 Age groups (years, % children) 3.1 to 5.0: 8 5.1 to 10.0: 50 10.1 to 15.0: 32 15.1 to 17.0: 10 Sex (female, %): 38 Follow-up time (years. Mean, SD, range) 2.7 (1.4), 0.2 to 6.3 Controls Total number of patients: 50 Age (years. Mean, SD, range) 9.7 (3.9), 3.4 to 16.9 Age groups (years, % children) 3.1 to 5.0: 14 5.1 to 10.0: 40 10.1 to 15.0: 34		ITB patients: 15 (13), 0 to 76 Controls: 13 (13), 0 to 67 P=0.06 Final Cobb angle (degrees: mean, SD, range) ITB patients: 28 (20), 0 to 87 Controls: 27 (21), 2 to 91 P=0.38 Progression of scoliosis (%) >5 degrees: ITB patients: 62 Controls: 70 P=0.40 >10 degrees: ITB patients:44 Controls: 36 P= 0.41 >50 degrees: ITB patients:4 Controls:4 P=1.00 Mean annual progression in Cobb angle, degrees per year (mean, SD, range) ITB patients: 6.6 (11.3), -4.9 to 63.7 Controls: 5.0 (6.1), -4.1 to 27.7 P=0.39 Results from multiple linear regression showed that adjusting for age, sex,		Population: none Intervention: none Comparison: none Outcomes assessed: none

	15.1 to 17.0: 12 Sex (female, %): 38 Follow-up time (years. Mean, SD, range) 3.0 (1.6), 0.3 to 6.9		topographic involvement and initial Cobb angle the mean progression of Cobb angle was 0.9 degrees per year greater in the ITB group compared with controls, however this result was not statistically significant		

Bibliographic details	Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality Assessment	Reviewer comment
Authors Hoving,M.A., van Raak,E.P., Spincemaille,G.H., van Kranen-Mastenbroek,V.H., van,Kleef M., Gorter,J.W., Vles,J.S., Dutch Study Group on Child Spasticity. **Year of publication** 2009 **Country of study** The Netherlands **Aim of Study** To study the efficacy at 12 months and safety up to 24 months after start of continuous infusion of intrathecal baclofen (CITB) in children with intractable spastic cerebral palsy **Ref ID** 64321 **Type of study** Prospective case series (follow-up of previous study)	**Inclusion Criteria** As described in Hoving 2007 and in addition having had a successful response to the testing (as previously defined by the authors) **Exclusion Criteria** As described in Hoving 2007 **Participant characteristics** Total: 17 children Sex: 9 females and 8 males Age at time of pump implantation: between 7 and 17 years Weight: range 17 to 84 kg Cerebral palsy type: 12 spastic, 5 spastic/dyskinetic, 3 diplegia, 14 tetraplegia GMFCS level: III (1), IV (2), V (14)	**Intervention** Programmable Synchromed infusion pump (no other details provided on the specific model) (Medtronic Inc., Minneapolis, MN) after 1 month Position pump in abdominal wall (n patients): Left subcutaneously: 7 Right subcutaneously: 2 Left subfascially: 3 Right subfascially: 4 Right subfascially/ subcutaneously: 1 SynchroMed (Medtronic Inc) pump model (n patients): EL 8627-18: 2 EL 8627-10: 1 EL 8627L-18: 1 EL 8626L-10: 2 II 8637-20: 11 Catheter model(n patients): 8709: 5 8731: 12 **Comparison** None **Background treatment** “Standard treatment” including any physiotherapy, speech therapy and occupational therapy. No other details provided 7 children took oral baclofen at	<u>Primary outcomes</u> Individually formulated problems Measured when: at 6 and at 12 months after CITB started Measured by: Depending on both the ability to understand the test and to draw a vertical line, the VAS was rated by the child or by a parent Instrument/test: Visual Analogue Scale (VAS) for individually formulated problems Unit of measurement: average of 3 individually formulated VAS scores per child Results at 6 months (change from baseline) (Mean, SD) (n=17) 4.1 (2.1) p=0.000 Results at 12 months (change from baseline) (Mean, SD) (n=17) 4.7 (2.0) p=0.000 Ease of care Measured when: at 6 and at 12 months after CITB started Measured by: Depending on both the ability to understand the test and to draw a vertical line, the VAS was rated by the	Outcomes assessors blinded to intervention: No Number of participants not completing treatment: None Number of participants with no available outcome data: None Selective outcome reporting: Yes. The outcomes of the Ashworth scale for individual muscles were not reported because there were “too many data” according to the authors. Ashworth scores at 6 months were not reported either	**Funding** Grants from the Research Fund of the University Hospital Maastricht. Grant from Medtronic Inc., Heerlen, the Netherlands. **Other information** Sample size: small for a case series Indirectness Population: None Intervention: None Comparison: None Outcomes assessed: None [STUDY 2009b]

		the time of pump implantation. 6 children gradually discontinued this use during the first 10 post operative days. In one child the dose was largely reduced	child or by a parent Instrument/test: Visual Analogue Scale (VAS) for individually formulated problems Unit of measurement: VAS scores Results change from baseline at 6 months (Mean, SD) (n=16) 4.4 (2.1) p=0.000 change from baseline at 12 months (Mean, SD) (n=16) 5.2 (2.1) p=0.000 Pain Measured when: at 6 and at 12 months after CITB started Measured by: Depending on both the ability to understand the test and to draw a vertical line, the VAS was rated by the child or by a parent Instrument/test: Visual Analogue Scale (VAS) for individually formulated problems Unit of measurement: VAS scores Straight 10cm horizontal line with anchor		

			points of ‘no pain’ (score 0) and ‘unbearable pain’ (score 10) Results change from baseline at 6 months (Mean, SD) (n=12) 4.5 (2.6) p=0.002 change from baseline at 12 months (Mean, SD) (n=12) 5.4 (2.7) p=0.002 Movement and function (activities and participation in the ICF-International Classification of Disability and Health) Measured when: at 6 and at 12 months after CITB started Measured by: unclear Instrument/test: Dutch version of the Paediatric Evaluation of Disability Inventory (PEDI)-PEDI caregiver assistance scale Unit of measurement: PEDI scores Results change from baseline at 6 months (median, range) (n=17) 0.0 (-16.6 to 32.7) p=0.893		

			change from baseline at 12 months (median, range) (n=17) 0.0 (-16.6 to 26.3) p=0.917 <u>Secondary outcomes</u> Spasticity Measured when: at 12 months after CITB started Measured by: an experienced paediatric physiotherapist. For each child scores were always rated by the same physiotherapist Instrument/test: Ashworth scale Unit of measurement: Ashworth scores bilaterally assessed in 7 lower-extremity muscle groups (hip adductors, flexors and extensors; knee flexors and extensors; and ankle plantarflexors and dorsiflexors) and 4 upper extremity muscle groups (elbow and wrist flexors and extensors). Scores of the total 22 muscles separately analysed Results (12-month-change scores): The Ashworth score decrease significantly in 5/8 upper extremity		

			muscle groups (0.008 ≤ p ≤ 0.046) and 9/14 lower-extremity muscle groups Movement and function (activities and participation in the ICF-International Classification of Disability and Health) Measured when: at 12 months after CITB started Measured by: unclear Instrument/test: Dutch version of Gross Motor Function Measure (both the GMFM-66 and the GMFM-88 versions) Dutch version of the Paediatric Evaluation of Disability Inventory (PEDI)-functional skills scale Unit of measurement: scores of previous tests (GMFM-88: 4-point ordinal scale; GMFM-66: interval scaling) Results change from baseline at 6 months		

			GMFM-66 overall (Mean, SD) (n=12) 1.4 (2.2) p=0.034 GMFM-88 lying and rolling (median, range) (n=12) 0.0 (-20.0 to 10.0) p=0.357 GMFM-88 sitting (median, range) (n=12) 3.3 (-15.0 to 15.0) p=0.045 GMFM-88 goal dimension (median, range) (n=9) 0.0 (2.0 to 10.0) p=0.041 PEDI functional skills (median, range) (n=17) 0.0 (-11.0 to 13.8) P=0.615 change from baseline at 12 months GMFM-66 overall (Mean, SD) (n=12) 1.6 (3.1) p=0.110 GMFM-88 lying and rolling (median, range) (n=12) -1.0 (-25.0 to 11.0) p=0.448 GMFM-88 sitting (median, range) (n=12) 3.3 (-4.0 to 22.0) p=0.022 GMFM-88 goal dimension (median, range) (n=9) 4.0 (0.0 to 26.0) p=0.007 PEDI functional skills		

			(median, range) (n=17) 0.0 (-15.0 to 15.8) P=0.158 Quality of Life Measured when: at 6 and at 12 months after CITB started Measured by: unclear Instrument/test: Dutch version of the Child-Health Questionnaire-Parent Form (CHQ-PF50) Unit of measurement: scores of CHQ-PF50, each domain is scaled from 0 to 100 with higher scores reflecting a better HRQL. Physical and psychosocial summary scores calculated using normative data from North American children Results change from baseline at 6 months (Mean, SD) physical summary (n=16) 3.8 (9.6) p=0.134 psychosocial summary (n=16) 6.2 (8.3) p=0.023		

			change from baseline at 12 months (Mean, SD) physical summary (n=16) 4.6 (10.7) p=0.163 psychosocial summary (n=16) 5.4 (9.0) p=0.088 Adverse events Measured when: from operation until 24 months after CITB started Measured by: unclear Instrument/test: standardised forms Definition of adverse events any undesirable experience occurring to a participant during the study whether or not related to CITB-included aggravation of symptoms or signs which were present before CITB started Serious adverse event: untoward medical occurrence or effect that: resulted in death, was life		

			threatening, required hospitalisation or prolongation of existing hospitalisation or resulted in persistent or significant disability or incapacity Results Total number of non-procedure or device related events: 51 during a follow-up of 312 patients-months (24 different events) Total number of children involved: 14 The most common non-procedure or device related events were (n events): temporary lethargy (8), excessive hypotonia (4, 3 of them enduring), temporary pressure sores (4), drooling (4, 2 of them enduing) 5 non-procedure or device related events were considered serious because they resulted in significant disability:		

			difficulty swallowing (1), dysarthria (1), excessive hypotonia (2) and epileptic seizure (1) Total number of procedure or device related events: 26 during a follow-up of 312 patients-months (24 different events) Total number of children involved: 11 3 procedure or device related events were considered serious and required children to undergo a second operation resulting in a prolonged hospital stay: 1 incomplete operation 1 abrupt lack of ITB effect 4 hours postoperatively 1 postoperative pain at pump site Procedure or device related events considered non		

			serious were (n events) Swelling at pump site: 7 Lumbar swelling: 3 Pruritus at pump site: 3 Moving pump: 3 Beeping pump: 2 Possible CSF leakage: 2 Wound leakage: 1 Pruritus at lumbar scar site: 1 Cystitis: 1 Acceptability and tolerability Measured when: at last follow-up visit Measured by: unclear Instrument/test: children and/or their parents were asked in they would participate in the test treatment and implantation procedures again Unit of measurement: children's and/or their parents' views on treatment		

