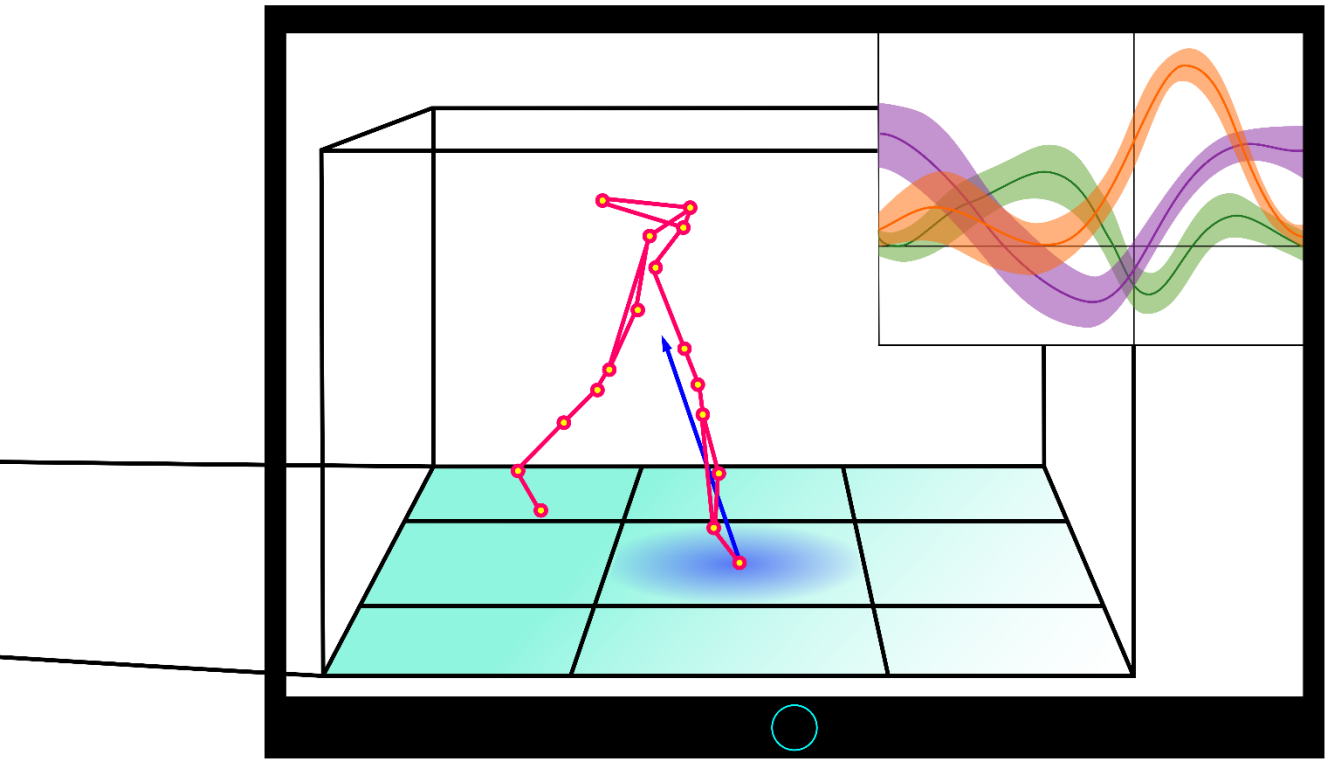
DOCTORAL THESIS

Clinically relevant gait parameters in children with bilateral spastic cerebral palsy

Cristina Gómez Pérez



UNIVERSITAT DE VIC
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Escola de Doctorat

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Clinically relevant gait parameters in children with bilateral spastic cerebral palsy

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Per als meus pares

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Resum

La paràlisi cerebral (CP) és la causa més freqüent de discapacitat motora crònica en la població infantil i descriu un conjunt de trastorns permanents que afecten el moviment i la postura, que s'atribueixen a lesions no progressives en el cervell en desenvolupament del fetus o de l'infant. L'espasticitat és sovint el trastorn motor predominant i causa problemes secundaris, com ara contractures, debilitat muscular, deformitats òssies i inestabilitat articular, que apareixen com a conseqüència del creixement i desenvolupament del sistema músculesquelètic. Aquests trastorns motors, actuant a diferents nivells, afecten la qualitat i l'eficiència de la marxa i d'altres aspectes de la funció motora, limitant les activitats de la vida diària i la participació en la societat dels nens amb CP. Per aquest motiu, bona part dels tractaments es centren a millorar o mantenir la capacitat de marxa.

L'anàlisi instrumentada de la marxa (IGA) és una eina de valoració que permet quantificar de forma precisa les característiques de la marxa, mitjançant dades objectives de diferent naturalesa (espai-temporals (ST), cinemàtiques, cinètiques i d'electromiografia superficial) que no es poden apreciar visualment ni mesurar en una exploració física estàtica. L'IGA s'utilitza en la valoració funcional dels nens amb CP per identificar els trastorns de la marxa, refinar la presa de decisions clíniques i avaluar els efectes dels tractaments sobre els trastorns de la marxa. La fiabilitat, validesa i sensibilitat als canvis de l'IGA, però, encara no han estat ben establertes. Un dels desavantatges de l'IGA és la gran quantitat de dades generades, que dificulten la interpretació clínica dels resultats.

La versió per a nens i joves de la Classificació Internacional del Funcionament, de la discapacitat i de la salut (ICF-CY) proporciona un marc universal per definir i classificar el funcionament i la discapacitat dels nens, mitjançant quatre components (funcions corporals (b) i estructures corporals (s), activitats i participació (d), factors ambientals (e) i factors personals) i 1685 categories. Hi ha dues categories de l'ICF-CY relacionades amb la marxa (funcions relacionades amb el patró de marxa (b770) i caminar (d450)) que poden ajudar a interpretar l'IGA dels nens amb CP. Paral·lelament, es poden distingir dos tipus de mesures de resultat de la marxa: les mesures de resultat del patró de marxa i les mesures de resultat de la capacitat de marxa.

L'objectiu d'aquesta tesi doctoral és seleccionar un conjunt de paràmetres de marxa que siguin clínicament rellevants per a la valoració de la marxa de nens amb CP espàstica bilateral. Tres requisits d'un paràmetre de marxa clínicament rellevant són: 1) la seva capacitat per distingir entre la marxa fisiològica i la marxa patològica, 2) la seva capacitat per detectar canvis en els

trastorns de la marxa, i 3) la seva capacitat per relacionar els trastorns de la marxa i els problemes clínics. Mitjançant una revisió sistemàtica, es van identificar els paràmetres de la marxa més freqüentment utilitzats i es va avaluar la seva sensibilitat als canvis. Mitjançant un estudi transversal observacional, es va avaluar la relació entre els paràmetres ST i els resultats clínics (deficiències a nivell de funcions i estructures corporals, i limitacions en l'activitat a nivell d'activitats i participació). També es va validar el mètode de detecció d'esdeveniments de la marxa (algoritme de Ghoussayni, basat en dades cinemàtiques) utilitzat en el càlcul dels paràmetres de marxa, incloent una nova adaptació per a la detecció del contacte inicial del peu (FS) en nens amb CP.

Es van identificar 89 paràmetres de la marxa, 56 dels quals van mostrar sensibilitat als canvis. Els paràmetres ST, seguits dels paràmetres cinemàtics, van ser els més utilitzats. Els paràmetres ST van mostrar correlacions amb les limitacions en l'activitat: una longitud de pas més curta, una amplada de pas més gran, una velocitat de marxa més lenta, un primer període de recolzament doble més llarg, un període de recolzament simple més curt i un temps fins l'enlairament del peu més llarg es van correlacionar amb un resultat més baix en l'escala Gross Motor Function Measure (tant en la puntuació total com en la dimensió E: caminar, córrer i saltar). Els paràmetres ST també van mostrar relació amb algunes deficiències: una cadència més baixa es va relacionar amb una espasticitat dels flexors del maluc més alta, una longitud de pas més curta amb una espasticitat dels flexors plantars del turmell més elevada i una velocitat de marxa més lenta amb una deformitat del peu (valg) en posició dempeus. L'algoritme de Ghoussayni utilitzant un llindar de 0.5 m/s (Gho05) no va mostrar diferències estadísticament significatives amb el mètode de referència (força de reacció del terra) a l'hora de detectar esdeveniments de la marxa. La nova adaptació de l'algoritme de Ghoussayni va distingir el tipus de FS dels nens amb CP (taló, punta o ambdós alhora).

En conclusió, l'IGA proporciona mesures de resultat sensibles als canvis per a la valoració de la marxa de nens amb CP espàstica bilateral. Tots els paràmetres ST excepte la cadència estan relacionats amb la funció motora grossa, i específicament amb la capacitat de marxa, a nivell d'activitats i participació, de manera que es poden interpretar com a mesures de resultat de la capacitat de marxa. La cadència, la longitud de pas i la velocitat de marxa també estan relacionades amb algunes deficiències, a nivell de funcions i estructures corporals, de manera que es poden interpretar com a mesures de resultat del patró de marxa. Gho05, incloent la nova adaptació, és un mètode vàlid per a detectar esdeveniments de la marxa en nens amb CP espàstica bilateral.

Abstract

Cerebral palsy (CP) is the most common cause of chronic childhood motor disability and it describes a group of permanent disorders affecting movement and posture that are attributed to non-progressive lesions in the developing fetal or infant brain. Spasticity is often the dominant motor disorder and it causes secondary problems like contractures, muscle weakness, bone deformities and joint instability that appear as a consequence of growth and development of the musculoskeletal system. These motor disorders, occurring at multiple levels, affect the quality and efficiency of gait, and other aspects of motor function, contributing to activity limitation and participation restriction. Thus, in children with CP, considerable efforts are focused on improving or maintaining walking ability.

The Instrumented gait analysis (IGA) is an assessment tool that allows a precise quantification of gait characteristics, through objective data that cannot be evaluated visually or measured on a static physical examination. It provides detailed information on four types of data recorded simultaneously: spatiotemporal (ST), kinematic, kinetic and surface electromyography data. The IGA is often used in the assessment of ambulatory children with CP for the identification and understanding of gait disorders, the refinement of clinical decision-making, and the evaluation and understanding of the effects of treatments on gait disorders. However, its psychometric properties (reliability, validity and responsiveness) have not been well established yet. One of the handicaps of the IGA is the large amount of data collected that makes it an instrument complicated to use and difficult to interpret.

The International Classification of Functioning, disability and health, Children and Youth version (ICF-CY) provides a universal framework for defining and classifying functioning and disability in children worldwide. It covers the functioning and disability through four different components (body functions (b) and body structures (s), activities and participation (d), environmental factors (e), and personal factors), using 1685 categories. There are two categories of the ICF-CY related to gait (gait pattern functions (b770) and walking (d450)) that can help to interpret the gait analysis of children with CP. Two types of gait outcome measures can be distinguished: outcome measures of gait pattern and outcome measures of walking.

The aim of the present doctoral thesis is to select a set of clinically relevant gait parameters for the gait analysis of children with bilateral spastic CP. Three requirements for a clinically relevant gait parameter are: 1) its capability to distinguish between physiological and pathological gait, 2) its capability to detect changes in gait disorders, and 3) its capability to link gait disorders and clinical problems. Through a systematic review, the gait parameters

most frequently used were identified and their responsiveness to treatments was evaluated. Through a cross-sectional observational study, the relationship between ST parameters and clinical outcomes (impairments at body functions and structures level, and activity limitations at activities and participation level) was evaluated. The gait event detection method used in the calculation of gait parameters (Ghoussayni's algorithm, based on kinematic data), including a new adaptation for detecting foot strikes (FS) in children with CP, was validated.

Eighty-nine gait parameters were identified and 56 of them showed responsiveness to treatments. ST parameters, followed by kinematic parameters, were the most frequently used. ST parameters showed correlations with activity limitations: shorter stride length, longer step width, slower gait speed, longer first double support, shorter single support, and longer time of toe off were correlated to lower Gross Motor Function Measure (total score, and dimension E: walking, running and jumping). ST parameters also showed relationship with impairments: lower cadence was related to higher hip flexors spasticity, shorter stride length was related to higher ankle plantar flexors spasticity, and slower gait speed was related to hindfoot deformity (valgus) in standing. Ghoussayni's algorithm using a threshold of 0.5 m/s (Gho05) showed no statistically significant differences with the gold standard (ground reaction forces) when detecting gait events. The new adaptation of Ghoussayni's algorithm distinguished how children with CP performed each FS (heel, toe or both at the same time).

In conclusion, the IGA yields responsive outcome measures for the gait assessment of children with bilateral spastic CP. All ST parameters, except cadence, are linked to gross motor function, and specifically to walking capacity, at activities and participation level, so they can be interpreted as outcome measures of walking. Cadence, stride length and gait speed are also linked to impairments, at body functions and structures level, so they can be interpreted as outcome measures of gait pattern. Gho05, including the new adaptation, is a valid method for detecting gait events in children with bilateral spastic CP.

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List of abbreviations

ADL = Activities of Daily Living

ASIS = Anterior Superior Iliac Spine

BoNT-A = Botulinum Neurotoxin A

CHQ = Child Health Questionnaire

CP = Cerebral Palsy

EMG = Electromyography

EVGS = Edinburgh Visual Gait Score

FAQ = Gillette Functional Assessment Questionnaire

FMS = Functional Mobility Scale

FS = Foot Strike

GGI = Gillette Gait Index

Gho05 = Ghoussayni's algorithm using a threshold of 0.5 m/s

GhoWS = Ghoussayni's algorithm using a Walking Speed dependent threshold

GMA = Prechtl's Assessment of General Movements

GMFCS = Gross Motor Function Classification System

GMFCS-E&R = Gross Motor Function Classification System – Expanded & Revised

GMFM = Gross Motor Function Measure

GPS = Gait Profile Score

GRF = Ground Reaction Forces

HINE = Hammersmith Infant Neurological Examination

ICF = International Classification of Functioning, Disability and Health

ICF-CY = International Classification of Functioning, disability and health, Children and Youth version

IGA = Instrumented Gait Analysis

LoA = Limits of Agreement

MAS = Modified Ashworth Scale

MMT = Manual Muscle Testing

MRI = Magnetic Resonance Imaging

MTS = Modified Tardieu Scale

ND = Non-Dimensional

PEDI = Pediatric Evaluation of Disability Inventory

PedsQL = Pediatric Quality of Life inventory

PODCI = Pediatric Outcomes Data Collection Instrument

PSIS = Posterior Superior Iliac Spine

pROM = Passive Range of Motion

RCT = Randomized Controlled Trial

ROM = Range of Motion

SEMLS = Single Event Multilevel Surgery

SPSS = Statistical Package for the Social Sciences

ST = Spatiotemporal

sEMG = Surface Electromyography

TO = Toe Off

WeeFIM = Functional Independence Measure for children

3D = Three-Dimensional

3DGA = Three-Dimensional gait analysis

6MWT = Six-Minute Walk Test

1

Introduction

1. INTRODUCTION

1.1. Context

The economic crisis of the last decade has led to a reduction in healthcare resources. Evaluating the efficacy of clinical interventions and moving towards evidence-based practice is essential to optimize healthcare resources. Every clinical process begins with an initial clinical assessment to determine the patient health status, define clinical goals, and select the treatment. During the treatment, periodic clinical assessments are performed to evaluate the patient progress, the achievement of the clinical goals, and thus the efficacy of the treatment.

Clinical assessment includes different types of outcome measures (questionnaires, tests, direct observations, interviews), and can be reported by the patient or by an external observer. It is important to know the advantages and disadvantages of each assessment tool to correctly interpret the results. Some common limitations are: 1) inherent subjectivity; 2) validity for specific populations; 3) low comparability of results due to the existence of different outcome measures validated to assess the same clinical problem; 4) difficulty to interpret the results; and 5) lack of responsiveness to treatments.

In recent years, the technology industry has shown great interest in the emerging healthcare market. Measurement systems for patients' objective clinical assessment are a current line of research, both in health sciences and biomedical engineering fields. Objective data improve patient clinical assessment, and facilitate the generation of evidence about treatments. Ineffective interventions should be revised and/or replaced by more effective ones in order to optimize healthcare resources.

Physical therapy aim to prevent, correct, or alleviate movement dysfunction; and promote, maintain, restore or improve the motor function. Movement assessment is a key task in this discipline. Motion analysis laboratories combine different technologies (motion capture systems, force plates, electromyography (EMG)) to provide objective and precise information about patient movements. However, these technologies are expensive and their application should be supported by evidence demonstrating their clinical utility.

In this context, the present research work is focused on the instrumented gait analysis (IGA), the study population is children with bilateral spastic cerebral palsy (CP), and the main research question is: which parameters are clinically relevant for the gait assessment in children with bilateral spastic CP?

1.2. Cerebral palsy

1.2.1. Definition

CP is an umbrella term encompassing etiologically diverse symptoms, which change with age (1). William John Little, an orthopedic surgeon who himself had an equinus deformity from early childhood secondary to poliomyelitis, is credited with the first descriptions of CP in 1843 (2,3). He was the first to recognize spastic paralysis, for many years known as Little's disease, and posited that these deformities of childhood were related to anoxia secondary to trauma occurring during labor (2,4). William Osler, a British physician, coined the term "cerebral palsy" in 1889 (2,5). Sigmund Freud, a neurologist and psychoanalyst, wrote many articles on CP, and disagreed with Little on its cause (2,6); he believed that CP might be caused by intrauterine abnormalities of brain development (2,6).

Different definitions of CP were developed over the years (2). In 1957, the Little Club, an informal club of neurologists, developed a unified definition of CP (2): "Cerebral palsy is a persisting qualitative motor disorder due to non-progressive interference with development of the brain occurring before the growth of the central nervous system is complete" (7). From 1987 to 1990, American and European CP investigators developed a common definition (2): "CP is an umbrella term covering a group of non-progressive, but often changing, motor impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of development" (8).

In 2004, in Bethesda, Maryland, an International Workshop on Definition and Classification of CP was held with the goal of updating the definition and classification of CP (9) in accordance with the new framework proposed by the International Classification of Functioning, Disability and Health (ICF) (10). The current definition, adopted by this group, recognizes that CP is more than a motor disability (2): "CP describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems" (9).

1.2.2. Etiology

The full causal path to CP is a complex interplay between several risk factors across, and not all are known (11,12). Risk factors can be classified according to the stage at which they occur: 1) preconception (concerning the broadly defined health and living conditions of the mother),

2) antenatal or prenatal (which are related to the course of pregnancy), 3) intrapartum or perinatal (from the 28th week of gestation through the 7th day after delivery), and 4) neonatal (during the first 28 days after birth) (1,13). For more than 100 years, it was believed that the vast majority of CP cases were related to infant brain hypoxia during perinatal period (14). Nowadays, antenatal factors seem to be responsible for nearly 75% of CP cases (14).

1.2.2.1.Preconception risk factors

A history of previous multiple miscarriage, stillbirth and neonatal death; maternal age; and prior maternal diagnoses (convulsions, intellectual disability, thyroid disease, diabetes, asthma, coagulation disorder, surgical history, mental illness, impaired fertility) (1,13).

1.2.2.2.Antenatal risk factors

Poly- or oligohydramnios; hemorrhage (second or third trimester); maternal disease in pregnancy (hypertension, psychiatric illness); placental abnormalities; intrauterine infection; intrauterine growth restriction; pre-eclampsia; genetic mutations; congenital anomalies; male sex; and multiple pregnancy (13,15,16).

1.2.2.3.Perinatal risk factors

Preterm delivery; premature membrane rupture; induction of labor; length of labor; meconium (stained liquor, aspiration); abnormal fetal presentation (breech, other than vertex); mode of delivery compared with spontaneous (caesarean section, instrumented delivery); sentinel events (cord around the neck; specifically tight cord, cord prolapse); placental abruption; hemorrhage; birth asphyxia; and low birthweight (13).

1.2.2.4.Neonatal risk factors

Convulsions; respiratory distress syndrome; hypoglycemia; jaundice; and infections including meningitis and sepsis (13).

New evidence suggests that many metabolic and non-progressive genetic disorders may present with motor dysfunction resembling CP, often characterized as CP mimics (17–20). Making a precise diagnosis of a metabolic or genetic disorder has important implications for the possibility of treatment, accurate prognosis and genetic counselling (19,20).

1.2.3. Prevention

Prevention strategies can be classified into antenatal and neonatal (21).

1.2.3.1.Antenatal

Magnesium sulfate before delivery of an infant less than 30 weeks' gestation prevents 30% of CP (22). Antenatal corticosteroids decrease intracranial hemorrhage and thereby also act as neuroprotection (22). Genetics testing could help to prevent CP in the near future (16).

1.2.3.2.Neonatal

In infants born preterm and mechanically ventilated, prophylactic caffeine prior to extubation effectively prevents CP (23). For babies born at term with neonatal encephalopathy or asphyxia, therapeutic hypothermia started within 6 hours of delivery is neuroprotective and prevents 15% of CP associated with intrapartum hypoxia (23).

1.2.4. Diagnosis

Historically, the diagnosis of CP has been made between age 12 and 24 months (24) but now it can be made before 6 months' corrected age (25). Diagnosis includes a clinical history, neuroimaging, and standardized neurological and motor assessments (25).

1.2.4.1.Clinical history

A detailed clinical history can help to identify risk factors (13).

1.2.4.2.Neuroimaging

Brain Magnetic Resonance Imaging (MRI) is commonly used to identify patterns predictive of CP that are associated to an estimated timing of damage (26). According to the Magnetic Resonance Imaging Classification System brain images in children with CP are classified into five main groups: A) maldevelopments; B) predominant white matter injury; C) predominant grey matter injury; D) miscellaneous; and E) normal (25,27) (see **Figure 1**).

MRI can also help with prognostication of motor severity and likelihood of co-occurring impairments, such as central vision impairment (11). The majority (84-91%) of infants with CP have detectable changes on MRI scanning (28). Conventional MRI has limitations in delineating white matter tracts precisely; powerful technique providing precise identification of white matter microstructure is Diffusion Tensor Imaging (29).

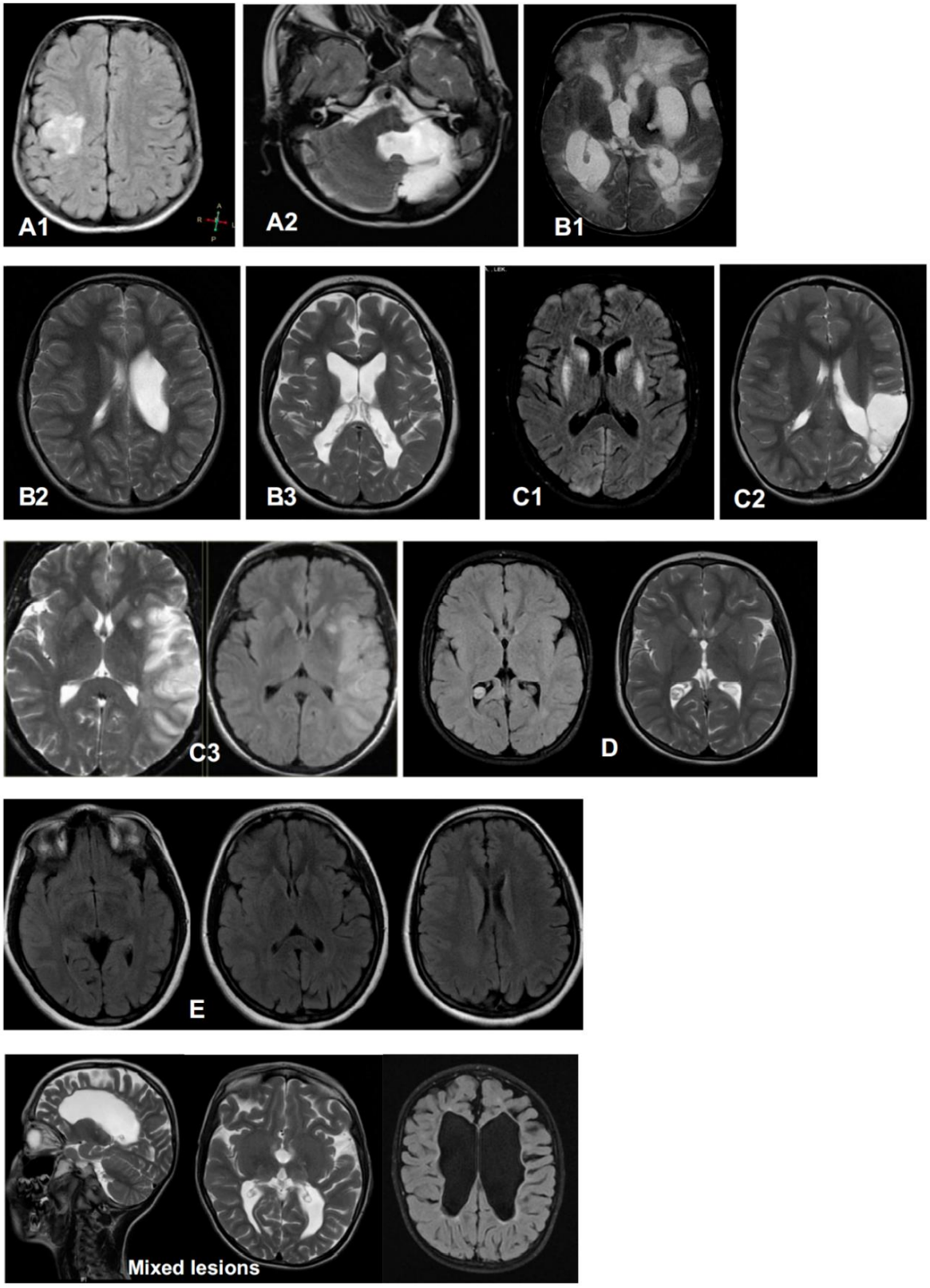

Figure 1. Examples of magnetic resonance imaging
A1, disorder of cortical formation; A2, other maldevelopments; B1, periventricular leukomalacia (PVL); B2, sequelae of intraventricular haemorrhage (IVH) or periventricular haemorrhagic infarction; B3, combination of PVL and IVH sequelae; C1, basal ganglia/thalamus lesion; C2, cortico-subcortical lesion; C3, arterial infarction; D, miscellaneous; E, normal imaging. Extracted from Sadowska et al. (1).

1.2.4.3.Standardized motor and neurological examination

The Prechtl's Assessment of General Movements (GMA) and the Hammersmith Infant Neurological Examination (HINE) have shown predictive validity for detecting cerebral palsy (30,31).

The GMA (32) assesses the spontaneous movement of infants, and is scored using a 3 to 5 minutes video (11). Two specific abnormal general movement patterns reliably predict later cerebral palsy: 1) a persistent pattern of cramped-synchronized general movements (movements appear rigid and do not have the normal smooth and fluent character; all limb and trunk muscles contract and relax almost simultaneously); and 2) the absence of fidgety movements (small movements of moderate speed with variable acceleration of neck, trunk and limbs in all directions are not observed from 9 to 20 weeks post-term) (32). Between 3 and 5 months post-term age, this tool has the highest sensitivity and specificity for detecting CP with values of about 98% and 91%, respectively (33).

The HINE (34) is a simple and scorable method designed for neurologically evaluating infants between 2 and 24 months of age (30). It includes 26 items that assess different aspects of neurological examinations such as cranial nerves, posture, movements, tone, and reflexes (34), and it can be completed in 5 to 10 minutes (30). Optimal scores are defined with cut-off values for CP at 3, 6, 9 and 12 months (35). The HINE allows identification of early abnormal signs related to other aspects of neurological function beyond the motor impairment such as cerebral visual impairment or feeding abnormalities (30). A good inter-observer reliability has been reported, even in inexperienced staff (34). The HINE has a sensitivity of 90% for detecting CP (30).

A trajectory of abnormal GMA or HINE scores, in combination with abnormal MRI, producing congruent findings, is even more accurate than individual clinical assessments for the diagnosis of CP (30,31).

1.2.5. Severity

Parents want to learn early about the severity of their child's condition for future planning (36). In infants younger than 2 years, the severity of the motor disability is difficult to accurately predict for different reasons such as developing motor skills (25). Prediction of motor severity should be made cautiously using standardized tools, including the cut-off scores of the HINE, combined with neuroimaging data (30). In children 2 years or older, severity is reliably classified using the Gross Motor Function Classification System (GMFCS) (37).

