

Monday 25 August 2014

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Interventions and Management

1. *Dev Med Child Neurol.* 2014 Aug 6. doi: 10.1111/dmcn.12551. [Epub ahead of print]

International Classification of Functioning, Disability and Health Core Sets for children and youth with cerebral palsy: a consensus meeting.

Schiariti V1, Selb M, Cieza A, O'Donnell M.

AIM: The objective of this article is to report on the Core Sets developed for children and youth aged 0 to 18 years, with cerebral palsy (CP) based on the pediatric International Classification of Functioning, Disability and Health (ICF) by the World Health Organization (WHO). **METHOD:** A formal decision-making and consensus process integrating evidence gathered from preparatory studies was followed. Preparatory studies included: a systematic literature review; an international expert survey; a qualitative study of children and youth with CP and their caregivers; and a clinical study. Relevant ICF categories were identified in a formal consensus process by international experts from different backgrounds. Twenty-six international experts chosen by WHO region with expertise in CP attended the consensus meeting. **RESULTS:** Overall, five ICF Core Sets were developed: a Comprehensive Core Set (135 ICF categories); a Common Brief (25 ICF categories); and three age-specific Core Sets: under 6 years (31 ICF categories), from 6 to <14 years (35 ICF categories) and from 14 to 18 years (37 ICF categories). **INTERPRETATION:** These ICF Core Sets for children and youth with CP are the first ICF-based tools developed for this population. The ICF Core Sets for children and youth with CP can be applied in clinical practice, research, teaching and administration. The application of the ICF Core Sets to this population will standardize the functional assessments of CP worldwide.

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[PMID: 25131642](https://pubmed.ncbi.nlm.nih.gov/25131642/) [PubMed - as supplied by publisher]

2. *Disabil Rehabil Assist Technol.* 2014 Aug 21:1-6. [Epub ahead of print]

The Cerebral Palsy Kinematic Assessment Tool (CPKAT): feasibility testing of a new portable tool for the objective evaluation of upper limb kinematics in children with cerebral palsy in the non-laboratory setting.

Preston N1, Weightman A, Culmer P, Levesley M, Bhakta B, Mon-Williams M.

Purpose: Efficacy of treatment to improve upper-limb activity of children with cerebral palsy (CP) is typically evaluated outside clinical/laboratory environments through functional outcome measures (e.g. ABILHAND kids).

This study evaluates CPKAT, a new portable laptop-based tool designed to objectively measure upper-limb kinematics in children with CP. Methods: Seven children with unilateral CP (2 females; mean age 10 years 2 months (SD 2 years 3 months), median age 9 years 6 months, range 6 years 5 months, MACS II-IV) were evaluated on copying, tracking and tracing tasks at their homes using CPKAT. CPKAT recorded parameters relating to spatiotemporal hand movement: path length, movement time, smoothness, path accuracy and root mean square error. The Wilcoxon signed ranks test explored whether CPKAT could detect differences between the affected and less-affected limb. Results: CPKAT detected intra-limb differences for movement time and smoothness (aiming), and path length (tracing). No intra-limb tracking differences were found, as hypothesised. These findings are consistent with other studies showing that movements of the impaired upper limb in unilateral CP are slower and less smooth. Conclusion: CPKAT provides a potential solution for home-based assessment of upper limb kinematics in children with CP to supplement other measures and assess functional intervention outcomes. Further validation is required. Implications for Rehabilitation This paper demonstrates the feasibility of evaluating upper limb kinematics in home using CPKAT, a portable laptop-based evaluation tool. We found that CPKAT is easy to set-up and use in home environments and yields useful kinematic measures of upper limb function. CPKAT can complement less responsive patient reported or subjectively evaluated functional measures for a more complete evaluation of children with cerebral palsy. Thus, CPKAT can help guide a multi-disciplinary team to more effective intervention and rehabilitation for children with cerebral palsy.