			Results 15/17 children and/or their parents stated that they would participate in all procedures again. Two parents were not sure in spite of the achieved individual treatment goal for their children. The doubts in one case were based on both the new onset seizures and the girl's stress during pump refills and in another case were based on a worsened trunk and head balance		

Bibliographic details	Participant Characteristics	Intervention characteristics	Outcome measures and results	Quality Assessment	Reviewer comment
Authors Ramstad,K., Jahnsen,R., Lofterod,B., Skjeldal,O.H. **Year of publication** 2010 **Country of study** Norway **Aim of Study** To explore the timing of effects of intrathecal baclofen therapy in children with cerebral palsy **Ref ID** 133153 **Type of study** Prospective case series	**Inclusion Criteria** 1. Child with cerebral palsy 2. Started continuous intrathecal baclofen therapy (CITB) during the inclusion period (September 2002 to September 2005) **Exclusion Criteria** Not reported **Participant characteristics** N = 38 (However, 3 children discontinued treatment, and data is only reported for the 35 who completed treatment) Age / months (median (range)): 103 (30 - 186) Sex: 25 M / 10 F Gross Motor Function Classification System level (n): III: 2 IV: 13 V: 20 Cerebral palsy diagnosis and classifications were made according to a 2006 consensus report. All children were bilaterally affected. In 26 patients, spasticity was the dominating motor impairment, and in 9 patients dyskinesia dominated over the spasticity	**Intervention** All children underwent a successful test treatment with intrathecal baclofen before they received a programmable Synchromed infusion pump. The catheter tip was placed at the thoracic level. Treatment was given as continuous intrathecal baclofen infusions, as either: - the same infusion rate throughout the day (simple mode) - varying infusion rate (complex mode) The dosage for each patient was based on individual needs, and the median dose was 132 micrograms per day (range 65 - 199) at six months, and 157 micrograms per day (range 86 - 576) at eighteen months. **Comparison** N/A **Background treatment** 14 children received anti-epileptic drugs daily. No children started with anti-epileptic drugs or underwent major surgery during the observation period. Standard treatments such as physiotherapy, occupational therapy and speech therapy were continued.	Assessments were made on the day before pump implantation (T0), and at 6 months (T1) and 18 months (T2) of CITB. <u>Sleep disturbances</u> Measured when: baseline, 6 months and 18 months Measured by: parental interview, but unclear who conducted interview and how Instrument/test: parental interview Unit of measurement: frequency of awakenings during the night on average in the last 4 weeks Results: <u>Number of awakenings (median (range))</u> T0: 1.0 (0 - 25) [n = 32] T1: 0.0 (0 - 10) [n = 29] T2: 0.0 (0 - 10) [n = 30] p-values for change: T0 - T1: 0.005 T0 - T2: 0.006 T1 - T2: 0.731 <u>Pain (frequency and severity</u> Measured when: baseline, 6	Outcome assessors blinded to intervention: unclear Number of participants not completing treatment: Three - one patient discontinued CITB after 3 months because the family suspected intolerable side effects (agitation). In two patients, the pump had to be removed because of infection, and the families did not want another pump Number of patients with no available outcome data: The 3 participants who stopped treatment have no data reported. Various outcomes have missing data for some out of the 35 participants who completed treatment; however it is not clear why this data is missing. Selective outcome reporting: no Other limitations: small sample size (N=35); exclusion criteria and any exclusions are not reported	**Funding** Source of funding not reported **Other information** Surgical revision of the drug delivery system was performed in 6 patients. In these cases, the assessment (T1) was postponed until 6 months after the problem had been resolved, and the assessment at T2 until twelve months after T1. <u>Statistical analysis</u> Due to the small sample size and skewed data, the authors used the Wilcoxon test to compare changes in outcome measures between baseline and T1 and T2. Medians and ranges are reported.

	that was also present.		months and 18 months Measured by: parental interview, but unclear who conducted interview and how Instrument/test: parental interview Unit of measurement: frequency of pain episodes when not sleeping on average in the last 4 weeks, and severity of pain on a 0 - 4 scale Results: <u>a. Pain: frequency (median (range))</u> T0: 2.0 (0 - 3) [n = 35] T1: 1.0 (0 - 3) [n = 31] T2: 1.0 (0 - 3) [n = 31] p-values for change in pain frequency T0 - T1: 0.000 T0 - T2: 0.005 T1 - T2: 0.019 <u>b. Pain: severity (median (range))</u> T0: 2.0 (0 - 3) [n = 35] T1: 1.0 (0 - 3) [n = 31] T2: 1.0 (0 - 3) [n = 31] p-values for change in pain severity T0 - T1: 0.005 T0 - T2: 0.011 T1 - T2: 0.550		

			Spasticity Measured when: baseline, 6 months and 18 months Measured by: experienced physiotherapists Instrument/test: Modified Ashworth Scale Unit of measurement: knee flexors right and left were measured using Modified Ashworth Scale Results: a. Spasticity: right knee flexors (median (range)) T0: 4.0 (2 - 6) [n = 27] T1: 4.0 (2 - 6) [n = 25] T2: 3.0 (1 - 6) [n = 26] p-values for change in spasticity of right knee flexors T0 - T1: 0.627 T2 - T0: 0.022 T1 - T2: 0.062 b. Spasticity: left knee flexors (median (range)) T0: 4.0 (2 - 6) [n = 27] T1: 3.5 (2 - 6) [n = 26] T2: 3.0 (1 - 6) [n = 28] p-values for change in spasticity of left knee flexors T0 - T1: 0.353 T2 - T0: 0.022		

			T1 - T2: 0.062 <u>Movement and function</u> - Measured when: baseline, 6 months and 18 months Measured by: experienced physiotherapists (GMFM-66) and parental interview (PEDI) Instrument/test: Gross Motor Function Measure (GMFM-66); Paediatric Evaluation of Disability Inventory (PEDI) Functioning Skills Scale and Caregiver Assistance Scale Unit of measurement: GMFM-66 total score; PEDI scaled scores Results: <u>a. GMFM-66 total score (median (range))</u> T0: 22.7 (0.0 - 48.3) [n = 35] T1: 22.0 (0.0 - 45.9) [n = 32] T2: 24.0 (0.0 - 47.1) [n = 31] p-values for change in GMFM-66 total score T0 - T1: 0.032 T0 - T2: 0.005 T1 - T2: 0.064		

			b. PEDI Functional Skills Scaled Scores (median (range)) - - Self-care T0: 33.6 (0.0 - 58.6) [n = 32] T1: 33.0 (0.0 - 61.8) [n = 28] T2: 36.0 (0.0 - 73.6) [n = 27] p-values for change in PEDI Functional skills self-care score T0 - T1: 0.246 T0 - T2: 0.027 T1 - T2: 0.124 - Mobility T0: 23.2 (0.0 - 53.1) [n = 32] T1: 20.9 (0.0 - 48.8) [n = 27] T2: 35.9 (0 - 54.8) [n = 27] p-values for change in PEDI Functional skills mobility score T0 - T1: 0.285 T0 - T2: 0.017 T1 - T2: 0.012 - Social Function T0: 57.9 (0.0 - 96.3) [n = 31] T1: 59.2 (0.0 - 96.3) [n = 27] T2: 64.1 (0.0 - 100.0) [n =		

			27] p-values for change in PEDI Functional skills social function score T0 - T1: 0.041 T0 - T2: 0.002 T1 - T2: 0.035 <u>c. PEDI Caregiver Assistance Scaled Scores (median (range))</u> - - Self-care T0: 15.9 (0.0 - 57.9) [n = 32] T1: 11.6 (0.0 - 63.4) [n = 28] T2: 11.6 (0.0 - 76.7) [n = 27] p-values for change in PEDI Caregiver assistance self-care score T0 - T1: 1.000 T0 - T2: 0.272 T1 - T2: 0.678 - Mobility T0: 11.7 (0.0 - 70.5) [n = 32] T1: 29.0 (0.0 - 58.8) [n = 28] T2: 36.9 (0.0 - 72.7) [n = 27] p-values for change in PEDI Caregiver		

			assistance mobility score T0 - T1: 0.066 T0 - T2: 0.008 T1 - T2: 0.034 - Social Function T0: 58.3 (0.0 - 100.0) [n = 30] T1: 66.9 (0.0 - 100.0) [n = 28] T2: 65.9 (0.0 - 100.0) [n = 26] p-values for change in PEDI Caregiver assistance social function score T0 - T1: 0.035 T0 - T2: 0.004 T1 - T2: 0.025		

Spasticity in children and young people with non-progressive brain disorders: management of spasticity, co-existing motor disorders and their early musculoskeletal complications

Orthopaedic surgery

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Archives of Physical Medicine and Rehabilitation **Authors** Yang,E.J., Rha,D., Kim,H.W., Park,E.S. **Year of publication** 2008 **Study location** South Korea **Ref ID** 111548 **Type of study** Retrospective cohort study **Aim of study** To compare the effects of BoNT-A injection into the hip adductor muscles with soft tissue surgery on hip displacement and identify the factors affecting outcomes of both BoNT injection and soft tissue surgery	**Inclusion Criteria** Children with CP admitted to hospital between Feb 2004 and Mar 2007 1) who had bilateral spastic CP 2) whose first hip radiographs were taken under 6 years of age 3) in whom radiographs of the hips were taken at least 3 times in intervals of more than 6 months. **Exclusion Criteria** Children with both a soft-tissue surgery and BoNT-A injection during the follow-up period were excluded **Baseline characteristics** 194 children with spastic CP were enrolled Diplegia : n=116, Quadriplegia : n=78 High functioning group : GMFCS I and II n= 58 Low functioning group : GMFCS III, IV and V n= 136	No intervention (138 hips of 69 children) Soft tissue surgery (130 hips of 65 children) Soft tissue surgery of hip adductor muscles BoNT-A (120 hips of 60 children) BoNT-A injection into hip adductor muscle BoNT-A brand: Not stated Average dose : 3U/kg body weight standardised by body weight during this time period Injection details : 1 ml syringe with 27-G needle Solution : contents of one vial of BoNT-A dissolved in 2ml isotonic saline Guidance : ultrasonography 7 children received an additional BoNT-A injection into both hip adductor muscles during the follow up period.	Hip Migration Percentage (MP) MP was measured by calculating the % femoral head lying outside the lateral border of the acetabulum as defined by bony landmarks on an anteroposterior pelvis radiograph Mean change in hip migration percentage (%) No intervention group : 4.7±10.3 BoNT group : -1.6±8.4 Surgery group : -3.3±6.1 Mean change per year in hip migration percentage (%) No intervention group : 4.4±11.3 BoNT group : -0.7±6.5 Surgery group : -1.6±4.4 Mean change per year in hip migration percentage (%) - high functioning children No intervention group (n=68) :	Study type : retrospective cohort study reviewing case notes Allocation to treatment unrelated to confounders : Unclear Attempt to balance groups for confounders : Yes Groups comparable at baseline : Yes (except for male: female ratio = 85%/15% in surgical group) Participants received similar care (except intervention?) : Yes Participants blinded to treatment : No Caregivers blinded to treatment : No No of participants for whom no data was available (each treatment arm) : None Length of follow up appropriate : Yes (mean 22 months) Definitions of outcomes given : Yes Outcomes assessed with valid	Ethical approval : Not stated Consent : Not stated Funding : Not stated