The GMFCS has been universally adopted to describe the motor function of children with CP (38). Its expanded and revised version (GMFCS-E&R) uses five ordinal levels across five age bands (under 2 years, 2-4 years, 4-6 years, 6-12 years, and 12-18 years), on the basis of the person's ability to self-initiate movement with a focus on sitting, transferring, and mobilizing (37). The general headings for each level are: [I] walks without limitations; [II] walks with limitations; [III] walks using a hand-held mobility device; [IV] self-mobility with limitations, may walk with physical assistance or use powered mobility; and [V] transported in a manual wheelchair (37) (see **Figure 2**). After classification with the GMFCS, children may be monitored as they age to evaluate if treatments result in improved GMFCS levels (39).

The GMFCS lacks a precise description of hand dexterity (1). The severity of motor disorders in upper limbs can be evaluated using the Manual Ability Classification System (40). It was designed to classify how children with CP aged 4 to 18 years use their hands when handling objects in daily activities (40). It consists of five levels: [I] children handle objects easily and successfully; [II] children handle most objects but with somewhat reduced quality and/or speed; [III] children handle objects with difficulty and require help to prepare and/or modify activities; [IV] children handle a limited selection of easily managed objects in adapted situations; and [V] children does not handle objects and has severely limited ability to perform even simple actions (40).

1.2.6. Classification

Different types of CP can be distinguished according to the associated movement disorders: 1) spastic: muscle hypertonia, usually accompanied by hyperreflexia and muscle weakness; 2) dyskinetic: uncontrollable involuntary movements, and altered muscle tension, including dystonia and athetosis; 3) ataxic: uncoordinated voluntary movements; and 4) mixed: various combinations of previous movement disorders (1,25,39). When more than one type of movement disorder is present, it is recommended to classify children according to the predominant disorder, also listing secondary disorders as these may impact on decision making (41).

Dyskinesia and ataxia usually affect all 4 limbs (25). Spasticity can be classified topographically as: 1) unilateral (lower and upper limbs unilateral affected); and 2) bilateral, including diplegia (lower limbs affected more than upper limbs) and quadriplegia (all 4 limbs and trunk affected) (25). Movement disorders and topography of cerebral palsy may emerge and change during the first 2 years of life (25).

GMFCS E & R between 6th and 12th birthday: Descriptors and illustrations

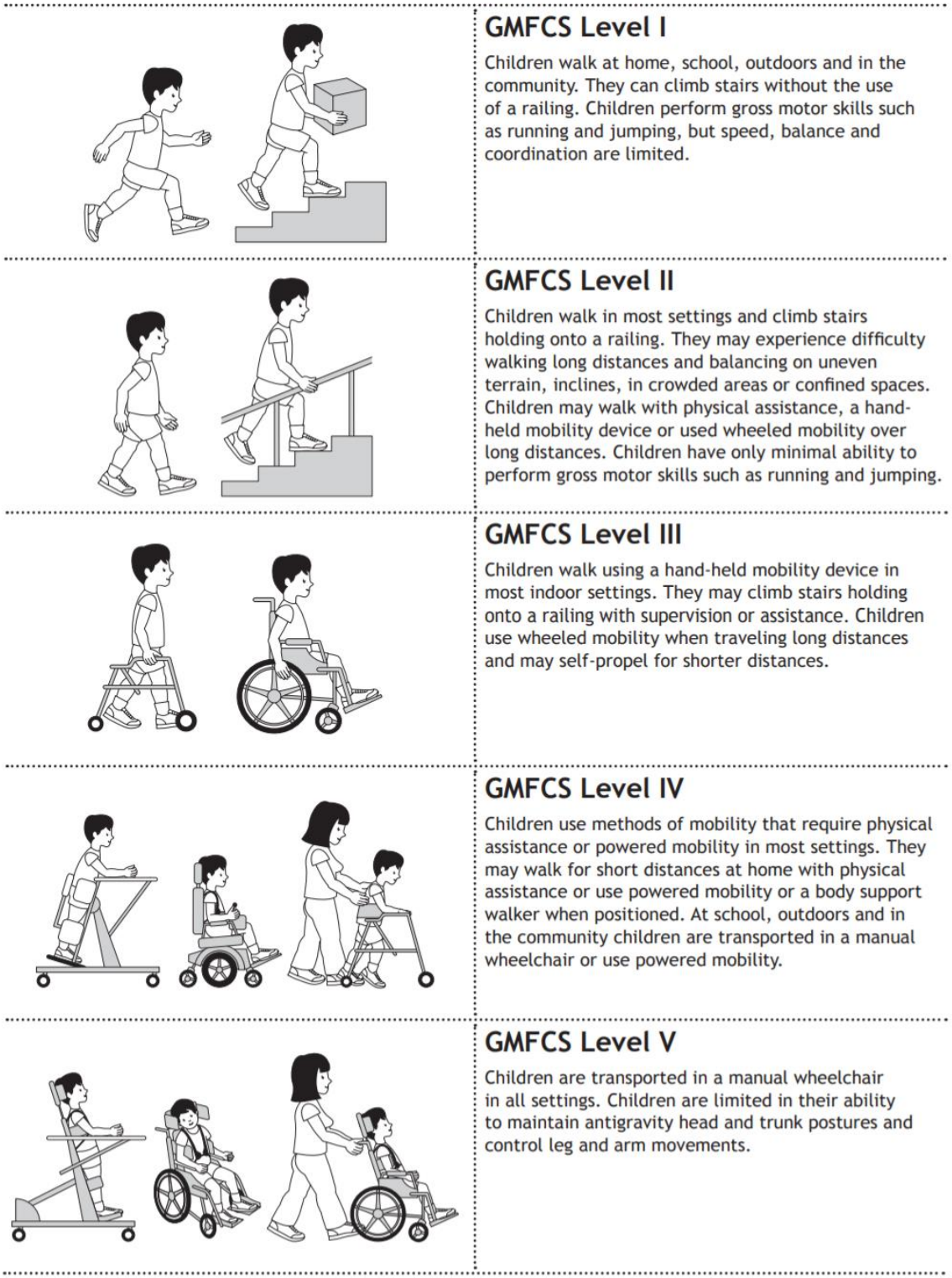

Figure 2. GMFCS-E&R between 6th and 12th birthday: descriptors and illustrations
GMFCS-E&R, Gross Motor Function Classification System – Expanded & Revised. Extracted from CanChild (42).

Children with unilateral CP almost always develop independent locomotion. On the contrary, in the case of bilateral CP, some children walk independently, some walk with aids and others can never achieve this function (43). Non-ambulant children typically receive their diagnosis by 6 months of age (11); while ambulant children with CP, particularly those with bilateral spastic CP, are a mean age of 23.9 months at diagnosis (24).

1.2.7. Epidemiology

CP is the most common motor disability of childhood (2) with a prevalence of above 2.11 per 1000 live births (44). However, the prevalence is not the same throughout the world (21,45). While in high-income countries such as Australia the prevalence has dropped to 1.4 per 1000 due to major discoveries in prevention, low-income countries such as Bangladesh have a prevalence of 3.4 per 1000 live births (21,45).

Most CP (92%) originates in the antenatal or perinatal period, with only 8% of cases attributed to postnatal causes (11). 57% of children with CP are born at term age, and the majority has no immediately identifiable risk factors for CP (36). The prevalence of CP in relation to birthweight per 1000 live births is: 60.04 in children under 1500 g, 8.33 in children between 1500 g and 2499 g, and 1.16 in children weighing over 2500 g (44). The prevalence of CP in relation to gestational age per 1000 live births is: 111.8 for children born before 28 weeks of gestation, 144.72 for children born between 28 weeks and 31 weeks, 6.75 for children born between 32 and 36 weeks, and 1.35 for children born after 36 weeks (44).

The severity is also not homogeneous around the world (21). In high-income countries such as Australia, 32% of children with CP have GMFCS level I, 27% level II, 12% level III, 14% level IV, and 15% level V (36). On the other hand, for example in Bangladesh, 43.6% of children with CP have severe motor impairments (GMFCS IV–V) (21,46). Regarding movement disorders, 85-91% of children with CP are spastic, 4-7% dyskinetic, 4-6% ataxic, and 2% mixed (25,36). In relation to topography, 38% of children have unilateral CP, 36% diplegia, and 26% quadriplegia (25,36).

1.2.8. Clinical features

The International Classification of Functioning, Disability and Health: Children and Youth version (ICF-CY) provides a universal and common language for clinical, public health and research applications to facilitate the documentation and measurement of functioning and disability, and relevant contextual factors in children (infancy, childhood and adolescence) (47). Functioning is an umbrella term encompassing all body functions, body structures, activities

and participation; disability is an umbrella term encompassing impairments, activity limitations and participation restrictions; and contextual factors define facilitators or barriers to functioning (47).

The ICF-CY covers the functioning and disability through two main components: 1) body functions (b) and structures (s), and 2) activities and participation (d); and the contextual factors through another two main components: 3) environmental factors (e), and 4) personal factors; using 1685 categories (47). Some ICF-CY definitions are shown in **Table 1**. For the activities and participation component, two constructs are available: 1) capacity (executing tasks in a standard environment), and 2) performance (executing tasks in the current environment) (47).

Table 1. Definitions of the International Classification of Functioning, Disability and Health: Children and Youth version

Component	Functioning	Disability
Body functions and structures	*Body functions* are the physiological functions of body systems (including psychological functions). *Body structures* are anatomical parts of the body such as organs, limbs and their components.	*Impairments* are problems in body function or structure such as a significant deviation or loss.
Activities and participation	*Activity* is the execution of a task or action by an individual.	*Activity limitations* are difficulties an individual may have in executing activities.
	Participation is involvement in a life situation.	*Participation restrictions* are problems an individual may experience in involvement in life situations.

Adapted from World Health Organization (47).

An ICF Core Set is a shortlist of ICF categories that are considered most relevant for describing the functioning of an individual with a particular health condition (48). The categories of the ICF Core Set for children and youth with CP related to motor disorders are listed in **Table 2**.

1.2.8.1.Body functions and structures

In children with CP, it is important to determine the nature and extent of abnormal tone (49). Tone is the resistance to passive stretch while a person is attempting to maintain a relaxed state of muscle activity (49). Hypertonia is defined as abnormally increased resistance to externally imposed movement about a joint (49), and it can be caused by spasticity, dystonia, rigidity, or a combination of these features (50).

Spasticity is often the dominant motor disorder in children with CP (41), along with loss of selective motor control (ability to activate a specific pattern of muscles in an isolated fashion (41)) and impaired balance (ability to maintain the line of gravity within the base of support with minimal postural sway (51)) (52). Spasticity is a form of muscle hypertonia in which resistance to passive movement grows with increasing velocity of movement, varies with direction of the movement, and/or rises rapidly above a threshold speed or joint angle (41). Spasticity is often a component of upper motor neuron syndrome and it is caused by an hyperactive stretch reflex

mechanism (41). The most affected muscles from spasticity in children with CP are: 1) in lower extremity: triceps surae (gastrocnemius and soleus), hamstrings, rectus femoris, hip adductors, and psoas; and 2) in upper extremity: shoulder external rotators, elbow, wrist and finger flexors, and forearm pronators (53).

Dystonia is defined as a movement disorder in which involuntary sustained or intermittent muscle contractions cause twisting and repetitive movements, abnormal postures, or both (50).

Rigidity is defined as an involuntary sustained muscle contraction in which the resistance to passive movement is independent of posture and speed of movement, and does not vary with the direction of movement (50). Voluntary activity in distant muscle groups does not lead to involuntary movements about the rigid joints (50).

Table 2. Categories of the ICF Core Set for children and youth with cerebral palsy related to motor disorders

Code	Category name	Description
s	**Body structures**	
s7	*Structures related to movement*	
s730	Structure of upper extremity	*No description available.*
s750	Structure of lower extremity	*No description available.*
s760	Structure of trunk	*No description available.*
b	**Body functions**	
b7	*Neuromusculoskeletal and movement-related functions*	
b710*	Mobility of joint functions	Functions of the range and ease of movement of a joint.
b715	Stability of joint functions	Functions of the maintenance of structural integrity of the joints.
b730	Muscle power functions	Functions related to the force generated by the contraction of a muscle or muscle groups.
b735*	Muscle tone functions	Functions related to the tension present in the resting muscles and the resistance offered when trying to move the muscles passively.
b740	Muscle endurance functions	Functions related to sustaining muscle contraction for the required period of time.
b755	Involuntary movement reaction functions	Functions of involuntary contractions of large muscles or the whole body induced by body position, balance and threatening stimuli.
b760*	Control of voluntary movement functions	Functions associated with control over and coordination of voluntary movements.
b765	Involuntary movement functions	Functions of unintentional, non- or semi-purposive involuntary contractions of a muscle or group of muscles.
b770	Gait pattern functions	Functions of movement patterns associated with walking, running or other whole body movements.
d	**Activities and participation**	
d4	*Mobility*	
d410	Changing basic body position	Getting into and out of a body position and moving from one location to another, such as rolling from one side to the other, sitting, standing, getting up out of a chair to lie down on a bed, and getting into and out of positions of kneeling or squatting.
d415*	Maintaining a body position	Staying in the same body position as required, such as remaining seated or remaining standing for work or school.
d420	Transferring oneself	Moving from one surface to another, such as sliding along a bench or moving from a bed to a chair, without changing body position.
d430	Lifting and carrying objects	Raising up an object or taking something from one place to another, such as when lifting a cup or toy, or carrying a box or a child from one room to another.
d435	Moving objects with lower extremities	Performing coordinated actions aimed at moving an object by using the legs and feet, such as kicking a ball or pushing pedals on a bicycle.
d440*	Fine hand use	Performing the coordinated actions of handling objects, picking up, manipulating and releasing them using one's hand, fingers and thumb, such as required to lift coins off a table or turn a dial or knob.

Table 2. Categories of the ICF Core Set for children and youth with cerebral palsy related to motor disorders

Code	Category name	Description
d445	Hand and arm use	Performing the coordinated actions required to move objects or to manipulate them by using hands and arms, such as when turning door handles or throwing or catching an object.
d450*	Walking	Moving along a surface on foot, step by step, so that one foot is always on the ground, such as when strolling, sauntering, walking forwards, backwards, or sideways.
d455	Moving around	Moving the whole body from one place to another by means other than walking, such as climbing over a rock or running down a street, skipping, scampering, jumping, somersaulting or running around obstacles.
d460*	Moving around in different locations	Walking and moving around in various places and situations, such as walking between rooms in a house, within a building, or down the street of a town.
d465	Moving around using equipment	Moving the whole body from place to place, on any surface or space, by using specific devices designed to facilitate moving or create other ways of moving around, such as with skates, skis, scuba equipment, swim fins, or moving down the street in a wheelchair or a walker.
d 470	Using transportation	Using transportation to move around as a passenger, such as being driven in a car, bus, rickshaw, jitney, pram or stroller, animal-powered vehicle, private or public taxi, train, tram, subway, boat or aircraft.

ICF, International Classification of Functioning, Disability and Health. * Included in the Brief ICF Core Set.

Adapted from Schiariti et al. (48).

Secondary musculoskeletal problems like muscle contracture (permanent shortening of a muscle-tendon unit (54)), muscle weakness (insufficient muscle activation (41)), bone deformity (abnormality in the shape or size of a bone), and joint instability (increased movement of a joint in any plane) appear as a consequence of growth and development of the musculoskeletal system, and are generally sequential and progressive over time (52,55). As muscles grow in response to stretching stimuli, muscle contractures due to hypertonia that are initially dynamic (over activity with no fixed shortening (55)) become fixed, as tight muscles fail to grow proportionately with the bones that they traverse (52). At the same time, due to the abnormal forces on the growing skeleton, bone deformities progress from flexible and passively correctable segmental malalignments to rigid skeletal deformities (55). Skeletal malalignment generally shortens the available lever arm (perpendicular distance between the joint center and the point of force application) compromising the ability of the muscle-tendon unit to generate an optimal moment, and causing joint instability (lever arm dysfunction) (52,55). There is evidence that spastic muscles are also weak in children with CP (49,56), and that strength and motor function are directly related (49,57).

The interaction of motor disorders and secondary musculoskeletal problems, occurring at multiple levels, affects the quality and efficiency of gait (52). The ICF-CY defines the category “gait pattern functions” (b770) as functions of movement patterns associated with walking, running or other whole body movements (47). This category includes walking and running patterns; and impairments such as spastic gait, hemiplegic gait, paraplegic gait, asymmetric gait, and limping and stiff gait pattern (47). The gait pattern of children with CP, referred to the manner or style of walking (58), is the result of muscle imbalance in the sagittal plane

(spasticity and contractures of hip flexors, knee flexors and ankle plantar flexors), and deformities in the sagittal and transversal planes, in addition to weakness and poor selective motor control (59). In children with CP, six different gait patterns have reached consensus: genu recurvatum, drop foot, true equinus, jump gait, apparent equinus, and crouch gait (60). These gait patterns are based on the IGA, specifically on kinematic data in sagittal plane (60).

In high-income countries, 33% of children with CP experience progressive hip displacement (39,61), defined as percentage of the femoral head that sits out-side the lateral margin of the acetabulum greater than 30% (62,63). Walking ability is a key point in the development of hip displacement, since dynamic compressive forces generated during walking are needed for the development of the required depth in acetabulum (64). Hip displacement was reported to be 11% in ambulatory children and 57% in non-ambulatory children (65).

1.2.8.2.Activities and participation

Motor impairments affect different aspects of motor function, contributing to activity limitations and participation restrictions (52,62). Motor function is the ability to perform movements (actions and tasks) that involve the use of different muscle groups (66,67). Motor skills are categorized in two groups: 1) gross motor skills: movements that require the use of large muscle groups of the arms, legs and/or trunk, such as crawling, walking and jumping; and 2) fine motor skills: movements that require the use of small muscle groups of the wrists, hands, fingers, feet and/or toes, such as playing the piano, writing and grasping an object (66,67).

The ICF Core Set for children and youth with CP highlights some relevant categories related to mobility (d4): changing basic body position, maintaining a body position, transferring oneself, lifting and carrying objects, moving objects with lower extremities, fine hand use, hand and arm use, walking, moving around, moving around in different locations, moving around using equipment, and using transportation (see **Table 2**) (48). “Walking” (d450) is part of this Core Set and it is defined as moving along a surface on foot, step by step, so that one foot is always on the ground, such as when strolling, sauntering, walking forwards, backwards, or sideways (47). This category includes walking short or long distances, walking on different surfaces, and walking around obstacles (47).

Activities of daily living (ADL), often termed basic ADL, include the fundamental skills typically needed to manage basic physical needs (68) such as washing, dressing, toileting, transferring, eating, and walking or moving around; and require the coordination of gross and fine motor skills (66). Basic ADL are generally categorized separately from instrumental ADL, which

include more complex activities related to independent living in the community (68) such as managing finances, medications, transportation and communication.

The ICF Core Set for children and youth with CP also highlights relevant categories related to: 1) self-care (d5): washing oneself, caring for body parts, toileting, dressing, eating, drinking, and looking after one's health; 2) domestic life (d6): preparing meals, and doing housework; 3) interpersonal interactions and relationships (d7): basic interpersonal interactions, complex interpersonal interactions, informal social relationships, family relationships, and intimate relationships; 4) major life areas (d8): preschool education, school education, acquiring, keeping and terminating a job, basic economic transactions, and engagement in play; and 5) community, social and civic life (d9): community life, and recreation and leisure (48).

Activity limitations and participation restrictions may lead to a reduced quality of life (69), defined as a person's feelings of well-being across many domains including physical, social, emotional and spiritual aspects of life (70). One of the possible future directions for development and application of ICF is establishing links with quality of life (47). It is important that there is conceptual compatibility between quality of life (a construct referred to subjective well-being) and disability constructs (referred to objective and exteriorized signs of the individual) (47).

1.2.8.3.Comorbidities

Different comorbidities that are not part of the core definition of CP also occur: chronic pain (75% of cases), intellectual disability (50%), inability to speak (25%), epilepsy (25%), incontinence (25%), behavioral disorders (25%), sleep disorders (20%), blindness (10%), and hearing loss (4%) (39,61).

1.2.9. Clinical assessment

Clinical assessment is the method used to measure the patient's health (functioning, disability), and draw conclusions. It includes a whole set of data sources (medical history, observation, physical examination, functional assessment, computer analysis methods, diagnostic imaging) that complement and reinforce each other (43,55).

The ICF-CY can help to standardize the selection of outcome measures in children with CP (47). There are instruments assessing body functions and structures such as muscle tone, muscle strength, contractures and range of motion (ROM), and deformities; and instruments assessing activities and participation such as gross motor function, ADL and quality of life (43).

Multilevel assessment is very important in CP to detect motor disorders, select the most appropriate treatment, and evaluate the changes occurring over time with the treatment (43).

When selecting outcome measures, psychometric properties (reliability, validity and responsiveness) should be considered (43) (see **Table 3**). Interpretability (the degree to which qualitative meaning, that is, clinical or commonly understood connotations, can be assigned to an instrument's quantitative scores or change in scores) is not considered a psychometric property, but an important characteristic of a measurement instrument (71).

Table 3. Definitions of psychometric properties

Psychometric property	Definition
Reliability	The degree to which a measurement is free from measurement error (71).
Intra-rater reliability	The stability of the data recorded by the same rater on different trials (72).
Inter-rater reliability	The stability of the data recorded by different raters who measure the same trial (72).
Test-retest reliability	The degree to which a test is stable and is capable of measuring a variable with consistency when administered repeatedly (72).
Internal consistency	The degree of the interrelatedness among different items of the same test (or the same subscale on a larger test) (71).
Validity	Degree to which an instrument measures the construct(s) it purports to measure (71)**.**
Content validity	The degree to which the content of an instrument is an adequate reflection of the construct to be measured (71).
Construct validity	The degree to which the scores of an instrument are consistent with the theoretical components of the construct to be measured (71,72)
Criterion validity	The degree to which the scores of an instrument are an adequate reflection of a gold standard (71).
Responsiveness	Ability of an instrument to detect change over time in the construct to be measured (71).

Adapted from Mokkink et al. (71) and Flamand et al. (72).

1.2.9.1.Body functions and structures

Physical examination is used to assess impairments (motor disorders and secondary musculoskeletal problems) such as hypertonia, muscle weakness, contractures, and bone deformities (49). Physical examination have some limitations: on the one hand, the information collected during a physical examination is based on static responses, whereas functional activities, for example walking, are dynamic; on the other hand, the method of assessment, the skill of the examiner, and the participation of the child can affect the usefulness of the examination (49). There are standardized definitions of the different elements of the examination that aim to provide a more homogeneous assessment (49).

Muscle tone

The Hypertonia Assessment Tool is a standardized 7-item assessment of the three types of pediatric hypertonia: spasticity (2 items), dystonia (3 items), and rigidity (2 items). Rating consists of scoring 0 (negative) or 1 (positive) for each item, and a positive score for at least one item of the subgroup confirms the presence of this subtype of hypertonia (72,73). It has

good reliability and validity for identifying spasticity and the absence of rigidity, and moderate findings for dystonia (73).

Spasticity comprises complex spinal and cortical components and yet no consensus has been reached regarding its appropriate measurement (72). Numerous measurement tools have been developed for assessing muscle spasticity, which can be grouped into three categories: 1) clinical scales: Ashworth Scale and Modified Ashworth Scale (MAS), Tardieu Scale and Modified Tardieu Scale (MTS), and the Composite Spasticity Scale; 2) biomechanical assessment tools: the Myotonometer, Wartenberg and three-dimensional (3D) pendulum tests, dynamometry, goniometry, inertial sensors, and the Stiffness tool with robotic-assisted gait orthosis; and 3) neurophysiological assessment tools: EMG, tonic stretch reflex testing, and the Hoffmann reflex of soleus muscle (72).

The lack of evidence on their psychometric properties (especially in relation to responsiveness) makes it difficult to recommend a single spasticity assessment tool over the others in children with CP (72). The neurophysiological tools are the most promising in terms of reliability and discriminating validity, but their applicability for clinical use remains an issue (cost, equipment, time required) (72). In a clinical setting, spasticity is still typically assessed by measuring the resistance to imposed passive movement of the limb through the available ROM, as done with the MAS and MTS (72).

The MAS qualifies the resistance (tone increase) of muscles to passive movement (72). A fast passive stretch of the muscle is performed to detect a catch (a sudden appearance of increased muscle activity, which leads to an abrupt stop or increased resistance during the joint movement) (74). The MAS uses a 6-point ordinal scale: [0] no increase in muscle tone; [1] slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the ROM when the affected part(s) is(are) moved in flexion or extension; [1+] slight increase in muscle tone, manifested by a catch followed by minimal resistance through the remainder of the ROM but the affected part(s) is(are) easily moved; [2] more marked increase in muscle tone through most of the ROM, but the affected part(s) is easily moved; [3] considerable increases in muscle tone, passive movement difficult; and [4] affected part(s) is (are) rigid in flexion or extension (75).

The MTS qualifies the resistance of spastic muscles to passive stretching at three different velocities: [V1] as slow as possible; [V2] the speed of the limb falling under gravity; and [V3] as fast as possible (72,76). The MTS measures two resulting joint angles using a goniometer: [R1] the angle of catch at which a muscle response (stretch reflex), provoked by the fast

velocity (V2 or V3) stretch; and [R2] the angle of full passive ROM obtained with low speed (V1) stretching. The R2 minus R1 (R2–R1) value is thought to describe the level of dynamic contracture in the joint (72,76).

Muscle strength

Muscle strength cannot be measured directly with non-invasive methods (77). It is evaluated by measuring the collective, or global, force of all muscles acting around a particular joint (77). In clinical and research settings, muscle strength is measured manually with Manual Muscle Testing (MMT), or instrumentally using force transducers such as a hand-held dynamometer (77).

MMT is an easy and quick way to assess significant weakness or muscle imbalance, and requires only a table and standardized positioning (49). It uses a 6-point scale: [0] no contraction; [1] flicker or trace contraction; [2] active movement, with gravity eliminated; [3] active movement against gravity; [4] active movement against gravity and resistance, and [5] normal power (77). MMT is very popular in clinical practice, but it has many limitations (77): 1) only scores 0 to 3 are considered objective, scores 4 and 5 are subjective and depend on the examiner's force-sensing abilities; 2) in patients with motor disorders such as CP, the testing position may require modification due to muscle shortening and/or muscle contractures, affecting the moment of force generated around the joint, which depends not only on its angular position, but also on the angular position of neighboring joints; 3) the MMT scale does not account for age-related and growth-related changes in force-generating ability (77). In pediatric population, MMT scores have been proven to be reliable, but not valid (77).

The hand-held dynamometer is a battery-operated device consisting of strain gauges that records force or torque, and it has shown to be a reliable tool to measure isometric strength in children with CP (78). Muscle groups are tested in their mid-muscle-length position (79). Muscle contractions of 5 seconds are used to allow subjects to gradually achieve maximal force (79). The mean value of peak forces (maximal voluntary contraction) out of three trials is considered for each muscle group (77,79). Normalization is required for body weight and lever length for strength comparisons (79). Validity of this examination still depends on appropriate positioning, whether stabilization is used, and the experience of the tester (49).

Selective motor control

Selective motor control involves isolating movements upon request, appropriate timing, and maximal voluntary contraction without overflow movement (49). It is measured using a muscle

selectivity grading scale, which includes three levels of control: [0] no ability to isolate movement; [1] partial ability to isolate movement; and [2] complete ability to isolate movement (49). There is a standardized positioning to assess selective motor control of lower limb muscle groups (49).

Range of motion and contractures

Loss of joint movement is a symptom of muscle contracture. Therefore, ROM is used to measure muscle contracture. The passive ROM (pROM) is the angular distance that a joint can be moved by the therapist (no effort from the patient), from a position of relative muscle shortening to a position of relative muscle lengthening at slow velocity (72). When assessing muscle contracture, it is important to understand the interaction of multiple muscle groups (49). Differentiation between contracted biarticular and monoarticular muscles is also important (49). The accuracy and repeatability of contracture and pROM measurements are improved by using a goniometer, and standardized techniques of limb-segment manipulation (55,80,81).

The Silverskiold test assesses and differentiates contractures of the gastrocnemius and the soleus (49). Firstly, with the child positioned in supine, the knee is flexed to 90º, the hindfoot is positioned in varus, and maximal ankle dorsiflexion (in degrees) is obtained (49). If dorsiflexion movement is diminished, soleus contracture is present (see **Figure 3a**). Next, as the knee is extended, if the ankle moves towards plantarflexion, gastrocnemius contracture is present (49) (see **Figure 3b**).

