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## Interventions and Management

### 1. Neurology. 2016 Mar 30. pii: 10.1212/WNL.0000000000002646. [Epub ahead of print]

#### **Brain stimulation and constraint for perinatal stroke hemiparesis: The PLASTIC CHAMPS Trial.**

Kirton A, Andersen J, Herrero M, Nettel-Aguirre A, Carsolio L, Damji O, Keess J, Mineyko A, Hodge J, Hill MD.

**OBJECTIVE:** To determine whether the addition of repetitive transcranial magnetic stimulation (rTMS) and/or constraint-induced movement therapy (CIMT) to intensive therapy increases motor function in children with perinatal stroke and hemiparesis. **METHODS:** A factorial-design, blinded, randomized controlled trial (clinicaltrials.gov/NCT01189058) assessed rTMS and CIMT effects in hemiparetic children (aged 6-19 years) with MRI-confirmed perinatal stroke. All completed a 2-week, goal-directed, peer-supported motor learning camp randomized to daily rTMS, CIMT, both, or neither. Primary outcomes were the Assisting Hand Assessment and the Canadian Occupational Performance Measure at baseline, and 1 week, 2 and 6 months postintervention. Outcome assessors were blinded to treatment. Interim safety analyses occurred after 12 and 24 participants. Intention-to-treat analysis examined treatment effects over time (linear mixed effects model). **RESULTS:** All 45 participants completed the trial. Addition of rTMS, CIMT, or both doubled the chances of clinically significant improvement. Assisting Hand Assessment gains at 6 months were additive and largest with rTMS + CIMT ( $\beta$  coefficient = 5.54 [2.57-8.51],  $p = 0.0004$ ). The camp alone produced large improvements in Canadian Occupational Performance Measure scores, maximal at 6 months (Cohen  $d = 1.6$ ,  $p = 0.002$ ). Quality-of-life scores improved. Interventions were well tolerated and safe with no decrease in function of either hand. **CONCLUSIONS:** Hemiparetic children participating in intensive, psychosocial rehabilitation programs can achieve sustained functional gains. Addition of CIMT and rTMS increases the chances of improvement. **CLASSIFICATION OF EVIDENCE:** This study provides Class II evidence that combined rTMS and CIMT enhance therapy-induced functional motor gains in children with stroke-induced hemiparetic cerebral palsy.

[PMID: 27029628](#)

### 2. Pak J Med Sci. 2016 Jan-Feb;32(1):181-4. doi: 10.12669/pjms.321.8491.

#### **Effectiveness of Constraint induced movement therapy as compared to bimanual therapy in Upper motor function outcome in child with hemiplegic Cerebral palsy.**

Zafer H, Amjad I, Malik AN, Shaukat E.

**OBJECTIVE:** This study aims at determining the effectiveness of constraint induced movement therapy as compared to bimanual therapy for improving functional status in children with hemiplegic cerebral palsy. **METHODS:** This study was a randomized control trial, children ( $n = 20$ ) with spastic hemiplegic cerebral palsy was randomly allocated to CIMT (constraint induced movement therapy) and BMT (bimanual therapy) group. The children with spastic hemiplegia, age between 1.5 and 12 year and having 10 degrees of wrist extension and 10 degrees of finger extension were included in study. Treatment regime was two hours of daily training six days a week for two weeks. Constraint was applied to CIMT group for six hours. The

outcome tool QUEST was used for baseline and post treatment assessment. RESULT: CIMT had superior outcome as compared to BMT in improving functional status ( $p=0.007$ ). On QUEST tool grasp and dissociated movements results were significant ( $p=0.005$ ) and ( $p=0.028$ ) respectively. Weight bearing and protective extension resulted in no significant outcome ( $p=0.080$ ) and ( $p=0.149$ ) respectively. Dissociated movements and grasp are significantly improved but there is no difference for weight bearing and protective extension in CIMT treated group as compared to BMT treated group. CONCLUSION: CIMT approach is better in improving functional status of child with cerebral palsy as compared to BMT. Significant improvement in grasp and dissociated movement is noted in group of CIMT while there was no significant improvement in weight bearing and protective extension in CIMT group when compared to BMT. CIMT is considered the appropriate treatment approach for unilateral conditions while BMT for bilateral conditions.