	Groups according to severity of hip displacement at initial MP assessment Mild subluxated group 20%≤MP<40% n=120 Moderate subluxated group 40%≤MP<60% n=70 Severe subluxated group 60%≤MP<90% n=4 Mean age at initial radiograph 39.3±12.9 months (range 18 to 70 months) Mean age at final radiograph 62.0±17.7 months (range 37 to 174) Mean duration of follow up 22.9±11.8 months(range 18 to 108) No significant differences at baseline between no intervention, soft tissue surgery and BoNT-A groups for any of the following : GMFCS score, initial MP, initial age, final age and duration of follow up, proportion of high and low functioning participants, proportion of participants with mild, moderate or severe subluxation		-2.8±5.0 BoNT group (n=40 legs) : -2.4±5.2 Surgery group (n=28 legs) : -3.4±4.8 Mean change per year in hip migration percentage (%) - low functioning children No intervention group (n=182 legs) : -0.5±5.6 BoNT group (n=90 legs) : -0.0±6.9 Surgery group (n=72 legs): -1.0±4.1 For each intervention (no invervention, BoNT and surgery) the higher functioning group's Mean Change HM% per year was statistically significantly greater than the low functioning group.	method : Yes Similar length of follow up for different groups: Yes Similar number of participants completed tx in each group : Yes Investigators blinded to patients' exposure to intervention : Unclear Investigators blinded to impt confounders/prognostic factors : Unclear Outcome assessors blinded to treatment :Unclear	

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical European Journal of Neurology **Authors** Molenaers,G., Desloovere,K., De,Cat J., Jonkers,I., De,Borre L., Pauwels,P., Nijs,J., Fabry,G., De,Cock P. **Year of publication** 2001 **Study location** Belgium **Ref ID** 117421 **Type of study** Retrospective cohort study **Aim of study** To provide objective evidence of two treatment options (multilevel botulinum toxin type A and multilevel surgery) for children with cerebral palsy. To evaluate the success of two multilevel treatment strategies for children with generalised joint impairments when each are applied in normal clinical conditions.	**Inclusion Criteria** Children randomly selected from a larger cohort of children treated between 1998 and 1999 at University Hospital Leuven. Children with a diagnosis of spastic CP with independent barefoot walking without walking aids before and after treatment. **Exclusion Criteria** None stated **Baseline characteristics** <u>BoNT and casting group</u> N= 29 pts, 43 treated limbs Diagnosis = 14 diplegia, 15 hemiplegia Age mean (range) = 6 years 2 months (4yrs 3m to 9 yrs 10m) Post treatment evaluation = 2 months post treatment Orthosis use pretreatment : Daytime - 5pts used leafspring AFOs, 6 pts used hinged AFOs, 1 pt used fixed AFOs. Night - 5 patients (3 limited use) Orthosis use posttreatment : Daytime - 19 pt used leafspring AFOs, 7 pts used hinged AFOs. Night - 26patients (5 limited use) Therapy pre-treatment = Mean of 2.4 sessions/wk Therapy post-treatment = Mean of 2.9 sessions/wk	<u>BoNT and casting treatment</u> BoNT A type : Botox Dilution : 50U/ml Maximum total dose : 50U Botox -A per site Dosage and Muscle Selection : Total dose averaged 25.5U/body weight (range 20-31 U/kg BW) for children with diplegia and 13.7U/body weight (range 6-20U/kg BW) for children with hemiplegia. Injections were fine tuned on a patient by patient basis following objective examination using full gait analysis and an extended clinical examination. Between 2 and 5 muscles were injected in each treated limb in one session. All patients received injections in gastrocnemius and medial hamstrings. Other muscles injected included soleus, tibialis posterior, adductors and iliopsoas Sedation and pain management : child sedated with mask anaesthesia <u>Casting</u> All patients were casted at the distal joints immediately before or after injections to	Outcomes were assessed at 2 months in the BoNT group and 12 months in the surgery group as it was decided to evaluate the children at a point of (presumed) maximum effect of treatment. BoNT group n=29 patients, 43 limbs Surgery group n=23 patients, 43 limbs Mean walking speed m/s BoNT group : Pre treatment = 1.06 (0.2) Post treatment = 1.03 (0.2) Surgery group : Pre treatment = 0.9 (0.2) Post treatment = 0.8 (0.2)	Study type : retrospective cohort study Allocation to treatment unrelated to confounders : Unclear Attempt to balance groups for confounders : No Groups comparable at baseline : No, Proportion of diplegia to hemiplegia different in each group, Age - BoNT group younger than the Surgery group. "Previous BoNT" higher in BoNT group compared to Surgery group (9 pts vs 1pt) and Previous Surgery" higher in Surgery group compared to BoNT group (11 pts vs 1pt) Participants received similar care (except intervention) : Unclear, description suggests that the surgical group may have received more intensive post-intervention therapy Participants blinded to treatment : No Caregivers blinded to treatment : No No of participants for whom no data was available (each treatment arm) : None Length of follow up appropriate : Assessments made at time of presumed maximum efficacy ie 2 months post treatment follow up in	Ethical approval : Not stated Consent : Not stated Funding : Not stated

	Previous surgery = 1 patient Previous BoNT treatment = 9 patients <u>Surgery group</u> N= 23 patients, 43 treated limbs Diagnosis = 20 diplegia, 3 hemiplegia Age (mean) (range) = 13 yrs 5 months (7yrs 4m to 21yrs 7m) Post treatment evaluation = 12 months post treatment Orthosis use pretreatment : Daytime - 1pt used leafspring AFOs, 4 pts used hinged AFOs. Night - 1 patient (limited use) Orthosis use posttreatment : Daytime - 5 pts used leafspring AFOs, 3 pts used hinged AFOs, 2 pts used ground reaction AFOs. Night - 18 6patients (1 limited use) Therapy pre-treatment = Mean of 2.6 sessions/wk Therapy post-treatment = Mean of 3.6 sessions/wk Previous surgery = 11 patients Previous BoNT treatment = 1 patient	correct mild contractures and to enhance the effect of the injections. Serial stretching casts (for a period of 10-28 days) were applied to bothe lower limbs (for children with diplegia and hemiplegia) with the ankle joint in neutral position or in 5° of dorsiflexion and the subtalar joint and midtarsal joints in a neutral position. On average cases were reapplied every 12 days. <u>Surgery</u> 3D gait analysis was used to delineate the gait deviations of each patient and to help to plan the surgical intervention. 7 patients had soft tissue surgery only, 16 patients had soft tissue surgery combined with corrections of bony deformities. Soft tissue procedures included: - Lengthening of the psoas, adductor longus, and medial hamstrings - Rectus femoris transfer to either gracilis or semitendinosus - Procedures involving gastrocnemius (Stryer or Achilles tendon lengthening in children with hemiplegia - Lengthening of peroneus		BoNT group and 12 months post treatment follow up in surgery group Definitions of outcomes given : Yes, outcomes assessed as part of gait analysis (details of instruments used given) Outcomes assessed with valid method : Yes Similar length of follow up for different groups: No 2 months post treatment follow up in BoNT group and 12 months post treatment follow up in surgery group Similar number of participants completed tx in each group : Yes Investigators blinded to patients' exposure to intervention : No Investigators blinded to impt confounders/prognostic factors : No Outcome assessors blinded to treatment : No	

		- Tibialis posterior lengthening or transfer - Tibialis anterior transfer - Flexor hallucis lengthening Bony deformity corrections included: - Acetabular corrections - Proximal femoral varus derotation osteotomy - Tibial realignment and foot stabilisation surgery (calcaneus lengthening combined with medial soft-tissue shortening and subtalar arthrodesis) All patients received a combination of surgical procedures at 3 levels in one session. All patients after BoNT or surgery had appropriate physiotherapy and orthotic management involving day orthoses and night splinting. This is described as "intensive" rehabilitation following surgery			

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Journal of Pediatric Orthopedics **Authors** Gorton,G.E.,III, Abel,M.F., Oeffinger,D.J., Bagley,A., Rogers,S.P., Damiano,D., Romness,M., Tylkowski,C. **Year of publication** 2009 **Study location** USA **Ref ID** 100823 **Type of study** Prospective cohort study **Aim of study** To prospectively examine whether lower extremity musculotendinous surgery in ambulatory children with CP improves impairments and function measured by gait and clinical outcome tools beyond changes fouond in a concurrent matched control group	**Inclusion Criteria** Diagnosis of CP, GMFCS level I to III, age 4 to 18 years, ability to complete gait analysis. This study of ambulatory children with CP is part of a 6 year prospective multicentre study across 7 paediatric orthopaedic facilities. **Exclusion Criteria** Earlier SDR, orthopaedic surgery within the previous year, BoNT injectinos within the last 6 months or a currently operating baclofen pump **Baseline characteristics** Total participants in each group Surgical Group : 75 who had lower extremity surgery and complete follow up assesment at 12 m after surgery Non-surgical Group : 75 who did not have surgery, either because is was not recommended based on full clinical assessment including 3D gait analysis or because the family did not elect to move forward with surgery during the study period, and who received standard care Variables used to match surgical and nonsurgical	Surgery Procedures included both soft tissue and bony surgery Soft tissue procedure only : 50/75 Bony procedures only : 5/75 Soft tissue and bony procedures :20/75 Soft tissue procedures included: rectus femoris transfer, hamstring lengthening, heelcord lengthening, adductor lengthening, psoas lenthening and other foot/ankle transfers Bony procedures included : femoral derotation osteotomy, tibia/fibula rerotation osteotomy, lateral column lengthening Standard care Observation, stretching and strengthening exercises, bracing and medication management. No surgery, BoNT injections or ITB pump insertion.	GMFM Dimension D Baseline Surgical = 83.0 (17.9) Baseline Nonsurgical= 82.2 (18.7) Follow-up Surgical = 83.0 (1.2) Follow-up Nonsurgical= 84.6 (1.2) ANCOVA P* = 0.331 MCID (0.5) = 1.8 GMFM Dimension E Baseline Surgical = 74.5 (26.4) Baseline Nonsurgical= 73.9 (26.1) Follow-up Surgical = 73.8 (1.3) Follow-up Nonsurgical= 76.0 (1.3) ANCOVA P* = 0.192 MCID (0.5) = 2.6 GMFM-66 Baseline Surgical = 75.0 (12.7) Baseline Nonsurgical= 74.4 (12.9) Follow-up Surgical = 75.0 (0.6) Follow-up Nonsurgical= 76.2 (0.6) ANCOVA P* = 0.172 MCID (0.5) = 1.3 PedsQL Physical Functioning Baseline Surgical = 55.8 (19.8) Baseline Nonsurgical= 59.0 (19.7) Follow-up Surgical = 60.5 (2.2) Follow-up Nonsurgical= 54.7	Study type : prospective cohort study Allocation to treatment unrelated to confounders : No Attempt to balance groups for confounders : Yes Groups comparable at baseline : Yes for matching variables Participants received similar care (except intervention) : Unclear Participants blinded to treatment : No Caregivers blinded to treatment : No No of participants for whom no data was available (each treatment arm) : None Length of follow up appropriate : Yes, 1 year Definitions of outcomes given : Yes, validated tools Outcomes assessed with valid method : Yes Similar length of follow up for different groups: Yes Similar number of participants completed tx in each group : Yes Investigators blinded to patients' exposure to intervention : No Investigators blinded to impt confounders/prognostic factors : No Outcome assessors blinded to	Ethical approval : Institutional Review Boards Consent : Obtained for participants Funding : Shriner Hospitals for Children Clinical Outcomes Study Advisory Board Grant no 9140

