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Interventions and Management

1. Preferred options and evidence for upper limb surgery for spasticity in cerebral palsy, stroke, and brain injury. Tranchida GV, Van Heest A.

J Hand Surg Eur Vol. 2019 Oct 9;1753193419878973. doi: 10.1177/1753193419878973. [Epub ahead of print]

Surgical interventions for the spastic upper extremity secondary to stroke, traumatic brain injury, and cerebral palsy aim to correct the common deformities of elbow flexion, forearm pronation, wrist and finger flexion, ulnar deviation, and thumb-in-palm deformity. After appropriate evaluation, as well as determining the goals of surgery, deformity correction can be achieved through single-event, multi-level surgery. Surgery includes a combination of soft tissue lengthening, tendon transfer, and joint stabilization procedures. Surgical treatment for shoulder adduction/internal rotation, elbow flexion, forearm pronation, wrist flexion, thumb-in-palm, and clenched fist deformities due to spasticity are discussed, and treatment outcomes are reviewed.

PMID: [31594425](#)

2. Systematic review of spinal deformities following multi-level selective dorsal rhizotomy. Wheelwright M, Selvey PJ, Steinbok P, Singhal A, Ibrahim G, Fallah A, Weil AG, Halvorson K, Tu A.

Childs Nerv Syst. 2019 Oct 8. doi: 10.1007/s00381-019-04375-x. [Epub ahead of print]

PURPOSE: Cerebral palsy is a common neurological disorder that involves spasticity of the extremities and can lead to lifelong disability. Selective dorsal rhizotomy (SDR) can improve spasticity and quality of life in these patients, but it may be associated with the development of spinal deformity. Risk factors for spinal deformity after SDR have not yet been systematically examined. **METHODS:** Medline, Embase, and Web of Science databases were queried for clinical studies reporting incidence of new or worsening spinal deformity, including scoliosis, after SDR. Variables that represent possible risk factors for deformity were correlated with reported incidence of deformity. **RESULTS:** Twenty-two articles for a total of 1485 patients met the inclusion criteria for this study. Deformity occurs among all patients with a weighted mean incidence of 28.0%. Scoliosis appears to be the most common deformity occurring with a weighted mean incidence of 31.6%. There is substantial heterogeneity between studies, limiting our analysis. Significant positive correlation was found between percent of patients that developed any type of deformity and the ratio of female to male patients, $p = 0.02$. Significant positive correlation was also found between percent of patients that develop scoliosis and the ratio of female to male patients, $p < 0.01$, and between scoliosis and the number of years to follow-up, $p < 0.01$. **CONCLUSION:** Spinal deformity is an important potential complication of SDR with scoliosis being the most common type of deformity. The major risk factor for postoperative deformity is female sex. Deformity was also found to significantly increase with extended follow-up, indicating a slow process that should be carefully monitored.

PMID: [31595313](#)

3. Are spasticity, weakness, selectivity, and passive range of motion related to gait deviations in children with spastic cerebral palsy? A statistical parametric mapping study.

Papageorgiou E, Simon-Martinez C, Molenaers G, Ortibus E, Van Campenhout A, Desloovere K.

PLoS One. 2019 Oct 11;14(10):e0223363. doi: 10.1371/journal.pone.0223363. eCollection 2019.

This study aimed to identify the relationships between clinical impairments and gait deviations in children with cerebral palsy (CP). A retrospective convenience sample of 367 children with CP was selected (3-18 years old) and divided in two groups based on clinical symptomatology [unilateral (uCP) / bilateral CP (bCP), (n = 167/200)]. All children underwent a three-dimensional gait analysis and a standardized clinical examination. Gait was inspected on a vector level (all sagittal motions combined), and an individual joint level (pelvis, hip, knee and ankle joint motions). Statistical non-parametric mapping was applied to identify specific parts of the gait cycle displaying relationships between the gait deviations of both groups and the impairment scores of spasticity, weakness, selectivity, and passive range of motion. Impairment scores were summarized in two ways: a) composite impairment scores (e.g. combined spasticity of all assessed muscles acting around the hip, knee and ankle joints) and b) joint specific impairment scores (e.g. spasticity of the muscles acting around the knee joint). Results showed that the vector and most of the individual motions were related to the composite scores. Direct and carry-over relationships were found between certain individual motions and joint impairment scores (around the same or neighboring joints, respectively). All correlations were more prominent for children with bCP compared to uCP, especially regarding the relationships of gait deviations with weakness and reduced selectivity. In conclusion, this study enabled the mapping of relationships between clinical impairments and gait deviations in children with CP, by identifying specific parts of the gait cycle that are related to each of these impairments. These results provide a comprehensive description of these relationships, while simultaneously highlighting the differences between the two CP groups. Integration of these findings could lead to a better understanding of the pathophysiology of gait deviations and, eventually, support individualized treatment planning.

PMID: [31603897](#)

4. Botulinum toxin type A in the treatment of lower limb spasticity in children with cerebral palsy.

Blumetti FC, Bellotti JC, Tamaoki MJ, Pinto JA.

Cochrane Database Syst Rev. 2019 Oct 8;10:CD001408. doi: 10.1002/14651858.CD001408.pub2. [Epub ahead of print]