[PMID: 27022371](#)

### **3. Dev Med Child Neurol. 2016 Mar 29. doi: 10.1111/dmcn.13105. [Epub ahead of print]**

#### **Effectiveness of motor interventions in infants with cerebral palsy: a systematic review.**

Morgan C, Darrah J, Gordon AM, Harbourne R, Spittle A, Johnson R, Fetters L.

AIM: To systematically review the evidence on the effectiveness of motor interventions for infants from birth to 2 years with a diagnosis of cerebral palsy or at high risk of it. METHOD: Relevant literature was identified by searching journal article databases (PubMed, Embase, CINAHL, Cochrane, Web of Knowledge, and PEDro). Selection criteria included infants between the ages of birth and 2 years diagnosed with, or at risk of, cerebral palsy who received early motor intervention. RESULTS: Thirty-four studies met the inclusion criteria, including 10 randomized controlled trials. Studies varied in quality, interventions, and participant inclusion criteria. Neurodevelopmental therapy was the most common intervention investigated either as the experimental or control assignment. The two interventions that had a moderate to large effect on motor outcomes (Cohen's effect size  $>0.7$ ) had the common themes of child-initiated movement, environment modification/enrichment, and task-specific training. INTERPRETATION: The published evidence for early motor intervention is limited by the lack of high-quality trials. There is some promising evidence that early intervention incorporating child-initiated movement (based on motor-learning principles and task specificity), parental education, and environment modification have a positive effect on motor development. Further research is crucial.

[PMID: 27027732](#)

### **4. Indian Pediatr. 2016 Mar 3;53(3):259-60.**

#### **Developmental Dysplasia of Spastic Hip in Children with Cerebral Palsy in Southern India.**

Vykuntaraju KN, Manohar V, Lakshman RR, Ramaswamy P.

We studied the proportion of developmental dysplasia of spastic hip in children with cerebral palsy. Children with cerebral palsy aged 2-12 years were enrolled. Migration percentage was measured on pelvic radiographs. Hip dysplasia was seen in 15 (12.7%) children.

[PMID: 27029696](#)

### **5. Dev Med Child Neurol. 2016 Mar;58 Suppl 4:78-82. doi: 10.1111/dmcn.13046.**

#### **Lessons learned from studying the functional impact of adaptive seating interventions for children with cerebral palsy.**

Ryan SE.

Little empirical evidence exists about the effectiveness of assistive technology interventions for children with cerebral palsy (CP) to inform clinical practice. This article reviews what we know about the functional impact of adaptive seating interventions - a common assistive technology type recommended for children with CP. A contemporary assistive technology outcomes framework is considered as a way to model the temporality and measure the effects of seating interventions and moderating cofactors. Three research studies are profiled to illustrate different research methods, measurement approaches, and follow-up periods to learn about adaptive seating outcomes. Recommendations for future research include the adoption of

common measurement indicators, consideration of quality assessment criteria, and the use of varied methodologies to generate new knowledge about functional outcomes. It is suggested that the proposed strategies will lead to new understandings, clinical applications, and ultimately improvements in the everyday lives of children with CP and their families.

[PMID: 27027612](#)

## 6. *Dev Neurorehabil.* 2016 Mar 28:1-11. [Epub ahead of print]

### **Clinical tools designed to assess motor abilities in children with cerebral palsy.**

Pavão SL, Silva FP, Dusing SC, Rocha NA.

**OBJECTIVE:** This systematic review aimed to list the tools used by rehabilitation professionals to test motor abilities in children with cerebral palsy (CP), to determine if these tools have psychometric properties specifically measured for CP, and to identify the main characteristics of these tools. **METHOD:** Web of Science, PEDro, PubMed/MEDLINE, Science Direct, and SciELO databases were searched to identify the tools. PubMed/MEDLINE was then searched to identify the studies assessing those tools' psychometric properties. The agreement-based standards for the selection of health measurement tools and the Terwee criteria were used to assess the quality and the results of each included study, respectively. **RESULTS:** Eighteen tools were identified. The psychometric properties of many of the tools used with children with CP have not been evaluated for this population. **CONCLUSION:** The psychometric properties evaluated often have a poor methodological quality of measurement. Overall, we suggest the tools with most empirical support to evaluate children with CP.