	groups at baseline Age Surgical Group : 11.3±3.1 Non-surgical Group : 11.3± 2.9 Height Surgical Group : 139.7 ± 19 Non-surgical Group : 139.8±18.3 Weight Surgical Group : 38.7±16.5 Non-surgical Group :40.5±18.4 GMFM Dimension E (%) Surgical Group : 74.5±26.4 Non-surgical Group : 73.9±26.1 Groups were not matched on pre-operative gait kinetcs, joint spasticity or other clinical indications typically used in determining appropriateness for musculoskeletal surgery.		(2.1) ANCOVA P* = 0.039 MCID (0.5) = 12.7 PedsQL Emotional Functioning Baseline Surgical = 67.6 (17.5) Baseline Nonsurgical= 66.9 (16.0) Follow-up Surgical = 68.8 (2.0) Follow-up Nonsurgical= 64.7 (1.9) ANCOVA P* = 0.109 MCID (0.5) = 10.5 PedsQL Social Functioning Baseline Surgical = 55.1 (20.5) Baseline Nonsurgical= 56.5 (19.2) Follow-up Surgical = 59.4 (2.5) Follow-up Nonsurgical= 55.4 (2.5) ANCOVA P* = 0.221 MCID (0.5) = 12.8 PedsQL School Functioning Baseline Surgical = 64.9 (17.3) Baseline Nonsurgical= 61.8 (16.3) Follow-up Surgical = 67.1 (2.0) Follow-up Nonsurgical= 64.6 (1.9) ANCOVA P* = 0.320 MCID (0.5) = 12.3 Velocity (%normal)	treatment : No	

			Baseline Surgical = 77.8 (23.7) Baseline Nonsurgical= 78.9 (22.3) Follow-up Surgical = 79.1 (2.0) Follow-up Nonsurgical= 78.6 (1.9) ANCOVA P* = 0.844 MCID (0.5) = 9.1		

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Journal of Bone and Joint Surgery - American Volume **Authors** Thomason,P., Baker,R., Dodd,K., Taylor,N., Selber,P., Wolfe,R., Graham,H.K. **Year of publication** 2011 **Study location** Australia **Ref ID** 132766 **Type of study** Randomised controlled study **Aim of study** To evaluate the magnitude of change between groups and over time on the basis of gait indices, physical measures, function, activity, mobility and health-related quality of life following single-event multilevel surgery in children 6-12 years old who had spastic diplegia.	**Inclusion Criteria** 1) Confirmed diagnosis of cerebral palsy with registration in the Victorian Cerebral Palsy Register 2) A spastic movement disorder 3) Aged 6 -12 years 4) GMFCS level of II or III 5) Suitability for multilevel surgery **Exclusion Criteria** 1) Diagnosis of dystonia 2) Prior orthopaedic surgery, selective dorsal rhizotomy, or intrathecal baclofen therapy 3) Any reasons why delaying surgery might cause harm, such as hip migration in excess of 25% on radiographs, painful breakdown of the midfoot, and progressive crouch gait (defined as a loss of knee extension of > 10 degrees in late stance) **Baseline characteristics** N=19 Baseline characteristics are reported in an appendix, not included with the paper.	This was a randomised controlled trial comparing: - single event multi-level surgery followed by intensive postoperative physical therapy - physical therapy alone Randomisation A consecutive sample of 30 children with spastic diplegic CP were assessed for eligibility, of which 19 met the inclusion criteria and were randomised. The randomisation was performed by the trial statistician, using a minimisation approach to ensure that the groups were well-matched. Random allocation was done via a computer program. Minimisation was based on GMFCS level (I or II), age (less or older than 9 years old), and type of surgery (osseous only, soft tissue only, or both). Interventions Surgery group (n=11) Single event multilevel surgery was defined as: at least one surgical procedure performed at two different anatomical	1. Comparative data: results of between group comparisons at 12 months Walking: GPS (median (IQR)) Baseline surgical: 13.7 (11.9, 15.2) Baseline control: 14.6 (10.5, 15.8) 12-month surgical: 9.1 (8.6, 12.6) 12-month control: 15.7 (13.9, 16.2) Difference between groups in change at 12 months (95% CI): -5.5 (-7.6, -3.4) p<0.001 Walking: GGI score (mean (SD)) Baseline surgical: 353 (211) Baseline control: 370 (194) 12-month surgical: 153 (81) 12-month control: 381 (196) Difference between groups in change at 12 months (95% CI): -218 (-299, -136) p<0.001 Function: GMFM-66 (mean (SD))	Small sample size; sample size calculation was not performed, due to the lack of pilot data Study type: randomised controlled trial, with additional prospective follow-up of one arm Appropriate randomisation: yes Allocation concealment: yes Groups comparable at baseline: unclear Participants blinded: no Outcome assessors blinded: unclear Participants received similar care except for intervention: yes Number of participants for whom no data was available: None Appropriate length of follow-up: yes	No children were lost to follow-up. Only the surgical arm were followed up for 24 months, as the control arm received surgery after 12 months. Ethical approval: Yes - granted by the Ethics in Human Research Committee of the Royal Children's Hospital, Melbourne Consent: Yes - informed written consent was obtained from parents of eligible children, following a minimum of two detailed interviews with the treating surgeons and the study coordinator. Funding: Received from the Hugh Williamson Foundation, the Murdoch Children's Research Institute, and the National Health and Medical Research Council, the Centre for Clinical Research Excellence in Gait Analysis and Gait Rehabilitation. Funding for the rehabilitation program was provided by the Post Intervention Physical Therapy Program

		levels (the hip, knee or ankle) on both sides of the body. The surgical recommendation was tailored to the child's needs as determined by a comprehensive evaluation, including a standardised physical examination, radiographic evaluation, and instrumented gait analysis. The multilevel surgical program included muscle tendon lengthening, tendon transfer, rotational osteotomy, and stabilisation of the hip and foot according to published guidelines. A total of 85 procedures were performed, with a mean of 8 procedures per child (SD 4). The children allocated to the surgical group had surgery performed by two experienced surgeons, within 4 weeks of the baseline assessment. Perioperative antibiotics and epidural infusions of 0.25% bupivacaine weer used. Children remained as inpatients for 5-7 days following surgery, and were discharged wearing below-the-knee plaster casts, with knee immobilisers and the use of appropriate assistive devices, as indicated by their GMFCS level.	Baseline surgical: 65.3 (11.1) Baseline control: 70.3 (11.3) 12-month surgical: 66.1 (8.9) 12-month control: 69.8 (11.4) Difference between groups in change at 12 months (95% CI): 0.3 (-4.5, 5.0) NS <u>Quality of life: CHQ-PF50 scores (mean (SD))</u> <u>a. Physical function</u> Baseline surgical: 47 (26) Baseline control: 62 (35) 12-month surgical: 58 (26) 12-month control: 76 (25) Difference between groups in change at 12 months (95% CI): -14 (-39, 11) NS <u>b. Social/emotional</u> Baseline surgical: 69 (34) Baseline control: 89 (21) 12-month surgical: 65 (36) 12-month control: 97 (8) Difference between groups in change at 12 months (95% CI): -32 (-62, -2) p<0.05 <u>c. Family cohesion</u>		

		The surgical group were assessed at 3 and 6 weeks postoperatively to check healing and provide custom-fitted ankle-foot orthoses. Physical therapy in the first 3 months was aimed at regaining function lost as a result of surgery. This was followed by an intensive program performed 3 times a week for twelve weeks, aimed at improving range of motion, strength, balance, and function. Control group (n=8) The control group underwent a progressive resistance strength training program. They continued their routine physical therapy program for the first three month. In the second three months, they commenced the lower limb progressive resistance strength training program, which was performed three times per week for twelve weeks in their usual therapy sessions. Exercises were targeted at strengthening the hip abductors and extensors, knee extensors, and ankle plantar flexors.	Baseline surgical: 72 (20) Baseline control: 69 (20) 12-month surgical: 83 (13) 12-month control: 69 (20) Difference between groups in change at 12 months (95% CI): 14 (-2, 30) NS 2. Case series data: results of 24 month follow-up in surgery group (n=11) GPS (median (IQR) Baseline: 13.7 (11.9, 15.2) Follow-up: 9.1 (7.8, 9.6) Difference (95% CI): -5.4 (-7.5, -3.3) p<0.05 GGI score (mean (SD)) Baseline: 353 (211) Follow-up: 139 (80) Difference (95% CI): -213 (-327, -100) p<0.05 GMFM-66 score (mean (SD)) Baseline: 65.3 (11.1) Follow-up: 70.2 (10.1) Difference (95% CI): 4.9		

		The frequency, duration and cost of therapy were matched for the treatment and control groups. Outcome assessment Quantitative 3D gait data were collected using a six-camera Vicon 370 system. Reflective markers were attached to the osseous landmarks. Gait Profile Score (GPS) and Gillette Gait Index (GGI) were assessed at baseline and at 12 months postoperatively. The children in the control group exited the study after the 12-month assessment and progressed to surgery. The children who have been randomised to surgery continued to be followed in a prospective cohort study for a minimum of three years. Results from 24 months are reported. Patient reported outcomes were assessed with the use of the Child Health Questionnaire - Parent Form 50 (CHQ-PF50), Australian authorised adaptation.	(0.98, 8.7) p<0.05 Quality of life: CHQ-PF50 physical function domain (mean (SD)) Baseline: 47 (26) Follow-up: 69 (18) Difference (95% CI): 22 (4, 39) p<0.05 Adverse events related to surgery (n (%)) - Mild (spontaneously resolving): 3 (27.3) [Three children had a total of 4 mild adverse events related to poor postoperative pain management. In 2 children, this was due to postoperative epidural malfunction. One child had difficulties with pain and excessive consumption of codeine, which was followed by constipation with emesis.] - Moderate (resolved completely following simple treatment): 3 (27.3) [Two had pain over		

		Analysis - An analysis-of-covariance between the groups at 12 months and a linear regression analysis with standard errors for comparison of baseline and 24 month values within the surgical group were carried out for all outcome measures.	femoral osteotomy plates, which resolved with implant removal. One had foot pain following os calcis lengthening, which resolved by 6 months after the surgery.]		