The Thomas test is used to measure the contracture of the hip flexor muscles (iliopsoas and rectus femoris) (49). It is performed with the child in a supine position and the pelvis held such that the anterior and posterior superior iliac spine (ASIS and PSIS) are aligned vertically (49). Contralateral hip and knee are flexed (82). An increase in the angle between the thigh and the table indicates a contracture of the hip flexor muscles (82). Unresponsiveness of the hip flexion to flexion of the knee indicates shortening of the psoas muscle, whereas an increase in hip flexion upon flexing the knee indicates rectus femoris muscle contracture (82) (see **Figure 4a**). Contracture of the rectus femoris can also be suspected based on a decrease in knee flexion when the child is at the edge of the table (82) (see **Figure 4b**).

The Duncan-Ely test assesses contracture of the biarticular rectus femoris, and differentiates it from contracture of the monoarticular vastii (49). With the child positioned in prone, the knee is flexed (49). Flexion of the hip indicates the presence of rectus femoris contracture (49). Biarticular muscle tests (such as Silverskiold test and Duncan-Ely test) reliably demonstrate

contracture of the biarticular muscle involved under general anesthesia, so they should routinely be included as part of the presurgical examination (49).

Contracture of hip adductor muscles can be distinguished from that of gracilis, semimembranosus, and semitendinosus by measuring hip abduction in three different ways, with the child in a supine position: 1) with hip and knee both flexed, the length of adductors is measured; 2) with hip in neutral and knee flexed off the side of the table, length of the adductors and gracilis is measured; and 3) with hip in neutral and knee fully extended, the length of gracilis, medial hamstrings and adductors is measured (49). Stabilization of the pelvis is essential for a correct measurement (49).

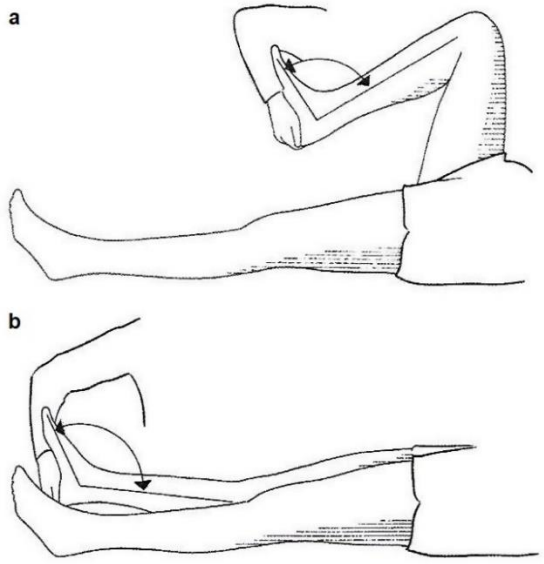

Figure 3. Silverskiold test
Extracted from Gage et al. (49).

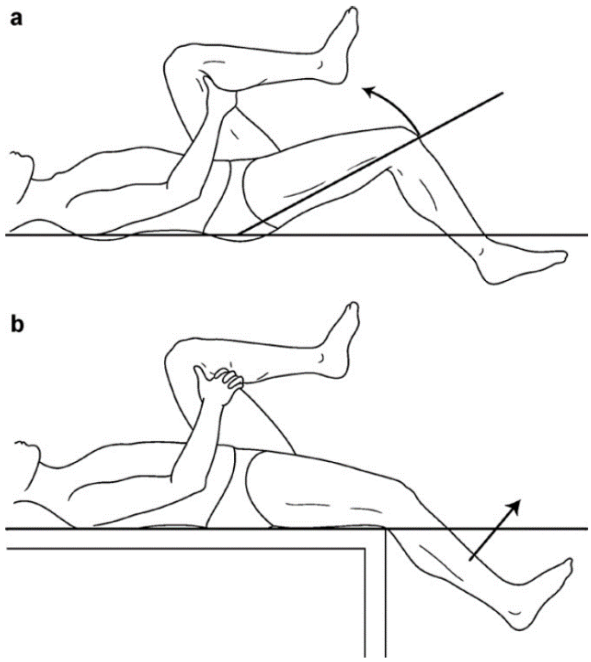

Figure 4. Thomas test
Extracted from Cottalorda et al. (82).

A knee-flexion contracture can be caused by four components: 1) shortened hamstrings; 2) shifted hamstrings due to excessive anterior tilt; 3) shortened proximal gastrocnemius; and 4) capsular contracture (49). Hamstring shift is calculated measuring the unilateral and bilateral popliteal angles and finding the difference between them (49). The unilateral popliteal angle is a measure of the functional hamstring contracture (with typical lordosis) (49). It is measured with the child in supine, the ipsilateral hip flexed to 90º, and the contralateral hip in neutral position (49). The knee is extended until the first endpoint of resistance is felt, and the angle (in degrees) lacking from full knee extension is measured (49). The bilateral popliteal angle is a measure of the true hamstring contracture (with neutral pelvis) (49). It is measured in supine, with the ipsilateral hip flexed to 90º, and the contralateral hip flexed until the ASIS and PSIS

are aligned vertically, to tip the pelvis posteriorly (49). The difference between the two angles represents the degree of hamstring shift (49) (see **Figure 5**).

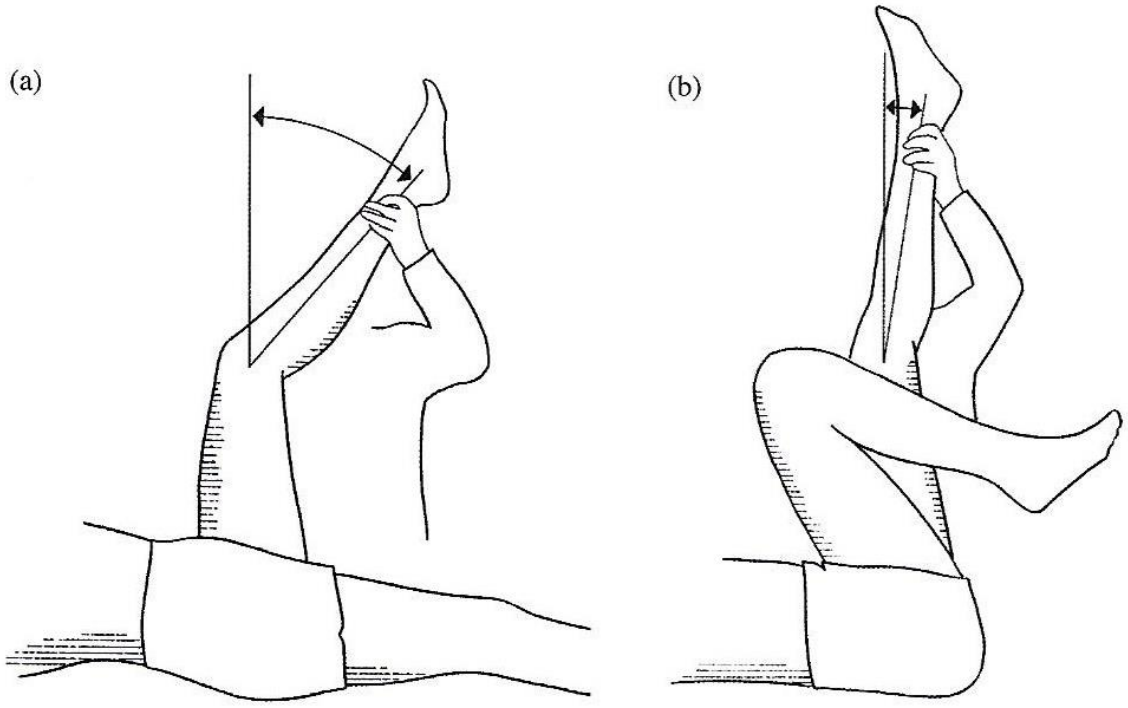

Figure 5. Unilateral and bilateral popliteal angles
(a), unilateral popliteal angle; (b), bilateral popliteal angle. Extracted from Gage et al. (49).

Bone deformities

Children with CP commonly have excessive femoral anteversion, referred to the relationship between the axes of the femoral neck and the femoral condyles, which is compensated with internal rotation of the femur and/or increased pelvic tilt (lumbar lordosis) in order to cover the femoral head (49). Femoral anteversion is assessed in the prone position, with the knee flexed to 90º (49). The clinician palpates the point of maximal trochanteric prominence and, with the fulcrum of the goniometer at the midpoint of the knee, the angle between the tibia and the vertical line is measured (49).

Children who walk with excessive knee flexion commonly have patella alta (49). With the child in supine and the knees extended, the top of the patella is palpated (49). If the superior edge of the patella is more than one finger width proximal to the adductor tubercle, patella alta is present (49). Extensor lag, defined as the difference between the active and the passive ROM during knee extension, is also suggestive of patella alta (49). It is measured with the child positioned supine, and the legs draped over the edge of the table (49). Patellar position can also be measured with lateral x-ray of the knee, taken in full knee extension (49).

Both excessive internal and external rotations of the tibia are common in children with CP (83). Tibial torsion can be measured in three different ways: 1) measurement of the thigh-foot angle: with the child in prone position, knee flexed to 90º, hindfoot in vertical position, and ankle dorsiflexed to 90º. The angle between the posterior axis of the femur, and the axis of the hindfoot with the point between the second and third metatarsals is measured (49); 2) measurement of the bi-malleolar axis: with the child in supine position and the knee fully extended, the thigh segment is rotated until the medial and lateral femoral condyles are parallel in the frontal plane. The angle between the malleolar axis and the condylar axis is measured. In case of foot deformities, the bimalleolar axis may be more accurate than the thigh-foot angle (49); and 3) the second toe test: with the child in prone position and knee fully extended, the leg is rotated to position the second toe pointing directly toward the floor. In this position, the knee is flexed and the angle between the tibia and the vertical line is measured. In case of equinus contracture and/or severe varus or valgus foot deformities, the second toe test is not accurate (49). Tibial torsion can also be measured using computed tomography (49).

Foot alignment is complex because it involves bone and joint deformities within the foot in addition to external rotational muscle forces (83). When assessing foot alignment, it is helpful to consider the foot and ankle as consisting of three segments: hindfoot or rearfoot, midfoot and forefoot (55) (see **Figure 6**), and the foot and ankle cardinal planes (49) (see **Figure 7**).

In the frontal plane, by visualizing the relationship of the bisector of the calcaneus relative to the bisector of the lower third of the leg, hindfoot position can be classified into: 1) vertical: when the relationship is linear; 2) varus: when the orientation of the hindfoot with respect to the lower third of the leg is inverted; and 3) valgus: when the line bisecting the calcaneus is everted in relation to the lower third of the leg (49) (see **Figure 8**). In the transverse plane, forefoot position can be classified into: 1) typical: no deviations; 2) adduction: deviations toward the midline; and 3) abduction: deviations away from the midline (49) (see **Figure 9**).

In the sagittal plane, equinus deformity consists of excessive plantar flexion of the hindfoot relative to the tibia (55,83). On the other hand, the medial longitudinal arch of the foot can be classified into normal, high, and low (flat foot). The Root test is used to distinguish flexible and structural flat foot (49). In the standing position, if there is a reconstitution of the medial longitudinal arch while heel is raised, flexible flat foot is present (49). Physical examination of foot malalignments can be evaluated further on radiographs, for structural abnormalities (55).

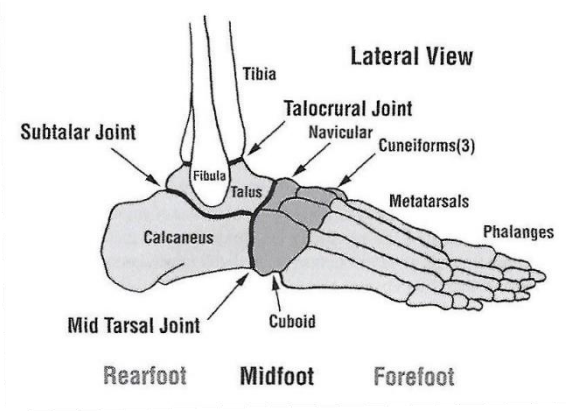

Figure 6. Foot bones and joints
Extracted from Gage et al. (49).

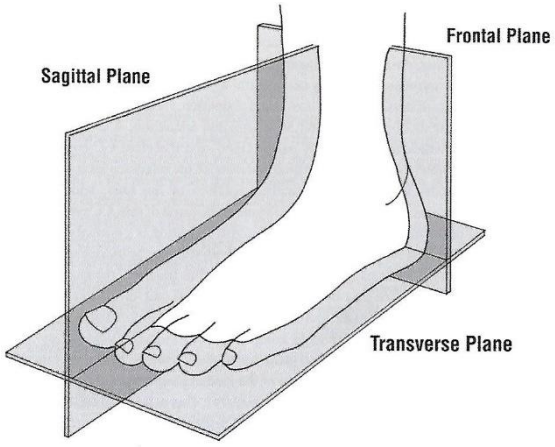

Figure 7. Foot cardinal planes
Extracted from Gage et al. (49).

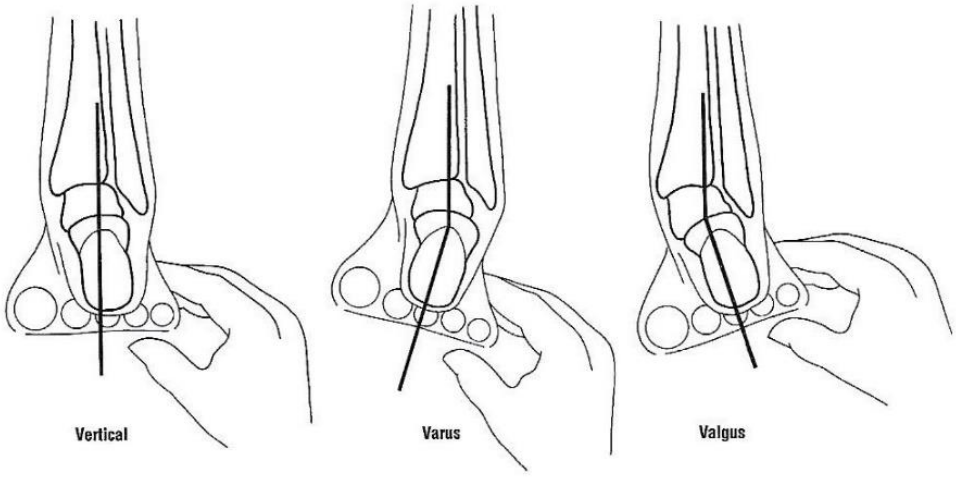

Figure 8. Hindfoot position in the frontal plane
Extracted from Gage et al. (49).

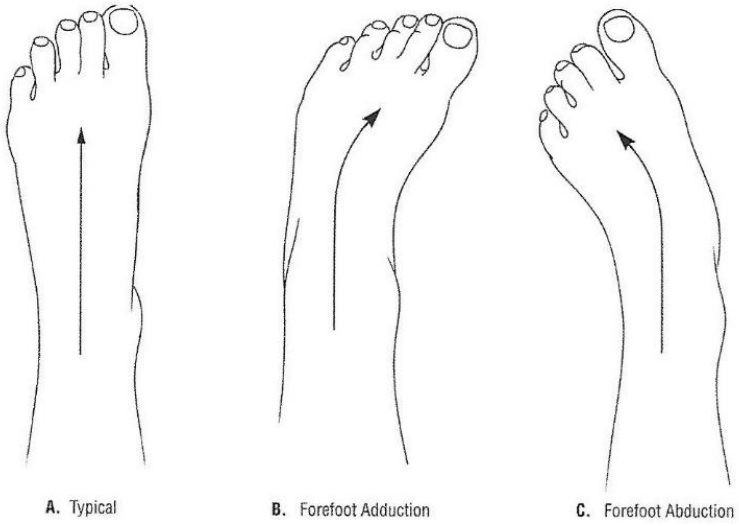

Figure 9. Forefoot position in the transverse plane
Extracted from Gage et al. (49).

Posture and balance

Many children with cerebral palsy have delayed or deficient posterior equilibrium responses (49). Assessment of static and dynamic posture will often give insight to areas of weakness, poor motor control, and compensation strategies (49). The Pediatric Balance Scale is a reliable and valid balance measure for school-age children with mild to moderate motor impairments (84–86), and it is frequently used in children with CP (43). It consists of 14 items such as "sitting to standing" and "standing on one foot" that are scored from 0 points (lowest function) to 4 points (highest function) with a maximum score of 56 points (84).

1.2.9.2.Activities and participation

Many scales are used for the functional assessment of children with CP such as the Gross Motor Functional Measure (GMFM), the Pediatric Evaluation of Disability Inventory (PEDI), and the Child Health Questionnaire (CHQ), which are the most frequently used (87).

The GMFM is the gold standard for assessing mobility in children with CP (87). It is a standardized observational instrument designed and validated to measure change in gross motor function over time in children with CP (88). It consists of five different dimensions: [A] lying and rolling; [B] sitting; [C] crawling and kneeling; [D] standing, and [E] walking, running and jumping (88). There are two versions of the GMFM: the GMFM-88 (89) and the GMFM-66 (90). The GMFM-88 is the original 88-item measure, and it is used to assess children using ambulatory aids and/or orthoses or shoes (88). Each item is scored from 0 (does not initiate) to 3 (completes), it allows testing one or more specific dimensions, and the total and/or goal total scores are given in percentage (88). The GMFM-66 is a 66 item subset of the original 88 items (88). The GMFM-66 is used to assess children walking barefoot, and items are ordered in terms of difficulty (88). It has a unidimensional scale ranging from 0 to 100 (88), and the total score is calculated using the GMFM-66 Ability Estimator Software (88). Both the reliability and the responsiveness of the GMFM are reasonable for measuring gross motor function in children with CP (91).

The PEDI provides information regarding functional performance, the level of assistance, and the extend of modifications required to perform ADL in young children (92,93). The PEDI primarily measures activities and participation (all the domains) across the following 3 measurement scales (87,93): 1) functional skills: includes 197 items, and each item is rated 0-1 for performance capability; 2) caregiver assistance: includes 20 items of complex functional activities, and each item is rated 0-5 for assistance level; and 3) modifications: includes 20 items of complex functional activities rated N (No modifications), C (Child-oriented), R

(Rehabilitation equipment), or E (Extensive modifications) (93). Scores are distributed from 0-100, with higher scores representing greater functionality (93). The PEDI can be administered via parent/caregiver report, structured interview, observation or professional judgement of the therapists or teachers, or by a combination of methods (93). The PEDI is a reliable, valid and responsive tool in children with CP (92,94).

The CHQ is a reliable and valid tool to measure health-related quality of life in children and adolescents (95,96). It covers most of the ICF-CY components including body functions, activities and participation, and contextual factors (87). This measure consists of a child report (CHQCF87, with 87 items) and 2 versions of parent-proxy report: 1) the long parent-report questionnaire (CHQ-PF50, with 50 items), and 2) the short parent-report questionnaire (CHQ-PF28, with 28 items) (95). Each item consists of 4–6 response options (95). The CHQ is not disease specific, so the scores of children with CP can be compared to children with typical development or with other disease conditions (49).

Other outcome measures included in the 15 most used multiple-item measures in children with CP are the Functional Independence Measure for children (WeeFIM), the Pediatric Outcomes Data Collection Instrument (PODCI) and the Pediatric Quality of Life inventory (PedsQL) (87).

1.2.9.3.Gait pattern and walking

There are two categories of the ICF-CY related to gait: gait pattern functions (b770), and walking (d450) (47). According to these categories, two different types of outcome measures used to assess gait have been distinguished: outcome measures of gait pattern (referred to the manner of walking), and outcome measures of walking (referred to the ability of walking) (97). The latter can be classified in outcome measures of walking capacity (walking in a standard environment), and outcome measures of walking performance (walking in the current environment) (47). On the other hand, there are two types of gait analysis: observational and instrumented (97). Some of the existing tools, which have different levels of evidence regarding psychometric properties in children with CP (97), are described below.

Gait pattern

The IGA is the gold standard for the evaluation of the gait pattern in CP (60,98). However, it is an expensive and unavailable technology in many centers (98), and its psychometric properties have not been well stablished in children with CP: the IGA has conflicting level of evidence for reliability because some gait parameters have good reliability while others do not; and its validity and responsiveness have not been thoroughly studied (97).

The Edinburgh Visual Gait Score (EVGS) is suggested as the best current available observational gait assessment tool to assess the gait pattern in children with CP (99). Gait videos in frontal and sagittal planes are analyzed according to 17 items for each inferior limb, which correspond to key elements of normal and pathological gait (98). Each item is graduated in a three scores range: [0] normal, [1] moderate deviation, and [2] marked deviation; and the maximum total score per limb is 34 (100). Six different anatomical levels are analyzed (trunk, pelvis, hip, knee, ankle and foot) in the transverse, frontal and sagittal planes; and stand and swing phases of the gait (98). The EVGS has unknown level of evidence regarding reliability, criterion validity and responsiveness; and limited level of evidence for construct validity (97). Its reliability is higher for distal segments, with greater experience in gait analysis of the observer, with more EVGS practice, and when used with higher functioning children (101).

Walking performance

The Functional Mobility Scale (FMS) classifies the functional mobility of children with CP, taking into account the range of assistive devices a child might use (102). The FMS aim to rate what the child actually does (performance), not what they can do or used to be able to do (capacity), so it is administered by the clinician via child/parent interview (102). The FMS rates walking ability at three distances (5 m, 50 m and 500 m) representing the child's mobility at home, at school and in the community setting (102). For each distance, a rating of 1-6 is given according to the need for assistive devices: [1] uses wheelchair; [2] uses walker or frame; [3] uses crutches; [4] uses sticks (canes); [5] independent on level surfaces; [6] independent on all surfaces (102). A rating of [C] is given if the child crawls for mobility at home (5 m), and an [N] if the child does not complete de distance (102). Orthotics which are regularly used should be included for the rating (102). The FMS has strong level of evidence for inter-rater reliability, and unknown level of evidence for construct validity and responsiveness (97,102–105).

The Gillette Functional Assessment Questionnaire (FAQ) is a 10-level, parent-report walking scale that aims to identify the child's usual level of function (106,107). The scale describes a range of walking abilities from non-ambulatory to ambulatory in all community settings and terrains (106), from 1 (the child cannot take any steps at all) to 10 (the child walks, runs, and climbs on level and uneven terrain without difficulty) (107). The FAQ has moderate level of evidence for inter-rater reliability and construct validity, and limited level of evidence for intra-rater reliability (97,106,108).

Walking capacity

The Six-Minute Walk Test (6MWT) is a measure of walking capacity used in children with CP (109,110). It assesses the distance walked over 6 minutes (109). It is recommended to use a 30-meter long hallway with a marker every 3 meters, and the turnaround points marked by a cone (111). Children may take as many standing rests as they like, but the timer should keep going and record the number of rests taken and the total rest time (111). Assistive devices can be used, but must be documented (111). The minimum amount of assistance required for a child to complete the task should be provided, and the greatest amount of assistance provided should be documented (111). When administering the test, the examiner should walk at least a half step behind the child (111). The 6MWT has moderate level of evidence regarding test retest reliability, and unknown level of evidence for construct validity (97,109,112,113).

Item		E: WALKING, RUNNING & JUMPING	SCORE				NT
*	65.	STD, 2 HANDS ON LARGE BENCH: CRUISES 5 STEPS TO R	0☐	1☐	2☐	3☐	65.
*	66.	STD, 2 HANDS ON LARGE BENCH: CRUISES 5 STEPS TO L	0☐	1☐	2☐	3☐	66.
*	67.	STD, 2 HANDS HELD: WALKS FORWARD 10 STEPS	0☐	1☐	2☐	3☐	67.
*	68.	STD, 1 HAND HELD: WALKS FORWARD 10 STEPS	0☐	1☐	2☐	3☐	68.
*	69.	STD: WALKS FORWARD 10 STEPS	0☐	1☐	2☐	3☐	69.
*	70.	STD: WALKS FORWARD 10 STEPS, STOPS, TURNS 180°, RETURNS	0☐	1☐	2☐	3☐	70.
*	71.	STD: WALKS BACKWARD 10 STEPS	0☐	1☐	2☐	3☐	71.
*	72.	STD: WALKS FORWARD 10 STEPS, CARRYING A LARGE OBJECT WITH 2 HANDS	0☐	1☐	2☐	3☐	72.
*	73.	STD: WALKS FORWARD 10 CONSECUTIVE STEPS BETWEEN PARALLEL LINES 20cm (8")APART	0☐	1☐	2☐	3☐	73.
*	74.	STD: WALKS FORWARD 10 CONSECUTIVE STEPS ON A STRAIGHT LINE 2cm (3/4") WIDE	0☐	1☐	2☐	3☐	74.
*	75.	STD: STEPS OVER STICK AT KNEE LEVEL, R FOOT LEADING	0☐	1☐	2☐	3☐	75.
*	76.	STD: STEPS OVER STICK AT KNEE LEVEL, L FOOT LEADING	0☐	1☐	2☐	3☐	76.
*	77.	STD: RUNS 4.5m (15'), STOPS & RETURNS	0☐	1☐	2☐	3☐	77.
*	78.	STD: KICKS BALL WITH R FOOT	0☐	1☐	2☐	3☐	78.
*	79.	STD: KICKS BALL WITH L FOOT	0☐	1☐	2☐	3☐	79.
*	80.	STD: JUMPS 30cm (12") HIGH, BOTH FEET SIMULTANEOUSLY	0☐	1☐	2☐	3☐	80.
*	81.	STD: JUMPS FORWARD 30 cm (12"), BOTH FEET SIMULTANEOUSLY	0☐	1☐	2☐	3☐	81.
*	82.	STD ON R FOOT: HOPS ON R FOOT 10 TIMES WITHIN A 60cm (24") CIRCLE	0☐	1☐	2☐	3☐	82.
*	83.	STD ON L FOOT: HOPS ON L FOOT 10 TIMES WITHIN A 60cm (24") CIRCLE	0☐	1☐	2☐	3☐	83.
*	84.	STD, HOLDING 1 RAIL: WALKS UP 4 STEPS, HOLDING 1 RAIL, ALTERNATING FEET	0☐	1☐	2☐	3☐	84.
*	85.	STD, HOLDING 1 RAIL: WALKS DOWN 4 STEPS, HOLDING 1 RAIL, ALTERNATING FEET	0☐	1☐	2☐	3☐	85.
*	86.	STD: WALKS UP 4 STEPS, ALTERNATING FEET	0☐	1☐	2☐	3☐	86.
*	87.	STD: WALKS DOWN 4 STEPS, ALTERNATING FEET	0☐	1☐	2☐	3☐	87.
*	88.	STD ON 15cm (6") STEP: JUMPS OFF, BOTH FEET SIMULTANEOUSLY	0☐	1☐	2☐	3☐	88.

TOTAL DIMENSION E ☐

Figure 10. Gross Motor Function Measure dimension E: walking, running and jumping
STD, standing; R, right; L, left. Extracted from CanChild (87).

The GMFM walking, running and jumping dimension is also used to assess walking capacity in children with CP (97). It consists of 24 items scored from 0 to 3 (88) (see **Figure 10**). The dimension E percentage score is calculated as Total Dimension E x 100 / 72 (88).

It was suggested that spatiotemporal (ST) parameters obtained through IGA may provide information regarding functional walking (49).

1.2.10. Treatment

Care for a child with CP is a long-term process, aimed at ensuring the child and their family the best possible quality of life (1). Treatment of children with CP varies depending on their specific symptoms (39). A multidisciplinary team is essential to address the various aspects of care, and adapt the treatment plan to the children's individual needs (39) (see **Table 4**).

Table 4. Multispecialty management team for patients with cerebral palsy

Team member	Role
Physician*	Team leader; synthesizes long-term, comprehensive plans and treatments.
Surgical specialist	Focuses on preventing contractures, hip dislocations, and spinal curvatures in addition to treatment of pain.
Physical therapist	Develops and implements care plans to improve movement and strength, and administers formal gait analyses.
Occupational therapist	Develops and implements care plans focused on activities of daily living.
Speech-language pathologist	Develops and implements care plans to optimize the patient's capacity for communication.
Social worker	Assists the patient's family in identifying community assistance programs.
Psychologist	Assists the patient and patient's family in coping with the stress and demands of the disability.
Educator	Develops strategies to address cognitive or learning disabilities.