[PMID: 27019351](#)

## 7. *Disabil Rehabil.* 2016 Mar 30:1-12. [Epub ahead of print]

### **What is the evidence for managing tone in young children with, or at risk of developing, cerebral palsy: a systematic review.**

Ward R, Reynolds JE, Bear N, Elliott C, Valentine J.

**BACKGROUND AND OBJECTIVES:** To conduct a systematic review of the evidence for the management of tone in infants 0-24 months of age, with or at risk of developing cerebral palsy. **METHOD:** This review was conducted and reported following the Preferred Reporting Items for Systematic Reviews and Meta-analyses Statement. The Cochrane Central Register of Controlled Trials, Embase, MEDLINE, CINAHL Plus and PsycINFO databases were systematically searched for relevant articles. Inclusion criteria were: children aged 0-24 months, identified as at risk of, or having cerebral palsy;  $\geq 25\%$  of participants  $\leq 24$  months, and included a standardized assessment of tone. Only peer reviewed journal articles were considered. Eligible studies were coded using the Oxford Levels of Evidence. Methodological quality was assessed using the PEDro scale for randomized controlled trials and the checklist for assessing the quality of quantitative studies of Kmet, Cook and Lee for non-randomized control trials. **RESULTS:** A total of 4838 studies were identified. After removing duplicates and unrelated studies, a total of 56 full text studies were reviewed. A total of five studies met inclusion criteria, two of which were RCTs, two pre-/post-test designs and one retrospective case audit. Interventions included BoNT-A, Oral Baclofen, Neurofacilitation of Developmental Reaction and Neurodevelopmental Therapy. The quality of evidence ranged from limited to moderate. **CONCLUSION:** The management of tone in infants and young children is not well described, with a dearth of high-level evidence to support intervention in the 0-24 month age-range. This is in contrast to a recent review completed by Novak et al. (2013) who report high levels of evidence of interventions for children with cerebral palsy, over 2 years of age. Implications for Rehabilitation High level of evidence to support clinical decision making for the management of tone in young children 0-24 months is not available. The lack of available evidence in the management of tone of young children underpins service delivery and intervention and impacts on patient outcomes. In the absence of clear research evidence, the systematic application of sensitive outcome measures is required to confirm treatment effects and generate new evidence. Hypertonia should not be managed in isolation. Consideration needs to be given to all components of the ICF-CY.

[PMID: 27027325](#)

## 8. *Pediatr Phys Ther.* 2016 Summer;28(2):199. doi: 10.1097/PEP.0000000000000254.

### **Commentary on "Six-Minute Walk Test in Children With Spastic Cerebral Palsy and Children Developing Typically".**

Hanson H, Rosenberg J.

[PMID: 27023139](#)

9. *Pediatr Phys Ther.* 2016 Summer;28(2):186. doi: 10.1097/PEP.000000000000262.

**Commentary on "The Effect of Ankle-Foot Orthoses on Community-Based Walking in Cerebral Palsy: A Clinical Pilot Study".**

Gonzalez S, Shen E, Taylor F.

[PMID: 27023137](#)

10. *Dev Med Child Neurol.* 2016 Mar 27. doi: 10.1111/dmcn.13106. [Epub ahead of print]

**Longitudinal development of hand function in children with unilateral spastic cerebral palsy aged 18 months to 12 years.**

Nordstrand L, Eliasson AC, Holmefur M.

**AIM:** The aim of the study was to describe the development of hand function, particularly the use of the affected hand in bimanual tasks, among children with unilateral cerebral palsy aged 18 months to 12 years. **METHOD:** A convenience sample of 96 children (53 males, 43 females) was assessed with the Assisting Hand Assessment (AHA) at regular intervals from the ages of 18 months to 12 years. The children ranged from 17 to 127 months (median age 24mo) at recruitment. Subgroups were created to identify differences in development using the child's AHA at 18 months and the Manual Ability Classification System (MACS). A nonlinear mixed effects model was used to analyze data according to a 'stable limit' development model. **RESULTS:** The results were based on 702 AHA sessions. The children showed a rapid development at a young age and reached 90% of their stable limit between 30 months and 8 years. The subgroups, based on the 18-month AHA and the MACS levels respectively, had distinctly different patterns of development. **INTERPRETATION:** The AHA at 18 months may be used to make a crude prediction of future development.