Spasticity in children and young people with non-progressive brain disorders: management of spasticity, co-existing motor disorders and their early musculoskeletal complications

Selective dorsal rhizotomy

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Developmental Medicine and Child Neurology **Authors** Steinbok,P., Reiner,A.M., Beauchamp,R., Armstrong,R.W., Cochrane,D.D., Kestle,J. **Year of publication** 1997 **Study location** Canada **Ref ID** 76280 **Type of study** Randomised controlled study **Aim of study** Prospective, single-blinded RCT to compare the efficacy of SDR with intensive physiotherapy to intensive physiotherapy alone in improving GMFM at 9 months in children	**Inclusion Criteria** 1) Age 3–7 years 2) Diagnosis of spastic diplegia CP (with no athetoid or ataxic component). 3) Spasticity severe enough to impair gross motor function. 4) Ability to sit on the edge of an examining table with arms in the air and able to stand up while holding on with hands. 5) Availability of sufficient PT services in child's home community 6) SDR considered appropriate for the child 7) Parental consent to randomisation of treatment **Exclusion Criteria** 1) Other neuromuscular problem. 2) Planned surgical procedure during the period of the study. 3) The child's problems were of such severity that a 9-month delay in performing a definitive procedure might	<u>Comparison</u> SDR + intensive therapy vs intensive therapy only Included in analysis: SDR+PT n = 14 PT only n = 14 <u>SDR</u> Operation performed within 1 month of assignment to treatment Partial rhizotomies from L2 to S2 performed via laminotomies from L1 to S1 Each posterior root was split into 3-6 rootlets and rootlets were stimulated within 4cm of the root exit foramen with 2 unipolar electrodes Responses to electrical stimulation determined which rootlets to cut to achieve predetermined desired effect. The general plan was to cut no more that 50% of S2 (to avoid bladder dysfunction) 40-50%	Primary outcome: Total score of GMFM Secondary outcome: Spasticity—Ashworth scale, muscle strength, range of motion, physiological cost index, Peabody fine motor scale, self-care assessment score and ambulatory status Follow-up: 9 months with comparison to baseline assessments Mean difference in GMFM dimensions at 9m (positive value in favour of SDR + Therapy group) Lying/rolling : -0.2 Sitting : 15 Crawl/kneel : -7.5 Standing : 2.3 Walk/run/jump : 6 Mean increase in total GMFM SDR+Therapy : 11.3% Therapy alone : 5.2% p= 0.007	Appropriate randomisation method: treatments assigned by random number table, by independent party not involved with patient care) Allocation concealment adequate : Yes Sample size calculation: 5.1% improvement in GMFM with 90% power at $\alpha = 0.05$ (estimated be reference to a previous study) Analysis: By treatment received Groups comparable at baseline : yes Participants blinded to treatment allocation : no Caregivers blinded to treatment allocation : yes Length of follow up similar for each group : yes No of participants not completing treatment (by group) : SDR + Therapy group n=1 Therapy only n=1 (both dropped out after randomisation)	Funding : Grants from British Columbia Healrh Care Research Foundation Consent: details not provided Ethical approval : Ethics Committee of the University of British Columbia

	compromise health **Baseline characteristics** Mean age (range) SDR + Therapy: 4.2 y (2.9–6.3); Therapy only : 3.9 y (2.9–6.4) Male % not reported No significant differences for GMFM, Ashworth scale, muscle strength, range of motion, physiological cost index, Peabody fine motor scale, self-care assessment score and ambulatory status at baseline	of L4 (to avoid excessive quadriceps hypotonia) and 50-79% of L2, L3 L5 and S1. Actual percentage of dorsal root tissue transacted: 40% for S2 42% for L4 58% for L2, L3, L5 and S1 combined Postoperative management standardised : gradual mobilisation after 48 hours bed rest, discharge on 6th postop day.Intesive physiotherapy received at home <u>Therapy</u> Therapy group started therapy within one month of assignment to treatment group and received the same amount and type of physiotherapy as the SDR + therapy group Children in both groups received : 9-month sequence for PT: 1) 3 hrs times per week for 3 months 2) 2 hrs times per week for 6 months All children wore leotards for sessions to obscure SDR surgical incisions from the therapist Therapy consisted of passive	Ashworth scale mean score reduction Hip SDR+Therapy : –1.4 (0.6) Therapy alone : –0.3 (0.6) p<0.001 Knee SDR+Therapy : –1.1 (0.5) Therapy alone : -0.1 (0.7) not given Ankle SDR+Therapy : –1.5 (0.6) Therapy alone : 0.0 (0.8) not given Range of motion (° diff) Hip SDR+Therapy : 15.8 (10.6) Therapy alone :–3.3 (8.6) p<0.001 Knee SDR+Therapy : 15.6 (15.6) Therapy alone : –2.1 (10.9) not given Ankle SDR+Therapy : 18.0 (5.9) Therapy alone : 17.5 (14.1) not given Self-care assessment score SDR+Therapy : 10.5 Therapy alone : 11.5 p= 0.78	Outcome assessors blinded to treatment : yes Outcome assessment methods valid : yes Investigators blinded to treatment allocation :unclear	

		ROM of the lower limb joints ; strenthening to hip abductors and extensors, knee extensors and ankle dorsiflexors ; for 40 mins of each hour long session, practice of normal patterns of movement based on neurodevelopmental theory. Physiotherapists were instructed to place as much emphasis on weightbearing as if the child had undergone SDR, in the sessions for children in both groups. Mean amount of therapy received over 9m study period (range) SDR + Therapy group = 81.8 (72 to 90 hours) Therapy only group = 81.3 hours (70 to 89 hours) Caregivers were advised no to stitue additional treatments for the children during the study period - this was monitored by the investigators	Ambulation status improvement SDR+Therapy : 50% (5/10) Therapy alone : 0% (0/11) Adverse events SDR+PT: Back pain (7%), urinary (7%), postoperative infection (7%) Therapy group : No complications		

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Pediatric Neurosurgery **Authors** Abbott,R. **Year of publication** 1992 **Study location** **Ref ID** 96090 **Type of study** Non-comparative study **Aim of study** To review 10 years experience of SDR with an emphasis on surgical outome concentrated on improvements in functional ability and adverse effects	**Inclusion Criteria** Total population N = 250 children who underwent SDR at New York University Medical Centre from 1986 - 1992 (approx) **Exclusion Criteria** Not stated **Baseline characteristics** Not stated	Not reported	SDR Adverse Effects Postoperative urinary retention (requiring intermittent catheterisation) = 13/250 (5.2%) Catheterisation required 18m post op = 1/250 (0.4%) Postoperative ileus (requiring 48H of NG suctioning) = 3/250 (1.2%) Loss of muscle range (requiring tendonotomy) = 8/250 (3.2%) Progressive hip dislocation (requiring varus derotation osteotomies of femur) = 6/250 (2.4%) (all crawlers pre-op who walked post -op)		

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Journal of Neurosurgery **Authors** Engsberg,J.R., Ross,S.A., Collins,D.R., Park,T.S. **Year of publication** 2006 **Study location** **Ref ID** 75889 **Type of study** **Aim of study**	**Inclusion Criteria** Diagnosis of spastic diplegic CP GMFCS classification Levels I to III The ability to walk (with or without orthoses, including crutches and canes) A minimum level of cognitive skills for active participation No surgical intervention within the preceding year Hypertonicity of the lower extremity measured with the modified Ashworth scale Ankle clonus Exaggerated deep tendon reflex in the legs Babinski sign Abnormal postures while sitting, standing, and walking Ability to perform barefoot walking for approximately 8 minutes for six to eight repetitions **Exclusion Criteria** Less than six months since any casting procedures or injections of botulinum toxin serotype A Age under 4 years (for reasons of cooperation with assessments) Children who had motor deficits resulting from	SDR intervention Needle electrodes were placed bilaterally in six major muscles of the lower extremity in preparation for intraoperative EMG examinations. A single-level laminectomy was performed at the L-1 vertebra. The L-1 spinal dorsal nerve roots were identified at the foraminal exit and separated from the ventral root. Next, individual dorsal roots were identified at the level of the cauda equina. Each root was then subdivided into four to seven smaller rootlets, and these rootlets were individually suspended over rhizotomy probes. Electrical stimulation was used to grade a reflex response from the lower-extremity muscles. Rootlets were then cut according to the response. This procedure was repeated on the remaining L-2 through S-2 dorsal roots, and the entire procedure was repeated on the contralateral side. The number of rootlets that were cut varied depending on the EMG response. Approximately 65% of the rootlets were cut. PT intervention	SDR-PT Group (29 children) ankle DF at initial contact Preop = −5 ± 7 Postop (8 mos) = −4 ± 6 Postop (20 mos) = −4 ± 6 ankle DF/PF ROM Preop =15 ± 8 Postop (8 mos) =16 ± 6 Postop (20 mos) = 16 ± 4 knee flex at initial contact Preop = 32 ± 12 Postop (8 mos) = 28 ± 11 Postop (20 mos) = 28 ± 12 knee flex/ext ROM‡ Preop = 44 ± 13 Postop (8 mos) = 49 ± 12 Post-PT (20 mos) = 52 ± 13§ hip flex/ext ROM‡ Preop = 43 ± 7 Postop (8 mos) = 46 ± 7 Postop (20 mos) = 46 ± 8 pelvic tilt ROM‡ Preop = 8 ± 3 Postop (8 mos) = 7 ± 3 Postop (20 mos) = 6 ± 3‡§ pelvis rotation ROM Preop = 19 ± 7 Postop (8 mos) = 17 ± 6 Postop (20 mos) = 18 ± 4§	Prospective or retrospective : Prospective Cross-sectional or longitudinal : longitudinal Design : observational Randomised : No Allocation concealment: no allocation concealment Similar prognosis at baseline : yes Blinded subjects : no Blinded therapists : no Blinded assessors : no >85% follow up : no ITT analysis : yes	

	neurological injury or illness that began after the 1st month of life Children with malformations of the central nervous system Moderate to severe dystonia, athetosis, ataxia, or severe cognitive delay Children whose parents reported that they were unable to follow simple commands and understand concepts such as “push as hard as you can” and “relax your muscles.” **Baseline characteristics** n=77 children with spastic diplegic CP were included, n=68 in final cohort SDR-PT group n=37 children included (mean ± SD, 9 ± 5.3 years of age) 6 children dropped out : no SDR after initial testing (3),lack of cooperation (1),no contact after the initial visit (1), because of the distance between the research site and the participant’s home (1) 31 children remained in the study Age (yrs) mean ± SD = 9.0 ± 5.3 Male = 15 Weight (kg) mean ± SD = 30.1 ± 17.8 GMFCS I = 12 GMFCS II = 11 GMFCS III = 8 Independent walking = 25	The SDR-PT group received PT from therapists in their hometowns four times per week for 8 months after discharge. Then treatments were reduced to three times per week for an additional 12 months. The PT-only group received the same number of PT sessions. Treatment in both groups was focussed on the trunk and lower extremities, on strengthening, and on functional activities. Billing data were used to confirm that both groups received the similar amounts of therapy.	trunk rotation ROM Preop = 15 ± 9 Postop (8 mos) = 11 ± 5 Postop (20 mos) = 12 ± 7 ext foot progression angle‡ Preop = −3 ± 18 Postop (8 mos) = −7 ± 15 Postop (20 mos) = −9 ± 15 Gait speed (cm/sec)‡ Preop = 81 ± 22 Postop (8 mos) = 91 ± 25 Postop (20 mos) = 101 ± 24§ GMFM (%) Preop = 87 ± 10 Postop (8 mos) = 88 ± 9 Postop (20 mos) = 92 ± 8§ PT-Only Group (36 children) ankle DF at initial contact Pre-PT −3 ± 7 Post-PT (8 mos) = −3 ± 7 Post-PT (20 mos) = −2 ± 6 ankle DF/PF ROM Pre-PT = 17 ± 7 Post-PT (8 mos) = 17 ± 6 Post-PT (20 mos) = 19 ± 7 knee flex at initial contact Pre-PT = 29 ± 8 Post-PT (8 mos) = 28 ± 9 Post-PT (20 mos) = 30 ± 8 knee flex/ext ROM‡		