[PMID: 25144388](#) [PubMed - as supplied by publisher]

3. Arch Phys Med Rehabil. 2014 Jul;95(7):1303-11. doi: 10.1016/j.apmr.2014.03.016. Epub 2014 Apr 4.

Botulinum toxin type B in the spastic arm: a randomized, double-blind, placebo-controlled, preliminary study.

Gracies JM1, Bayle N2, Goldberg S2, Simpson DM2.

OBJECTIVE: To determine the efficacy and safety of 2 doses of botulinum toxin type B (rimabotulinumtoxinB, BoNT/B) in spastic upper limb muscles. **DESIGN:** Randomized, double-blind, placebo-controlled trial with a 3-month follow-up. **SETTING:** Tertiary care center. **PARTICIPANTS:** Referred sample of adult hemiparetic patients (N=24) with disabling elbow flexor overactivity after stroke or traumatic brain injury. **INTERVENTIONS:** Injection of 10,000U of rimabotulinumtoxinB (fixed 2500U dose into elbow flexors; n=8), 15,000U (5000U into elbow flexors; n=8), or placebo (n=8) into overactive upper limb muscles selected as per investigator's discretion. **MAIN OUTCOME MEASURES:** At 1 month postinjection, active range of elbow extension (goniometry; primary outcome); active upper limb function (Modified Frenchay Scale [MFS]); subjective global self-assessment (GSA) of arm pain, stiffness, and function; rapid alternating elbow flexion-extension movement frequency over the maximal range; elbow flexor spasticity grade and angle (Tardieu), and tone (Ashworth). **RESULTS:** No adverse effects were associated with either BoNT/B dose. Both doses improved active elbow extension versus placebo (+8.3°; 95% confidence interval, 1.1°-15.5°; analysis of covariance, P=.028). The high dose of BoNT/B also improved subject-perceived stiffness (P=.005) and the composite pain, stiffness, and function GSA (P=.017), effects that persisted 3 months from injection. No MFS change was demonstrated, although subjects with a baseline MFS <70/100 seemed more likely to benefit from BoNT/B. **CONCLUSIONS:** In this short-term study, BoNT/B up to 15,000U into spastic upper limb muscles, including the elbow flexors, was well tolerated and improved active elbow extension and subject-perceived stiffness.

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[PMID: 24709034](#) [PubMed - indexed for MEDLINE]

4. J Phys Ther Sci. 2014 Jul;26(7):1003-7. doi: 10.1589/jpts.26.1003. Epub 2014 Jul 30.

Immediate Effect of Postural Insoles on Gait Performance of Children with Cerebral Palsy: Preliminary Randomized Controlled Double-blind Clinical Trial.

Neto HP1, Grecco LA2, Duarte NA3, Christovão TC3, Franco de Oliveira LV4, Dumont AJ3, Galli M5, Oliveira CS4.

Purpose: Improved gait efficiency is one of the goals of therapy for children with cerebral palsy (CP). Postural insoles can allow more efficient gait by improving biomechanical alignment. The aim of the present study was to

assess the effect of postural insoles on gait performance of children with CP classified as levels I or II of the Gross Motor Function Classification System (GMFCS). **Subjects and Methods:** the study was a randomized controlled double-blind clinical trial. After meeting the legal aspects and the eligibility criteria, 10 children between four and 12 years old were randomly divided into a two groups: a control group (n=5), and an experimental group (n=5). Children in the control group used a placebo insoles, and children in the experimental group used postural insoles. Evaluation consisted of three-dimensional gait analysis under three conditions: barefoot, shoes without insoles and shoes with postural insoles or shoes with placebo insoles. **Results:** Regarding the immediate effects of insole use, significant improvements in gait velocity and cadence were observed in the experimental group in comparison to the control group. **Conclusion:** The use of postural insoles led to improvements in gait velocity and cadence of the children with cerebral palsy classified as levels I or II of the GMFCS.

[PMID: 25140083](#) [PubMed] [PMCID: PMC4135184](#)

5. J Orthop Res. 2014 Aug 19. doi: 10.1002/jor.22719. [Epub ahead of print]

Stiff muscle fibers in calf muscles of patients with cerebral palsy lead to high passive muscle stiffness.