[PMID: 27017925](#)

11. *Pediatr Phys Ther.* 2016 Summer;28(2):170. doi: 10.1097/PEP.000000000000253.

**Commentary on "Benefits and Enjoyment of a Swimming Intervention for Youth With Cerebral Palsy: An RCT Study".**

Appel J.

[PMID: 27023135](#)

12. *Pediatr Phys Ther.* 2016 Summer;28(2):161. doi: 10.1097/PEP.000000000000256.

**Commentary on "Modified Constraint-Induced Movement Therapy as a Home-Based Intervention for Children With Cerebral Palsy".**

Rabin L, Dittbenner L, Sarreal A, Sarreal J.

[PMID: 27023134](#)

## Prevention and Cure

**13. Cochrane Database Syst Rev. 2016 Mar 29;3:CD010527. doi: 10.1002/14651858.CD010527.pub2.**

### **Melatonin for women in pregnancy for neuroprotection of the fetus.**

Wilkinson D, Shepherd E, Wallace EM.

**BACKGROUND:** Melatonin is an antioxidant with anti-inflammatory and anti-apoptotic effects. Animal studies have supported a fetal neuroprotective role for melatonin when administered maternally. It is important to assess whether melatonin, given to the mother, can reduce the risk of neurosensory disabilities (including cerebral palsy) and death, associated with fetal brain injury, for the preterm or term compromised fetus. **OBJECTIVES:** To assess the effects of melatonin when used for neuroprotection of the fetus. **SEARCH METHODS:** We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 January 2016). **SELECTION CRITERIA:** We planned to include randomised controlled trials and quasi-randomised controlled trials comparing melatonin given to women in pregnancy (regardless of the route, timing, dose and duration of administration) for fetal neuroprotection with placebo, no treatment, or with an alternative agent aimed at providing fetal neuroprotection. We also planned to include comparisons of different regimens for administration of melatonin. **DATA COLLECTION AND ANALYSIS:** Two review authors planned to independently assess trial eligibility, trial quality and extract the data. **MAIN RESULTS:** We found no randomised trials for inclusion in this review. One study is ongoing. **AUTHORS' CONCLUSIONS:** As we did not identify any randomised trials for inclusion in this review, we are unable to comment on implications for practice at this stage. Although evidence from animals studies has supported a fetal neuroprotective role for melatonin when administered to the mother during pregnancy, no trials assessing melatonin for fetal neuroprotection in pregnant women have been completed to date. However, there is currently one ongoing randomised controlled trial (with an estimated enrolment target of 60 pregnant women) which examines the dose of melatonin, administered to women at risk of imminent very preterm birth (less than 28 weeks' gestation) required to reduce brain damage in the white matter of the babies that were born very preterm. Further high-quality research is needed and research efforts should be directed towards trials comparing melatonin with either no intervention (no treatment or placebo), or with alternative agents aimed at providing fetal neuroprotection (such as magnesium sulphate for the very preterm infant). Such trials should evaluate maternal and infant short- and longer-term outcomes (including neurosensory disabilities such as cerebral palsy), and consider the costs of care.

[PMID: 27022888](#)

**14. Dev Med Child Neurol. 2016 Mar;58 Suppl 4:53-60. doi: 10.1111/dmcn.13051.**

### **Prognostic significance of neurological signs in high-risk infants - a systematic review.**

Hamer EG, Hadders-Algra M.

The aim of this paper was to systematically review the literature on the significance of specific neurological signs in infancy, in particular in infants at risk for developmental problems such as cerebral palsy (CP). A literature search was performed using the databases PubMed, Embase, Web of Science, and AMED. Papers on infantile reactions ('primitive reflexes') and postural reactions were included if data were available allowing for calculation of sensitivity, specificity, or positive and negative predictive value for CP or atypical developmental outcome. Our search identified 23 articles on 20 different neurological signs. Properties of six neurological signs were reported in at least three different papers. The data indicated that, in early infancy, an absent Moro or plantar grasp response may be predictive for adverse developmental outcome. After early infancy, persistence of the Moro response and asymmetric tonic neck reflex was clinically significant. Prediction of a delayed emergence of the parachute reaction increases with age. Abnormal performances on the pull-to-sit manoeuvre and vertical suspension test have predictive significance throughout infancy. The neurological signs reviewed have some predictive value in infants at risk. For most of the signs, criteria for abnormality and significance are age-dependent.