*Family physician or pediatrician, with support or direction from a neurologist or psychiatrist trained to help children with developmental disabilities, if available.

Extracted from Vitrikas et al. (39).

This section is focused on the treatment of motor skills, but the treatment of children with CP also involves managing the common comorbidities (39), and assisting families in coping with development of children communication, social, academic, and eventually professional skills as they grow into adulthood (39,114). Discussing expectations with families to help them develop realistic goals is essential (39).

An intervention may target multiple desirable treatment outcomes, for example, reduction of spasticity (at body functions and structures level) and improvement in functional mobility (at activities and participation level) (21). On the other hand, to achieve a goal where multiple goal-limiting factors are present, combination of interventions might be beneficial (for example, if the goal is to improve functional mobility, pharmacological agent to reduce background spasticity might make it easier to learn to move, but principally targeted functional mobility training intervention will also be required) (21) (see **Figure 11**).

1.2.10.1.Body functions and structures

Treatment of spasticity is important for preventing and correcting muscle contractures, and bone and joint deformities; controlling pain; and maintaining function (39). The following pharmacological agents and neurosurgical procedures effectively reduce spasticity: Botulinum NeuroToxin A (BoNT-A) (115), intrathecal baclofen (116,117), diazepam (118), and selective dorsal rhizotomy (119). Tizanidine (118), hippotherapy (120–122), acupuncture (123), and whole body vibration are probably effective (21) (see **Figure 11**). In the context of spasticity management, there is an intense research focus on improved understanding of pathology, histochemistry, and muscle architecture in CP (124). Children with CP appear to have elevated proinflammatory cytokines and genes involved in the extracellular matrix of their skeletal muscles, combined with increased intramuscular collagen and reduced ribosomal production (125). These findings could prompt a reconsideration of BoNT-A treatment, which induces therapeutic weakness and potential muscle fibrosis (126).

Muscle contracture is a common complication, particularly for children with spastic CP (21). Contracture prevention and management should be thought of as a continuum (21), including: 1) to prevent contracture: high intensity self-generated active movement (127); 2) before contracture develops: active movement and BoNT-A; 3) when a contracture has begun to develop (early moderate contracture): serial casting (four weeks after BoNT-A injections, changing the casts at 3-day intervals to reduce weakness induced) followed by active strength training (128) and goal-directed training (129) to make functional use of the new range gained; and 4) when a contracture is severe (greater than 20°) and/or before: orthopedic surgery should be considered to maintain alignment, muscle length, and optimize biomechanics (single-event multi-level surgery is a powerful intervention to simultaneously address the biomechanics of gait and minimize repeat surgeries) (130,131). Ankle robotics (132), biofeedback (133), BoNT-A plus electrical stimulation (134), and whole-body vibration (135) may help manage contracture (see **Figure 11**).

Hip disorders are among the most common musculoskeletal issues in children with CP (39). Approximately 36% of children with CP have a hip disorder, and the incidence increases with higher GMFCS level (136). Routine hip surveillance, including periodic examinations and radiography, can help identify developing problems earlier and prevent poor outcomes (39). Comprehensive multidisciplinary intervention (including botulinum toxin, weight-bearing, motor training, and orthopedic surgery) at the right time and the right dose can prevent hip dislocation (137).

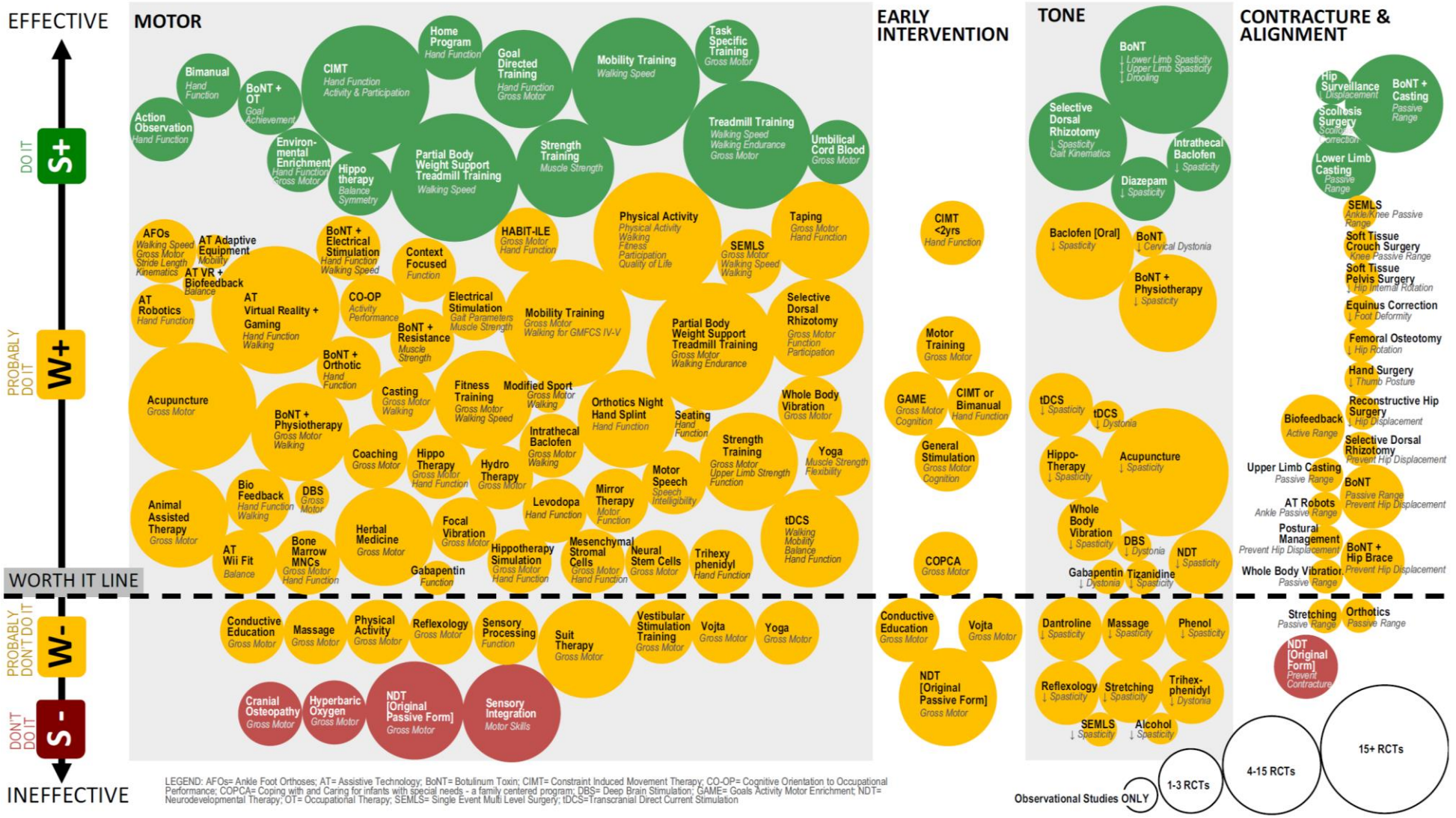

Figure 11. Treatments' evidence alert system
Extracted from Novak et al. (21).

1.2.10.2.Activities and participation

With the emergence of the task-oriented approach, the focus of interventions has shifted from eliminating impairments to enhancing activities and participation by emphasizing fitness, motor function, participation, and quality of life (138).

Substantive clinical trial data support the efficacy of training-based interventions for improving motor function. They consist of practice of real-life tasks and activities, using self-generated active movements, at a high intensity, where the practice directly targets the achievement of a goal set by the child (21), including: 1) to improve hand function: action observation training (139,140), bimanual training (141–143), Constraint-induced movement therapy (144–147), goal-directed training (129), home programs using goal-directed training (148), and environmental enrichment to promote task performance (149); and 2) to improve walking: mobility training, treadmill training, and partial body weight support treadmill training (150,151).

There are adjunctive interventions that when combined with task-specific motor training may augment its positive effects (21), including: electrical stimulation (152–154), taping (155–157), transcranial direct current stimulation (158,159), and virtual reality serious gaming (160–163). Some complementary and alternative medicine interventions such as hippotherapy (120–122) and acupuncture (123) may also improve motor skills (21). Strength training and BoNT-A have also positive effects on motor function (21). Physical activity interventions probably improve fitness, physical activity, ambulation, mobility, participation, and quality of life (164–166) (see **Figure 11**).

Nowadays, it is possible to diagnose CP before 6 months' corrected age, enabling much earlier intervention (25). Child-active motor learning early interventions (including baby-constraint-induced movement therapy (167), baby-bimanual (168), goals activity motor enrichment (169,170), and small steps (171)) may improve motor function (172) (see **Figure 11**).

1.2.10.3.Gait pattern and walking

In children with CP, considerable efforts are focused on improving or maintaining walking ability (52,97), and developing the most optimal gait pattern (52,131). These goals are accomplished by interventions at body functions and structures level such as surgery, pharmacology, orthotics and physical therapy; and interventions at activity and participation level such as mobility training, treadmill training and physical activity (21,52,97,131). Using reliable, valid and responsive outcome measures is crucial to evaluate the success of these interventions (97).

1.3. Instrumented gait analysis

1.3.1. Definition

The IGA is a gait assessment tool that allows a precise quantification of gait characteristics, through objective data that cannot be appreciated visually or measured on a static physical examination (83). The IGA provides detailed information about the intricacies of the individual's gait, as well as about how far the individual's gait pattern deviates from normal (49). Four main types of data can be recorded simultaneously: ST, kinematic, kinetic and surface EMG (sEMG) data (173,174). The IGA is often used in the assessment of ambulatory children with CP (175), for multiple purposes including: 1) the identification and understanding of gait deviations (and recognition of typical pathological gait patterns); 2) the refinement of clinical decision-making; and 3) the evaluation and understanding of the effects of treatments on gait deviations (52,83,173). However, the reliability, validity, responsiveness and clinical utility of the IGA have not been well established (52,97), and its clinical use still remains variable and controversial (55,174,176).

The IGA is a biomechanically based approach (55). Biomechanics is the study of the properties, processes, and behavior of biological systems under the action of mechanical forces (177). It includes kinematics, referred to the description of motion regardless of forces; and kinetics, referred to the study of the relations between the forces and their effects on bodies at rest (statics), or in motion (dynamics) (178). Biomechanics is supported by various biomedical sciences such as mechanics, engineering, anatomy and physiology (179).

Gait analysis was initiated in some form in 384 B.C. by Aristotle, who started theoretically analyzing human gait by thinking about it as a problem (180). In 1836, Eduard and Willhelm Weber used a stop watch, measuring tape, and a telescope to demonstrate the influence of walking speed on step length and cadence (180). Marey and Carlet (1849-1892) invented a shoe with pressure transducers for measuring the forces at the foot, giving for the first time an idea of the M-shape of the ground reaction force during walking (180). The first 3D gait analysis (3DGA) was conducted by Otto Fischer (1861-1917, mathematician), who affixed glowing gas discharge tubes to his subjects and instructed them to walk in the dark (180). All measurement systems at that time were very time-consuming and cumbersome, making them not suitable for everyday and clinical applications (180). In 1972, David Sutherland (surgeon) and John Hagy (engineer) reported a video-based motion tracking system that took only about 20 minutes to conduct and 2 hours for data processing (180). Later, the development of modern

computers and sensor technology enabled clinicians and researchers to study human gait in a clinical setting (180).

1.3.2. Measurement systems

There are different gait and movement analysis methods that can objectify and quantify the gait pattern (180). They can be divided into: 1) complex systems with high accuracy, such as marker-based gait analysis or pedobarography, which often have very high acquisition costs, are time-consuming, bound to controllable laboratory conditions, and require trained personnel for system-operation, data processing and interpretation of results; and 2) alternative systems, often accompanied by insufficient accuracy, such as small wearable sensors or markerless motion capture systems, which are cost-effective, compact, and easy to use under everyday conditions outside the laboratory (180).

1.3.2.1.Marker-based gait analysis

Marker-based systems are considered the gold standard in the IGA (180,181). They use either active (light-emitting) or passive (retro-reflective) spherical skin markers with a diameter of 4 - 25 mm (180) directly attached to either specific anatomical landmarks of the human body, or corresponding body segments using marker clusters or position sensors (180). The most widely used biomechanical model for the analysis of the lower extremities is the Plug-in Gait model (182), a variant of the Conventional Gait Model (183). The Plug-in Gait model allows 3DGA using 16 markers (8 right and 8 left) located at: ASIS, PSIS, thigh wand marker, lateral knee, shank wand marker, lateral ankle, top of the second metatarsal head, and posterior aspect of the heel (182,184). This model can be optionally expanded to allow for the analysis of upper body movements during locomotion (180) (see **Figure 12**).

Optical motion tracking systems generally use infrared technology with a minimum of two cameras necessary to identify the position of markers in the 3D space (185). A sampling frequency of 50 Hz has been rated as sufficient for gait analysis, however, optoelectronic techniques are able to measure human movement at sampling speeds of more than 1000 Hz with spatial resolutions of up to 1 mm (180,186), enabling detailed analyses of high speed motions with high reliability (180,185).

Biomechanical models commonly implement captured marker positions in combination with anthropometric measures to calculate human body joint kinematics and kinetics (180). The Plug-in Gait model separates the lower body into seven segments consisting of the pelvis,

femurs, tibias and feet, each consisting of an orthogonal local coordinate system and linked by 3 degrees of freedom spherical joints (183,187).

Based on these principles, joint (hip, knee and ankle) and segment (pelvis and foot) kinematics (angles and angular velocities) in sagittal (flexion-extension), frontal (adduction-abduction) and transverse (internal-external rotation) planes; and ST parameters such as gait speed, cadence or step length can be obtained from marker-based movement analysis (180). Synchronized force plates allow for the calculation of additional kinetic parameters such as joint moments and joint powers, calculated from ground reaction forces (GRF) and equations of motion through inverse dynamics (180). Synchronized sEMG provides information about the timing and intensity of muscles activity (173).

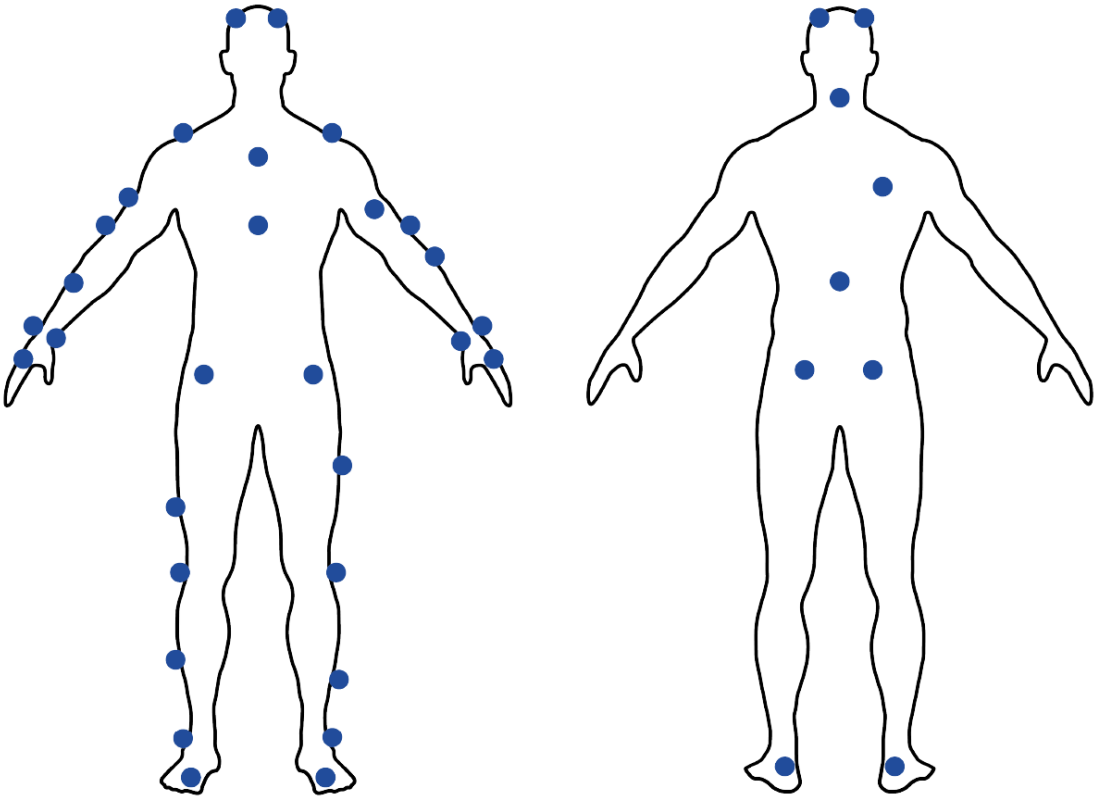

Figure 12. Vicon Plug-in Gait model (front and back)
Extracted from Albert et al. (184).

Marker-based gait and movement analysis has limitations that must be considered: 1) the use of markers on the skin surface causes inaccuracies in the determination of the joint positions due to soft tissue artifacts; 2) biomechanical models usually assume simplified joints which do not fully represent the complexity of human anatomy; and 3) the misplacement of surface markers can also lead to substantial errors regarding the prediction of joint centers (188).

1.3.2.2.Pedobarography

Pedobarography is a kinetic measurement device that provides a detailed analysis of foot dynamics by measuring the pressure (force/area) under the foot (180). Detailed information on pressure values and pressure distribution can only be provided by electronic devices (180). Pedobarographic systems deliver many parameters: 1) pressure distribution, given in absolute values (N/cm²), in relation to specific foot region, or in comparison to the contralateral site; 2) force (N); 3) contact area (cm²); 4) contact time (% roll-over process) (180); 5) gait line and its progression along the sole of the foot (velocity of Center of Pressure, cm/s); and 6) pressure-time-integrals (N/cm²∗s) (180). There are two different types of pedobarographic measurement devices: platform systems and insole/in-shoe systems (189).

Platform systems offer the possibility of a very detailed analysis of the bare foot without external perturbation by shoes or orthopedic insoles (180). Sensor resolution is often quite high (1 - 4 sensors/cm²), offering a detailed analysis of even very small anatomic structures (180). However, most platforms have limited sensor area sizes, restraining the analysis to only one or two steps during one walking trial (180).

In-shoe devices are placed in the shoe, and evaluate the pressure at the contact interface between the sole of the foot and the shoe or orthopedic insole (189). These systems are portable, and able to be used indoors and outdoors, on different terrains and during different tasks as well (180). During measurement, every single step is detected, enabling the analysis of a large number of gait cycles (180). However, the spatial sensor resolution of insole systems is often lower than in platform systems (180).

In terms of technology, various sensors are used in plantar pressure measurement devices: capacitive, resistive, piezoelectric and piezoresistive sensors (190). Resistive systems offer high sensor resolution, but are influenced by temperature and humidity (180). Capacitive and piezoelectric systems are easily calibrated and provide reliable and repeatable data, but are rather expensive (189,190). All pressure sensors other than piezoelectric are only capable of detecting vertical force components (180). Piezoelectric sensors respond to vertical and shear forces, but only measure the summation of all force components (189).

1.3.2.3.Wearable sensors

Wearable sensors are becoming smaller and lighter, making it possible to measure gait and movement parameters outside of the laboratory setting (191–193). Accelerometry-based methodologies, also called Inertial Measurement Units, can be used to identify postures and

classify several daily movements by threshold-based or statistical classification systems (180). Magnetic and Inertial Measurement Units offer a combination of several inertial sensors such as acceleration sensors, gyroscope sensors and magnetometers (194) that allows for the evaluation of joint and segment kinematics (180).

Sensor based trackers provide ST parameters (step count, gait speed, cadence, stride length, foot clearance (195–198), right-left asymmetry, double support, stance and swing time (195), inter-stride variability (199)), and kinematic data for all planes and joints/segments (180). It is important to know if the 3D orientation of an inertial sensor to an inertial reference is obtained as absolute, or if the orientation of a segment is obtained relative to another (200).

Some limitations of wearable sensors are (180): 1) they are susceptible to noise and interference of external factors such as wireless networks or X-ray radiation, which cannot be controlled in the clinical environment; 2) they have a limited battery duration; and 3) their accuracy is often insufficient for usage in clinical and scientific movement analysis (191).

Sensorized clothing is a recent activity tracking technology created by sensor threads integrated into mesh wire, for example elastic polymer threads woven into either the garment or bandages (180). The stretching and relaxation of the elastic polymer string can be registered via resistive sensors (180). The change in polymer thread length causes a change in voltage, which can then be correlated with joint kinematics (180). These data can be evaluated using artificial intelligence techniques such as a neural network (197,201).

1.3.2.4.Markerless motion capture systems

There are different types of markerless motion capture systems: floor based sensor systems that represent an easy-to-handle technique; and some more complex and detailed procedures related to image processing such as pattern recognition (180).

Floor sensors are integrated into specialized mats and pressure or force data are collected when walking is detected (191,202). Subjects can walk a range of steps on the mat, allowing for the determination of ST parameters such as gait speed, step length and step width (180). Depending on the used sensor technique, pressure or forces recorded under the feet can be also reported (191,203). Some advantages of the floor sensors are: 1) the ease of handling; 2) low acquisition costs; 3) portability; 4) no specialists are necessary for the measurement; and 5) patients may walk in their preferred clothing (180).

Pattern recognition systems are active, that is, emit light information to collect the structures of objects (203). Stereoscopic projections are technically simple and low-cost pattern

recognition systems that facilitate object detection and identification, and can provide useful information about human posture and movements (180). A commonly used method is depth measurement: a projector emits light information into the laboratory spectrum, images are collected by a camera and compared to the reference pattern at known distances stored in the system's memory, and a map of distances is calculated (180) using techniques such as camera triangulation, laser range scanner or Time-of-Flight methods (191). 3D cameras based on a triangulation principle are available commercially such as Microsoft Kinect, which can be used for gait analysis, providing ST parameters such as stride time and joint kinematics such as hip and knee flexion-extension (181,204–207). Some advantages of active systems are: 1) low cost; 2) simplicity of equipment; 3) ease of handling; and 4) possibility of continuous feedback about posture or movement performance (180). However, active systems are dependent on light conditions, and only usable in a controlled environment (203).

1.3.3. Gait cycle

Walking can be defined as an activity in which the body advances at a slow to moderate pace by moving the feet in a coordinated fashion (208), and gait as the manner or style of walking (58). During gait, a regular and repetitive sequence of events occurs: foot strike (FS), opposite toe off (TO), reversal of fore shear to aft shear, opposite FS, TO, foot clearance, tibia vertical, and successive FS (209); so gait can be separated into periodic cycles (173). A gait cycle is the movement from one FS to the successive FS on the same side (209). The gait cycle is divided in two phases: 1) stance phase, which begins with FS and ends with TO; and 2) swing phase, which begins with TO and ends with FS (209). The gait cycle can also be divided in different periods: 1) first double support or loading response: from FS to opposite TO; 2) single support: from opposite TO to opposite FS, divided by the event of reversal of fore to aft shear into midstance and terminal stance; 3) second double support or preswing: from opposite FS to TO; 4) initial swing: from TO to foot clearance; 5) midswing: from foot clearance to tibia vertical; and 6) terminal swing: from tibia vertical to FS (209) (see **Figure 13**).

Gait events such as FS and TO are essential in different stages of the IGA (210), for example for the gait cycle segmentation, and the calculation of ST parameters (209,211). FS is defined as the timing when foot contacts the ground and foot forward progression stops, and TO as the timing when toe leaves the ground or toe starts forward progression (212). These comprehensive definitions cover both healthy and pathological subjects, and include kinetic and kinematic components (212). Gait event detection is one of the most time-consuming processes in IGA (212). Accurate automated event detection is important to increase the efficiency and repeatability of IGA (210,212).

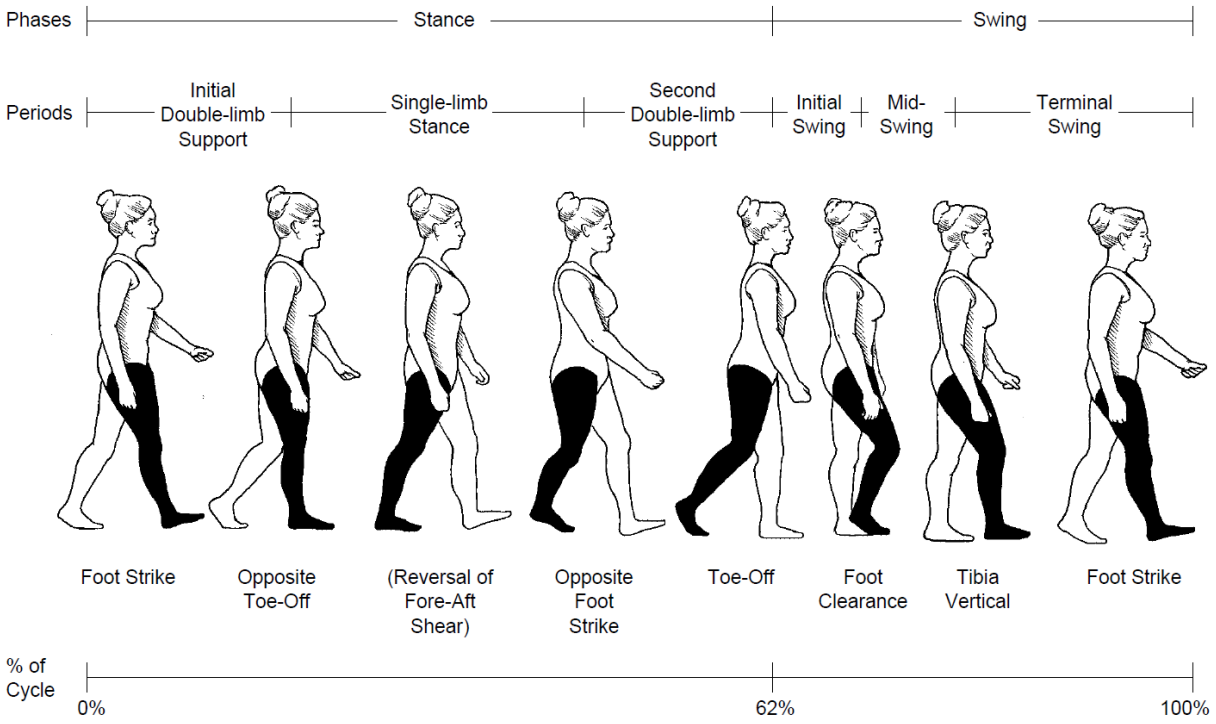

Figure 13. Typical normal gait cycle
Extracted from Chambers et al. (209).

GRF are considered the gold standard in the detection of gait events (212,213). However, force plates are not always available in gait analysis laboratories (210,212) and/or applicable in pathological populations such as CP (212,213). In these cases, marker detection systems (3D marker coordinates) take relevance as alternative methods to GRF (212). Moreover, they present some advantages in comparison to GRF, such as the possibility of detecting gait events for several strides within the measurement volume, or their applicability in treadmill walking (210).

There exist different gait event detection methods based on kinematic data (212,213). Some of them are listed here using the primary author's last name: 1) Hreljac (214): based on peak vertical deceleration of the heel marker (FS), and anterior-posterior acceleration of the toe marker (TO); 2) Hsue (215): based on the peak anterior-posterior deceleration (FS) and acceleration (TO) of the heel marker; 3) Ghoussayni (210): based on the sagittal plane descending velocity threshold of the heel marker (FS), and ascending velocity threshold of the toe marker (TO); and 4) Zeni (216): based on the peak anterior position of the heel marker (FS), and posterior position of the toe marker (TO) relative to the sacrum marker. When comparing these automated algorithms for the detection of gait events in children with CP, using visual inspection (212) or force plates (213) as a reference, the algorithm reported by Ghoussayni et al. (210) (hereafter called Ghoussayni's algorithm) shows the best results. Two

empirically set thresholds have been used: 0.05 m/s (210) (in healthy adult subjects) and 0.5 m/s (212,213) (in children with CP). Another threshold, walking speed dependent, was proposed to increase the accuracy of Ghoussayni's algorithm in children with CP (212). However, in that case, no statistical results were reported in the study (212).