	Needs device to walk = 6 PT group n= 40 children included (mean ± SD, 9.7 ± 4.5 years) 3 children dropped out : lack of cooperation (1), shunt malfunction (1), severe change in scoliosis after the initial visit (1) 37 children remained in the study Age (yrs) mean ± SD = 9.7 ± 4.5 Male = 19 Weight (kg) mean ± SD = 34.5 ± 19.8 GMFCS I = 12 GMFCS II = 20 GMFCS III = 5 Independent walking = 35 Needs device to walk = 2 No disablility group Data from 40 participants with no disability were also collected but are not relevant to this review .		Pre-PT = 45 ± 12 Post-PT (8 mos) = 46 ± 13 Post-PT (20 mos) = 47 ± 13 hip flex/ext ROM‡ Pre-PT = 43 ± 7 Post-PT (8 mos) = 43 ± 7 Post-PT (20 mos) = 43 ± 7 pelvic tilt ROM‡ Pre-PT = 7 ± 3 Post-PT (8 mos) = 8 ± 3 Post-PT (20 mos) = 7 ± 3 pelvis rotation ROM Pre-PT = 17 ± 7 Post-PT (8 mos) = 18 ± 7 Post-PT (20 mos) = 18 ± 7 trunk rotation ROM Pre-PT = 12 ± 6 Post-PT (8 mos) = 12 ± 6 Post-PT (20 mos) = 12 ± 6 ext foot progression angle‡ Pre-PT = −7 ± 13 Post-PT (8 mos) = −8 ± 12 Post-PT (20 mos) = −5 ± 11 Gait speed (cm/sec)‡ Pre-PT = 91 ± 26 Post-PT (8 mos) = 90 ± 22 Post-PT (20 mos) = 93 ± 22 GMFM (%) Pre-PT = 89 ± 7 Post-PT (8 mos) = 90 ± 7 Post-PT (20 mos) = 91 ± 7§		

			‡ Significantly different pre- to 20m post-treatment change compared with that found for the PT group ($p < 0.05$). § Significantly different from pretreatment or initial visit ($p < 0.05$).		

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Developmental Medicine and Child Neurology **Authors** Wright,F.V., Sheil,E.M., Drake,J.M., Wedge,J.H., Naumann,S. **Year of publication** 1998 **Study location** Canada **Ref ID** 76369 **Type of study** Randomised controlled study **Aim of study** To determine whether SDR leads to improved functional outcome after 1 year in children with spastic diplegia compared with a control group receiving the equivalent amount of physiotherapy and occupational therapy.	**Inclusion Criteria** (1) Diagnosis of CP. (2) Predominant spastic diplegia that interferes with functional tasks such as sitting, standing and walking (3) Ability to walk ≥ 3 m with an assistive device of underarm support (4) Adequate trunk control to allow at least 60 s of independent sitting. (5) Reasonable underlying lower-extremity strength (minimum grade 3 at hip and knees) **Exclusion Criteria** (1) Major fixed contractures of lower extremity ie >30 degrees at hips and knees. (2) Major previous orthopaedic surgery eg rectus femoris transfers **Baseline characteristics** 31/100 children attending a rhizotomy clinic were eligible for inclusion in the study 7/31 declined to participate as families wanted the rhizothomy procedure to start as early as possible Therefore total N=24 All had spastic diplegia that interfered with functional tasks such as sitting, standing or walking and the spasticity	Comparison: SDR + Therapy vs Therapy only SDR + therapy group: n = 12 Therapy only : n = 12 SDR : Performed under general anaesthesia No neuromuscular blocking agents used Urinary catheter inserted after anaesthesia EMG acticity recorded using surface electrodes over the quadriceps, hamstrings, anterior tibial and gastrocnemius muscles A partial laminectomy of L2 to L5 was performed and the posterior roots of L2 to S2 were isolated and confirmed as being sensory. The roots were subdivided along natural planes into between 2 and 6 rootlets which were tested in sequence for their threshold to constant current stimulation at 50Hz. Those rootlets with the lowest threshold were divided (on average 50% of each dorsal root was transected). All procedures were performed by the same	Follow-up: 6 months, and 1 year Primary outcome : GMFM-88 NB A change of 6 percentage points in the total score or within a dimension is considered to be clinically important. Mean GMFM scores Lie/roll @ baseline SDR + Therapy group = 92.8 (9.4) Therapy only group = 91.2 (8.3) Lie/roll @ 6 m SDR + Therapy group = 94.4 (6.7) Therapy only group = 95.9 (2.8) Lie/roll @ 12m SDR + Therapy group = 98.7 (1.9) Therapy only group = 96.2 (3.1) Sit @ baseline SDR + Therapy group = 74.3 (22.2) Therapy only group = 83.7 (16.1)	Randomisation method: Appropriate Sample size calculation: Not given Analysis: Intention to treat Loss to follow-up: 0% Blinding: None (in effect) Appropriate randomisation method : Yes, blocking by age was performed prior to randomisation (<6 yrs and ≥ 6 yrs) then assignment of values from a uniform distribution on the interval (0, 1). Allocation concealment adequate : Yes Groups comparable at baseline : Yes for age and sex. Participants blinded to treatment allocation : No Caregivers blinded to treatment allocation : Yes (but could distinguish treatment groups) Length of follow up similar for each group : Yes No of participants not completing treatment (by group) : None Outcome assessment methods valid : Yes Investigators blinded to treatment allocation : Yes (but	Funding : the Easter Seal Research Institute of Canada and the United Cerebral Palsy Resarch and Education Consent: Informed consent obtained from parents Ethical approval : Not stated

	was considered to be a major limiting factor to gross motor progress. 4/24 also had upper extramity spasticity that was strongly evidence during functional activities. Sex : Female =10, Male = 14 Mean age at enrollment = 58.0 months ± SD 12.7 months Age range at enrollment = 41 - 91 months Baseline physiotherapy and biomechanical assessments were conducted. In the SDR group, these were conducted no more than 3 wks before surgery was performed and follow up was conducted from the day of surgery for 1 year. In the therapy only group, follow up for 1 year started on the baseline assessments completion. No significant differences between the groups for mean age (SDR+therapy group = 57.8m vs Therapy only group 58.3), for sex ratio in each group (Male - 58% in both groups)	neurosurgeon Postoperative analgesia was IV morphine (typically 30µg/kg/hr) usually for 3 or 4 days. Patients were nursed in bed during this time and were turned every 4 hours. Physiotherapy to amintain ROM was started on the second or third postoperative day. Therapy programs Each child's local physiotherapist and occupational therapist developed a list of pre-randomisation therapy goals and the behaviours that would indicate goal accomplichment for the next 3-6 months These treatment goals were followed by the therapy only group in 2 hour-long sessions/wk (c120mins/wk) and focussed on ROM, strengthening through functional activities, facilitation of normal movement patterns and postural control, standing and gait-related activities and work on fine motor skills and functional abilities.The physiotherapist generally concentrated on lower limb,	Sit @ 6m SDR + Therapy group = 87.9 (15.1) Therapy only group = 85.6 (17.9) Sit @ 12m SDR + Therapy group = 87.7 (15.2) Therapy only group = 87.9 (15.8) Crawl/kneel @ baseline SDR + Therapy group = 62.9 (26.9) Therapy only group = 71.1 (19.4) Crawl/kneel @ 6m SDR + Therapy group = 68.4 (24.0) Therapy only group = 76.3 (15.8) Crawl/kneel @ 12m SDR + Therapy group = 77.3 (19.2) Therapy only group = 76.9 (10.4) Stand @ baseline SDR + Therapy group = 21.8 (15.9) Therapy only group = 19.6 (17.2) Stand @ 6m SDR + Therapy group = 30.1 (23.4)	could distinguish treatment groups) Limitations : None Other considerations :None	

		whilst the occupational therapist focussed on upper limb and functional skills. Children in the SDR and therapy group were given a new set of short term goals determined postoperatively by the hospital physiotherapist and occupational therapist team. In the initial post-operative period these were consistent for all children as they were based on local post-SDR rehabilitation guidelines. For the remainder of their 6 week in-patient stay the same physiotherapist and occupational therapist treated all 12 children for 45 mins of physiotherapy each day and for 45 mins of occupational therapy twice/wk. The focus initially was on ROM and positioning, upper and lower extremity strengthening, particularly of the trunk musculature, hip extensors and abductors and knee extensors via work on isolated movements and facilitation of more normal movement patterns and postural control. Standing and gait related activities and work on fine motor	Therapy only group = 23.7 (12.1) Stand @ 12m SDR + Therapy group = 33.1 (23.5) Therapy only group = 27.1 (19.6) Walk/run/jump @ baseline SDR + Therapy group = 10.6 (8.2) Therapy only group = 13.2 (14.2) Walk/run/jump @ 6m SDR + Therapy group = 14.8 (7.8) Therapy only group = 14.5 (15.4) Walk/run/jump @ 12m SDR + Therapy group = 23.4 (19.5) Therapy only group = 15.7 (17.1) Total score @ baseline SDR + Therapy group = 51.9 (13.4) Therapy only group = 56.5 (12.2) Total score @ 6m SDR + Therapy group = 58.7 (13.5) Therapy only group = 58.5 (10.7)		

		skills and cuntional activities were gradually introduced as the child's strength and control improved. On transfer to outpatient care, the child's regular community therapists were sent specific treatment guidelines and set individual treatment goals for the remainder of the child's study year with therapy frequency set at 2 hour-long sessions/wk (c120mins/wk)	Total score @ 12m SDR + Therapy group = 64.0 (13.2) Therapy only group = 60.9 (12.5) Secondary outcomes Tone using modified Ashworth Active ROM lower limb Passive ROM lower limb Distance walked in 60 secs using the child's usual gait device scoring for the foot–floor contact pattern ankle-stretch reflex isometric contractions video gait analysis Modified Ashworth @ elbow baseline SDR + Therapy group = 4.0 (1.3) Therapy only group = 5.0 (0.5) Modified Ashworth @ elbow 6m SDR + Therapy group = 4.0 (0.7) Therapy only group = 4.0 (0.6) Modified Ashworth @ elbow 12m SDR + Therapy group = 4.0 (1.2) Therapy only group = 4.0		