BACKGROUND: Cerebral palsy (CP) is the most common cause of physical disabilities in children in high-income countries. Spasticity is the most common motor disturbance in CP. Botulinum toxin type A (BoNT-A) is considered the first-line treatment for focal spasticity in people with CP. **OBJECTIVES:** To evaluate the effectiveness and safety of BoNT-A compared to other treatments used in the management of lower limb spasticity in children with CP. **SEARCH METHODS:** We searched CENTRAL, PubMed, four other databases, and two trial registers in October 2018. We also searched the reference lists of relevant studies and reviews and contacted experts in the field. We did not apply any date or language restrictions. **SELECTION CRITERIA:** Randomised controlled trials of children with CP, aged between birth and 19 years, treated with BoNT-A injections in the lower limb muscles compared to other interventions. The primary outcomes were gait analysis and function. The secondary outcomes were joint range of motion, quality of life, satisfaction, spasticity, and adverse events. **DATA COLLECTION AND ANALYSIS:** Two review authors independently selected studies, extracted data, assessed risk of bias, and rated the quality of the evidence using GRADE. A third review author arbitrated in case of disagreements. We conducted meta-analyses of available data whenever possible, analysing dichotomous data with risk ratios (RR), and continuous data with mean differences (MD) or standardised mean differences (SMD), with 95% confidence intervals (CI). We considered a 5% significance level for all analyses. Whenever possible, we analysed outcomes at the time points at which they were assessed: short term (2 to 8 weeks); medium term (12 to 16 weeks); and long term (> 24 weeks). **MAIN RESULTS:** We included 31 randomised controlled trials assessing 1508 participants. Most studies included ambulatory patients with more than one motor type of CP, and with a mean age of between three and seven years. There was a slight predominance of males. Studies compared BoNT-A in the lower limb muscles to usual care or physiotherapy (14 studies), placebo or sham (12 studies), serial casting (4 studies), or orthoses (1 study). We rated studies as at high or unclear risk of bias mainly due to random sequence generation, allocation concealment, blinding of participants and personnel, and blinding of outcome assessment. BoNT-A versus usual care or physiotherapy BoNT-A might improve overall gait scores at medium-term follow-up (MD 2.80, 95% CI 1.55 to 4.05; 1 study, 40 children; very low-quality evidence) and is moderately effective at improving function at short-term (SMD 0.59, 95% CI 0.23 to 0.95; 2 studies, 123 children) and medium-term (SMD 1.04, 95% CI 0.16 to 1.91; 4 studies, 191 children) follow-up (all very low-quality evidence). BoNT-A improves ankle range of motion, satisfaction, and ankle plantarflexors spasticity at one or more time points (very low-quality evidence). The proportion of adverse events in the BoNT-A group was 0.37 (95% CI 0.08 to 0.66; I² = 95%; very low-quality evidence). No adverse events were reported in the control group. BoNT-A versus placebo or sham BoNT-A improves overall gait scores at short-term (RR 1.66, 95% CI 1.16 to 2.37, P = 0.006; 4 studies, 261 assessments) and medium-term (RR 1.90, 95% CI 1.32 to 2.74, P < 0.001; 3 studies, 248 assessments) follow-up, and may improve peak ankle dorsiflexion in stance (MD 15.90 degrees, 95% CI 4.87 to 26.93, P =

0.005; 1 study, 19 children) and in swing (MD 10.20 degrees, 95% CI 4.01 to 16.39, $P = 0.001$; 1 study, 19 children) at short-term follow-up (all moderate-quality evidence). BoNT-A is not more effective than placebo or sham at improving function at short-term (SMD 0.24, 95% CI -0.35 to 0.83, $P = 0.42$; 4 studies, 305 children) or long-term (SMD -0.07, 95% CI -0.48 to 0.35, $P = 0.76$; 2 studies, 91 children) follow-up, but has a small positive effect at medium-term follow-up (SMD 0.28, 95% CI 0.06 to 0.49, $P = 0.01$; 5 studies, 327 children) (all moderate-quality evidence). BoNT-A improves passive ankle range of motion, satisfaction, and ankle plantarflexors spasticity at one or more time points (moderate-quality evidence). There was no difference between groups in the rate of adverse events at short-term follow-up (RR 1.29, 95% CI 0.87 to 1.93, $P = 0.21$; 12 studies, 918 children; moderate-quality evidence). BoNT-A versus serial casting There was no difference between groups for overall gait scores at short-term (MD 0.00, 95% CI -1.66 to 1.66); medium-term (MD 0.65, 95% CI -1.21 to 2.51); or long-term (MD 0.46, 95% CI -1.33 to 2.25) follow-up in one study with 18 children (moderate-quality evidence). BoNT-A improved instrumented gait analysis only in terms of ankle dorsiflexion at initial contact (MD 6.59 degrees, 95% CI 1.39 to 11.78, $P = 0.01$; 2 studies, 47 children). There was no difference between groups for peak ankle dorsiflexion in stance and swing, and gait speed at any time point (moderate- and low-quality evidence). BoNT-A is not more effective than serial casting at improving function, ankle range of motion, and spasticity at any time point (moderate- and low-quality evidence). BoNT-A is not associated with a higher risk of adverse events than serial casting (RR 0.59, 95% CI 0.03 to 11.03; 3 studies, 64 children; low-quality evidence). BoNT-A versus orthoses There was no difference between groups for function at medium-term follow-up (MD 11.14, 95% CI -0.05 to 22.33; 1 study, 43 children), but BoNT-A is more effective than orthoses at improving hip range of motion and hip adductors spasticity (all very low-quality evidence). **AUTHORS' CONCLUSIONS:** The quality of the evidence was low or very low for most of the outcomes analysed. We found limited evidence that BoNT-A is more effective than placebo or a non-placebo control at improving gait, joint range of motion, satisfaction, and lower limb spasticity in children with CP, whereas the results for function were contradictory. The rate of adverse events with BoNT-A is similar to placebo. BoNT-A is not more effective than ankle serial casting to treat ankle contractures for any of the assessed outcomes, but is more effective than orthotics at improving range of motion and spasticity.

PMID: [31591703](#)

5. Predicting gait adaptations due to ankle plantarflexor muscle weakness and contracture using physics-based musculoskeletal simulations.

Ong CF, Geijtenbeek T, Hicks JL, Delp SL.

PLoS Comput Biol. 2019 Oct 7;15(10):e1006993. doi: 10.1371/journal.pcbi.1006993. [Epub ahead of print]

Deficits in the ankle plantarflexor muscles, such as weakness and contracture, occur commonly in conditions such as cerebral palsy, stroke, muscular dystrophy, Charcot-Marie-Tooth disease, and sarcopenia. While these deficits likely contribute to observed gait pathologies, determining cause-effect relationships is difficult due to the often co-occurring biomechanical and neural deficits. To elucidate the effects of weakness and contracture, we systematically introduced isolated deficits into a musculoskeletal model and generated simulations of walking to predict gait adaptations due to these deficits. We trained a planar model containing 9 degrees of freedom and 18 musculotendon actuators to walk using a custom optimization framework through which we imposed simple objectives, such as minimizing cost of transport while avoiding falling and injury, and maintaining head stability. We first generated gaits at prescribed speeds between 0.50 m/s and 2.00 m/s that reproduced experimentally observed kinematic, kinetic, and metabolic trends for walking. We then generated a gait at self-selected walking speed; quantitative comparisons between our simulation and experimental data for joint angles, joint moments, and ground reaction forces showed root-mean-squared errors of less than 1.6 standard deviations and normalized cross-correlations above 0.8 except for knee joint moment trajectories. Finally, we applied mild, moderate, and severe levels of muscle weakness or contracture to either the soleus (SOL) or gastrocnemius (GAS) or both of these major plantarflexors (PF) and retrained the model to walk at a self-selected speed. The model was robust to all deficits, finding a stable gait in all cases. Severe PF weakness caused the model to adopt a slower, "heel-walking" gait. Severe contracture of only SOL or both PF yielded similar results: the model adopted a "toe-walking" gait with excessive hip and knee flexion during stance. These results highlight how plantarflexor weakness and contracture may contribute to observed gait patterns.