Normal gait has five prerequisites that are frequently lost in pathological gait: 1) appropriate swing phase pre-positioning of the foot (for performing the FS with the heel); 2) stability in stance; 3) sufficient foot clearance during swing; 4) an adequate step length; and 5) energy conservation (49). Children with CP perform FS in different ways (with the heel, toe, and/or both at the same time) (100), and it is not always possible to distinguish them visually. This fact should be taken into account when detecting FS. Ghoussayni et al. (210) validated their automated algorithm with healthy adults, so they did not address this issue. Bruening and Ridge (212) classified the children in different gait patterns, and used the toe marker in place of the heel marker for the detection of FS in the equinus group. Gonçalves et al. (213) also considered different gait patterns, but they detected FS using the heel marker in all cases.

1.3.4. Gait parameters

The IGA provides a large amount of data of different nature: ST, kinematic, kinetic, and sEMG data (173,174,217). Clinicians and researchers have the challenge to extract the clinically relevant information from this large amount of data (218). Different methods have been used to select relevant gait parameters, from conventional manual procedures based on subjective available clinical expert knowledge to novel automated procedures based on objective mathematical techniques (219). Two requirements for a clinically relevant gait parameter are: 1) its capability to distinguish between physiological and pathological gait, and 2) its capability to separate between two therapy stages within the same patient group (219). The responsiveness of gait parameters to interventions should be established with caution due to the risk of type I (false positive: the mistake of inferring an experimental effect when none exists in reality) (220) and type II (false negative: the mistake of missing real effects) errors (221).

1.3.4.1.Spatiotemporal parameters

ST analysis is defined as techniques which study entities using their topological, geometric, or geographic properties and include the dimension of time in the analysis (222). ST parameters are gait parameters that provide information about the spatial and temporal characteristics of gait, based on the gait cycle, such as gait speed (m/s), cadence (steps/min), stride time (s),

stride length (m), step length (m), step width (m), single support (% of gait cycle), double support (%), stance phase (%) and swing phase (%) (173) (see **Table 5**).

Table 5. Operational definitions of spatiotemporal parameters

Spatiotemporal parameter	Operational definition
Spatial parameter	
Step length (m)	Anterior-posterior distance from the heel of one footprint to the heel of the opposite footprint.
Stride length (m)	Anterior-posterior distance between heels of two consecutive footprints of the same foot (left to left, right to right).
Step width (m)	Lateral distance from heel center of one footprint to the line of progression formed by two consecutive footprints of the opposite foot.
Temporal parameter	
Cadence (steps/min)	Number of steps per minute, sometimes referred to as step rate.
Step time (s)	Time elapsed from initial contact of one foot to initial contact of the opposite foot.
Stride time (s)	Time elapsed between the initial contacts of two consecutive footfalls of the same foot.
Stance time (s)	Time elapsed between the initial contact and the last contact of a single footfall.
Swing time (s)	Time elapsed between the last contact of the current footfall to the initial contact of the next footfall of the same foot.
Single support time (s)	Time elapsed between the last contact of the opposite footfall to the initial contact of the next footfall of the same foot.
Double support time (s)	Sum of the time elapsed during two periods of double support in the gait cycle.
Temporophasic parameter	
Stance time (%)	Stance time normalized to stride time.
Swing time (%)	Swing time normalized to stride time.
Single support time (%)	Single support time normalized to stride time.
Double support time (%)	Double support time normalized to stride time.
Spatiotemporal parameter	
Gait speed (m/s)	Calculated by dividing the distance walked by the ambulation time.
Stride speed (m/s)	Calculated by dividing the stride length by the stride time.

Adapted from Hollman et al. (223).

Reference values of ST parameters from typically developing children are necessary when analyzing and interpreting outcome measures of children with gait disorders (224). Different studies have presented normative data for ST parameters in children, using different measurement systems (224–226) (see **Table 6**).

Table 6. Normative spatiotemporal parameters data (mean ± standard deviation) in children, stratified into age groups

Spatiotemporal parameter	5-6 years	7-8 years	9-10 years	11-13 years	14-21 years
Stride length (m) (224)	0.99 ± 0.11	1.10 ± 0.13	1.20 ± 0.13	1.32 ± 0.13	1.34 ± 0.16
Step width (m) (226)	0.071 ± 0.025			0.075 ± 0.025	
Gait speed (m/s) (224)	1.11 ± 0.12	1.19 ± 0.16	1.25 ± 0.17	1.34 ± 0.14	1.28 ± 0.15
Cadence (steps/min) (224)	138.95 ± 9.06	131.09 ± 11.79	124.20 ± 9.02	122.03 ± 10.94	115.35 ± 8.18
Stance (%) (224)	57.91 ± 1.82	58.68 ± 1.99	58.62 ± 1.59	57.81 ± 1.22	58.93 ± 1.64
Swing (%) (224)	42.09 ± 1.82	41.32 ± 1.99	41.38 ± 1.59	42.19 ± 1.22	41.07 ± 1.64
Double support (%) (224)	16.29 ± 3.61	17.57 ± 3.79	17.28 ± 3.11	15.67 ± 2.37	17.85 ± 3.29

Adapted from Voss et al. (224) and McKay et al. (226).

Significant differences in ST parameters have been observed between children with typical development and children with CP (227). The scores for gait speed, cadence, and stride length are lower, and the score for step width is higher in children with CP compared with typically developing children (227). The periods of right and left single support are shorter, and those

of right and left double support are longer in children with CP compared with typically developing children (227).

ST parameters, as well as kinetic parameters, can be affected by anthropometric measures such as weight and height (for example, tall people have longer stride lengths) (228–230). When comparing gait parameters between a child and a reference group, between two children with significantly different body sizes, or between the same child at different time points, we should try to minimize variability due to physical characteristics (228,231,232). The scaling problem can be solved presenting the data as non-dimensional (ND) numbers, although these numbers are more difficult to interpret (228). ND normalization aim to remove systematic dependences of a parameter on relevant factors such as age, mass and leg length (230,231). It converts gait parameters into ratios, each with a function of leg length and/or body mass (231). In the case of ST parameters, **Equation 1, Equation 2** and **Equation 3** have been defined (228,231,232).

Equation 1 $$ND\ stride\ length = \frac{stride\ length(m)}{leg\ length(m)}$$

Equation 2 $$ND\ gait\ speed = \frac{gait\ speed\left(\frac{m}{s}\right)}{\sqrt{gravity\left(\frac{m}{s^2}\right) \times leg\ length(m)}}$$

Equation 3 $$ND\ cadence = cadence(s^{-1}) \times \sqrt{\frac{leg\ length(m)}{gravity\left(\frac{m}{s^2}\right)}}$$ being $$cadence(s^{-1}) = \frac{1}{stride\ time(s)}$$

1.3.4.2.Kinematic parameters

Kinematic data describe the motion occurring simultaneously at different segments (pelvis and foot) and joints (hip, knee and ankle) in the three planes (sagittal, frontal and transverse) during the gait cycle (55). Kinematic calculation assume no relative movement between the skin surface marker and the underlying skeletal landmark (55). Segment angles represent the absolute orientation of a body segment with respect to the inertial or laboratory frame. On the other hand, joint angles represent the relative orientation between two adjacent body segments (that is, orientation of the distal segment with respect to the proximal segment local frame). Euler angles are generally used to decompose the 3D general orientation in three successive elementary rotations (173). Kinematic data are usually presented as curves over the entire gait cycle, along with the typical curves associated with normal gait for comparison (52) (see **Figure 14**).

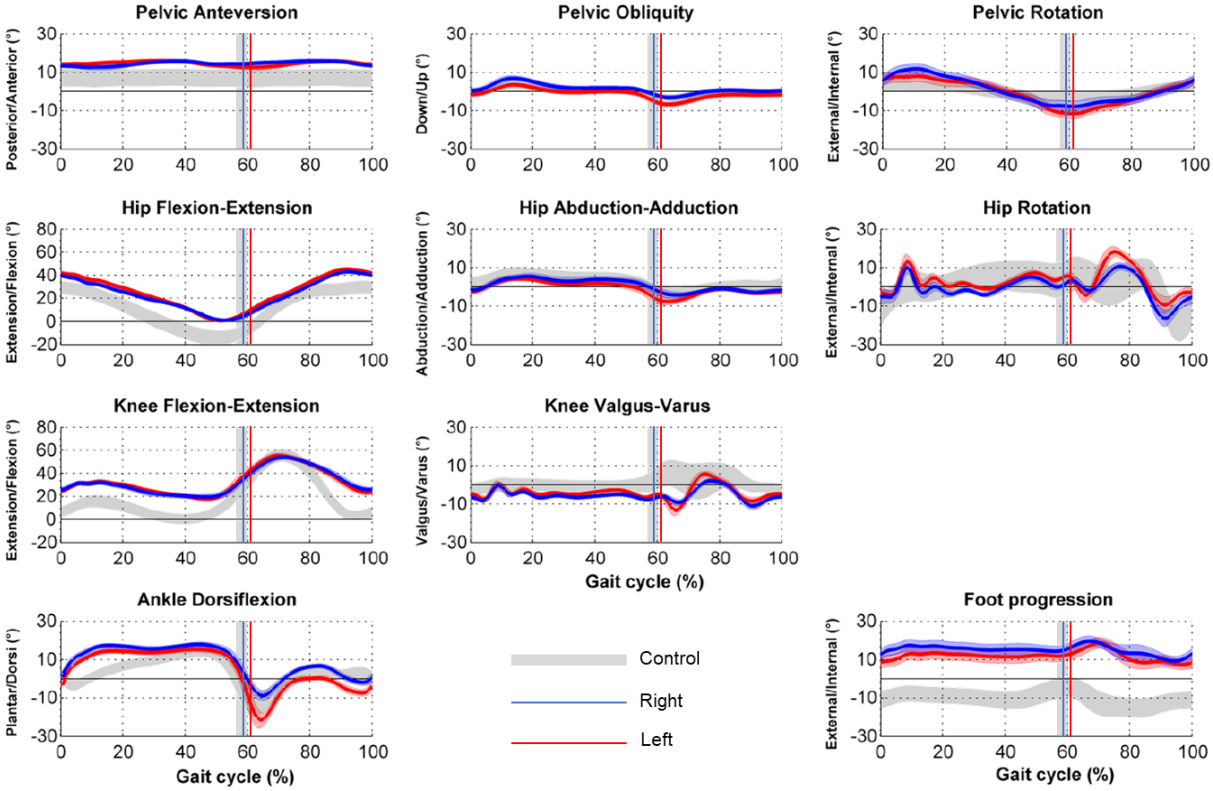

Figure 14. Example of kinematic data in clinical gait analysis report for bilateral spastic cerebral palsy
Normalized gait cycle is represented on the abscissa (horizontal axis), and joint/segment angle on the ordinate (vertical axis); the vertical bar at about 60% of the gait cycle separates stance and swing phases; the gray band indicates the typical mean ± 1 standard deviation; the blue line correspond to the right side; the red line correspond to the left side. Adapted from Armand et al. (173).

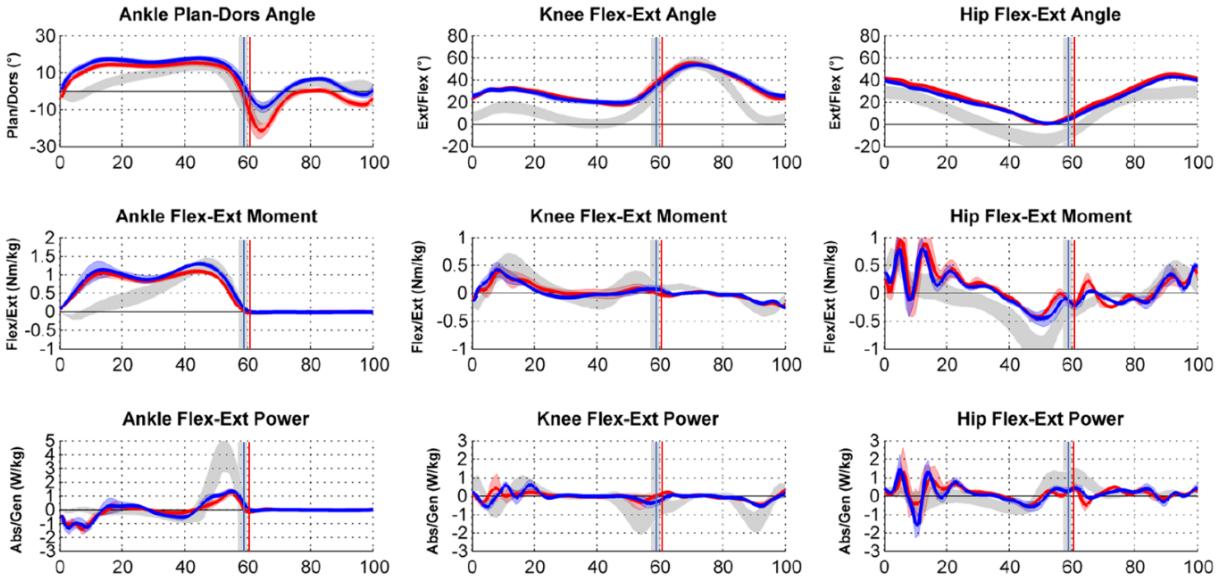

Figure 15. Example of kinetic data in clinical gait analysis report for bilateral spastic cerebral palsy
Normalized gait cycle is represented on the abscissa, and joint angle/moment/power on the ordinate; the vertical bar at about 60% of the gait cycle separates stance and swing phases; the gray band indicates the typical mean ± 1 standard deviation; the blue line correspond to the right side; the red line correspond to the left side. Adapted from Armand et al. (173).

1.3.4.3.Kinetic parameters

Kinetic data describe the forces applied by an individual at different joints (hip, knee and ankle) in a body plane (sagittal plane) during the gait cycle (173). Kinetics are subdivided into joint moments and powers (49). Internal joint moments are the resultant of various muscle forces acting around a joint, associated to an angular motion (49). Joint powers are associated with the time rate of muscles' mechanical work (178), distinguishing between: 1) concentric or shortening contraction: muscles do positive work (generation); 2) eccentric or lengthening contraction: muscles do negative work (absorption); and 3) isometric contraction: muscles length is constant and no work is done (49). Joint moments and joint powers can be calculated by inverse dynamics, from GRF, inertial parameters, and kinematic data (173). Kinetic data are also presented as curves over the entire gait cycle, along with the typical curves of normal gait for comparison (52) (see **Figure 15**).

Kinematic and kinetic data analysis can be performed in two different ways: scalar gait parameters analysis and full gait curves analysis (218). Scalar gait parameters analysis (which refers to specific vector components in specific time instants of the gait cycle) is the most frequently used in intervention studies, but there is no consensus on which parameters should be evaluated (218).

1.3.4.4.Surface electromyography data

sEMG data describe the timing and intensity of the muscle activity during the gait cycle (173). Surface electrodes, located following recommended procedures (233), are used to measure the electrical potential generated by a muscle when it is activated (55). The electrical signal magnitude is indirectly related to the muscle force, which could be estimated normalizing the electrical potential to the maximum manual muscle contraction (55). However, children with CP may have impaired selective motor control, compromising the ability to assess the maximum manual muscle contraction (55). Therefore, sEMG data are commonly presented as raw signals, which do not indicate muscle strength (55) (see **Figure 16**).

1.3.4.5.Summary indexes

Summary indexes are used for global quantification of gait deviations compared to the normal gait pattern (234). They are calculated from IGA data, and provide a single value that can be interpreted as a summary of the overall quality of an individual's gait (217). However, they do not provide detailed information about how gait is impaired (234). Moreover, there is no established relation between the normalcy of gait pattern and function (235).

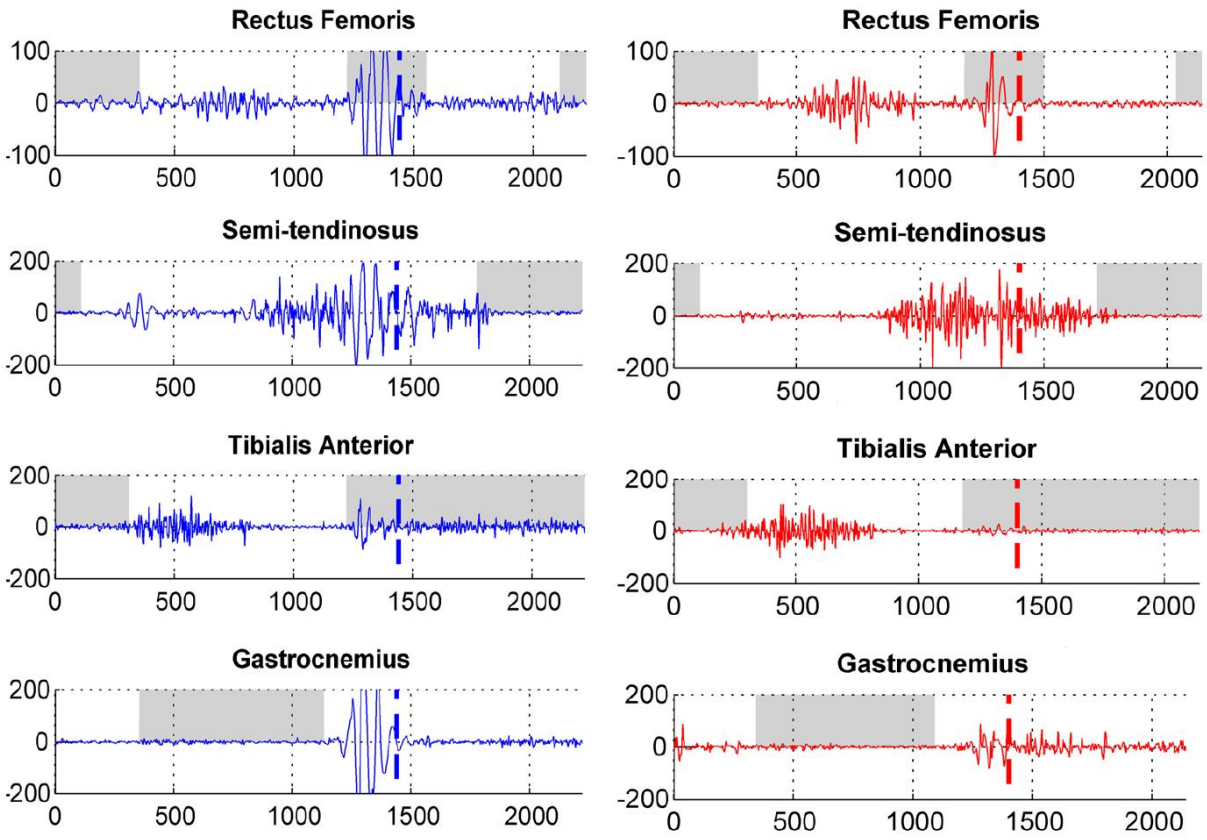

Figure 16. Example of surface electromyography data in clinical gait analysis report for bilateral spastic cerebral palsy
Gait cycle is represented on the abscissa, and muscle activation on the ordinate; the gray band indicates the typical muscle activation timing; the blue line correspond to the right side; the red line correspond to the left side; the discontinuous vertical bar separates stance and swing phases. Adapted from Armand et al. (173).

The most commonly used summary indexes are those based on kinematic data (234) such as the Gillette Gait Index (GGI) (235), also called Normalcy Index, which is calculated from three ST parameters and 13 kinematic parameters (217). Its result is a dimensionless number with a normal mean value of 15.9 (range 8.2 to 26.9), the higher the number the larger the deviation from typical gait (236). On the other hand, there are summary indexes based on kinetic data, for example the Gait Deviation Index – Kinetics (237), and others based on EMG data, for example the Kerpape-Rennes EMG-based Gait Index (234).

1.3.5. Gait patterns

Gait classification systems aim to help clinicians and researchers to categorize the gait of children with CP, and most of them are based on 3DGA for being the gold standard in CP gait analysis (60). Six multiple joint patterns for children with CP, which describe sagittal plane kinematic deviations, have reached consensus in literature (60): A) genu recurvatum: full knee extension or hyperextension during stance, with almost normal hip motion during stance and impaired ankle motor control, resulting in plantar flexion or reduced dorsiflexion (238); B) drop

foot: drop foot during swing but adequate dorsiflexion ROM, increased knee flexion at terminal swing, initial contact and loading response, hip hyperflexion during swing, and increased lordosis throughout the gait cycle (239); C) true equinus: ankle in equinus during stance, full knee extension, full hip extension, and pelvis within normal ROM or anteversion (59); D) jump gait: ankle in equinus, particularly in late stance, knee and hip in hyperflexion in early stance, followed by extension to a variable degree in late stance, and pelvis within normal ROM or anteversion (59); E) apparent equinus: ankle normal ROM, knee and hip in hyperflexion throughout stance, and pelvis within normal ROM or anteversion (59); and F) crouch gait: ankle in excessive dorsiflexion throughout stance, knee and hip in hyperflexion, and pelvis in normal ROM, anteversion or retroversion (59) (see **Figure 17**). However, association of gait patterns to clinical symptoms remain to be established (60).

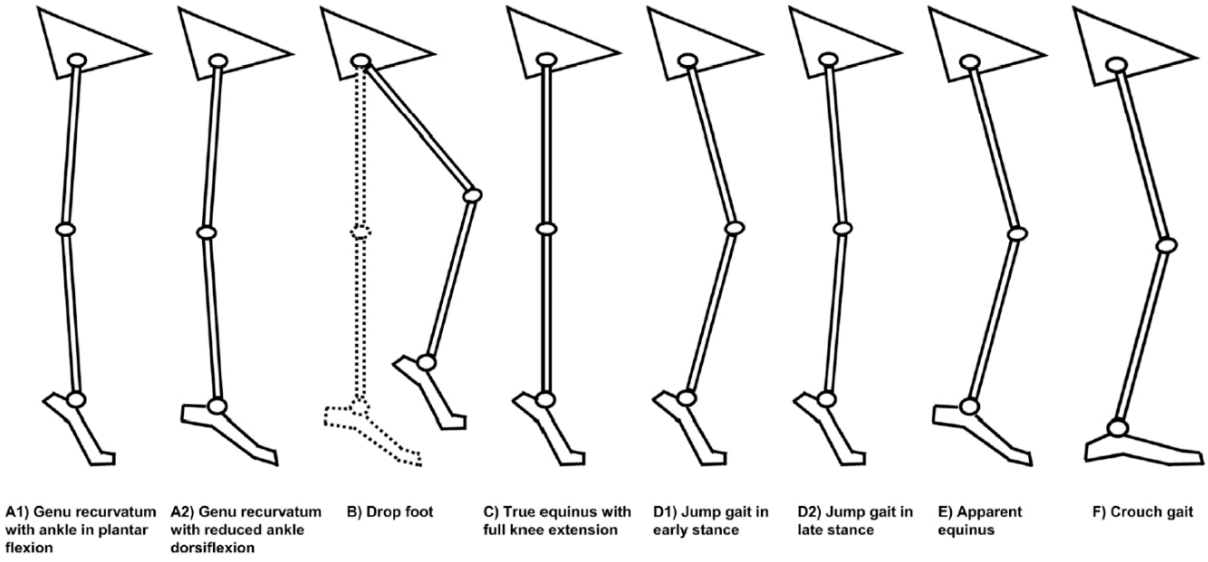

Figure 17. Multiple joint patterns in children with cerebral palsy
Extracted from Papageorgiou et al. (60).

It was suggested that gait patterns associated with equinus, such as true equinus and jump gait, may be the most common patterns in younger children at the beginning of independent walking. Moreover, the age gradient from these patterns to other patterns associated with increased flexion, such as apparent equinus and crouch gait, may reflect the natural history for children with spastic diplegia (59).

1.3.6. Interpretation

One of the handicaps of the IGA is the large amount of data collected and analyzed, that makes it an instrument complicated to use and difficult to interpret (217). A methodology for properly interpreting data from the IGA has not been defined clearly (174). Understanding the links

between gait disorders and impairments, that is, between gait parameters and clinical outcomes, is essential for correctly interpreting the IGA (173).

Several studies have tried to stablish relationships between gait disorders and impairments, with discrepancies in the results due to heterogeneity in sample characteristics, selected gait parameters, included clinical outcomes, and applied statistical methods (240). Many studies are focused on kinematics (57,240–250), for being the basis of most gait classification systems (60,251). Some studies have reported relationships between ST parameters and clinical outcomes (57,241–245,252–254); however, most of them only studied cadence, stride length and/or gait speed (57,241,242,245,252,253), and specific types of clinical outcomes (241,242,244,245,253,254) (see **Table 7**). Other studies have reported relationships between clinical outcomes and kinetic parameters (241–243,245,248,255,256), sEMG data (243,257), and summary indexes (236,241,258–262).

Table 7. Studies on relationship between spatiotemporal parameters and clinical outcomes in children with CP

	Spatiotemporal parameter							Impairment					Activity limitation				
Study	Gait speed	Stride length	Cadence	Step width	Double support	Single support	Time of toe off	Weakness	Selectivity	Spasticity	Contracture/ROM	Deformity	GMFM	FAQ	WeeFIM	PODCI	PedsQL
Hösl (245)	●	●	●									●					
Goudriaan (241)	●							●									
Shin (242)	●	●	●					●									
Kurz (254)	●			●									●				
Ross (57)	●	●	●					●		●							
Sullivan (252)	●	●	●										●	●	●	●	●
Desloovere (243)	●	●	●				●	●	●	●	●	●					
Damiano (244)	●	●	●		●	●							●				
Drouin (253)	●	●	●										●				

CP, cerebral palsy; ROM, range of motion; GMFM, Gross Motor Function Measure; FAQ, Gillette Functional Assessment Questionnaire; WeeFIM, Functional Independence Measure for children; PODCI, Pediatric Outcomes Data Collection Instrument; PedsQL, Pediatric Quality of Life inventory. ●, outcome measure studied.

Own elaboration.

The IGA is one of the many inputs into the clinical decision-making (175). When identifying walking problems, differences are detected when using the IGA or the clinical assessment (263). The IGA is not a substitute for the clinical assessment but should be used to provide evidence and enhance clinical decision-making (83), because clinical assessment do not offer sufficient objectivity, validity, reliability and volume of information (49). The use of a diagnostic matrix, based on different sources of information (clinical history, diagnostic imaging, physical examination, functional assessment) and including the IGA, is crucial for the achievement of an evidence-based practice in the optimization of walking ability of children with CP (55).

2

Hypotheses and objectives

2. HYPOTHESES AND OBJECTIVES

2.1. Hypotheses

2.1.1. General hypothesis

The IGA yields outcome measures responsive to treatments, and able to objectively assess gait pattern and walking in children with bilateral spastic CP.

2.1.2. Specific hypotheses

Eight specific hypotheses were defined:

1. Kinematic parameters are the most frequently used gait parameters in children with bilateral spastic CP.
2. Gait parameters are responsive to treatments in children with bilateral spastic CP.
3. The proposed adaptation of Ghoussayni's algorithm for the detection of FS in children with CP distinguishes how each FS is performed (heel, toe or both at the same time).
4. Both Ghoussayni's algorithm using a threshold of 0.5 m/s (Gho05) and Ghoussayni's algorithm using a walking speed dependent threshold (GhoWS) are valid alternatives to GRF for detecting gait events in children with bilateral spastic CP.
5. GhoWS provides closer results to GRF than Gho05.
6. Gait event detection methods have an effect on ST parameters.
7. ST parameters are related to clinical outcomes both at body functions and structures level, and at activities and participation level, according to the ICF-CY.
8. ST parameters provide clinical information regarding both gait pattern and walking.

2.2. Objectives

2.2.1. General objective

To identify a set of clinically relevant gait parameters responsive to treatments, and able to objectively assess gait pattern and walking in children with bilateral spastic CP.

2.2.2. Specific objectives

Ten specific objectives were defined:

1. To critically evaluate and summarize the current evidence base related to the clinical use of the IGA for the assessment of gait disorders in children with bilateral spastic CP.
2. To identify the gait parameters most frequently used in the gait analysis of children with bilateral spastic CP.
3. To evaluate the responsiveness to treatments of gait parameters in children with bilateral spastic CP.
4. To propose a new adaptation of Ghoussayni's algorithm for the objective detection of FS in children with CP.
5. To compare Ghoussayni's thresholds (Gho05 and GhoWS) with the gold standard gait event detection method (GRF).
6. To find out whether Gho05 and GhoWS are valid methods for the detection of gait events in children with bilateral spastic CP.
7. To evaluate which threshold (Gho05 or GhoWS) provides closer results to GRF.
8. To study the effect of gait event detection methods on ST parameters.
9. To evaluate the relationship between ST parameters and different types of clinical outcomes (including measures of body functions and structures, and activities and participation) according to the ICF-CY.
10. To find out whether ST parameters provide clinical information regarding gait pattern and walking.