Mathewson MA1, Chambers HG, Girard PJ, Tenenhaus M, Schwartz AK, Lieber RL.

Cerebral palsy (CP), caused by an injury to the developing brain, can lead to alterations in muscle function. Subsequently, increased muscle stiffness and decreased joint range of motion are often seen in patients with CP. We examined mechanical and biochemical properties of the gastrocnemius and soleus muscles, which are involved in equinus muscle contracture. Passive mechanical testing of single muscle fibers from gastrocnemius and soleus muscle of patients with CP undergoing surgery for equinus deformity showed a significant increase in fiber stiffness ($p < 0.01$). Bundles of fibers that included their surrounding connective tissues showed no stiffness difference ($p = 0.28$). When in vivo sarcomere lengths were measured and fiber and bundle stiffness compared at these lengths, both fibers and bundles of patients with CP were predicted to be much stiffer in vivo compared to typically developing (TD) individuals. Interestingly, differences in fiber and bundle stiffness were not explained by typical biochemical measures such as titin molecular weight (a giant protein thought to impact fiber stiffness) or collagen content (a proxy for extracellular matrix amount). We suggest that the passive mechanical properties of fibers and bundles are thus poorly understood.

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[PMID: 25138654](#) [PubMed - as supplied by publisher]

6. Med Sci Sports Exerc. 2014 Sep;46(9):1808-15. doi: 10.1249/MSS.000000000000299.

Validation of Accelerometer Cut Points in Toddlers with and without Cerebral Palsy.

Oftedal S1, Bell KL, Davies PS, Ware RS, Boyd RN.

AIM: The purpose of this study was to validate uni- and triaxial ActiGraph cut points for sedentary time in toddlers with cerebral palsy (CP) and typically developing children (TDC). **METHODS:** Children (n = 103, 61 boys, mean age = 2 yr, SD = 6 months, range = 1 yr 6 months-3 yr) were divided into calibration (n = 65) and validation (n = 38) samples with separate analyses for TDC (n = 28) and ambulant (Gross Motor Function Classification System I-III, n = 51) and nonambulant (Gross Motor Function Classification System IV-V, n = 25) children with CP. An ActiGraph was worn during a videotaped assessment. Behavior was coded as sedentary or nonsedentary. Receiver operating characteristic-area under the curve analysis determined the classification accuracy of accelerometer data. Predictive validity was determined using the Bland-Altman analysis. **RESULTS:** Classification accuracy for uniaxial data was fair for the ambulatory CP and TDC group but poor for the nonambulatory CP group. Triaxial data showed good classification accuracy for all groups. The uniaxial ambulatory CP and TDC cut points significantly overestimated sedentary time (bias = -10.5%, 95% limits of agreement [LoA] = -30.2% to 9.1%; bias = -17.3%, 95% LoA = -44.3% to 8.3%). The triaxial ambulatory and nonambulatory CP and TDC cut points provided accurate group-level measures of sedentary time (bias = -1.5%, 95% LoA = -20% to 16.8%; bias = 2.1%, 95% LoA = -17.3% to 21.5%; bias = -5.1%, 95% LoA = -27.5% to 16.1%). **CONCLUSION:** Triaxial accelerometers provide useful group-level measures of sedentary time in children with CP across the spectrum of functional abilities and TDC. Uniaxial cut points are not recommended.

[PMID: 25134003](#) [PubMed - in process]

7. Bone. 2014 Aug 15. pii: S8756-3282(14)00304-4. doi: 10.1016/j.bone.2014.08.003. [Epub ahead of print]

Time since onset of walking predicts tibial bone strength in early childhood.

Ireland A1, Rittweger J2, Schönau E3, Lamberg-Allardt C4, Viljakainen H4.