PMID: [31589597](#)

6. [Impact of resistive therapy on gait parameters in children with cerebral palsy: systematic review and meta-analysis].

Collado-Garrido L, Paras-Bravo P, Calvo-Martin P, Santibanez M.

Rev Neurol. 2019 Oct 16;69(8):307-316. doi: 10.33588/rn.6908.2019081. [Article in Spanish; Abstract available in Spanish from the publisher]

INTRODUCTION: Cerebral palsy is one of the main causes of disability in childhood. Resistive therapy has proved to be

beneficial in increasing strength and motor function in these patients, but its impact on gait is not yet clear. AIM: To analyse the impact of resistive therapy on improving gait through a systematic review and meta-analysis. PATIENTS AND METHODS: A search was conducted in Medline, ISI Web of Knowledge and PEDro for clinical trials in which resistive therapy was used and at least one gait parameter was assessed. RESULTS: Nine controlled studies and one single-arm study were identified. In terms of pre-post difference, the overall intragroup effect was in favour of the intervention, with null heterogeneity (standardised mean difference: 0.32; 95% CI: 0.19-0.44). The standardised mean differences were also positive as they restricted each of the gait parameters analysed: 0.36, 0.35 and 0.22 for step cadence, gait speed and step length, respectively. As regards the difference between groups, the results showed high heterogeneity, and the mean difference was also favourable, especially for speed (7.3 cm/s; 95% CI: 2.67-11.92), cadence (5.66 steps; 95% CI: 1.86-9.46) and, to a lesser extent, step length (3.25 cm; 95% CI: -1.69 to 8.19). CONCLUSION: The results support the impact of resistive therapy on gait improvement, especially in terms of the gait speed and step cadence parameters.

PMID: [31588984](#)

7. Effect of physical therapy interventions on spatiotemporal gait parameters in children with cerebral palsy: a systematic review.

Corsi C, Santos MM, Moreira RFC, Dos Santos AN, de Campos AC, Galli M, Rocha NACF.

Disabil Rehabil. 2019 Oct 7:1-10. doi: 10.1080/09638288.2019.1671500. [Epub ahead of print]

Aim: To investigate the effect of physical therapy interventions on spatiotemporal gait parameters in children with cerebral palsy. Methods: Six databases were searched: PubMed, Embase, Web of Science, Science Direct, Lilacs, and Scopus. Two independent reviewers worked on primary study selection based on titles, abstracts, and full text reading. We included randomized controlled trials investigating the role of therapeutic interventions on gait kinematics in children with cerebral palsy. The independent reviewers extracted information about study population, intervention type, main outcomes, and methodological quality according to PEDro Scale. The body of evidence was synthesized through GRADE. Results: Twenty-six studies were found addressing the following treatment categories: functional electrical stimulation, transcranial stimulation, gait training, muscular strengthening, vibratory platform training, and serial casting. A moderate level of evidence was identified for vibratory platform training, gait training, transcranial stimulation (positive effect), and isolated muscle strengthening (negative effect) in relation to gait velocity. Electrical stimulation showed a moderate level of evidence regarding stride length. The evidence for other outcomes was of low or very low quality. Conclusion: Vibratory platform, gait training, electrical stimulation, and transcranial stimulation were effective to improve spatiotemporal gait parameters, especially velocity in children with cerebral palsy. Implication for rehabilitation Improvement and maintenance of gait of children with cerebral palsy is a great challenge to rehabilitation professionals Vibratory platform, gait training, electrical stimulation, and transcranial stimulation improve gait parameters. Isolated strength training was not effective to improve gait parameters in Cerebral Palsy. Long-term effect of most techniques on gait parameters until unclear.

PMID: [31588810](#)

8. Validity and reliability of the Dynamic Gait Index in children with hemiplegic cerebral palsy.

Evkaya A, Karadag-Saygi E, Karali Bingul D, Giray E.

Gait Posture. 2019 Sep 23;75:28-33. doi: 10.1016/j.gaitpost.2019.09.024. [Epub ahead of print]

BACKGROUND: Dynamic Gait Index (DGI) is a performance-based tool can be applied in a short time and evaluates dynamic balance and gait ability. RESEARCH QUESTION: Is the DGI valid and reliable for assessing gait and balance disorders in children with hemiplegic cerebral palsy (CP)? METHODS: Sixteen children with hemiplegic CP (5 females, 11 males; mean age 10y 3mo, SD 2y 7mo; range 6-14y; Gross Motor Function Classification System (GMFCS) levels I [n = 9], II [n = 7]) and 16 age-matched typically developing (TD) (8 females, 8 males; mean age 9y 9mo, SD 2y 6mo; range 6-14y) participated. The relationship between the DGI, Four-Square Step Test (FSST), Timed Up and Go Test (TUG) and Pediatric Berg Balance Scale (PBS) was analyzed. To determine the test-retest reliability, the DGI was performed twice and; for the inter-rater reliability, only DGI was reapplied by a different rater on the same day. Internal consistency was obtained by Cronbach- α value. Validity was tested by Spearman correlation coefficient and reliability was calculated by Intraclass correlation coefficient (ICC). RESULTS: There was a significant difference between hemiplegic CP and TD and between the children with GMFCS level I and II in the comparison of results of the DGI and other tests. All items on the DGI had appropriate internal consistency (Cronbach- α = 0.969). The test-retest (ICC = 0.970 CI(0.915- 0.990)) and inter-rater (ICC = 0.983 CI(0.882- 0.998)) reliabilities were found to be excellent. A negative, moderate correlation between FSST and DGI (r_s = -0.673, p = 0.004); a positive, high correlation between PBS (r_s = 0.724, p = 0.002) and DGI and a negative, high correlation between TUG and DGI (r_s = -0.828, p < 0.001) was detected. SIGNIFICANCE: DGI with features such as its feasibility in a short time, being simple but distinctive

and not requiring heavy equipment is a valid and reliable method in children with hemiplegic CP.

PMID: [31590067](#)

9. Determinants of motor rehabilitation satisfaction in people with cerebral palsy: a national survey in France (ESPaCe).

Cornec G, Drewnowski G, Desguerre I3, Toullet P4, Boivin J2, Bodoria M5, De La Cruz J6, Brochard S7; ESPaCe group.