3

Methods

3. METHODS

This doctoral thesis is divided into three studies:

1. A systematic review of gait parameters used as outcome measures in children with bilateral spastic CP.
2. A validation study of Ghoussayni's algorithm (using two different thresholds) as gait event detection method in children with bilateral spastic CP.
3. A correlational study between gait parameters and clinical outcomes in children with bilateral spastic CP.

The following reporting guidelines were used:

- PRISMA 2009 (264), for systematic reviews.
- STARD 2015 (265), for diagnostic accuracy studies.
- STROBE 2007 (266), for observational studies.

Some reporting recommendations were also taken into account, regarding gait studies (267), CP studies (268), and statistical analysis (269).

This research work did not involve contact with humans, since data were collected retrospectively from a previous study made at the Motion Analysis Laboratory of the Institut Guttmann (Badalona, Spain). Therefore, approval by the Ethics Committee of the Institut Guttmann was not needed. It was approved by the Teaching and Research Committee of the Institut Guttmann on May 26, 2015.

3.1. Study 1: Gait parameters in children with bilateral spastic cerebral palsy: a systematic review of randomized controlled trials

3.1.1. Search strategy

In order to identify the key articles on this topic, a systematic search was undertaken within the following online databases: PubMed, Web of Science and Scopus. Constraints were applied for year of publication (2000-2016), language (English) and document type (clinical trial). Search through PubMed was also limited for species (humans) and text availability (abstract). The user query used was: (cerebral palsy OR spastic diplegia) AND (child OR adolescent) AND (gait OR walking OR ambulation OR locomotion) AND (spatiotemporal parameters OR kinematics OR kinetics OR electromyography OR three-dimensional gait analysis OR 3D gait analysis OR instrumented gait analysis OR quantitative gait analysis OR computerized gait analysis).

3.1.2. Eligibility criteria

Articles were included if they satisfied the following criteria: 1) randomized controlled trials (RCT) with statistical analysis of the results; 2) percentage of participants with diagnosis of bilateral spastic CP > 60%; 3) mean age of the sample between 6 and 18 years old; and 4) IGA for obtaining outcome measures, including ST, kinematic, kinetic and/or sEMG parameters.

3.1.3. Risk of bias

To check the validity of the RCT selected, the Cochrane risk of bias tool (270) was used. This tool allows the analysis of the adequacy of different features related to the risk of bias: random sequence generation, allocation sequence concealment, blinding, incomplete outcome data, and selective outcome reporting. Included studies needed to be RCT so we initially analyzed the way randomization was carried out (participants' selection bias). On the other hand, this review aimed to evaluate the responsiveness of gait parameters to treatments so we secondly analyzed the risk of type I and type II errors due to the gait parameters' selection bias. The analysis of the risk of bias involves answering "low risk of bias", "high risk of bias", or "unclear risk of bias" (lack of information or uncertainty over the potential for bias) (270).

3.1.4. Data collection

A data extraction sheet was developed, pilot-tested on the 14 first included studies and refined accordingly. Firstly, information related to participants and study characteristics was extracted in order to establish the comparability of the included studies: eligibility criteria, participants, study design, intervention, and assessment. Secondly, gait parameters were classified, according to their nature, in ST, kinematic, kinetic, sEMG and summary indexes, and their significant results (intragroup or intergroup statistical analysis) were collected in order to determine their responsiveness to interventions. Both text and tables data were considered. Only outcomes which were statistically analyzed and significant results obtained from randomized interventions were included. Significant results obtained from a combination of experimental and control group data, and kinematic parameters calculated from video observation were excluded. Finally, results were summarized in tables.

3.1.5. Additional analysis

From the data collection, an additional analysis was performed to study the responsiveness of gait parameters to different treatments. In this analysis, interventions were grouped into different types and the gait parameters that showed significant results for each type of intervention were determined.

3.2. Study 2: Gait event detection using kinematic data in children with bilateral spastic cerebral palsy

Data were collected retrospectively from a previous study made at the Motion Analysis Laboratory of the Institut Guttmann (Badalona, Spain).

3.2.1. Participants

The potentially eligible participants were children with a diagnosis of bilateral spastic or mixed CP, age between 4 and 14 years, GMFCS (38) levels I to III (see **Figure 2**), and ability to carry out simple verbal instructions. No child had moderate or severe pain, or severe visual impairment. Exclusion criteria were: 1) disability to walk 7 m independently without assistive devices; and 2) unavailability to detect at least one valid gait event using GRF. The previous study was approved by the Research Ethics Committee of the Institut Guttmann (Badalona, Spain), and parents gave written informed consent for participating in the study.

3.2.2. Instrumented gait analysis

Each child walked barefoot, without orthosis or assistive devices, at self-selected speed on a 7-meter walkway. A minimum of three trials were collected. Two reflective markers (radius 15 mm) were placed on each foot (right and left), one on the posterior end of the calcaneus (heel marker) and the other on the second metatarsal head (toe marker), based on the Plug-in Gait model (182) (see **Figure 12**). 3D marker coordinates were measured using a six infrared cameras system (SMART-D, BTS Bioengineering, Milan, Italy). GRF were measured using two force plates (9286BA, Kistler, Granollers, Spain). Data were synchronously collected at 140 Hz and filtered using a fourth order low pass Butterworth filter with a cutoff frequency of 6 Hz. Additionally, lateral and frontal views of feet motion were video recorded.

3.2.3. Gait event detection using GRF (gold standard)

Gait events were detected using a 10 N threshold from the vertical component of GRF. FS was estimated as the first frame with GRF vertical component above 10 N, and TO as the first frame below 10 N. Events were considered valid when only one foot was in contact with the force plate and its heel or toe (depending on the event type) was clearly located on the force plate.

3.2.4. New adaptation of Ghoussayni's algorithm for the detection of foot strike in children with cerebral palsy

We defined a new adaptation of Ghoussayni's algorithm for detecting FS in children with CP. The new adaptation consisted of calculating sagittal plane velocities of the two foot markers (heel and toe) (210), and comparing the timing (in frames) when each one fell below a given threshold. Three different situations made it possible to distinguish three types of FS: 1) heel strike: when heel marker velocity fell below the threshold before than toe marker velocity, 2) toe strike: when toe marker velocity fell below the threshold before than heel marker velocity, and 3) both at the same time: when both (heel and toe) marker velocities fell below the threshold at the same time. FS was estimated as the first frame with sagittal plane velocity of at least one of the two foot markers (heel and/or toe) below the threshold.

In the present study, this new adaptation of Ghoussayni's algorithm was applied using two different thresholds: 0.5 m/s (Gho05, see **Section 3.2.5**), and a walking speed dependent threshold (GhoWS, see **Section 3.2.6**).

3.2.5. Gait event detection using Gho05

The gait events previously detected with GRF were estimated using Ghoussayni's algorithm (210) with a threshold of 0.5 m/s (212). FS was estimated as the first frame with sagittal plane velocity of at least one of the two foot markers (heel and/or toe) below 0.5 m/s, using the new adaptation of Ghoussayni's algorithm. TO was estimated as the first frame with sagittal plane velocity of the toe marker above 0.5 m/s.

3.2.6. Gait event detection using GhoWS

The gait events previously detected using GRF and Gho05 were also estimated using Ghoussayni's algorithm (210) with a walking speed dependent threshold (212). Bruening and Ridge (212) defined the threshold (for FS and TO) as a simple function of walking speed, according to the correlation between walking speed and sagittal plane velocity of foot markers at the gait events (FS and TO) (see **Equation 4** and **Equation 5**). Walking speed was calculated as stride speed (m/s), dividing stride length by stride time (211,223). Stride length (m) was computed as the distance between the heel marker at two successive FS of the same foot (211), and stride time (s) as the time difference between two successive FS of the same foot (211). Both variables were computed from a gait cycle containing the gait event that was being estimated, in order to obtain a stride speed as close as possible to the true walking

speed at that moment. The two successive FS used to calculate the stride speed were estimated using Gho05 due to the difficulty to detect two successive FS from GRF only.

Equation 4 $FS\ threshold = 0.78 \times Walking\ Speed$

Equation 5 $TO\ threshold = 0.66 \times Walking\ Speed$

FS was estimated as the first frame with sagittal plane velocity of at least one of the two foot markers (heel and/or toe) below the FS threshold (see **Equation 4**), using the new adaptation of Ghoussayni's algorithm. TO was estimated as the first frame with sagittal plane velocity of the toe marker above the TO threshold (see **Equation 5**).

3.2.7. Spatiotemporal parameters

We compared ST parameters calculated from gait events detected using Gho05 and GhoWS. Gait cycles containing at least one of the gait events detected previously (using GRF, Gho05 and GhoWS) were selected. The fundamental events of each gait cycle (initial FS, opposite TO, opposite FS, TO and final FS) were detected using Gho05 and GhoWS. The following ST parameters were calculated: stride length, stride time, stride speed, first double support (percentage of the gait cycle from initial FS to opposite TO), single support (percentage of the gait cycle from opposite TO to opposite FS), and time of TO (percentage of the gait cycle from initial FS to TO) (see **Figure 18**). We could not detect the five fundamental events of a gait cycle using GRF so it was not possible to calculate ST parameters from GRF.

3.2.8. Statistical Analysis

The sample size (understood as the number of gait events) was calculated considering the difference (in frames) between the events detected by Ghoussayni's algorithm and those detected by GRF that was obtained in a previous study (213). With a difference of 2.1 frames, accepting an alpha risk of 0.05 and a beta risk of 0.2 in a two-sided test, and anticipating a drop-out rate of 0% (for being a retrospective study), the minimum sample size required was 35. Statistical analysis was done separately for FS and TO, so a minimum of 35 FS and 35 TO were required (271).

The correct statistical approach to assess the comparability between methods is not obvious (272). When a new method is evaluated by comparison with a gold standard, we try to assess the degree of agreement (273). The correlation coefficient is frequently proposed as an indicator of agreement (272–274), for example, to evaluate the criterion validity (degree to which the scores of an instrument are an adequate reflection of a gold standard) (71,275). However, the correlation coefficient analyzes the relationship between one variable and

another, not the differences, and it is not recommended as a method for assessing the comparability between methods (272). Bland and Altman (273) developed a statistical method to analyze the agreement between two quantitative measurements (Bland-Altman plot), by studying the mean bias and constructing limits of agreement (LoA) (272). However, it is a descriptive method and therefore it does not allow conclusions to be drawn beyond the analyzed data. The statistical significance of differences between methods is an inferential method, so it can be used to test hypotheses.

Pearson correlation coefficients were used to evaluate the linear relationship between the gold standard (GRF) and the two Ghoussayni's thresholds (Gho05 and GhoWS). Bland-Altman plots (273) were used to evaluate the degree of agreement between GRF and the other methods. In Bland-Altman plots, mean bias was calculated as the average of the differences (in frames) between GRF and the other methods, and LoA as the mean bias ±2SD (273). Bland-Altman plots only define LoA, without assessing whether these limits are acceptable or not (272). Acceptable limits must be previously defined, based on clinical needs, biological considerations or other goals (272). We defined acceptable limits of -5 and 5 frames, that is, -35.7 and 35.7 ms, based on the accuracy window of 33 ms used by Bruening and Ridge (212). Difference of means tests for non-normal distribution paired data were used to analyze the statistical significance of differences between the three methods (Friedman test), and between ST parameters calculated from Gho05 and GhoWS (Wilcoxon test). Mean differences (and 95% confidence intervals for differences) were also reported. A *P*-value lower than 0.05 was considered. Microsoft Excel and the Statistical Package for the Social Sciences (SPSS v.26) were used.

3.3. Study 3: Relationship between spatiotemporal parameters and clinical outcomes in children with bilateral spastic cerebral palsy

Data were collected retrospectively from a previous study made at the Motion Analysis Laboratory of the Institut Guttmann (Badalona, Spain).

3.3.1. Participants

The potentially eligible participants were children with a diagnosis of bilateral spastic or mixed CP, age between 4 and 14 years, GMFCS (38) levels I to III (see **Figure 2**), and ability to carry out simple verbal instructions. No child had surgery within the previous 12 months, BoNT-A injections within the previous 4 months, moderate or severe pain, severe visual impairment, or lower limb asymmetry above 3% of the height. Exclusion criteria were: 1) disability to walk 4 m independently without assistive devices; and 2) unavailability to process at least six gait cycles (three right and three left). The previous study was approved by the Research Ethics Committee of the Institut Guttmann (Badalona, Spain), and parents gave written informed consent for participating in the study.

3.3.2. Instrumented gait analysis

Each child walked barefoot, without orthosis or assistive devices, at self-selected speed on a 7-meter walkway. A minimum of three trials were collected. Two reflective markers (15 mm radius) were placed on each foot (right and left), one on the posterior end of the calcaneus (heel marker) and the other on the second metatarsal head (toe marker), according to the foot marker placement of the Plug-in Gait model (182) (see **Figure 12**). 3D marker coordinates were measured using a six infrared cameras system (SMART-D, BTS Bioengineering, Milan, Italy). Data were recorded at a sample frequency of 140 Hz, and filtered using a fourth order low pass Butterworth filter with a cutoff frequency of 6 Hz. Additionally, lateral and frontal views of feet motion were video recorded.

Gait events (FS and TO) were objectively detected using Gho05 (see **Section 3.2.5**). For each child, six gait cycles (three right and three left) were selected. For each gait cycle, seven ST parameters were computed: 1) cadence (steps/min) was calculated dividing 120 by stride time, considering stride time (s) as the time difference between two consecutive FS of the same foot (211) (see **Equation 6**); 2) stride length (m) was computed as the distance between the heel marker at two consecutive FS of the same foot (211); 3) step width (m) was computed as the medio-lateral distance between the heel markers (right and left) at two consecutive FS; 4) gait speed (m/s) was calculated as stride speed, dividing stride length by stride time (211); 5) first

double support (% of the gait cycle) was computed as the time difference between initial FS and opposite TO, normalized to stride time; 6) single support (%) was calculated as the time difference between opposite TO and opposite FS, normalized to stride time; and 7) time of TO (%) was computed as the time difference between initial FS and TO, normalized to stride time (see **Figure 18**).

Equation 6 $$Cadence\left(\frac{steps}{min}\right) = \frac{1\ cycle}{stride\ time(s)} \times \frac{2\ steps}{1\ cycle} \times \frac{60\ s}{1\ \text{min}} = \frac{120}{stride\ time(s)}$$

For each ST parameter, the mean value corresponding to the six gait cycles was calculated. Cadence was normalized (ND normalization) to leg length according to Stansfield et al. (232) (see **Equation 3**), due to its statistically significant correlation with relevant factors such as age, weight, and leg length (see **Table 8**).

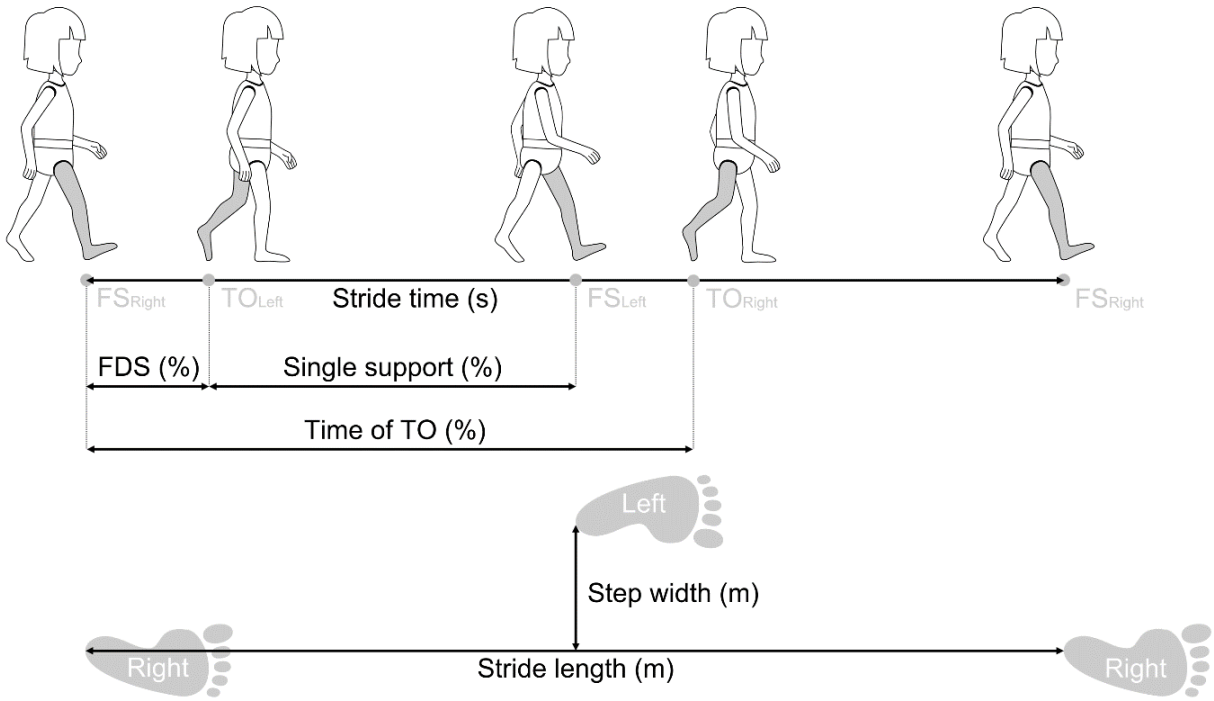

Figure 18. Graphical representation of spatiotemporal parameters
FS, foot strike; TO, toe off; FDS, first double support. Own elaboration.

Table 8. Correlation coefficients between spatiotemporal parameters and relevant factors

	Spatiotemporal parameters				
Relevant factors	**Cadence (steps/min)**	**ND cadence**	**Stride length (m)**	**Step width (m)**	**Gait speed (m/s)**
Age (y)	-0.725**	-0.408	0.209	0.205	-0.141
Weight (kg)	-0.553*	-0.247	0.307	-0.108	0.011
Leg length (m)	-0.767**	-0.439	0.228	0.110	-0.136

ND, non-dimensional. * p < 0.05; ** p < 0.01; *** p < 0.001. NA, not applicable.

Own elaboration.

3.3.3. Clinical assessment

Children were physically examined (including measures of spasticity, contractures and pROM, and deformities), and functionally assessed (including measures of gross motor function) by a physical therapist.

Spasticity was measured bilaterally in hip flexors, hip adductors, knee flexors, knee extensors, and ankle plantar flexors, using the MAS (72). Contractures and pROM measures included bilateral hip flexors contracture, hip abduction, hip rotations (internal and external), knee flexors contracture, and ankle plantar flexors contracture. Hip flexors contracture was evaluated using two methods: 1) as rectus femoris contracture (presence), using the Duncan-Ely test (49); and 2) as hip flexors contracture (presence), using the Thomas test (82) (See **Figure 4**). Hip abduction (degrees) was measured in supine, both with knee and hip flexed and extended (243). Hip rotations (degrees) were measured in prone, with knee flexed to 90º (82). Knee flexors contracture was evaluated as hamstring contracture (degrees), using the bilateral popliteal angle (49) (see **Figure 5**). Ankle plantar flexors contracture (degrees) was evaluated using the Silverskiold Test (49) (see **Figure 3**). Deformities were evaluated bilaterally, including: 1) femoral anteversion (degrees) in prone, with the knee flexed to 90º (49); 2) patella alta (presence) in supine, with the knee extended (49); 3) tibio-femoral angle (degrees) in supine; 4) tibial torsion, using the measurement of the bi-malleolar axis (degrees) (49); 5) hindfoot (neutral, varus or valgus) both in prone (unloaded) and standing (loaded) (49,82) (see **Figure 8**); 6) arch of the foot (normal, high or low) in standing (49); 7) flat foot (presence), using the Root test (49); 8) forefoot (neutral, abduction or adduction) in prone (49,82) (see **Figure 9**); and 9) toe (normal, hallux valgus or claw) in supine (82). The mean value of right and left sides (for quantitative clinical outcomes), and the most affected side (for qualitative clinical outcomes) were considered to take into account the interrelationship of the two sides (276) and its effect on overall gait disorders.

Gross motor function was evaluated using the GMFM-66 (score) and the dimension E (walking, running and jumping) of the GMFM-88 (%) (89,90) (see **Figure 10**).

3.3.4. Statistical Analysis

The sample size was calculated considering the correlation coefficients obtained between gait speed and the GMFM (dimension E or total score) in previous studies (244,252,253). With a correlation coefficient of 0.66, accepting an alpha risk of 0.05 and a beta risk of 0.2 in a two-sided test, and anticipating a drop-out rate of 0% (for being a retrospective study), the minimum sample size needed was 16 (271). The normality distribution of ST parameters was tested with

the Shapiro-Wilk test. Difference of means tests for both normal distribution independent samples (ANOVA and Student's t) and non-normal distribution independent samples (Mann-Whitney U and Kruskal-Wallis) were used to analyze the statistical significance of differences between independent samples of ST parameters in relation to qualitative clinical outcomes. Pearson correlation coefficients were used to evaluate the correlation between ST parameters and quantitative clinical outcomes. A p-value lower than 0.05 was considered. The software SPSS v.26 was used for statistical analysis.

4

Results

4. RESULTS

4.1. Study 1: Gait parameters in children with bilateral spastic cerebral palsy: a systematic review of randomized controlled trials

4.1.1. Study selection

The search of PubMed, Web of Science and Scopus databases provided a total of 334 citations, taking into account the above-mentioned user query and the search constraints (see **Section 3.1.1**). The last search was run on August 10th, 2017. After adjusting for duplicates, 199 studies remained. After reviewing the title and the abstract, 150 studies were discarded because they clearly did not meet the inclusion criteria. The full text of the remaining 49 studies was examined in more detail. Finally, 21 studies met the inclusion criteria and were included in the literature review (277–297). In one article (287), only one of the studies (phase I) was included. All the studies finally selected for the review were RCT, published in English in the period 2000 to 2016. See the flow diagram in **Figure 19**.

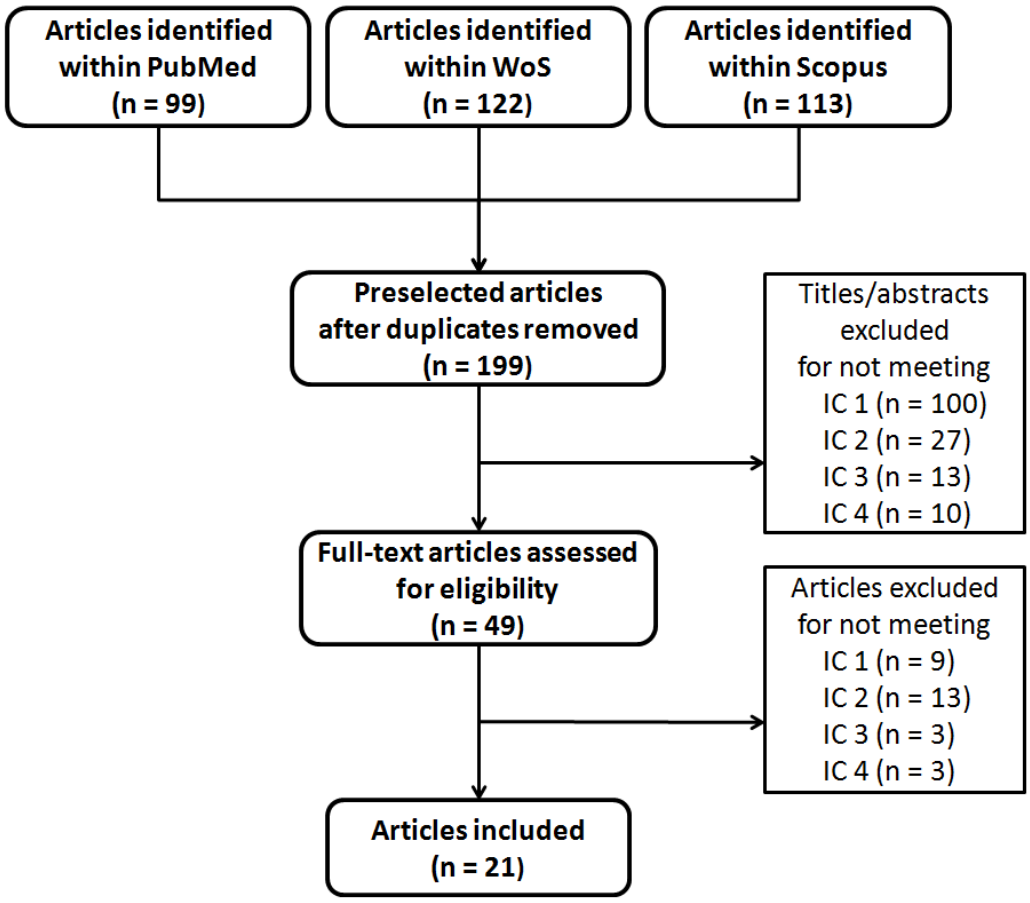

Figure 19. Flow diagram of study 1
WoS, Web of Science; IC, inclusion criteria. Own elaboration.

4.1.2. Eligibility criteria

The inclusion criteria of participants in the different studies include information related to diagnosis (21 studies), age range (16), gross motor function (20), ROM (nine), severity of motor disorders (spasticity and/or muscle weakness; six), secondary musculoskeletal problems (contractures and deformities; 14), medical history (surgery, drugs and/or rehabilitation; 19), sensory impairments (visual, auditory or perceptual; seven), degree of comprehension (13), anthropometric measures (height and/or weight; three), and treatment contraindications (four).

4.1.3. Participants

The included studies involved a total of 528 children with spastic CP. The majority of the participants had a diagnosis of bilateral spastic CP (n = 488, 92%), at least 419 (79%) spastic diplegic, and the mean age of the children was 8.6 years. The ability to walk of the participants was mainly defined through the GMFCS. Seven studies only included participants with independent walking (GMFCS levels I and/or II), 10 studies included participants able to walk with or without walking aids (GMFCS levels I, II and/or III) and four studies additionally included participants able to walk with external support (GMFCS levels I, II, III and/or IV) (see **Table 9**).

Other characteristics were detailed only in some studies, for example, sex (15 studies), anthropometric measures like weight, height or body mass index (10), the gait pattern (five), the use of walking aids or orthosis (three), and the history of surgery, physical therapy, or BoNT-A injections (three).

4.1.4. Study design

Eighteen studies used a parallel group design: different interventions were applied to at least two different groups (experimental and control groups). The other three studies used a crossover design: there were two different interventions (A and B) and all the children received both interventions in a randomized order. Two studies defined a typically developing control group but only data from the CP groups was taken into account in the review (see **Table 9** and **Table 10**).

4.1.5. Intervention

A big variety of interventions were studied in the included studies: surgical procedure (single event multilevel surgery (SEMLS), distal rectus femoris transfer, and/or selective dorsal rhizotomy; four studies), BoNT-A (four), casting (four), orthopedic device (ankle-foot orthosis, strapping system, and/or postural insole; three), individually defined physical therapy (one),

strength training program (whole body vibration training, resistance, and/or active exercises or neuromuscular electrical stimulation; five), balance training program (one), gait training program (gait trainer, treadmill training, or partial body-weight-supported treadmill training; three), hippotherapy (one), and transcranial direct current stimulation (one) (see **Table 10**).