[PMID: 27027608](#)

15. *Dev Med Child Neurol.* 2016 Mar;58 Suppl 4:46-52. doi: 10.1111/dmcn.13047.

**Motor and cognitive outcome after specific early lesions of the brain - a systematic review.**

Hielkema T, Hadders-Algra M.

The aim of this systematic review was to study motor and cognitive outcome in infants with severe early brain lesions and to evaluate effects of side of the lesion, sex, and social economic status on outcome. A literature search was performed using the databases Pubmed and Embase. Included studies involved infants with either cystic periventricular leukomalacia (cPVL), preterm, or term stroke (i.e. parenchymal lesion of the brain). Outcome was expressed as cerebral palsy (CP) and intellectual disability (mental retardation). Median prevalence rates of CP after cPVL, preterm, and term stroke were 86%, 71%, and 29% respectively; of intellectual disability 50%, 27%, and 33%. Most infants with cPVL developed bilateral CP, those with term stroke unilateral CP, whereas after preterm stroke bilateral and unilateral CP occurred equally often. Information on the effects of sex and social economic status on outcome after specific brain lesions was very limited. Our findings show that the risk for CP is high after cPVL, moderate after preterm stroke, and lowest after term stroke. The risk for intellectual disability after an early brain lesion is lower than that for CP. Predicting outcome at individual level remains difficult; new imaging techniques may improve predicting developmental trajectories.

[PMID: 27027607](#)

16. *Dev Med Child Neurol.* 2016 Mar;58 Suppl 4:22-7. doi: 10.1111/dmcn.13044.

**Anticipatory control and spatial cognition in locomotion and navigation through typical development and in cerebral palsy.**

Belmonti V, Cioni G, Berthoz A.

Behavioural evidence, summarized in this narrative review, supports a developmental model of locomotor control based on increasing neural integration of spatial reference frames. Two consistent adult locomotor behaviours are head stabilization and head anticipation: the head is stabilized to gravity and leads walking direction. This cephalocaudal orienting organization aligns gaze and vestibula with a reference frame centred on the upcoming walking direction, allowing anticipatory control on body kinematics, but is not fully developed until adolescence. Walking trajectories and those of hand movements share many aspects, including power laws coupling velocity to curvature, and minimized spatial variability. In fact, the adult brain can code trajectory geometry in an allocentric reference frame, irrespective of the end effector, regulating body kinematics thereafter. Locomotor trajectory formation, like head anticipation, matures in early adolescence, indicating common neurocomputational substrates. These late-developing control mechanisms can be distinguished from biomechanical problems in children with cerebral palsy (CP). Children's performance on a novel navigation test, the Magic Carpet, indicates that typical navigation development consists of the increasing integration of egocentric and allocentric reference frames. In CP, right-brain impairment seems to reduce navigation performance due to a maladaptive left-brain sequential egocentric strategy. Spatial integration should be considered more in rehabilitation.

[PMID: 27027604](#)

17. *Dev Med Child Neurol.* 2016 Mar;58 Suppl 4:7-11. doi: 10.1111/dmcn.13040.

**Prenatal ischemia deteriorates white matter, brain organization, and function: implications for prematurity and cerebral palsy.**

Coq JO, Delcour M, Massicotte VS, Baud O, Barbe MF.

Cerebral palsy (CP) describes a group of neurodevelopmental disorders of posture and movement that are frequently associated with sensory, behavioral, and cognitive impairments. The clinical picture of CP has changed with improved neonatal care over the past few decades, resulting in higher survival rates of infants born very preterm. Children born preterm seem particularly vulnerable to perinatal hypoxia-ischemia insults at birth. Animal models of CP are crucial for elucidating underlying mechanisms and for development of strategies of neuroprotection and remediation. Most animal models of CP are based on hypoxia-ischemia around the time of birth. In this review, we focus on alterations of brain organization and functions, especially sensorimotor changes, induced by prenatal ischemia in rodents and rabbits, and relate these alterations to neurodevelopmental disorders found in preterm children. We also discuss recent literature that addresses the relationship between neural and myelin plasticity, as well as possible contributions of white matter injury to the emergence of brain dysfunctions induced by prenatal ischemia.