Ann Phys Rehabil Med. 2019 Oct 3. pii: S1877-0657(19)30143-5. doi: 10.1016/j.rehab.2019.09.002. [Epub ahead of print]

BACKGROUND: User satisfaction is a key indicator of healthcare quality. **OBJECTIVE:** We aimed to identify factors associated with satisfaction with motor rehabilitation (MR) in children and adults with cerebral palsy at a national level, using determinants related to patient characteristics, healthcare organisation and practice features. **METHODS:** This study was part of ESPaCe, a national survey aimed at documenting the views of individuals with cerebral palsy and their families regarding MR services via a questionnaire, developed by a multidisciplinary group. The ESPaCe questionnaire included the Client Satisfaction Questionnaire (CSQ-8), whose total score was the primary outcome of this study. Survey participation was promoted nation-wide. The questionnaire could be completed by the person with cerebral palsy or their main carer. Analysis included the description of determinants across CSQ-8 quartiles and generalised linear modelling of the CSQ-8 score. **RESULTS:** From June 2016 to June 2017, 1010 eligible participants (354 children, 145 adolescents and 511 adults) responded to the questionnaire, and 750 completed the CSQ-8. Univariate analysis suggested that multiple factors affected satisfaction with MR. On multivariate sequential adjustment, the factors that decreased satisfaction (all $p < 0.001$) were being an adolescent, Gross Motor Function Classification System levels IV/V, frequent pain, receiving physiotherapy in private practice and poor access to a physiotherapist with specific CP training. Factors that increased satisfaction (all $p < 0.001$) were presence of an MR coordinator, exchanges between healthcare professionals, provision of information regarding MR organisation, and goal setting and effective pain management by the physiotherapist. Organisation and practice features improved the predictive ability of patient characteristics ($R^2 = 0.40$) (0.14). **CONCLUSION:** This study suggests that measures to improve the quality of healthcare for individuals with cerebral palsy should focus on improving pain management by the physiotherapist, establishing a therapeutic alliance, and greater provision of CP-specific practice education for healthcare professionals.

PMID: [31586683](#)

10. Randomised controlled pilot feasibility trial of an early intervention programme for young infants with neurodevelopmental impairment in Uganda: a study protocol.

Nampijja M, Webb E, Nanyunja C, Sadoo S, Nalugya R, Nyonyintono J, Muhumuza A, Ssekidde M, Katumba K, Magnusson B, Kabugo D, Cowan FM, Martinez-Biarge M, Zuurmond M, Morgan C, Lester D, Seeley J, Tann CJ.

BMJ Open. 2019 Oct 9;9(10):e032705. doi: 10.1136/bmjopen-2019-032705.

INTRODUCTION: Early intervention programmes (EIPs) for infants with neurodevelopmental impairment have been poorly studied especially in low-income settings. We aim to evaluate the feasibility and acceptability of a group participatory EIP, the 'ABAaNA EIP', for young children with neurodevelopmental impairment in Uganda. **METHODS AND ANALYSIS:** We will conduct a pilot feasibility, single-blinded, randomised controlled trial comparing the EIP with standard care across two study sites (one urban, one rural) in central Uganda. Eligible infants ($n = 126$, age 6-11 completed months) with neurodevelopmental impairment (defined as a developmental quotient < 70 on Griffiths Scales of Mental Development, and, or Hammersmith Infant Neurological Examination score < 60) will be recruited and randomised to the intervention or standard care arm. Intervention arm families will receive the 10-modular, peer-facilitated, participatory, community-based programme over 6 months. Recruited families will be followed up at 6 and 12 months after recruitment, and assessors will be blinded to the trial allocation. The primary hypothesis is that the ABAaNA EIP is feasible and acceptable when compared with standard care. Primary outcomes of interest are feasibility (number recruited and randomised at baseline) and acceptability (protocol violation of arm allocation and number of sessions attended) and family and child quality of life. Guided by the study aim, the qualitative data analysis will use a data-led thematic framework approach. The findings will inform scalability and sustainability of the programme. **ETHICS AND DISSEMINATION:** The trial protocol has been approved by the relevant Ugandan and UK ethics committees. Recruited families will give written informed consent and we will follow international codes for ethics and good clinical practice. Dissemination will be through peer-reviewed publications, conference presentations and public engagement. **TRIAL REGISTRATION NUMBER:** ISRCTN44380971; protocol version 3.0, 19th February 2018.

PMID: [31601606](#)

11. Spasticity and pain in adults with cerebral palsy.

Flanigan M, Gaebler-Spira D, Kocherginsky M, Garrett A, Marciniak C.

Dev Med Child Neurol. 2019 Oct 10. doi: 10.1111/dmcn.14368. [Epub ahead of print]

AIM: To evaluate whether spasticity measures are related to pain in adults with cerebral palsy (CP). **METHOD:** This cross-sectional study recruited individuals aged 16 to 89 years with a diagnosis of CP. Participants completed the Penn Spasm Frequency Scale (PSFS), Brief Pain Inventory (BPI), and PROMIS Pain Interference measures. The Modified Ashworth Scale (MAS) and Tardieu spasticity angles of six joints were rated and summed to composite MAS and Tardieu scores for each participant. Associations between spasticity and pain measures were evaluated. **RESULTS:** Forty-seven participants (27 females, 20 males) with a mean age of 35 years 7 months (range 18-77y) spanning all Gross Motor Function Classification System (GMFCS) levels were included. Twenty-six participants reported their average pain level on BPI as greater than 0 over the past week (median pain level 4.0). Median PSFS was 1.0 (range 0.0-1.0) and this correlated with average BPI and Pain Interference T scores (median 40.7; $\rho=0.33$ and $\rho=0.31$ respectively [both $p=0.01$]). When adjusted for pain medication use and age, MAS correlated with BPI ($\rho=0.30$; $p=0.04$). Other pain and spasticity measures, or GMFCS level, were not significantly related with pain interference or BPI rating. Age was weakly associated with BPI (slope=0.10; $p<0.01$). **INTERPRETATION:** PROMIS Pain Interference was lower than population-based norms. Patient-rated spasm frequency demonstrated better association with pain levels and interference than physician-rated MAS and Tardieu. **WHAT THIS PAPER ADDS:** Pain was not associated with Gross Motor Function Classification System level. Pain increased with age, as anticipated. Self-reported spasm scores were associated with increased pain in contrast to clinical examination scales. Adjusted, summed spasticity on the Modified Ashworth Scale was associated with pain scores on the Brief Pain Inventory. Although pain is experienced by adults with cerebral palsy, pain did not interfere with activities.

PMID: [31602643](#)**12. Obstructive Sleep Apnea in Children With Autism.**

Tomkies A, Johnson RF, Shah G, Caraballo M, Evans P, Mitchell RB.

J Clin Sleep Med. 2019 Oct 15;15(10):1469-1476. doi: 10.5664/jcsm.7978.