Table 9. Participants' characteristics of study 1

	Sample size, n		Mean age,	Sex, n		Diagnosis, n				GMFCS	Participants' selection risk of bias	
Study	E	C	years	M	F	SD	SQ	SH	ST	level	RSG	AC
Neto et al. (277)	5	5	8	NR	NR	10				I, II	?	?
Abd El-Kafy et al. (278)	15	15	8.8	13	17	30				I, II	+	?
Franki et al. (279)[a]	5	5	6.2[b]	6	4	[c]	[c]			I, II, III	+	+
Abd El-Kafy (280)	19/19[d]	19	7.3	31	26	57				I, II	+	+
Grecco et al. (281)	12	12	7.9	7	17	24				II, III	?	+
Lee et al. (282)	15	15	9.8	15	15	[c]	[c]			[e]	?	?
Dreher et al. (283)	17	15	11.2	20	12	32				I, II, III	+	?
Smania et al. (284)	9	9	13.3	10	8	11	7			I, II, III, IV	+	?
Van der Houwen et al. (285)	12	10	7.6	14	8	21		1		I, II, III	?	?
Johnston et al. (286)	14	12	9.5	14	12	12	12		2	II, III, IV	?	?
McGibbon et al. (287)	25	22	8.5	27	20	25	9	7	6[f]	I, II, III, IV	?	+
Smith et al. (288)[a]	NR	NR	7.5	NR	NR	15				I	?	?
Al-Abdulwahab et al. (289)	21	10	7.7	NR	NR	31				[g]	?	?
Seniorou et al. (290)	11	9	12.5	10	10	20				I, II, III	?	?
McNee et al. (291)[a]	5	4	7.1	4	5	6		3		I, II, III	+	?
Engsberg et al. (292)	3/4/2[d]	3	9.9	3	9	12				I, II, III	?	?
Patikas et al. (293)	19	20	9.7	NR	NR	39				[g]	?	?
Kay et al. (294)	11	12	7.1	12	11	13	1	9		[g]	+	?
Bottos et al. (295)	5	5	6.3	7	3	10				[e]	?	?
Desloovere et al. (296)	17	17	6.8	NR	NR	22		12		[e]	-	-
Graubert et al. (297)	18	11	6.8	NR	NR	29				[h]	+	+

E, experimental group; C, control group; M, male; F, female; SD, spastic diplegia; SQ, spastic quadriplegia; SH; spastic hemiplegia; ST, spastic triplegia; GMFCS, Gross Motor Function Classification Scale; RSG, random sequence generation; AC, allocation concealment; NR, not reported; +, low risk of bias; ?, unclear risk of bias; -, high risk of bias. [a]Crossover design; [b]Median of age; [c]Diagnosis: SD or SQ; [d]More than one experimental group; [e]Independent walking; [f]Diagnosis: Mixed; [g]Independent or aided walking; [h]Nonambulator, assisted ambulatory or independent ambulatory.

Own elaboration.

4.1.6. Instrumented gait analysis

All included studies assessed participants at least twice. Eight studies made preintervention and postintervention assessments, seven studies made preintervention and follow-up assessments, and four studies made preintervention, postintervention and follow up assessments. Three studies made assessments in different conditions: with and without the intervention device (see **Table 10**).

When performing the IGA, different measurement tools were used synchronously (integrated solutions) or independently: 3DGA system, force plate, sEMG and video recording. 3DGA was used in 19 studies to obtain kinematic and/or ST parameters. The number of infrared cameras went from five to 16 (six being the most common) and the recording frequency from 100 to 120

Hz. The markers were reflective with a diameter between 9 and 25 mm. Eight studies used force plates to obtain kinetic data and the number of platforms ranged from one to three (two being the most common). Five studies used sEMG to obtain muscle activation data, and information about channels supported, sample frequency, amplifier, transmitter, filters (high-pass and low-pass) and electrodes (type, area, and interelectrodes distance) was reported. Eight studies used a video system as a complement to the other measurement tools (see **Table 10**).

Table 10. Studies' characteristics

	Intervention			Instrumented gait analysis		Gait parameters' selection risk of bias
Study	E	C	Assessment timing	Measurement tool	Data type	
Neto et al. (277)	PI	Placebo	Barefoot/ Shoes/+Insoles	3DGA	ST	-
Abd El-Kafy et al. (278)	BT+CT	CT	Pre/Post	3DGA+Video	ST	-
Franki et al. (279)[a]	ITP	GTP	Pre/Post	3DGA+FP +sEMG	ST, kinematics, summary indexes	+
Abd El-Kafy (280)	CT+SS/ +SAFO[b]	CT	Pre/Post	3DGA+Video	ST, kinematics	+
Grecco et al. (281)	TT+tDCS	TT +Placebo	Pre/Post/1mo	3DGA+Video	ST, kinematics, summary indexes	+
Lee et al. (282)	WBVT+CT	CT	Pre/Post	3DGA	ST, kinematics	-
Dreher et al. (283)	SEMLS+CT	SEMLS +DRFT+CT	Pre/1y	3DGA+FP	ST, kinematics, summary indexes	-
Smania et al. (284)	GT	CT	Pre/Post/1mo	3DGA	ST, kinematics	-
Van der Houwen et al. (285)	BoNT-A +CR	CT	Pre/6wks	Video+sEMG	sEMG	+
Johnston et al. (286)	PBWSTT	CT	Pre/Post/1mo	3DGA	ST	-
McGibbon et al. (287)	HT	BS	Pre/Post	Video+sEMG	sEMG	+
Smith et al. (288)[a]	DAFO	HAFO	Barefoot/DAFO /HAFO	3DGA+Video +FP	ST, kinematics, kinetics	-
Al-Abdulwahab et al. (289)	NMES		Pre/NMES/Post	3DGA	ST	-
Seniorou et al. (290)	SEMLS+CT +RS	SEMLS+CT +AE	Pre/Post/1y	3DGA	ST, kinematics	-
McNee et al. (291)[a]	CAST		Pre/Post	3DGA+FP	ST, kinematics, summary indexes	-
Engsberg et al. (292)	D-STR/ P-STR/ DP-STR[b]		Pre/Post	3DGA+Video +FP	ST, kinematics, kinetics	-
Patikas et al. (293)	SEMLS+CT +STR	SEMLS+CT	Pre/1y/2y	3DGA+FP	ST, kinematics, kinetics, summary indexes	-
Kay et al. (294)	BoNT-A +CAST	CAST	Pre/3mo/1y	3DGA	Kinematics	-
Bottos et al. (295)	BoNT-A +CAST+CT	BoNT-A +CT	Pre/1mo/4mo	3DGA+FP +sEMG	ST, kinematics, kinetics, sEMG	-
Desloovere et al. (296)	CAST post BoNT-A +CT	CAST pre BoNT-A +CT	Pre/2mo	3DGA+Video +FP+sEMG	ST, kinematics, kinetics, sEMG	-
Graubert et al. (297)	SDR+CT	CT	Pre/1y	3DGA	ST, kinematics	-

[a]Cross-over design; [b]More than one experimental group. E, experimental group; C, control group; PI, postural insole; BT, balance training; CT, conventional therapy; ITP, individualized therapy program; GTP, general therapy program; SS, strapping system; SAFO, static ankle foot orthosis; TT, treatmill training; tDCS, transcranial direct current stimulation; WBVT, whole body vibration training; SEMLS, single event multilevel surgery; DRFT, distal rectus femoris transfer; GT, gait trainer; BoNT-A, botulinum toxin A; CR, comprehensive rehabilitation; PBWSTT, partial body-weight-supported treadmill training; HT, hippotherapy; BS, barrel-sitting; DAFO, dynamic ankle foot orthosis; HAFO, hinged ankle foot orthosis; NMES, neuromuscular electrical stimulation; RS, resistance strengthening; AE, active exercise; CAST, casting; D-STR, dorsiflexion strength training; P-STR, plantarflexion strength training; DP-STR, dorsi-and plantarflexion strength training; STR, strength training; SDR, selective dorsal rhizotomy; Pre, pre-intervention assessment; Post, post-intervention assessment; 3DGA, three dimensional gait analysis; FP, force plate; ST, spatiotemporal; sEMG, surface electromyography; +, low risk of bias; ?, unclear risk of bias; -, high risk of bias.

Own elaboration.

In all the studies, participants were asked to walk on a walkway. In 12 studies, the length of the walkway was specified, with a mean value of 8 m. In 11 studies, the minimum number of walking trials (collected and/or selected) was reported, ranging from two to six trials. Two studies reported the maximum number of walking trials (eight and 10 respectively). Fifteen studies reported the walking speed that was indicated to participants. In all cases, self-selected walking speed was chosen. Some studies also described whether participants walked barefoot (eight studies) or with usual footwear (two), with orthosis or insoles (four), and/or with walking aids (five). Ten studies used data from children with typical development as normative reference.

All the studies used the IGA for obtaining outcome measures (it was one of the inclusion criteria of the review). Additionally, the IGA was used to define the gait pattern of the participants (two studies), the rehabilitation devices setup (two), and the BoNT-A target muscles (two).

4.1.7. Risk of bias

The risk of bias assessment was focused on the participants' selection and the gait parameters' selection. When assessing the participants' selection bias, the random sequence generation and the allocation concealment were studied. Different techniques were reported in the included studies. Regarding the random sequence generation, the following criteria was applied when analyzing the risk of bias: 1) computer random number generation, minimization, and block randomization with block size masked were considered as "low risk of bias"; 2) alternation was considered as "high risk of bias"; and 3) envelopes and block randomization without specifying the sequence generation technique were considered as "unclear risk of bias". In relation to the allocation concealment: 1) sequentially numbered, opaque, sealed envelopes and central randomization (performed by a person independent to the study) were considered as "low risk of bias"; 2) alternation was considered as "high risk of bias"; and 3) envelopes with one or two of the requirements (sequentially numbered, opaque, and sealed), computer randomization without specifying the allocation method, and random allocation schedule without specifying that it was not open were considered as "unclear risk of bias". Three studies showed a low risk of bias in both features and seven studies showed a low risk of bias in one of them (with the other one classified as unclear). In 10 studies, the whole randomization process was classified as unclear and one study showed a high risk of participants' selection bias (see **Table 9**).

The assessment of the gait parameters' selection bias was based on the ideal hypothesis testing defined by Pataky et al. (220) and the following criteria were applied: 1) directed

hypotheses (claim response in specific gait parameters) followed by analyses of the same specific gait parameters and non-directed hypotheses (broadly claim kinematic, kinetic, or sEMG response) followed by full gait curves analyses were considered as “low risk of bias”; and 2) specific gait parameters analyses following non-directed hypotheses (broadly claim ST, kinematic, kinetic, or gait response) and directed hypotheses followed by analyses of more specific gait parameters than those defined in the hypotheses were considered as “high risk of bias”. We considered as hypothesis the information contained in the last paragraph of the introduction section of the included studies, independently of the terminology used (hypothesis, aim, objective, goal, or purpose). Sixteen studies showed high risk of gait parameters’ selection bias, and five studies showed low risk (see **Table 10**).

No subgroup analyses of the results were done considering the risk of bias results because it is not possible to know if the bias really existed and any judgment could be unfair.

4.1.8. Outcomes

This section summarizes the gait parameters used as outcome measures in the included studies. The reported parameters were classified in ST, kinematic (“joint angles” referring to ankle, knee and hip, and “segment angles” referring to foot and pelvis), kinetic, sEMG, and summary indexes.

Only three included studies provided detailed parameters definitions (279,281,283). Gait parameters with different terminology were grouped together if they had a similar meaning (e.g. “minimum knee flexion in stance” (283) and “maximum knee extension in stance” (296)) and a common terminology was provided in order to homogenize the definition criteria. Sometimes, it was difficult to establish the correct definition for each gait parameter. For example, it is not clear if the gait parameter “ankle angle at initial swing” (284) refers to a specific time instant of the gait cycle (TO) or to the mean value during a gait subphase (initial swing). Some ST parameters were defined according to Grecco et al. (281). The nomenclature of kinematic and kinetic parameters was divided in three different items related to their definition: value, time-series and gait phase (e.g. the minimum value of the hip flexion-extension angle at stance phase was named MIN_HipFlexExt_St), based on Wolf et al. (219), and a short definition was given for each item. The definition of the summary indexes was also provided (see **Table 11**). sEMG data were catalogued by muscles, independently of the statistical parameter used in each study.

For each parameter, it was determined whether statistically significant differences were observed, either in the intragroup or intergroup analysis, considering a p-value < 0.05.

Table 11. Gait parameters definitions

Type	Nomenclature	Definition
SPATIOTEMPORAL		
	Gait speed	Mean velocity of progression in longitudinal direction. In meters/second. (281)
	Cadence	Number of steps in a time unit. In steps/minute. (281)
	Stride length	Longitudinal distance between successive points of heel contact of the same foot. In meters. (281)
	Step width	Distance between the rear end of the right and left heel centerlines along the mediolateral axis. In meters. (281)
	Time of toe off	Instant in the gait cycle in which toe off occurs. It also refers to the duration of stance phase. In percentage of gait cycle.
	Single support	Percentage of the gait cycle in which one foot is in contact with the floor. (173) It includes MSt and TSt.
	Double support	Percentage of the gait cycle in which both feet are in contact with the floor. There are two double support periods during a gait cycle (LR and PSw). (173)
KINEMATIC AND KINETIC		
Value		
	MAX	Maximum value. (219) In degrees (angle), N·m (moment) and W (power).
	MIN	Minimum value. (219) In degrees (angle), N·m (moment) and W (power).
	MAPO	Temporal position of the maximum value. (219) In percentage of gait cycle.
	MIPO	Temporal position of the minimum value. (219) In percentage of gait cycle.
	ROM	Range of motion (MAX-MIN). (219) In degrees (angle), N·m (moment) and W (power).
	MEAN	Mean value (219), in degrees (angle), N·m (moment) and W (power), calculated as: $MEAN_i = \frac{1}{T}\sum_{t=1}^{T} x_{i,t}$ where $x_{i,t}$ is the value of a gait variable *i* at a specific instant *t* in the gait cycle, and T is the number of instants into which the gait cycle was divided.
	GVS	The Gait Variable Score is the root mean square (RMS) difference between a normalized temporal kinematic variable (joint or segment angle) and the average kinematic variable from a reference group, calculated point-by-point across the gait cycle (279,281,298): $GVS_i = \sqrt{\frac{1}{T}\sum_{t=1}^{T}\left(x_{i,t} - \bar{x}_{i,t}^{ref}\right)^2}$ where $x_{i,t}$ is the value of a gait variable *i* at a specific instant *t* in the gait cycle, $\bar{x}_{i,t}^{ref}$ is the mean value of that variable at the same instant for the reference population, and T is the number of instants into which the gait cycle was divided. In degrees.
Time-series		
Foot kinematics		
	FootPro	Foot progression orientation in the frontal plane.
	FootInExRot	Foot rotation orientation in the transverse plane.
Ankle kinematics		
	DorsPlantFlex	Ankle dorsi-plantar flexion angle in the sagittal plane.
Knee kinematics		
	KneeFlexExt	Knee flexion-extension angle in the sagittal plane.
	KneeFlexExtVe	Knee flexion-extension velocity in the sagittal plane. It can be calculated as the temporal gradient (slope) of the KneeFlexExt angle: $v_{i,t} = \frac{1}{2}\left(x_{i,t+1} - x_{i,t-1}\right)$ where $x_{i,t}$ is the value of a gait variable *i* at a specific instant *t* in the gait cycle. (219)
Hip kinematics		
	HipFlexExt	Hip flexion-extension angle in the sagittal plane.
	HipAddAbd	Hip adduction-abduction angle in the frontal plane.
	HipInExRot	Hip internal-external rotation angle in the transverse plane.
Pelvis kinematics		
	PelvicTilt	Pelvic tilt orientation in the sagittal plane.
	PelvicObl	Pelvic obliquity orientation in the frontal plane.
	PelvicRot	Pelvic rotation orientation in the transverse plane.
Ankle kinetics		
	PlantDorsFlexMo	Internal ankle moment in the sagittal plane. It indicates muscle activity of plantar-flexors (positive values) and dorsi-flexors (negative values). (209)
	AnkleGenAbsPo	Ankle power in the sagittal plane. Generation power indicates concentric contraction and absorption power indicates eccentric contraction. (299)
Knee kinetics		
	KneeGenAbsPo	Knee power in the sagittal plane. Generation power indicates concentric contraction and absorption power indicates eccentric contraction. (299)
Hip Kinetics		

Table 11. Gait parameters definitions

Type	Nomenclature	Definition
	HipGenAbsPo	Hip power in the sagittal plane. Generation power indicates concentric contraction and absorption power indicates eccentric contraction. (299)
Gait phase		
Events		
	IC	Initial contact is the instant in which the initial foot strike occurs (0% of gait cycle). (209)
	ForeAftShear	Instant in which reversal of fore to aft shear occurs. (209)
	TOff	Instant in which toe off occurs (≈62% of gait cycle). (209)
Subphases		
	LR	Loading response or initial double-limb support goes from IC (0% of gait cycle) to opposite toe-off (≈12% of gait cycle). (209)
	MSt	Midstance refers to initial single-limb stance and goes from opposite toe-off (≈12% of gait cycle) to ForeAftShear (209) (or heel off if it occurs).
	TSt	Terminal stance refers to terminal single-limb stance and goes from ForeAftShear (or heel off if it occurs) to opposite foot strike (≈50% of gait cycle). (209)
	PSw	Preswing or second double-limb support goes from opposite foot strike (≈50% of gait cycle) to TOff. (209)
	ISw	Initial swing goes from TOff to foot clearance (≈75% of gait cycle). (209)
	MSw	Midswing goes from foot clearance (≈75% of gait cycle) to tibia vertical (≈85% of gait cycle). (209)
	TSw	Terminal swing goes from tibia vertical (≈85% of gait cycle) to second foot strike (100% of gait cycle). (209)
Phases		
	St	Stance is the phase in which the foot is in contact with the floor. It is from IC to TOff. It lasts for about 62% of gait cycle. (209)
	POff	Push off goes from ForeAftShear (or heel off if it occurs) to TOff. (300) It includes TSt and PSw and it is part of the Stance phase.
	Sw	Swing is the phase in which the foot is not in contact with the floor. It is from TOff to second foot strike. It lasts for about 38% of gait cycle. (209)
Gait cycle		
	Stri	Stride is the movement from one foot strike (initial) to the successive foot strike (second) on the same side. (209)
SUMMARY INDEXES		
	GGI	The Gillette Gait Index, also called the Normalcy Index, uses multivariate statistical methods to quantify the deviation of a subject's gait from an unimpaired control group. It is calculated from three spatiotemporal parameters (timing of toe off, gait speed normalized by leg length and cadence) and 13 kinematic parameters (MEAN_PelvicTilt_Stri, ROM_PelvicTilt_Stri, MEAN_PelvicRot_Stri, MIN_HipFlexExt_Stri, ROM_HipFlexExt_Stri, MIN_HipAddAbd_Sw, MEAN_HipInExRot_St, KneeFlexExt_IC, MAPO_KneeFlexExt_Stri, ROM_KneeFlexExt_Stri, MAX_DorsPlantFlex_St, MAX_DorsPlantFlex_Sw and MEAN_FootPro_Stri). (217) Schutte et al (301) described its calculation.
	GPS	Gait Profile Score is the RMS difference between a gait trial and averaged data from people with no gait pathology. It is calculated from 15 kinematic parameters (GVS_PelvicTilt_Stri, GVS_PelvicObl_Stri, GVS_PelvicRot_Stri, and GVS_HipFlexExt_Stri, GVS_HipAddAbd_Stri, GVS_HipInExRot_Stri, GVS_KneeFlexExt_Stri, GVS_DorsPlantFlex_Stri, GVS_FootPro_Stri for right and left sides). A GPS score can be determined for each side based on the nine GVS scores for that side (217,281): $GPS = \sqrt{\frac{1}{N}\sum_{i=1}^{N} GVS_i^2}$. In degrees.

Own elaboration.

4.1.8.1.Spatiotemporal parameters

Eighteen studies analyzed ST data. Seven different parameters were reported: gait speed (17 studies), cadence (also expressed as cycle time) (15), stride length (also expressed as step length) (17), step width (two), time of TO (also expressed as stance phase or swing phase) (six), single support (one), and double support (one). Gait speed was calculated in m/s, cm/s, or m/min (15 studies) and it was also normalized to account for leg length (one). Cadence was

calculated in steps/min or cycles/min (10 studies) and, when expressed as cycle time, in s or ms (four). Stride length was calculated in m or cm (13 studies) and percentage of height (one). Time of TO, single support, and double support were calculated in percentage of cycle. Statistically significant changes ($p<0.05$) within groups (intragroup analysis) and/or between groups (intergroup analysis) were observed for five ST parameters: gait speed (11 studies), cadence (seven), stride length (nine), time of TO (one) and single support (one) (see **Table 12**).

Table 12. Instrumented gait analysis: spatiotemporal and segment angles parameters

	Spatiotemporal							Segment angles												
								Foot				Pelvis								
								FP	TP			SP			FP			TP		
Study	Gait speed	Cadence	Stride length	Step width	Time of toe off	Single support	Double support	MEAN_FootPro_St	MEAN_FootInExRot_St	ROM_FootInExRot_Stri	GVS_FootInExRot_Stri	MEAN_PelvicTilt_Stri	ROM_PelvicTilt_Stri	GVS_PelvicTilt_Stri	MEAN_PelvicObl_Stri	ROM_PelvicObl_Stri	GVS_PelvicObl_Stri	MEAN_PelvicRot_Stri	ROM_PelvicRot_Stri	GVS_PelvicRot_Stri
Neto et al. (277)	EG	EG	N		N		N													
Abd El-Kafy et al. (278)	ECG	ECG	ECG		ECG															
Franki et al. (279)			EG								N			N			C			E
Abd El-Kafy (280)	ECG	ECG	ECG																	
Grecco et al. (281)	EG	EG	N	N	N						N			EG			N			N
Lee et al. (282)	E	E	E																	
Dreher et al. (283)	N	N	N		N															
Smania et al. (284)	EG	N	EG																	
Johnston et al. (286)	EC	C	E																	
Smith et al. (288)	EC	EC	EC																	
Al-Abdulwahab et al. (289)	E		E	N																
Seniorou et al. (290)	E																		N	
McNee et al. (291)	N	N	N			G														
Engsberg et al. (292)	N	N	N																	
Patikas et al. (293)	N	N	N		N															
Bottos et al. (295)	G	N	G		N															
Desloovere et al. (296)	N	N	N					E	E			N	N		N	N		N	E	
Graubert et al. (297)	N	N	N							G			N							

SP, sagittal plane; FP, frontal plane; TP, transverse plane. N, no significant differences; E, significant differences within the experimental group (intra-group analysis); C, significant differences within the control group (intra-group analysis); G, significant differences between groups (inter-group analysis).

Own elaboration.

4.1.8.2.Kinematic parameters

Fifteen studies analyzed kinematics of the lower limb, including segment angles: foot (four studies) and pelvis (five); and joint angles: ankle (12), knee (13) and hip (10); in the three planes: sagittal (15), frontal (four) and transverse (four). Four studies analyzed kinematics at the five levels (foot, ankle, knee, hip, and pelvis) and in the three planes (sagittal, frontal, and transverse). There were 64 different kinematic parameters explicitly reported: foot (four

parameters), ankle (14), knee (18), hip (19) and pelvis (nine); sagittal plane (44), frontal plane (eight), and transverse plane (12). Significant changes were found in 38 kinematic parameters: foot (three parameters), ankle (10), knee (13), hip (eight), and pelvis (four); sagittal plane (30), frontal plane (three), and transverse plane (five) (see **Table 12, Table 13** and **Table 14**).

4.1.8.3.Kinetic parameters

Five studies analyzed kinetics, including ankle, knee, and hip moment (five studies) and power (three) in the sagittal plane. Joint moment was calculated in N·m/kg (normalized to body mass) (four studies) and joint power in W (one) or W/kg (two). Eight different parameters were reported: PlantDorsFlexMo_IC (one study), MAX_PlantDorsFlexMo_LR (two), MAX_PlantDorsFlexMo_POff (five), MIN_AnkleGenAbsPo_LR (one), MAX_AnkleGenAbsPo_POff (three), MIN_KneeGenAbsPo_LR (one), MIN_HipGenAbsPo_St (one), and MAX_HipGenAbsPo_St (one). Significant changes were observed in four kinetic parameters: MAX_PlantDorsFlexMo_LR (one study), MAX_PlantDorsFlexMo_POff (two), MIN_AnkleGenAbsPo_LR (one), and MAX_HipGenAbsPo_St (one) (see **Table 15**).

4.1.8.4.sEMG parameters

Four studies analyzed sEMG data. Each one used different parameters related to sEMG: root mean square difference, mean asymmetry score (in mV), dynamic EMG score (in percentage of number of patients in which muscle is active during gait cycle), and maximal linear envelope of EMG (dynamic rectified EMG recordings in mV). Eight muscle groups were studied: gastrocnemius (three studies), soleus (one), tibialis anterior (two), rectus femoris (two), vastus lateralis (one), lateral hamstrings (one), medial hamstrings (two), and adductor (one). Significant changes within or between groups were found in all the muscles (at least in one study) except in vastus lateralis (see **Table 15**).

4.1.8.5.Summary indexes

Five studies analyzed one of these summary indexes: the GGI (three), and the Gait Profile Score (GPS) (two). Significant changes were found in both indexes (see **Table 15**).

Table 13. Instrumented gait analysis: hip (sagittal and frontal plane) and ankle angles parameters

	Ankle														Hip													
	Sagittal plane																											Frontal plane
Study	DorsPlantFlex_IC	MAX_DorsPlantFlex_LR-MSt	DorsPlantFlex_ForeAftShear	MAX_DorsPlantFlex_St	MAPO_DorsPlantFlex_St	DorsPlantFlex_TOff	MIN_DorsPlantFlex_Sw	MEAN_DorsPlantFlex_MSw	MAX_DorsPlantFlex_Sw	MEAN_DorsPlantFlex_Stri	ROM_DorsPlantFlex_St	ROM_DorsPlantFlex_POff	ROM_DorsPlantFlex_Sw	GVS_DorsPlantFlex_Stri	HipFlexExt_IC	HipFlexExt_ForeAftShear	MIN_HipFlexExt_St	HipFlexExt_TOff	MEAN_HipFlexExt_MSw	MAX_HipFlexExt_Sw	MEAN_HipFlexExt_Stri	ROM_HipFlexExt_St	GVS_HipFlexExt_Stri	MEAN_HipAddAbd_St	MEAN_HipAddAbd_Sw	ROM_HipAddAbd_St	GVS_HipAddAbd_Stri
Franki et al. (279)														N									N				N
Abd El-Kafy (280)																ECG											
Grecco et al. (281)														N									N				EG
Lee et al. (282)										E										N							
Smania et al. (284)	N		N			N		N							EG	EG		EG	G								
Smith et al. (288)	EC			EC			EC		EC											N							
McNee et al. (291)				G					G								G										
Engsberg et al. (292)	N			N					N																		
Patikas et al. (293)						N											N										
Kay et al. (294)				EC					EC																		
Bottos et al. (295)	N			N			N																				
Desloovere et al. (296)	EC	E		EC	E			EC				N	EC		N		N			N		N		N	N	N	
Graubert et al. (297)											G		G									G				N	

N, no significant differences; E, significant differences within the experimental group (intra-group analysis); C, significant differences within the control group (intra-group analysis); G, significant differences between groups (inter-group analysis).

Own elaboration.

Table 14. Instrumented gait analysis: hip (transverse plane) and knee angles parameters

	Knee																	Hip						
	Sagittal plane																	Transverse Plane						
Study	KneeFlexExt_IC	MAX_KneeFlexExt_St	KneeFlexExt_ForeAftShear	MIN_KneeFlexExt_St	MIPO_KneeFlexExt_St	KneeFlexExt_TOff	MAX_KneeFlexExt_Sw	MAPO_KneeFlexExt_Sw	MEAN_KneeFlexExt_MSw	MIN_KneeFlexExt_TSw	MEAN_KneeFlexExt_Stri	MEAN_KneeFlexExt_St	ROM_KneeFlexExt_Stri	ROM_KneeFlexExt_St	ROM_KneeFlexExt_Sw	MAX_KneeFlexExtVe_Stri	Amount delayed KneeFlexExt_Sw	GVS_KneeFlexExt_Stri	HipInExRot_IC	HipInExRot_ForeAftShear	MAX_HipInExRot_Stri	MEAN_HipInExRot_TSt	MEAN_HipInExRot_MSw	GVS_HipInExRot_Stri
Franki et al. (279)																		G						N
Abd El-Kafy (280)			ECG																	EC				
Grecco et al. (281)																		G						N
Lee et al. (282)											N													
Dreher et al. (283)	EC			EC	N		EG	EC				EC	CG	C	ECG	ECG								
Smania et al. (284)	N		N			N			N															
Smith et al. (288)							E																	
Seniorou et al. (290)	N			E																	N			
McNee et al. (291)				N																				
Engsberg et al. (292)				E																				
Patikas et al. (293)										N														
Desloovere et al. (296)	N	N		E	E	N	N							E			E		N	N		N	N	
Graubert et al. (297)														G	N									

N, no significant differences; E, significant differences within the experimental group (intra-group analysis); C, significant differences within the control group (intra-group analysis); G, significant differences between groups (inter-group analysis).