[PMID: 27027601](#)

**18. Mov Disord. 2016 Mar 31. doi: 10.1002/mds.26618. [Epub ahead of print]**

**Clinical and imaging findings of progressive supranuclear palsy with predominant cerebellar ataxia.**

Shimohata T, Kanazawa M, Yoshida M, Saito Y, Iwai K, Yasuda T, Inukai A, Takahashi H, Nishizawa M, Aiba I.

[PMID: 27030358](#)

**19. Pediatr Neurol. 2016 Mar 3. pii: S0887-8994(15)30232-0. doi: 10.1016/j.pediatrneurol.2016.02.012. [Epub ahead of print]**

**Neonatal Magnesium Levels Between 24 and 48 Hours of Life and Outcomes for Epilepsy and Motor Impairment in Premature Infants.**

Ostrander B, Bardsley T, Korgenski EK, Greene T, Bonkowsky JL.

**OBJECTIVE:** Elevated rates of epilepsy and motor impairments including cerebral palsy are observed in children who were born prematurely. Maternal antenatal magnesium supplementation has been associated with decreased rates of cerebral palsy in infants born prematurely. Our objective was to determine whether the neonatal serum magnesium level between 24 and 48 hours after birth is associated with better long-term neurodevelopmental outcomes (epilepsy, motor impairment) in premature infants. **METHODS:** We performed a retrospective cohort analysis in infants born less than 37-weeks gestation over a ten-year period. Prenatal, perinatal, and postnatal clinical and demographic information was collected. Crude and adjusted odds ratios were estimated under generalized linear models with generalized estimating equations to examine the association of the neonatal serum magnesium level between 24 and 48 hours after birth with the risk of epilepsy and/or motor impairment (spasticity; hypotonia; cerebral palsy). **RESULTS:** The final cohort included 5461 infants born less than 37-weeks gestation from 2002 to 2011. The adjusted relative risk ratio for the combined outcomes of epilepsy and/or motor impairment, controlling for gestational age, current age, maternal magnesium supplementation, maternal steroid administration, five-minute Apgar score, neonatal infection, need for vasopressor use, and birth weight and with serum magnesium level as the main independent variable, was 0.85 ( $P = 0.24$ ). Stratified analyses by gestational age less than 32 or greater than 32 weeks were not significantly associated with adverse neurodevelopmental outcome (risk ratio = 0.79 and 1.2,  $P = 0.12$  and 0.49, respectively). A multivariate analysis for the risk of motor impairment alone had a risk ratio of 0.94 ( $P = 0.72$ ). **CONCLUSION:** This study demonstrates that the neonatal magnesium level between 24 and 48 hours of life in premature infants is not significantly associated with the risk for developing epilepsy or motor impairment.

[PMID: 27025188](#)

**20. Pediatr Phys Ther. 2016 Mar 29. [Epub ahead of print]**

**Relationship Between Central Hypotonia and Motor Development in Infants Attending a High-Risk Neonatal Neurology Clinic.**

Segal I, Peylan T, Sucre J, Levi L, Bassan H.

**PURPOSE:** To study the relationship between central hypotonia and motor development, and to determine the relative contribution of nuchal, truncal, and appendicular hypotonia domains to motor development. **METHODS:** Appendicular, nuchal, and truncal tones of high-risk infants were assessed, as was their psychomotor developmental index (PDI). Infants with peripheral hypotonia were excluded. **RESULTS:** We included 164 infants (mean age  $9.6 \pm 4$  months), 36 with normal tone in all 3 domains and 128 with central hypotonia. Twenty-six of the latter had hypotonia in 1 domain and 102 had multiple combinations of 3 domains. Hypotonia domains were distributed as follows: truncal ( $n = 115$ ), appendicular ( $n = 93$ ), and nuchal ( $n = 70$ ). Each domain was significantly associated with PDI scores ( $P < .001$ ) but not with a later diagnosis of cerebral palsy. On linear regression, nuchal hypotonia had the strongest contribution to PDI scores ( $\beta = -0.6$  [nuchal],  $-0.45$  [appendicular], and  $-0.4$  [truncal],  $P < .001$ ). **CONCLUSIONS:** Central hypotonia, especially nuchal tone, is associated with lowered motor development scores.

[PMID: 27027244](#)