STUDY OBJECTIVES: To describe the demographic and clinical characteristics of children with autism spectrum disorder (ASD) referred for polysomnography (PSG) and to look for predictors of obstructive sleep apnea (OSA) and severe OSA in these children. **METHODS:** This is a retrospective case series of children ages 2 to 18 years who underwent PSG between January 2009 and February 2015. Children were excluded if they had major comorbidities, prior tonsillectomy, or missing data. The following information was collected: age, sex, race, height, weight, tonsil size, and prior diagnosis of allergies, asthma, gastroesophageal reflux disease, seizure disorder, developmental delay, cerebral palsy, or attention deficit hyperactivity disorder. Predictors of OSA were evaluated. **RESULTS:** A total of 45 children were included with a mean (standard deviation [SD]) age of 6.1 years (2.8). The patients were 80% male, 49% Hispanic, 27% African American, 22% Caucasian, and 2.2% other. Of these children 26 (58%) had OSA (apnea-hypopnea index [AHI] > 1 event/h) and 15 (33%) were obese (body mass index, body mass index z-score \geq 95th percentile). The mean (SD) AHI was 7.7 (15.0) events/h (range 1.0-76.6). A total of 9 (20%) had severe OSA (AHI \geq 10 events/h). There were no demographic or clinical predictors of OSA in this group. However, increasing weight served as a predictor of severe OSA and African American or Hispanic children were more likely obese. **CONCLUSIONS:** The absence of demographic or clinical predictors of OSA supports using general indications for PSG in children with ASD.

PMID: [31596212](#)**13. Transition from paediatric to adult care in adolescents with neurological diseases and handicap.**

Chabrol B, Milh M.

Rev Neurol (Paris). 2019 Oct 7. pii: S0035-3787(19)30857-4. doi: 10.1016/j.neurol.2019.09.001. [Epub ahead of print]

The transfer of adolescents from paediatric care to adult health facilities is often difficult for the patients and their families and can lead to a breakdown in medical follow-up and therefore serious complications. Existing recommendations for the successful transition of patients with chronic disorders do not specifically address patients with handicap. Preparations for the transfer must be made well in advance. They must aim to achieve the autonomisation of adolescents by making them responsible and providing them with the knowledge that will enable them to manage their care themselves, the know-how to

react appropriately if there is any change in their condition, and to move comfortably within the adult health system. This requires the active participation of the patient, his or her family and the paediatric and adult care teams. It involves multidisciplinary management plus the production and maintenance of an educational therapy programme. Finally, the identification of doctors trained in handicap, relevant sub-specialists and even expert patients could enable improvements in the continuum of complete and appropriate care for these patients within adult medicine.

PMID: [31601451](#)

14. Improving the Health of Individuals With Cerebral Palsy: Protocol for the Multidisciplinary Research Program MOVING ON WITH CP.

Alriksson-Schmidt A, Jarl J, Rodby-Bousquet E, Lundkvist Josenby A, Westbom L, Himmelmann K, Stadskleiv K, Ödman P, Svensson I, Antfolk C, Malesevic N, Jeglinsky I, Saha S, Hägglund G.

JMIR Res Protoc. 2019 Oct 9;8(10):e13883. doi: 10.2196/13883.

BACKGROUND: Cerebral palsy (CP) is one of the most common early onset disabilities globally. The causative brain damage in CP is nonprogressive, yet secondary conditions develop and worsen over time. Individuals with CP in Sweden and most of the Nordic countries are systematically followed in the national registry and follow-up program entitled the Cerebral Palsy Follow-Up Program (CPUP). CPUP has improved certain aspects of health care for individuals with CP and strengthened collaboration among professionals. However, there are still issues to resolve regarding health care for this specific population. **OBJECTIVE:** The overall objectives of the research program MOVING ON WITH CP are to (1) improve the health care processes and delivery models; (2) develop, implement, and evaluate real-life solutions for Swedish health care provision; and (3) evaluate existing health care and social insurance benefit programs and processes in the context of CP. **METHODS:** MOVING ON WITH CP comprises 9 projects within 3 themes. Evaluation of Existing Health Care (Theme A) consists of registry studies where data from CPUP will be merged with national official health databases, complemented by survey and interview data. In Equality in Health Care and Social Insurance (Theme B), mixed methods studies and registry studies will be complemented with focus group interviews to inform the development of new processes to apply for benefits. In New Solutions and Processes in Health Care Provision (Theme C), an eHealth (electronic health) procedure will be developed and tested to facilitate access to specialized health care, and equipment that improves the assessment of movement activity in individuals with CP will be developed. **RESULTS:** The individual projects are currently being planned and will begin shortly. Feedback from users has been integrated. Ethics board approvals have been obtained. **CONCLUSIONS:** In this 6-year multidisciplinary program, professionals from the fields of medicine, social sciences, health sciences, and engineering, in collaboration with individuals with CP and their families, will evaluate existing health care, create conditions for a more equal health care, and develop new technologies to improve the health care management of people with CP. **INTERNATIONAL REGISTERED REPORT IDENTIFIER (IRRID):** DERR1-10.2196/13883.

PMID: [31599737](#)

15. Cerebral Palsy: Early Markers of Clinical Phenotype and Functional Outcome.

Einspieler C, Bos AF, Kriber-Tomantschger M, Alvarado E, Barbosa VM, Bertocelli N, Burger M, Chorna O, Del Secco S, DeRegnier RA, Hüning B, Ko J, Lucaccioni L, Maeda T, Marchi V, Martín E, Morgan C, Mutlu A, Nogolová A, Pansy J, Peyton C, Pokorný FB, Prinsloo LR, Ricci E, Saini L, Scheuchenegger A, Silva CRD, Soloveichick M, Spittle AJ, Toldo M, Utsch F, van Zyl J, Viñals C, Wang J, Yang H, Yardımcı-Lokmanoğlu BN, Cioni G, Ferrari F, Guzzetta A, Marschik PB.

J Clin Med. 2019 Oct 4;8(10). pii: E1616. doi: 10.3390/jcm8101616.