Bone strength in adulthood is known to be affected by health at birth and early childhood. Habitual bone loading is a primary determinant of bone strength in later childhood and adulthood. However, the effects of physical activity in early childhood (e.g. crawling, standing and walking) on bone strength are unknown. Fifty-three children (twenty-seven males) were included in a longitudinal study in their early infancy. Shortly after birth (0.3 ± 0.3 months), details of mass and height were obtained along with a pQCT scan at 20% distal-proximal tibia length. At 14.8 ± 0.5 months of age the same data were collected, along with details of age at onset of standing, crawling, supported and unsupported walking. Time since onset of walking unsupported was associated with greater bone mass, cortical bone area, pericortical circumference and polar moment of inertia of both total and cortical bone (all $P < 0.05$). There were no significant associations between other physical activity timepoints and bone measures. Age at onset of walking was not significantly related to mass, length or bone measures at birth. The results suggest that time since attainment of independent walking - representing exposure of the tibia to the large reaction and muscular forces associated with locomotion - is a primary determinant of bone strength in early childhood. This finding raises the possible opportunity of physical activity interventions at young age in paediatric populations associated with low childhood bone strength and late walking (e.g. low birth weight, cerebral palsy and Down's Syndrome, etc.).

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[PMID: 25132490](#) [PubMed - as supplied by publisher]

8. J Clin Densitom. 2014 Apr-Jun;17(2):281-94. doi: 10.1016/j.jocd.2014.01.005. Epub 2014 Mar 19.

Bone health in children and adolescents with chronic diseases that may affect the skeleton: the 2013 ISCD Pediatric Official Positions.

Bianchi ML1, Leonard MB2, Bechtold S3, Högl W4, Mughal MZ5, Schönau E6, Sylvester FA7, Vogiatzi M8, van den Heuvel-Eibrink MM9, Ward L10; International Society for Clinical Densitometry.

The aim of this Task Force was to review the use of dual-energy X-ray absorptiometry (DXA) in children and adolescents with underlying chronic diseases that pose risk factors for compromised bone health, such as inflammation, glucocorticoid therapy, or decreased mobility. The Task Force systematically analyzed more than 270 studies, with an emphasis on those published in the interval since the original 2007 Position Statements. Important developments over this period included prospective cohort studies demonstrating that DXA measures of areal bone mineral density (aBMD) predicted incident fractures and the development of robust reference data and strategies to adjust for bone size in children with growth impairment. In this report, we summarize the current literature on the relationship between DXA-based aBMD and both fracture (vertebral and non-vertebral) outcomes and non-fracture risk factors (e.g., disease characteristics, ambulatory status, and glucocorticoid exposure) in children with chronic illnesses. Most publications described the aBMD profile of children with underlying diseases, as well as the cross-sectional or longitudinal relationship between aBMD and clinically relevant non-fracture outcomes. Studies that addressed the relationship between aBMD and prevalent or incident fractures in children with chronic illnesses are now emerging. In view of these updated data, this report provides guidelines for the use of DXA-based aBMD in this setting. The initial recommendation that DXA is part of a comprehensive skeletal healthy assessment in patients with increased risk of fracture is unchanged. Although the prior guidelines recommended DXA assessment in children with chronic diseases at the time of clinical presentation with ongoing monitoring, this revised Position Statement focuses on the performance of DXA when the patient may benefit from interventions to decrease their elevated risk of a clinically significant fracture and when the DXA results will influence that management.

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[PMID: 24656723](#) [PubMed - indexed for MEDLINE]

9. *Dev Med Child Neurol.* 2014 Sep;56 Suppl 5:2-112. doi: 10.1111/dmnc.12539.

Abstracts of the American Academy for Cerebral Palsy and Developmental Medicine 68th Annual Meeting, 10-13 September 2014, San Diego, USA.

[No authors listed]

[PMID: 5138380](#) [PubMed - in process]

10. *IEEE Trans Neural Syst Rehabil Eng.* 2014 Aug 13. [Epub ahead of print]

FORCe: Fully Online and automated artifact Removal for brain-Computer interfacing.

Daly I, Scherer R, Billinger M, Muller-Putz G.