			(0.6) Modified Ashworth @ knee baseline SDR + Therapy group = 5.0 (1.2) Therapy only group = 5.0 (0.7) Modified Ashworth @ knee 6m SDR + Therapy group = 4.0 (0.9) Therapy only group = 5.0 (0.6) Modified Ashworth @ knee 12m SDR + Therapy group = 4.0 (0.7) Therapy only group = 5.0 (0.7) Modified Ashworth @ ankle baseline SDR + Therapy group = 5.0 (0.7) Therapy only group = 6.0 (0.4) Modified Ashworth @ ankle 6m SDR + Therapy group = 4.0 (0.7) Therapy only group = 6.0 (0.4) Modified Ashworth @ ankle 12m		

			SDR + Therapy group = 4.5 (0.7) Therapy only group = 6.0 (0.4) Active ROM hip extension @ baseline SDR + Therapy group = -22.5 (25.3) Therapy only group =-44.2 (31.3) Active ROM hip extension @ 6m SDR + Therapy group = -26.5 (20.0) Therapy only group = -28.6 (15.3) Active ROM hip extension @ 12m SDR + Therapy group = -20.3 (18.7) Therapy only group = -38.3 (27.9) Active ROM knee extension @ baseline SDR + Therapy group = -26.7 (18.7) Therapy only group = -32.5 (17.4) Active ROM knee extension @ 6m SDR + Therapy group = -10.2 (10.9) Therapy only group = -28.6 (15.3)		

			Active ROM knee extension @ 12m SDR + Therapy group = - 11.3 (15.4) Therapy only group = -24.3 (14.9) Active ROM ankle dorsiflexion @ baseline SDR + Therapy group = -25.8 (18.1) Therapy only group = -27.9 (21.4) Active ROM ankle dorsiflexion @ 6m SDR + Therapy group = -13.0 (19.9) Therapy only group = -32.7 (20.1) Active ROM ankle dorsiflexion @ 12m SDR + Therapy group = -6.3 (10.3) Therapy only group = -35.4 (19.9) Passive ROM hip extension @ baseline SDR + Therapy group = -15.0 (10.2) Therapy only group = -20.4 (12.7) Passive ROM hip extension @ 6m SDR + Therapy group =		

			-7.7 (9.1) Therapy only group = -18.6 (7.7) Passive ROM hip extension @ 12m SDR + Therapy group = -7.5 (9.9) Therapy only group = -12.9 (12.7) Passive ROM knee extension @ baseline SDR + Therapy group = -12.9 (18.3) Therapy only group = -12.1 (12.7) Passive ROM knee extension @ 6m SDR + Therapy group = -8.4 (15.9) Therapy only group = -11.1 (11.3) Passive ROM knee extension @ 12m SDR + Therapy group = -6.5 (12.5) Therapy only group = -8.7 (11.1) Passive ROM popliteal angle @ baseline SDR + Therapy group = 37.1 (17.5) Therapy only group = 46.7 (14.4)		

			Passive ROM popliteal angle @ 6m SDR + Therapy group = 32.5 (16.6) Therapy only group = 50.5 (14.7) Passive ROM popliteal angle @ 12m SDR + Therapy group = 32.5 (19.3) Therapy only group = 46.8 (9.8) Passive ROM ankle dorsiflexion (knee extended) @ baseline SDR + Therapy group = -5.0 (20.2) Therapy only group = -9.6 (17.9) Passive ROM ankle dorsiflexion (knee extended) @ 6m SDR + Therapy group = 6.9 (13.7) Therapy only group = -11.8 (17.6) Passive ROM ankle dorsiflexion (knee extended) @12m SDR + Therapy group = 3.8 (11.5) Therapy only group = -12.0 (16.4)		

			Timed walk @ baseline SDR + Therapy group = 23.9 (25.9) Therapy only group = 30.1 (25.1) Timed walk @ 6m SDR + Therapy group = 28.9 (27.7) Therapy only group = 38.1 (25.9) Timed walk @ 12m SDR + Therapy group = 39.8 (32.2) Therapy only group = 26.6 (18.6)		

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Archives of Physical Medicine and Rehabilitation **Authors** Buckon,C.E., Thomas,S.S., Piatt,J.H.,Jr., Aiona,M.D., Sussman,M.D. **Year of publication** 2004 **Study location** USA **Ref ID** 75792 **Type of study** Non-randomised controlled study **Aim of study** To compare the efficacy of selective dorsal rhizotomy versus orthopaedic surgery using multidimensional outcomes measures (National Centre for Medical Rehabilitation Research disablement framework)	**Inclusion Criteria** Children found by an MDT to be appropriate for SDR or orthopaedic soft tissue procedures. Eligibity for SDR: -aged between 4 and 10 years -predominantly spastic -have good trunk control -history of prematurity -no significant ataxia or athetosis -good lower extremity antigravity strength -no significant scoliosis -ambulatory with or without assistive devices -cooperative -ability to isolate lower extremity movements -lower extremity contracture < 10º Eligibility for orthopaedic surgery: -kinematic dysfunction with evidence of dynamic limitation of motion -spasticity on static examination, which would benefit from muscle and tendon lengthening, release or transfer **Exclusion Criteria**	Interventions - 1. Selective Dorsal Rizhotomy (SDR) (n=18) SDR performed through osteoplastic laminotomy. Posterior nerve roots from L2 to S1 divided into 3–6 rootlets. At L2, 30%– 50% of rootlets sectioned without stimulation. Rootlets from L3 to S1 sectioned on basis of electromyographic results after stimulation and presurgical assessment results (mean of 42% of rootlets cut, range 36%–48%). Post-SDR hospitalisation for 1 month. Twice daily PT and once daily OT from day 4 to discharge. PT 2–3 times a week and OT 1–2 times a week for first 6 months, then PT 1–2 times a week to 1 year. 2. Orthopaedic surgery (n=7) Aponeurotomy/tenotomy, between 4 and 7 procedures performed per patient. Patients received post-surgical therapy that was standard for interventions received. Children with soft tissue procedures began PT on days 2	(p values refer to significant within-group change) GMFM total (change scores) (mean (SD)) a. SDR 6 months: 1.98 (5.22); p=0.13 (NS) 1 year: 3.39 (7.82); p=0.08 (NS) 2 years: 6.32 (8.38); p=0.01 b. Orthopaedic surgery 6 months: 0.96 (4.45); p=0.59 (NS) 1 year: 5.90 (4.89); p=0.02 2 years: 7.51 (8.04); p=0.05 PEDI Functional skills PEDI-self care (change scores) (mean (SD)) - a. SDR 6 months: 3.27 (4.37); p≤0.006 1 year: 6.18 (6.91); p≤0.001 2 years: 11.89 (6.81); p≤0.0001 b. Orthopaedic surgery 6 months: 1.1 (4.82); p≤0.57 (NS) 1 year: 5.5 (5.27); p≤0.03 2 years: 8.17 (6.29); p≤0.02 PEDI-mobility (change scores) (mean (SD))	Follow-up issues: Completeness of follow-up not reported. Study design issues: Prospective study Sample size calcualtion not reported The post-surgical physiotherapy care was not standardised between the groups as it was focused to the remedial need, and may have influenced outcome. All outcomes were evaluated by two investigators who were trained in using the scales. Assessors were not blinded to treatment allocation. Study population issues: Ambulatory = 92% There were no significant differences between groups at baseline in any of the clinical outcomes measured. Mean proportion of dorsal nerve rootlets sectioned in the SDR group: 43.3% (reported by NICE IPG analyst)	Recruitment period: over 3 years (dates not reported) Follow-up: 2 years No safety data was presented in the study report Conflict of interest/source of funding: no commercial party conferred a benefit on the author.

	Not stated **Baseline characteristics** Total sample size n=25 children Characteristics Children with spastic diplegia -Age: SDR group: 71.3 months (mean); orthopaedic surgery group: 78.6 months (mean) -Sex: 76% (19/25) male -GMFCS (I, II, III): SDR: 17%, 44%, 39% Orthopaedic surgery: 29%, 14%, 57%	and 3. 5/7 received casting. Discharged on day 5. Casts removed after 2–4 weeks. Readmitted for 2 weeks of PT twice daily and OT (where indicated) once daily. Patients then discharged and received weekly outpatient therapy for 2–4 months. Comparison SDR vs. orthopaedic surgery with post-surgical physiotherapy in both groups. Parents chose the treatment therapy after discussions with clinicians.	- a. SDR 6 months: 1.41 (3.80); p≤013 (NS) 1 year: 3.73 (7.94); p≤0.06 (NS) 2 years: 7.51 (7.11); p≤0.001 b. Orthopaedic surgery 6 months: -1.50 (6.26); p≤0.55 (NS) 1 year: 1.84 (5.79); p≤0.43 (NS) 2 years: 7.34 (7.52); p≤0.04 PEDI-social skills (change scores) (mean (SD)) - a. SDR 6 months: 1.22 (5.95); p≤0.39 (NS) 1 year: 3.19 (6.56; p≤0.06 (NS) 2 years: 7.82 (6.63); p≤0.0004 b. Orthopaedic surgery 6 months: 7.41 (5.23); p≤0.01 1 year: 2.59 (3.73); p≤0.12 (NS) 2 years: 7.67 (4.95); p≤0.006 PEDI Caregiver assistance PEDI-self care (change scores) (mean (SD)) - a. SDR 6 months: 2.82 (9.77); p≤0.24 (NS)		

			1 year: 3.07 (10.73); p≤0.22 (NS) 2 years: 10.53 (8.33); p≤0.0002 b. Orthopaedic surgery 6 months: 0.59 (12.13); p≤0.90 (NS) 1 year: 1.60 (9.66); p≤0.67 (NS) 2 years: 5.50 (5.27); p≤0.033 <u>PEDI-mobility (change scores) (mean (SD))</u> - a. SDR 6 months: 0.78 (5.15); p≤0.53 (NS) 1 year: 8.01 (11.97); p≤0.11 2 years: 13.58 (13.76); p≤0.02 b. Orthopaedic surgery 6 months: 2.59 (8.63); p≤0.46 (NS) 1 year: 4.84 (6.82); p≤0.11 (NS) 2 years: 5.83 (9.64); p≤0.16 (NS) <u>PEDI-social skills (change scores) (mean (SD))</u> - a. SDR 6 months: 1.12 (13.56); p≤0.73 (NS) 1 year: 3.07 (10.40); p≤0.23 (NS) 2 years: 7.00 (10.31); p≤0.02		

			b. Orthopaedic surgery 6 months: 1.44 (14.67); 0.80 (NS) 1 year: -3.14 (8.89); p≤0.39 (NS) 2 years: 2.53 (14.59); p≤0.66 (NS)		