The Prechtl General Movement Assessment (GMA) has become a cornerstone assessment in early identification of cerebral palsy (CP), particularly during the fidgety movement period at 3-5 months of age. Additionally, assessment of motor repertoire, such as antigravity movements and postural patterns, which form the Motor Optimality Score (MOS), may provide insight into an infant's later motor function. This study aimed to identify early specific markers for ambulation, gross motor function (using the Gross Motor Function Classification System, GMFCS), topography (unilateral, bilateral), and type (spastic, dyskinetic, ataxic, and hypotonic) of CP in a large worldwide cohort of 468 infants. We found that 95% of children with CP did not have fidgety movements, with 100% having non-optimal MOS. GMFCS level was strongly correlated to MOS. An MOS > 14 was most likely associated with GMFCS outcomes I or II, whereas GMFCS outcomes IV or V were hardly ever associated with an MOS > 8. A number of different movement patterns were associated with more severe functional impairment (GMFCS III-V), including atypical arching and persistent cramped-synchronized movements. Asymmetrical segmental movements were strongly associated with unilateral CP. Circular arm movements were associated with dyskinetic CP. This study demonstrated that use of the MOS contributes to understanding later CP prognosis, including early markers for type and severity.

PMID: [31590221](#)

16. [Children born too soon and outcomes].

Ådén U, Sävman K, Norman M.

Lakartidningen. 2019 Oct 7;116. pii: FR6D. [Article in Swedish]

Advances in perinatal intensive care have resulted in increased survival of the most immature preterm infants (born before 28 gestational weeks) and these new survivors are now entering school. While the clear majority of all children born preterm have a normal development, the extremely preterm infant is at a considerable risk for long term disabilities and rates of adverse development increase at lower gestational ages. Lung function is commonly affected in children born extremely preterm, and many have treatment for obstructive symptoms. The incidences of major neuromotor impairments, i.e. cerebral palsy, are low, but there is an increasing awareness of common cognitive and neuropsychiatric problems in extremely preterm children and their special needs in school. Extremely preterm children therefore need follow up of lung function and neurodevelopment at least until school start.

PMID: [31593283](#)**17. [Mechanisms of brain injury of the premature baby].**

Cerisola A, Baltar F, Ferrán C, Turcatti E.

Medicina (B Aires). 2019;79 Suppl 3:10-14. [Article in Spanish; Abstract available in Spanish from the publisher]

Preterm birth is one of the main country health indicators. It is associated with high mortality and significant morbidity in preterm newborns with cerebral palsy and potential long-term neurodevelopmental disabilities like cognitive and learning problems. The main lesions could be: a) white matter injuries, generally associated with cortical and other regions of grey matter neuronal-axonal disturbances; b) intracranial hemorrhage that includes germinal matrix, intraventricular and parenchymal, c) cerebellum injuries. The white matter lesions include cystic and non-cystic (with microscopic focal necrosis) periventricular leukomalacia and non-necrotic diffuse white matter injury. Multiple etiologic factors are associated with these injuries. Anatomical and physiological characteristics of periventricular vascular structures predispose white matter to cerebral ischemia and, interacting with infection/inflammation factors, activate microglia, generating oxidative stress (mediated by free oxygen and nitrogen radicals), pro-inflammatory cytokine and glutamate toxicity, energetic failure and vascular integrity disturbances. All these factors lead to a particular vulnerability of pre-oligodendrocytes that will affect myelination. Hypoxia-ischemia also may produce selective neuronal necrosis in different cerebral regions. Germinal matrix is a highly vascularized zone beneath ependymal or periventricular region that constitutes a capillary bed with a particular structural fragility that predispose it to hemorrhage.

PMID: [31603836](#)**18. Diagnosis of Bilirubin Encephalopathy in Preterm Infants with Dyskinetic Cerebral Palsy.**

Kitai Y, Hirai S, Okuyama N, Hirotsune M, Mizutani S, Ogura K, Ohmura K, Okumura A, Arai H.

Neonatology. 2019 Oct 4:1-7. doi: 10.1159/000502777. [Epub ahead of print]

INTRODUCTION: Very preterm infants are susceptible to bilirubin neurotoxicity, the signs of which are unclear during early infancy. We investigated children born preterm and later diagnosed with bilirubin encephalopathy (BE) to gain insights into accurate early diagnosis. **METHODS:** We identified 93 children born preterm and clinically diagnosed with BE who visited our hospital between 2006 and 2018. Perinatal history, findings of auditory brainstem response (ABR), brain magnetic resonance imaging (MRI), and functional outcomes were investigated retrospectively based on chart review. **RESULTS:** The mean gestational age and birth weights were 27.2 weeks and 991 g, respectively. During the neonatal period, only 3% (2/71) had exchange transfusions, and none were diagnosed with acute BE. ABR was abnormal in 64% (51/80), but the majority (34/51) required no hearing aids. Brain MRI taken between 6 and 18 months of age revealed bilateral T2 hyperintensity of the globi pallidi in 91% (60/66); subsequently, the rate decreased with age. Functional communication outcomes were markedly superior to gross motor and hand function outcomes. **CONCLUSION:** For early diagnosis of BE, brain MRI is recommended at a corrected age of between 6 and 18 months, especially for those with abnormal ABR during early infancy, and even with no apparent history of marked neonatal hyperbilirubinemia.

PMID: [31587006](#)

19. Severe skull deformity in a child with shunted hydrocephalus.

Tabibkhoeei A, Taheri M, Ebrahimniya F.

Br J Neurosurg. 2019 Oct 10;1-4. doi: 10.1080/02688697.2019.1671954. [Epub ahead of print]

Introduction: We report a rare case of skull deformity in a child with shunted hydrocephalus. **Case report:** A 2.5-year-old boy with a history of cerebral palsy (CP), shunted hydrocephalus and seizures was admitted to our children's hospital with status epilepticus. This was initially controlled with anesthesia. He referred to us intubated. Head examination found a skull deformity (brachycephaly). Head CT revealed a remarkable deformity and bilateral chronic subdural hematomas. MRI demonstrated voluminous extra-axial masses over the cerebral convexities with high signal on T1 and T2 sequences in favor of hematoma. The patient had a bilateral frontoparietal craniotomy and evacuation of subdural/epidural hematomas. Neurological status improved on the next day but because of co-existent medical problems, the patients gradually deteriorated and died. **Conclusion:** Shunt-induced craniosynostosis is rarely seen nowadays thanks to early detection and treatment of infantile hydrocephalus. But in the setting of child neglect or low socioeconomic culture, it can occur. Although it usually results in a skull deformity similar to the primary craniosynostosis such as scaphocephaly, brachycephaly, it can induce a macrocephalic skull and subsequently associated chronic haematomas.

PMID: [31599176](#)**20. Impact of peri-intraventricular haemorrhage and periventricular leukomalacia in the neurodevelopment of preterms: A systematic review and meta-analysis.**

Gotardo JW, Volkmer NFV, Stangler GP, Dornelles AD, Bohrer BBA, Carvalho CG.

PLoS One. 2019 Oct 10;14(10):e0223427. doi: 10.1371/journal.pone.0223427. eCollection 2019.