A fully automated and online artifact removal method for the electroencephalogram (EEG) is developed for use in brain-computer interfacing. The method (FORCe) is based upon a novel combination of wavelet decomposition, independent component analysis, and thresholding. FORCe is able to operate on a small channel set during online EEG acquisition and does not require additional signals (e.g. electrooculogram signals). Evaluation of FORCe is performed offline on EEG recorded from 13 BCI participants with cerebral palsy (CP) and online with three healthy participants. The method outperforms the state-of-the-art automated artifact removal methods Lagged auto-mutual information clustering (LAMIC) and Fully automated statistical thresholding (FASTER), and is able to remove a wide range of artifact types including blink, electromyogram (EMG), and electrooculogram (EOG) artifacts.

[PMID: 25134085](#) [PubMed - as supplied by publisher]

11. *Indian Pediatr.* 2014 Aug 8;51(8):613-619.

INCLen Diagnostic Tool for Neuromotor Impairments (INDT-NMI) for Primary Care Physician: Development and Validation.

Gulati S1, Aneja S, Juneja M, Mukherjee S, Deshmukh V, Silberberg D, Bhutani VK, Pinto JM, Durkin M, Tudu P, Pandey RM, Nair MK, Arora NK; INCLen Study Group; INCLen Study Group. Collaborators (42)

OBJECTIVE: To develop and validate a diagnostic tool for use by primary care physicians for diagnosing neuro-motor impairment among 2-9 year old children in primary care settings. **STUDY DESIGN:** Modified Delphi technique involving national (n=49) and international (n=6) experts was used for development of INDT-NMI. The tool was then validated through a cross sectional study. **SETTING:** Neurology specialty clinics of three tertiary care pediatric centers in New Delhi, India. **PARTICIPANTS:** 454 children aged 2-9 years [mean (SD) age: 60.4 (23.7) mo], selected through systematic random sampling, underwent assessment for identification and classification of neuromotor impairments (NMI). **INTERVENTION:** All study subjects were first administered INDT-NMI (candidate test) by a trained physician followed by expert assessment for NMI and other neurodevelopment disorders (NDD) by team of two pediatric neurologists (Gold standard). **RESULTS:** According to expert evaluation, 171 (37.8%) children had neuromotor impairments. There were four categories of subjects: NMI alone (n=66); NMI+other NDDs (n=105); Other NDDs without NMI (n=225) and 'Normal' group (n=58). Using expert evaluation as gold standard, overall sensitivity of the INDT-NMI was 75.4% and specificity was 86.8%. INDT-NMI helped graduate physicians to correctly classify 86.6% (112/129) children with NMI into different types (cerebral palsy, neuromotor diseases and other NMI). Graduate physicians assigned 40 children (8.8%) as 'indeterminate', 38 (95%) of whom had either NDD and/or NMI and thus merited referral. Misclassification of NMI occurred in those with mild changes in muscle tone, dystonia, or ataxia and associated NDDs. **CONCLUSIONS:** Graduate primary care physicians with a structured short training can administer the new tool and diagnose NMI in 2-9 year old children with high validity. INDT-NMI requires further evaluation in actual primary care settings.

[PMID: 25128993](#) [PubMed - as supplied by publisher]

Prevention and Cure

12. Am J Epidemiol. 2014 Aug 19. pii: kwu179. [Epub ahead of print]

Prenatal Exposure to Perfluoroalkyl Substances and the Risk of Congenital Cerebral Palsy in Children.

Liew Z, Ritz B, Bonefeld-Jørgensen EC, Henriksen TB, Nohr EA, Bech BH, Fei C, Bossi R, von Ehrenstein OS, Streja E, Uldall P, Olsen J.