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Developmental Medicine and Child Neurology **Authors** McLaughlin,J.F., Bjornson,K.F., Astley,S.J., Graubert,C., Hays,R.M., Roberts,T.S., Price,R., Temkin,N. **Year of publication** 1998 **Study location** USA **Ref ID** 96092 **Type of study** Randomised controlled study **Aim of study** To investigate the efficacy and safety of SDR in children with spastic diplegia	**Inclusion Criteria** 1) Age 3 – 18 years 2) Diagnosis of spastic diplegia. 3) Good prognosis for community or indoor ambulation with conventional treatment. 4) Ability to participate for the duration of study. 5) Availability of sufficient PT services in child's home community. 6) Intellectual function at 36-month-old level or higher. 7) Expressive language: 36-month-old level or higher **Exclusion Criteria** 1) Other neurological motor abnormalities. 2) Fixed musculoskeletal contractures of more than 15° at hips or knees and 30° at ankles. 3) Other musculoskeletal problems requiring effective conventional intervention. 4) Medical contraindications to a prolonged elective anaesthetic, abnormal spine anatomy, uncontrolled seizure disorder, or other chronic conditions that would compromise either the postoperative course after SDR or the child's participation in an intensive PT program	Comparison: SDR+PT vs PT only SDR+PT : n = 21 PT only : n = 17 <u>SDR</u> One surgeon performed all SDRs Inhalational anaesthesia was used and monitored to avoid suppression of EMG responses Neuromuscular blockers were not used A narrow laminectomy (bone rongeurs)or laminotomy (Anspach lamina cutter) was performed from T12 to S2 Bilateral visual and EMG identification of each ventral (0.2mA) and dorsal (1-20mA) roots Dorsal rootlets giving abnormal repnses subdivided by blunt dissention 4 channel EMG recording unit , clinical inspection and muscle palpation used to detect muscle group responses to rootlet stimulation Postoperative pain managed with IV morphine and IV midazolam for 2-3 days Children hospitalised for 5-7 days Percentage of dorsal root tissue transacted:26%	Primary outcome: Spasticity—spasticity measurement system. Functional mobility—GMFM score Secondary outcome: Spasticity—Ashworth scale and clinical assessment of signs of spasticity. Functional mobility—rating of child's ambulation status Adverse events : A structured adverse event questionnaire was administered to parents either face-to-face or over the telephone every 3 m for 24 m by the investigators. Adverse events were rated for severity and whether they were related to treatment or CP. <u>Changes in spasticity</u> Mean Ashworth scale score reduction @ 6 m (read from graph) SDR+Therapy : -1.0 Therapy alone : -0.15 Mean difference = 0.85 Median Ashworth scale score reduction @ 12 m SDR+Therapy : -0.88 Therapy alone : -0.13 Median difference -1.0 (-1.3 to -0.7) <0.001	Appropriate randomisation method: Yes, sealed envelope technique with statistician uninvolved with study. Allocation concealment adequate : Unclear, two children swopped from the therapy group to the SDR + therapy group Patients were stratified by age (3-11 yrs and 12-18yrs) and ambulatory (ability to walk 50 feet without upper extremity aids) status by a block with a cell size of 4 Sample size calculation: 10% difference in GMFM with 90% power at α = 0.05 (2-sided) and spasticity measurement system difference of 10 Nm/rad with 80% power at α = 0.05 (2-sided) Sample size obtained (ie SDR + Therapy vs Therapy alone, n=21 vs n=17) sufficient for 10% difference in GMFM with 90% power and 10 Nm/rad difference in total SMS path with 46% power. Analysis: By treatment Groups comparable at baseline : yes Participants blinded to treatment allocation : no Caregivers blinded to treatment allocation : no	Funding : Was sought to purchase therapy services for the Therapy only group and for the SDR+therapy group where insurance did not cover the children's therapy costs. Consent: Consent from children (if functioning at 7 year old level or higher), written consent from adolescents and each guardian Ethical approval : Children's Hospital Regional Medical Centre Institutional review board

	Baseline characteristics N = 38 Mean age (range) SDR+PT: 6.1 y (2.9–14.3) PT: 6.8 y (3.0–17.3) Male Sex% SDR+PT: 52% PT: 55% No significant difference between groups for -Race -Caregiver's marital status -Socioeconomic status -Insurance coverage -Gestational age -Birthweight -Cause of CP -Ambulatory ability -Cognitive status -Number of children with associated impairments	(14%–50%) from L1 to S2 <u>Therapy</u> Over a 12-month sequence each child within the SDT + therapy or Therapy group only was scheduled to receive : 1) 2 hrs per day for 5days/wk for 4 wks performed by experienced therapists for which the families stayed in hospital 2) 1 hr per day, 4–5 days/wk for 5 m prescribed by investigators and performed by community therapists 3) 1 hr per day, 1–4 days/wk for 6 m prescribed by investigators and performed by community therapists on a voluntary basis The emphasis and techniques used in the SDR group were appropriate for this group. 20 difference categories of treatment were documented by the treating therapists	Median Ashworth scale score reduction @ 24 m SDR+Therapy : - 0.88 Therapy alone : 0.00 Median difference -1.0 (-1.4 to -0.7) <0.001 <u>Changes in function</u> Mean difference in GMFM dimensions at 12m (95% CI) (positive value in favour of SDR + Therapy group) Lying/rolling : -0.8 (-3.5 to 1.8) p=0.53 Sitting : 1.2 (-5.8 to 8.2) p=0.73 Crawl/kneel : -0.1 (-6.8 to 6.6) p=0.98 Standing : 2.6 (-8.4 to 14.0) p=0.63 Walk/run/jump : 0.5 (-6.0 to 7.0) p=0.88 Mean difference in GMFM dimensions at 24m (95% CI) Lying/rolling : -0.1 (-2.2 to 2.1) p=0.97 Sitting : -1.6 (-8.5 to 5.4) p=0.65 Crawl/kneel : -0.3 (-7.0 to 6.4) p= 0.93 Standing : 1.6 (-16.0 to 9.1) p= 0.59 Walk/run/jump : 1.6 (-8.0 to 11.0) p=0.74 Mean increase in total GMFM score @ 12m	Length of follow up similar for each group : yes No of participants not completing treatment (by group) : SDR + Therapy group n=2, Therapy only n=2 (and 1 child stopped participating after 6 month intensive treatment) Outcome assessment methods valid : yes Investigators blinded to treatment allocation : no	

			SDR+Therapy : 4.9% Therapy alone : 4.2% 0.72 Mean increase in total GMFM score @24 m SDR+Therapy :7.0% Therapy alone :7.2% 0.94 Ambulation status improvement @ 12 m SDR+Therapy :19% Therapy alone :18% NS Ambulation status improvement @ 24 mo SDR+Therapy : 38% Therapy alone :18% 0.20 <u>Adverse events</u> No severe adverse events related to either treatment Back pain SDR+Therapy: 29% Therapy alone: 0% Lower-extremity pain SDR+Therapy: 48% Therapy alone: 94% Weakness SDR+Therapy: 19% Therapy alone: 18% Urinary problem SDR+Therapy: 14%		

			Therapy alone: 0% Emotion/behavioural SDR+Therapy: 29% Therapy alone: 35% Other (musculoskeletal) SDR+Therapy: 14% Therapy alone: 0% Sensory SDR+Therapy: 19% Therapy alone: 0%		

Bibliographic details	Number of Participants Characteristics	Intervention characteristics	Outcome measures and results	Quality assessment	Reviewer comment
Periodical Childs Nervous System **Authors** Kim,D.S., Choi,J.U., Yang,K.H., Park,C.I. **Year of publication** 2001 **Study location** Korea **Ref ID** 96093 **Type of study** Non-randomised controlled study **Aim of study** To review 10years experience of SDR with an emphasis on surgical outcomes, concentrating on the improvement in functional ability and adverse events	**Inclusion Criteria** Selection criteria were patients with spastic hemiplegia of cerebrovascular sequelae or spastic quadriparesis resulting from an incomplete cervical cord who had undergone SDR more that one year previously to the start of the study. **Exclusion Criteria** Not stated **Baseline characteristics** N=208 Patients with spastic CP =198 Patients with hemiplegia after a cerebrovascular insult = 8 Patients with spastic quadriparesis after cervical cord injury = 2 Mean age = 5.9 years (range 2-13 years)	Surface ENG electrodes were placed on selected muscle groups on both legs. Gastrocnemius was used to identify S1, the hamstrings for L5, anterior tibialis for L4, quadriceps for L3 and hip adductors for L2. The anal sphincter muscle was monitored for S2. Laminectomies were performed from L1 to S1 in the first 58 patients (48 children and 10 adults). Subsequently, laminoplasties from L1 to L5 followed by upper sacral laminectomies were performed in 150 children. At each level the posterior root was separated into three or four rootlets which were each stimulated and the EMG pattern recorded on surface electrodes. Rootlets' spasticity were ranked from grade 0 - 4. Those that demonstrated gradually decreasing or steady squared off electrical responses were spared, but any rootlets ranked higher were cut. The testing cutting or sparing procedure was repeated on all rootlets from S2 to L2 and was continued at L1 where 50% of the bilateral	Average duration of follow up = 4.2 years (range 1-9 years) 20/208 (9.6%) patients experienced post-op temporary urinary retention resolving spontaneously in 18 patients within 4 wks of SDR surgery. 2 patients suffered from long-standing urinary incontinence because of atonic bladder. Post-op urinary incontinence in 1 child markedly improved after clean intermittant catheterisation for 2 years, however it did not return to normal in one child after 3 years. A post-op spinal deformity was seen in 12/208 (5.8%) patients - radiological only, and not functionally important Scoliosis was found in 5/58 patients undergoing laminectomy and in 2/150 patients undergoing laminoplasty 2/208 patients required orthopaedic surgery because of progressive hip migration> 208/208 patients experienced post-op back pain which was	Case series providing non-comparative data. Only outcomes pertaining to specific adverse events related to surgery are extracted. Observational study (low)	

		roots were cut without EMG testing. A continuous IV fentanyl or morphine drip was administered as needed for pain relief until post-op day 3. Foley catheterss were discontinued on post-op day 1 or 2. Patients were transferred to a rehab dept on post-op day 7 if there were no complications. Children then began gentle stretching, rolling and mat exercises and were allowed to sit as they tolerated this.	well controlled with iv fentanyl or morphine drip. 7/208 (3.4%) patients experienced long standing back pain. Lower limb spasticity (Ashworth score), passive range of motion, muscle strength, ambulatory function (Peacock grade) and gait pattern were assessed (but not presented here as is non comparative data)		