CONTEXT: Whether all degrees of periventricular leukomalacia (PVL) and peri-intraventricular haemorrhage (PIVH) have a negative impact on neurodevelopment. **OBJECTIVE:** To determine the impact of PVL and PIVH in the incidence of cerebral palsy, sensorineural impairment and development scores in preterm neonates. Registered in PROSPERO (CRD42017073113). **DATA SOURCES:** PubMed, Embase, SciELO, LILACS, and Cochrane databases. **STUDY SELECTION:** Prospective cohort studies evaluating neurodevelopment in children born preterm which performed brain imaging in the neonatal period. **DATA EXTRACTION:** Two independent researchers extracted data using a predesigned data extraction sheet. **STATISTICAL METHODS:** A random-effects model was used, with Mantel-Haenszel approach and a Sidik-Jonkman method for the estimation of variances, combined with Hartung-Knapp-Sidik-Jonkman correction. Heterogeneity was assessed through the I² statistic and sensitivity analysis were performed when possible. No funnel plots were generated but publication bias was discussed as a possible limitation. **RESULTS:** Our analysis concluded premature children with any degree of PIVH are at increased risk for cerebral palsy (CP) when compared to children with no PIVH (3.4, 95% CI 1.60-7.22; 9 studies), a finding that persisted on subgroup analysis for studies with mean birth weight of less than 1000 grams. Similarly, PVL was associated with CP, both in its cystic (19.12, 95% CI 4.57-79.90; 2 studies) and non-cystic form (9.27, 95% CI 5.93-14.50; 2 studies). We also found children with cystic PVL may be at risk for visual and hearing impairment compared to normal children, but evidence is weak. **LIMITATIONS:** Major limitations were the lack of data for PVL in general, especially for the outcome of neurodevelopment, the high heterogeneity among methods used to assess neurodevelopment and the small number of studies, which led to meta-analysis with high heterogeneity and wide confidence intervals. **CONCLUSIONS:** There was no evidence supporting the hypothesis that PIVH causes impairment in neuropsychomotor development in our meta-analysis, but review of newer studies show an increased risk for lower intelligence scores in children with severe lesions, both PIVH and PVL. There is evidence to support the hypothesis that children with any degree of PIVH, especially those born below 1000 grams and those with severe haemorrhage, are at increased risk of developing CP, as well as children with PVL, both cystic and non-cystic.

PMID: [31600248](#)**21. Clinical outcomes of pallidal deep brain stimulation for dystonia implanted using intraoperative MRI.**

Sharma VD, Bezchlibnyk YB, Isbaine F, Naik KB, Cheng J, Gale JT, Miocinovic S, Buetefisch C, Factor SA, Willie JT, Boulis NM, Wichmann T, DeLong MR, Gross RE.

J Neurosurg. 2019 Oct 11:1-13. doi: 10.3171/2019.6.JNS19548. [Epub ahead of print]

OBJECTIVE: Lead placement for deep brain stimulation (DBS) using intraoperative MRI (iMRI) relies solely on real-time intraoperative neuroimaging to guide electrode placement, without microelectrode recording (MER) or electrical stimulation.

There is limited information, however, on outcomes after iMRI-guided DBS for dystonia. The authors evaluated clinical outcomes and targeting accuracy in patients with dystonia who underwent lead placement using an iMRI targeting platform. **METHODS:** Patients with dystonia undergoing iMRI-guided lead placement in the globus pallidus pars internus (GPi) were identified. Patients with a prior ablative or MER-guided procedure were excluded from clinical outcomes analysis. Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) scores and Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) scores were assessed preoperatively and at 6 and 12 months postoperatively. Other measures analyzed include lead accuracy, complications/adverse events, and stimulation parameters. **RESULTS:** A total of 60 leads were implanted in 30 patients. Stereotactic lead accuracy in the axial plane was 0.93 ± 0.12 mm from the intended target. Nineteen patients (idiopathic focal, $n = 7$; idiopathic segmental, $n = 5$; DYT1, $n = 1$; tardive, $n = 2$; other secondary, $n = 4$) were included in clinical outcomes analysis. The mean improvement in BFMDRS score was $51.9\% \pm 9.7\%$ at 6 months and $63.4\% \pm 8.0\%$ at 1 year. TWSTRS scores in patients with predominant cervical dystonia ($n = 13$) improved by $53.3\% \pm 10.5\%$ at 6 months and $67.6\% \pm 9.0\%$ at 1 year. Serious complications occurred in 6 patients (20%), involving 8 of 60 implanted leads (13.3%). The rate of serious complications across all patients undergoing iMRI-guided DBS at the authors' institution was further reviewed, including an additional 53 patients undergoing GPi-DBS for Parkinson disease. In this expanded cohort, serious complications occurred in 11 patients (13.3%) involving 15 leads (10.1%). **CONCLUSIONS:** Intraoperative MRI-guided lead placement in patients with dystonia showed improvement in clinical outcomes comparable to previously reported results using awake MER-guided lead placement. The accuracy of lead placement was high, and the procedure was well tolerated in the majority of patients. However, a number of patients experienced serious adverse events that were attributable to the introduction of a novel technique into a busy neurosurgical practice, and which led to the revision of protocols, product inserts, and on-site training.

PMID: [31604331](#)

22. Utilization of electromyography during selective obturator neurotomy to treat spastic cerebral palsy accompanied by scissors gait.

Ren S, Liu W, Wang L, Guo C, Pang Q.

J Integr Neurosci. 2019 Sep 30;18(3):305-308. doi: 10.31083/j.jin.2019.03.146.

Selective obturator neurotomy is a commonly used neurosurgical intervention for spastic cerebral palsy with scissors gait. Here we report the use of surface electromyography to assess the accuracy and effect of selective obturator neurotomy procedures. Selective obturator neurotomy was carried out on 18 patients while using intraoperative electromyography. Contractions of adductor muscles were recorded by electromyography before and after neurotomy and assessed using root mean square and integrated electromyography tests. Passive and voluntary movements were recorded for all patients. Our results show that adductor spasms and adductive deformity of hip were improved in all patients with spastic cerebral palsy. Adductor muscle spatiality was improved significantly, confirmed by a significant decrease in the values of root mean square and integrated electromyography in both passive and voluntary movements after surgery. We show that electromyography is an effective tool for accurately and safely targeting nerve tracts during selective obturator neurotomy. Thus, we demonstrate a valuable noninvasive method to objectively evaluate the effect of treatment in spastic cerebral palsy patients.

PMID: [31601080](#)

23. Dorsal root ganglion axons facilitate and guide cortical neural outgrowth: In vitro modeling of spinal cord injury axonal regeneration.