Perfluoroalkyl substances (PFASs) are persistent pollutants and endocrine disruptors that may affect fetal brain development. We investigated whether prenatal exposure to PFASs increases the risk of congenital cerebral palsy (CP). The source population for this study includes 83,389 liveborn singletons and mothers enrolled in the Danish National Birth Cohort during 1996-2002. We identified 156 CP cases by linking the cohort to the Danish National Cerebral Palsy Register, and we randomly selected 550 controls using a case-cohort design. We measured 16 PFASs in maternal plasma collected in early or midpregnancy, and 6 PFASs were quantifiable in more than 90% of the samples. We found a higher risk of CP in boys with higher maternal PFAS levels; per 1-unit (natural-log ng/mL) increase, the risk ratios were 1.7 (95% confidence interval: 1.0, 2.8) for perfluorooctane sulfonate and 2.1 (95% confidence interval: 1.2, 3.6) for perfluorooctanoic acid. We also observed a dose-response pattern of CP risk in boys per quartile of maternal level of perfluorooctane sulfonate and perfluorooctanoic acid (P for trend < 0.01). PFASs were associated with both unilateral and bilateral spastic CP subphenotypes. No association between PFASs and CP was found in girls. Prenatal exposures to PFASs may increase the risk of CP in boys, but the finding is novel and replication is needed.

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[PMID: 25139206](#) [PubMed - as supplied by publisher]

13. Ann Neurol. 2014 Aug 18. doi: 10.1002/ana.24251. [Epub ahead of print]

Clinical Whole Exome Sequencing in Child Neurology Practice.

Srivastava S1, Cohen JS, Vernon H, Barañano K, McClellan R, Jamal L, Naidu S, Fatemi A.

Objective. Whole exome sequencing (WES) represents a significant breakthrough in clinical genetics as a powerful tool for etiological discovery in neurodevelopmental disorders. To better characterize the genetic landscape of neurodevelopmental disorders, we analyzed patients in our pediatric neurogenetics clinic who underwent WES. **Methods.** We performed a retrospective cohort study on 78 patients with various neurodevelopmental disabilities and unrevealing workup prior to WES. We characterized their molecular diagnoses, clinical features, and whether their previous treatment plan changed due to WES results. **Results.** The overall presumptive diagnostic rate for our cohort was 41% (n=32 out of 78 patients). Nineteen patients had a single autosomal dominant (AD) disorder, 11 had a single autosomal recessive (AR) disorder, one had an X-linked dominant disorder, and one had both an AD and AR disorder. The 32 patients with pathogenic or likely pathogenic variants exhibited various neurobehavioral and neuroimaging abnormalities, including: intellectual disability/developmental delay (n=28), cerebral palsy like encephalopathy (n=11), autism spectrum disorder (n=5), delayed/hypomyelination (n=7), and cerebellar abnormalities (n=9). The results of WES affected management for all patients with a presumptive diagnosis, triggering reproductive planning (n=27), disease monitoring initiation (n=4), investigation of systemic involvement of the disorder(s) (n=6), alteration of presumed disease inheritance pattern (n=7), changing of prognosis (n=10), medication discontinuation (n=5) or initiation (n=2), and clinical trial education (n=3). **Interpretation.** The high diagnostic yield of WES supports its use in pediatric neurology practices. It may also lead to earlier diagnosis, impacting medical management, prognostication, and family planning. WES therefore serves as a critical tool for the child neurologist.

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[PMID: 25131622](#) [PubMed - as supplied by publisher]

14. Neurol Neurochir Pol. 2014;48(2):130-5. doi: 10.1016/j.pjnns.2013.05.003. Epub 2014 Feb 15.

Alternating hemiplegia of childhood: new diagnostic options.

Gergont A1, Kacinski M2.

A syndrome of alternating hemiplegia of childhood (AHC) is a rare disorder first presented in 1971. AHC is characterized by transient episodes of hemiplegia affecting either one or both sides of the body. Age of onset is before 18 months and the common earliest manifestations are dystonic or tonic attacks and nystagmus. Hemiplegic episodes last minutes to days and the frequency and duration tend to decrease with time. Motor and intellectual development is affected, deficits may also develop later. Epileptic seizures occur in some patients. Neuroimaging of the brain usually reveals no abnormalities. The variability of individual clinical presentations and evolution of symptoms have made diagnosis difficult. Therefore the problems of misdiagnosis could account for the low prevalence of this syndrome. This paper hopes to present actual data on AHC, especially of the results of genetic research and new diagnostic tools.

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[PMID: 24821639](#) [PubMed - indexed for MEDLINE]