Xu ZX, Albayar A, Dollé JP, Hansel G, Bianchini J, Sullivan PZ, Kacy Cullen D, Smith DH, Ozturk AK.

Restor Neurol Neurosci. 2019 Sep 28. doi: 10.3233/RNN-190933. [Epub ahead of print]

BACKGROUND: Spinal cord injury (SCI) patients represent a heterogeneous group, with injuries ranging from partial compression to complete transection. Patients with complete injuries are unlikely to exhibit recovery and suffer from paralysis as well as the loss of bowel and bladder function. One treatment option is the formation of a bridge through a lesion site, whereby transplanted cells or biocompatible scaffolds guide the regenerating axons across the site of injury. Moreover, the viability of transplanted dorsal root ganglia (DRGs) into rat spinal cord has been previously demonstrated. **OBJECTIVE:** We aim to demonstrate the feasibility of using DRG axons as a bridging tool to help guide the axonal growth of cortical neurons. **METHODS:** Cortical neurons were isolated from embryonic rats and two aggregated populations were cultured at increasing distances in isolation and in a co-culture with DRG explants. Growth rates of the sprouting axons and connections between the two populations were observed over a period of twelve days. **RESULTS:** DRG explants demonstrated the ability to grow robust axonal connections that can connect two explants separated by up to 10mm, however, CNAs could not achieve connections in distances greater than 2mm. The co-culture of CNAs with DRG explants facilitated axonal growth between two populations of CNAs at distances they cannot otherwise traverse. **CONCLUSIONS:** Our findings support the use of DRG axons to facilitate

the growth of cortical neurons in a process of axon-facilitated axon regeneration. We believe these results could have implications for the treatment of SCI.

PMID: [31594262](#)

24. Controlled Trial of Two Incremental Milk-Feeding Rates in Preterm Infants.

Dorling J, Abbott J, Berrington J, Bosiak B, Bowler U, Boyle E, Embleton N, Hewer O, Johnson S, Juszczak E, Leaf A, Linsell L, McCormick K, McGuire W, Omar O, Partlett C, Patel M, Roberts T, Stenson B, Townend J; SIFT Investigators Group.

N Engl J Med. 2019 Oct 10;381(15):1434-1443. doi: 10.1056/NEJMoa1816654.

BACKGROUND: Observational data have shown that slow advancement of enteral feeding volumes in preterm infants is associated with a reduced risk of necrotizing enterocolitis but an increased risk of late-onset sepsis. However, data from randomized trials are limited. **METHODS:** We randomly assigned very preterm or very-low-birth-weight infants to daily milk increments of 30 ml per kilogram of body weight (faster increment) or 18 ml per kilogram (slower increment) until reaching full feeding volumes. The primary outcome was survival without moderate or severe neurodevelopmental disability at 24 months. Secondary outcomes included components of the primary outcome, confirmed or suspected late-onset sepsis, necrotizing enterocolitis, and cerebral palsy. **RESULTS:** Among 2804 infants who underwent randomization, the primary outcome could be assessed in 1224 (87.4%) assigned to the faster increment and 1246 (88.7%) assigned to the slower increment. Survival without moderate or severe neurodevelopmental disability at 24 months occurred in 802 of 1224 infants (65.5%) assigned to the faster increment and 848 of 1246 (68.1%) assigned to the slower increment (adjusted risk ratio, 0.96; 95% confidence interval [CI], 0.92 to 1.01; P = 0.16). Late-onset sepsis occurred in 414 of 1389 infants (29.8%) in the faster-increment group and 434 of 1397 (31.1%) in the slower-increment group (adjusted risk ratio, 0.96; 95% CI, 0.86 to 1.07). Necrotizing enterocolitis occurred in 70 of 1394 infants (5.0%) in the faster-increment group and 78 of 1399 (5.6%) in the slower-increment group (adjusted risk ratio, 0.88; 95% CI, 0.68 to 1.16). **CONCLUSIONS:** There was no significant difference in survival without moderate or severe neurodevelopmental disability at 24 months in very preterm or very-low-birth-weight infants with a strategy of advancing milk feeding volumes in daily increments of 30 ml per kilogram as compared with 18 ml per kilogram. (Funded by the Health Technology Assessment Programme of the National Institute for Health Research; SIFT Current Controlled Trials number, ISRCTN76463425.).

PMID: [31597020](#)

25. [Expert consensus on etiological diagnostic strategies for cerebral palsy].

Subspecialty Group of Rehabilitation, the Society of Pediatrics, Chinese Medical Association.

Zhonghua Er Ke Za Zhi. 2019 Oct 2;57(10):746-751. doi: 10.3760/cma.j.issn.0578-1310.2019.10.004. [Article in Chinese; Abstract available in Chinese from the publisher]

PMID: [31594059](#)

Prevention and Cure

26. Systematic review of controlled clinical studies using umbilical cord blood for regenerative therapy: Identifying barriers to assessing efficacy.

Aziz J, Liao G, Adams Z, Rizk M, Shorr R, Allan DS.

Cytotherapy. 2019 Oct 3. pii: S1465-3249(19)30843-6. doi: 10.1016/j.jcyt.2019.08.004. [Epub ahead of print]

Clinical use of umbilical cord blood (UCB) for novel indications in regenerative therapy continues to rise, however, whether new indications are proven is less clear. An updated systematic search of the literature, focusing only on controlled clinical studies, is needed to properly assess potential efficacy. After updating our systematic search to April 1, 2018 (PROSPERO protocol CRD42016040157), a total of 16 studies were identified that addressed the treatment of cerebral palsy (four studies), type 1 diabetes (three studies), and nine other novel potential indications where only a single controlled study was identified. In the four controlled studies of patients with cerebral palsy, three used allogeneic cells and reported greater improvement in motor-related scores at 1, 3 and 6 months compared with controls. The results were mixed for other scores at other time points,

including additional measures of mental and motor function. One study of autologous UCB treatment reported an improvement in motor function scores at 12 months compared with controls. In the three controlled studies of type 1 diabetes, two studies used autologous cells whereas one used allogeneic cord blood cells to "educate" autologous lymphocytes. Taken together, there was no clear difference in HbA1c levels or daily insulin requirements between treated patients and controls. For the nine published reports with a single controlled study, eight used allogeneic UCB cells and seven infused mesenchymal stromal cells derived from UCB. All but one study reported benefit. Many other published reports that lack a control group were not included in our analysis. More controlled studies are needed that use similar approaches regarding cell source and outcome measures at similar time points. Pooled estimates of results from multiple studies will be essential as published studies remain modest in size. Patients should continue to be enrolled in clinical trials because there are no novel potential indications remain unproven.

PMID: [31587876](#)