Own elaboration.

Table 15. Instrumented gait analysis: kinetic and surface electromyography parameters and summary indexes

	Kinetic																	Summary indexes	
	Ankle					Knee		Hip		Surface electromyography									
	Moment			Power															
Study	PlantDorsFlexMo_IC	MAX_PlantDorsFlexMo_LR	MAX_PlantDorsFlexMo_POff	MIN_AnkleGenAbsPo_LR	MAX_AnkleGenAbsPo_POff	MIN_KneeGenAbsPo_LR	MIN_HipGenAbsPo_St	MAX_HipGenAbsPo_St	Gastrocnemius	Soleus	Tibialis anterior	Rectus femoris	Vastus lateralis	Lateral hamstrings	Medial hamstrings	Adductor	GGI	GPS
Franki et al. (2014) (279)																		N
Grecco et al. (2014) (281)																		EG
Dreher et al. (2012) (283)																	EC	
Van der Houwen et al. (2011) (285)									G			N			N			
McGibbon et al. (2009) (287)																EG		
Smith et al. (2009) (288)	N		EC		N													
McNee et al. (2007) (291)																	N	
Engsberg et al. (2006) (292)			N															
Patikas et al. (2006) (293)			N		N	N	N										N	
Bottos et al. (2003) (295)		N	N						N		N							
Desloovere et al. (2001) (296)		EC	EC	EC	N			C	EC	EC	C	C	N	C	EC			

N, no significant differences; E, significant differences within the experimental group (intra-group analysis); C, significant differences within the control group (intra-group analysis); G, significant differences between groups (inter-group analysis).

Own elaboration.

4.1.9. Gait parameters responsiveness to different treatments

Interventions were grouped in eight different types: surgery, BoNT-A plus casting, orthopedic devices, strength training, balance training, gait training, individualized therapy, and hippotherapy. Surgery produced significant changes in kinematic parameters, mainly at knee (nine parameters), and one summary index (GGI). BoNT-A and/or casting showed significant differences in ST, kinematic (foot, ankle, knee, hip, and pelvis), kinetic (ankle and hip), and sEMG parameters. Orthopedic devices showed significant results in ST, kinematic (ankle, knee, and hip), and ankle kinetic parameters. Strength training significantly changed ST and kinematic (ankle and knee) parameters. Balance training produced significant results in ST parameters. Gait training showed significant results in ST and kinematic parameters, mainly at hip (five parameters), and one summary index (GPS). Individualized therapy significantly changed ST and kinematic (knee and pelvis) parameters. Hippotherapy showed significant changes in sEMG data (adductor muscle activity) (see **Table 16**).

Table 16. Gait parameters responsiveness to different treatments

		Kinematic						Kinetic			
Interventions	**Spatiotemporal**	**Foot**	**Ankle**	**Knee**	**Hip**	**Pelvis**	**SI**	**Ankle**	**Knee**	**Hip**	**sEMG**
Surgery (283,297)	N	ROM_FootInExRot_Stri	ROM_DorsPlantFlex_St, ROM_DorsPlantFlex_Sw	KneeFlexExt_IC, MIN_KneeFlexExt_St, MAX_KneeFlexExt_Sw, MAPO_KneeFlexExt_Sw, MEAN_KneeFlexExt_St, ROM_KneeFlexExt_Stri, ROM_KneeFlexExt_St, ROM_KneeFlexExt_Sw, MAX_KneeFlexExtVe_Stri	ROM_HipFlexExt_St	N	GGI	X	X	X	X
BONT-A + Casting (285,291,294–296)	Gait speed, Stride length, Single support	MEAN_FootPro_St, MEAN_FootInExRot_St	DorsPlantFlex_IC, MAX_DorsPlantFlex_LR-MSt, MAX_DorsPlantFlex_St, MAPO_DorsPlantFlex_St, MEAN_DorsPlantFlex_MSw, MAX_DorsPlantFlex_Sw, ROM_DorsPlantFlex_Sw	MIN_KneeFlexExt_St, MIPO_KneeFlexExt_St, ROM_KneeFlexExt_St,	MIN_HipFlexExt_St	ROM_PelvicRot_Stri	N	MAX_PlantDorsFlexMo_LR, MAX_PlantDorsFlexMo_POff, MIN_AnkleGenAbsPo_LR	X	MAX_HipGenAbsPo_St	Soleus, Tibialis anterior, Gastrocnemius, Rectus femoris, Lateral hamstrings, Medial hamstrings
Orthopedic device (277,280,288)	Gait speed, Cadence, Stride length	X	DorsPlantFlex_IC, MAX_DorsPlantFlex_St, MIN_DorsPlantFlex_Sw, MAX_DorsPlantFlex_Sw	KneeFlexExt_ForeAftShear, MAX_KneeFlexExt_Sw	HipFlexExt_ForeAftShear, HipInExRot_ForeAftShear	X	X	MAX_PlantDorsFlexMo_POff	X	X	X
Strength training (282,289,290, 292,293)	Gait speed, Cadence, Stride length	X	MEAN_DorsPlantFlex_Stri	MIN_KneeFlexExt_St	N	N	N	N	N	N	X
Balance training (278)	Gait speed, Cadence, Stride length, Time of toe off	X	X	X	X	X	X	X	X	X	X
Gait training (281,284,286)	Gait speed, Cadence, Stride length	N	N	GVS_KneeFlexExt_Stri	HipFlexExt_IC, HipFlexExt_ForeAftShear, HipFlexExt_TOff, MEAN_HipFlexExt_MSw, GVS_HipAddAbd_Stri	GVS_PelvicTilt_Stri	GPS	X	X	X	X
ITP (279)	Stride length	N	N	GVS_KneeFlexExt_Stri	N	GVS_PelvicRot_Stri	N	X	X	X	X
Hippotherapy (287)	X	X	X	X	X	X	X	X	X	X	Adductor

BONT-A, botulinum toxin A; ITP, individualized therapy program; SI, summary indexes. X, not analyzed; N, no significant differences.

Own elaboration.

4.2. Study 2: Gait event detection using kinematic data in children with bilateral spastic cerebral palsy

Twenty-two potentially eligible participants were identified. Six children were excluded (see **Figure 20**). Sixteen children (seven males and nine females) with a diagnosis of bilateral spastic CP and a mean age of 8.9 ± 2.7 years were included (see **Table 17**). Sixty-two trials were collected and 51 of them contained at least one valid event. Ninety-eight gait events (50 FS and 48 TO) were detected, first with GRF, and afterwards with Gho05 and GhoWS. Three types of FS were distinguished: heel strike (n=30), toe strike (n=6), and both at the same time (n=14) (see **Table 17**).

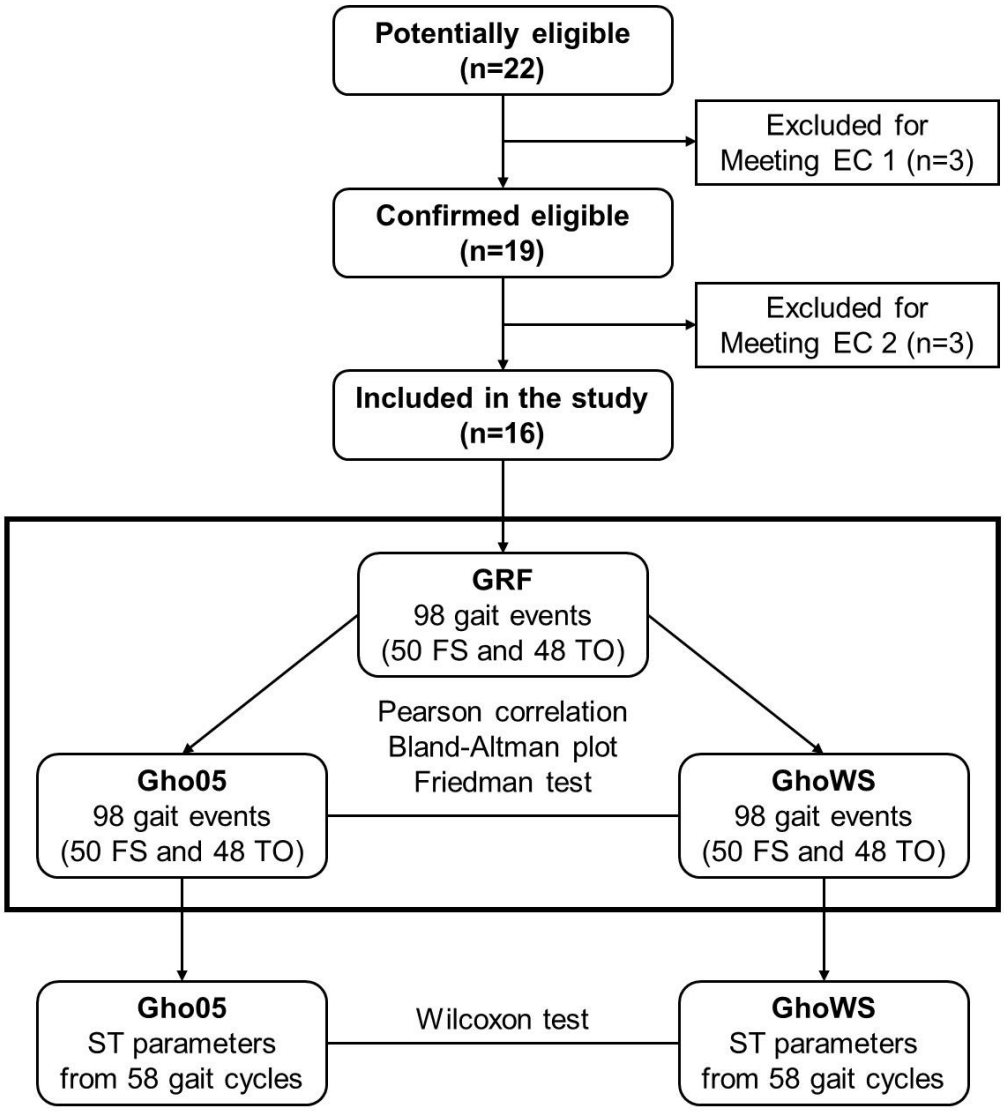

Figure 20. Flow diagram of study 2
EC, exclusion criteria; GRF, ground reaction forces; Gho05, Ghoussayni's algorithm using a threshold of 0.5 m/s; GhoWS, Ghoussayni's algorithm using a walking speed dependent threshold; FS, foot strike; TO, toe off; ST, spatiotemporal. Own elaboration.

Table 17. Participants' characteristics of study 2

ID	Sex	CP, type	GMFCS, level	Age, y	Weight, kg	Height, m	Mean WS[a] (SD), m/s	Foot strike[b], type (n)	Orthosis	Assistive device
1	Male	Mixed	III	6.3	17.4	1.10	0.55 (0.08)	Toe (2), both (1)	Yes	No
2	Female	Spastic	II	9.4	22.5	1.30	0.95 (0.19)	Heel (2), both (2)	Yes	No
3	Male	Spastic	III	9.9	34.9	1.32	0.50 (0.05)	Heel (4)	Yes	Crutches
4	Female	Spastic	III	12.1	41.5	1.47	1.11 (0.12)	[c]	Yes	Crutches
5	Male	Spastic	II	7.9	26.8	1.32	0.92 (0.08)	Toe (1)	Yes	No
6	Female	Spastic	III	8.1	46.2	1.25	0.66 (0.03)	Heel (1), both (2)	No	Walker
7	Male	Spastic	II	12.1	50.2	1.57	0.91 (0.01)	Heel (1), both (1)	No	No
8	Female	Spastic	II	8.8	24.2	1.25	0.95 (0.01)	Both (3)	Yes	No
9	Female	Mixed	II	11.5	28.5	1.32	0.43 (0.08)	Toe (2)	No	Walker
10	Male	Spastic	II	12.8	33.4	1.45	1.01 (0.03)	Heel (2)	No	No
11	Female	Spastic	I	4.9	21.3	1.09	1.08 (0.05)	Heel (5), both (1)	Yes	No
12	Male	Spastic	II	8.3	29.9	1.31	0.91 (0.11)	Heel (1), both (1)	Yes	No
13	Female	Mixed	II	12.5	34.4	1.44	1.03 (0.06)	Heel (6), toe (1)	No	No
14	Female	Spastic	II	6.9	18.1	1.10	0.93 (0.17)	Heel (2), both (2)	Yes	No
15	Female	Mixed	I	5.6	18.4	1.08	1.15 (0.04)	Heel (6)	No	No
16	Male	Spastic	II	5.8	27.9	1.20	0.99 (0.15)	Both (1)	Yes	No

ID, identification; CP, cerebral palsy; GMFCS, Gross Motor Functional Classification System; WS, walking speed; SD, standard deviation. [a]Mean value of the walking speeds calculated for the detection of gait events using Ghoussayni's algorithm with a walking speed dependent threshold (GhoWS); [b]Estimated using the new adaptation of Ghoussayni's algorithm with a threshold of 0.5 m/s (Gho05): heel strike (heel marker velocity fell below the threshold before than toe marker velocity), toe strike (toe marker velocity fell below the threshold before than heel marker velocity), both at the same time (both –heel and toe- marker velocities fell below the threshold at the same time); [c]No valid foot strike was detected using ground reaction forces (GRF).

Own elaboration.

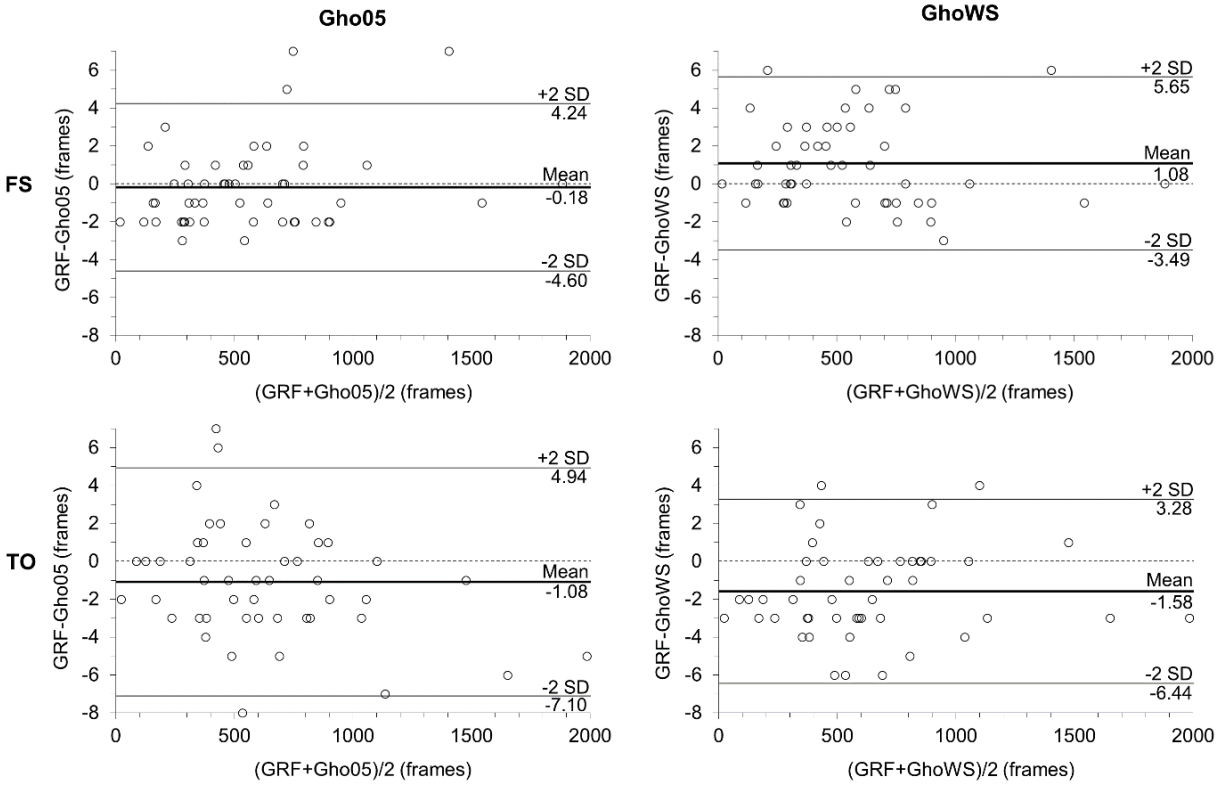

Figure 21. Bland-Altman plots between GRF and Ghoussayni's thresholds (Gho05 and GhoWS), for FS and TO
GRF, ground reaction forces; Gho05, Ghoussayni's algorithm using a threshold of 0.5 m/s; GhoWS, Ghoussayni's algorithm using a walking speed dependent threshold; SD, standard deviation; FS, foot strike; TO, toe off. Own elaboration.

Correlation coefficients between the gold standard (GRF) and the other methods were 0.99 ($p<0.01$) both for Gho05 and GhoWS, and both for FS and TO. Bland-Altman plots are shown in **Figure 21**. For FS, the mean bias was smaller between GRF and Gho05 than between GRF and GhoWS (-0.18 and 1.08 frames, respectively); and LoA were -4.60 and 4.24 frames between GRF and Gho05, and -3.49 and 5.65 frames between GRF and GhoWS, exceeding (GhoWS) the acceptable limits (-5 and 5 frames). For TO, the mean bias was smaller between GRF and Gho05 than between GRF and GhoWS (-1.08 and -1.58 frames, respectively); and LoA were -7.10 and 4.94 frames between GRF and Gho05, and -6.44 and 3.28 frames between GRF and GhoWS, exceeding (both Gho05 and GhoWS) the acceptable limits.

The statistical significance of differences, mean difference, and 95% confidence interval for the difference between the three methods are shown in **Table 18**. For FS, there were no statistically significant ($p<0.05$) differences between GRF and the two Ghoussayni's thresholds. For TO, there were statistically significant differences between GRF and GhoWS, but not between GRF and Gho05. In both cases (FS and TO), there were statistically significant differences between Gho05 and GhoWS.

Table 18. Statistical significance of differences and mean difference (95% confidence interval for the difference) between GRF, Gho05 and GhoWS

	GRF and Gho05		GRF and GhoWS		Gho05 and GhoWS	
Gait event	F	Mean difference (95% CI)	F	Mean difference (95% CI)	F	Mean difference (95% CI)
Foot strike (frame)	2.300	-0.18 (-0.81; 0.45)	2.000	1.08 (0.43; 1.73)	4.300***	1.26 (0.89; 1.63)
Toe off (frame)	1.633	-1.08 (-1.96; -0.21)	4.338***	-1.58 (-2.29; -0.88)	2.705*	-0.50 (-1.07; 0.07)

Gho05, Ghoussayni's algorithm using a threshold of 0.5 m/s; GhoWS, Ghoussayni's algorithm using a walking speed dependent threshold; GRF, ground reaction forces; F, standardized Friedman test statistic in absolute value; CI, confidence interval for the difference. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Own elaboration.

ST parameters from 58 gait cycles defined using Gho05 and GhoWS were compared. There were statistically significant differences between ST parameters calculated from Gho05 and GhoWS in the cases: first double support, single support, and time of TO (see **Table 19**).

Table 19. Statistical significance of differences and mean difference (95% confidence interval for the difference) between ST parameters calculated from Gho05 and GhoWS

Spatiotemporal parameter	Standardized Wilcoxon test statistic in absolute value	Mean difference (95% CI)
Stride length (m)	1.217	-0.0005 (-0.0012; 0.0003)
Stride time (s)	0.570	-0.0011 (-0.0025; 0.0002)
Stride speed (m/s)	1.217	0.0005 (-0.0003; 0.0013)
First double support (%)	3.714***	-1.3729 (-2.0071; -0.7386)
Single support (%)	3.782***	1.4347 (0.7737; 2.0958)
Time of toe off (%)	3.643***	-1.2682 (-1.8748; -0.6616)

ST, spatiotemporal; Gho05, Ghoussayni's algorithm using a threshold of 0.5 m/s; GhoWS, Ghoussayni's algorithm using a walking speed dependent threshold; CI, confidence interval for the difference. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Own elaboration.

4.3. Study 3: Relationship between spatiotemporal parameters and clinical outcomes in children with bilateral spastic cerebral palsy

Twenty-two potentially eligible participants were identified. Three children were excluded (see **Figure 22**). Nineteen children (nine males and ten females) with a diagnosis of bilateral spastic CP, a mean age of 9.6 ± 2.8 years, and GMFCS levels I to III were included in the present study (see **Table 20**). Mean and standard deviation of ST parameters, grouped by GMFCS, are shown in **Table 21**.

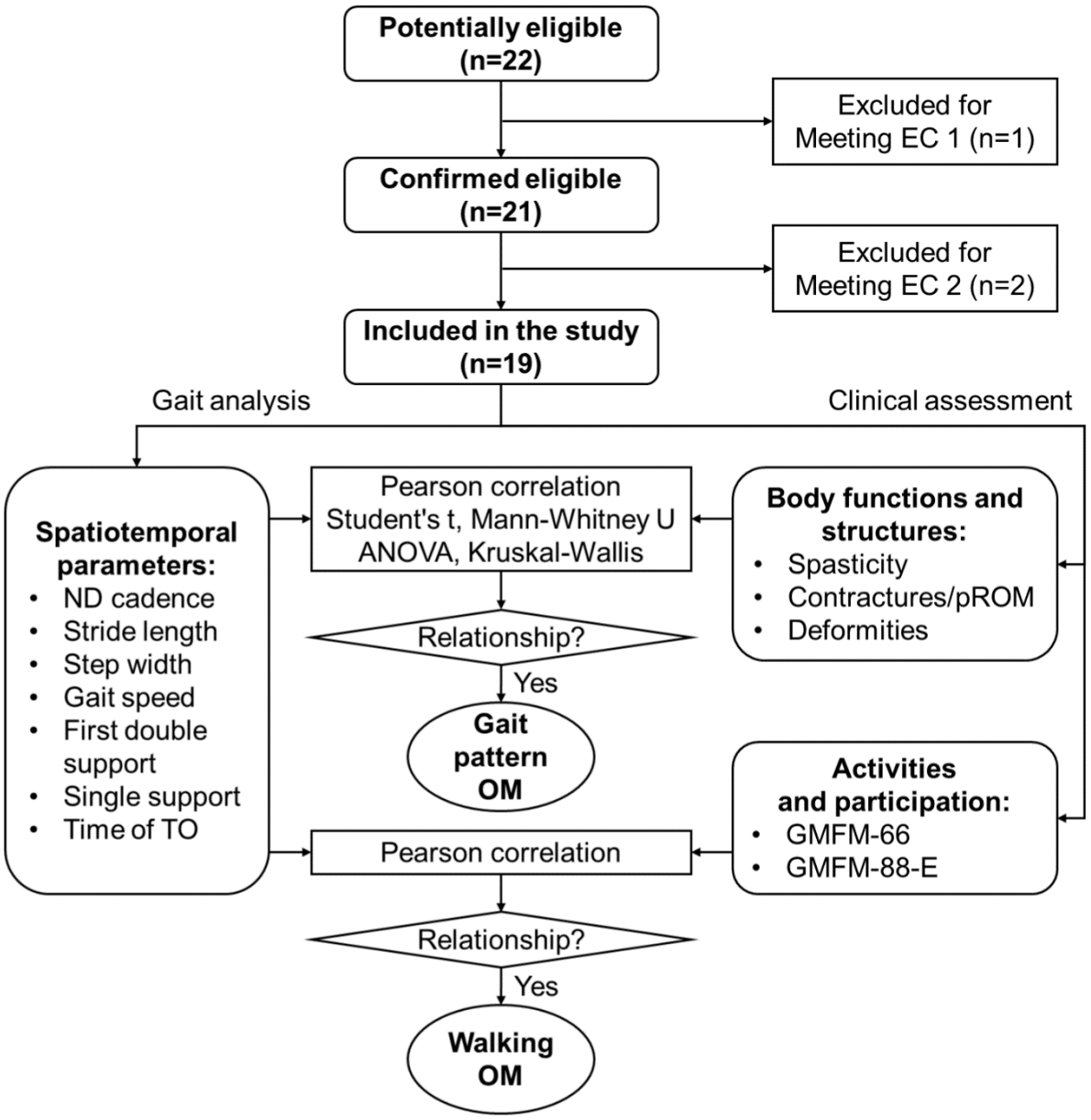

Figure 22. Flow diagram of study 3
EC, exclusion criteria; ND, non-dimensional normalization; TO, toe off; pROM, passive range of motion; GMFM-66, Gross Motor Function Measure 66; GMFM-88-E, Gross Motor Function Measure 88 dimension E (walking, running, jumping); OM, outcome measure. Own elaboration.

Table 20. Participants' characteristics of study 3

ID	Sex	CP type	GMFCS, level	Age, y	Weight, kg	Height, m	Leg length, m	PT, HPW	BoNT-A	Surgery	Orthosis	AD
1	Male	Mixed	III	6.3	17.4	1.10	0.55	1.50	Yes	No	Yes	No
2	Female	Spastic	II	9.4	22.5	1.30	0.66	0.75	Yes	No	Yes	No
3	Male	Spastic	III	9.9	34.9	1.32	0.70	1.00	Yes	Yes	Yes	Crutches
4	Female	Spastic	III	12.1	41.5	1.47	0.74	3.50	Yes	Yes	Yes	Crutches
5	Male	Spastic	II	7.9	26.8	1.32	0.66	2.00	Yes	Yes	Yes	No
6	Female	Spastic	III	8.1	46.2	1.25	0.65	2.50	Yes	Yes	No	Walker
7	Male	Spastic	II	12.1	50.2	1.57	0.82	1.00	Yes	No	No	No
8	Female	Spastic	II	8.8	24.2	1.25	0.63	0.00	Yes	No	Yes	No
9	Female	Mixed	III	13.3	39.9	1.54	0.79	1.50	No	No	No	Wheelchair
10	Female	Mixed	II	11.5	28.5	1.32	0.71	1.00	No	No	No	Walker
11	Male	Mixed	II	12.7	39.7	1.57	0.85	0.50	Yes	Yes	No	No
12	Female	Spastic	I	13.2	54	1.54	0.81	1.00	Yes	No	No	No
13	Male	Spastic	II	12.8	33.4	1.45	0.77	1.00	Yes	Yes	No	No
14	Female	Spastic	I	4.9	21.3	1.09	0.53	2.00	Yes	Yes	Yes	No
15	Male	Spastic	II	8.3	29.9	1.31	0.69	1.50	Yes	No	Yes	No
16	Female	Mixed	II	12.5	34.4	1.44	0.76	0.50	No	No	No	No
17	Male	Spastic	III	6.5	19.1	1.05	0.55	1.00	Yes	No	Yes	Crutches
18	Female	Spastic	II	6.9	18.1	1.10	0.56	2.00	No	No	Yes	No
19	Male	Spastic	II	5.8	27.9	1.20	0.61	2.00	No	No	Yes	No

ID, identification; CP, cerebral palsy; GMFCS, Gross Motor Functional Classification System; PT, physical therapy; BoNT-A, botulinum neurotoxin A; AD, assistive device.

Own elaboration.

Table 21. Spatiotemporal parameters (mean and standard deviation), grouped by GMFCS

	GMFCS							
	Level I (n=2)		Level II (n=11)		Level III (n=6)		TOTAL (n=19)	
Spatiotemporal parameters	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Cadence (steps/min)	130.20	27.80	115.94	19.90	124.34	20.24	120.09	20.12
ND cadence	0.28	0.02	0.25	0.04	0.26	0.03	0.26	0.03
Stride length (m)	1.00	0.18	0.86	0.22	0.65	0.18	0.81	0.23
Step width (m)	0.10	0.02	0.11	0.05	0.15	0.07	0.12	0.05
Gait speed (m/s)	1.07	0.04	0.84	0.25	0.67	0.23	0.81	0.25
First double support (% GC)	8.55	2.00	12.28	6.54	16.18	4.99	13.12	6.06
Single support (% GC)	41.69	2.19	38.11	6.31	34.67	4.67	37.40	5.77
Time of toe off (% GC)	58.47	2.44	62.21	6.37	65.88	4.47	62.98	5.82

GMFCS, Gross Motor Functional Classification System; SD, standard deviation; ND, non-dimensional normalization; GC, gait cycle.

Own elaboration.

All ST parameters, except ND cadence, showed statistically significant ($p<0.05$) correlations with the GMFM-66 and the GMFM-88-E. Higher gross motor function was related to longer stride length, shorter step width, higher gait speed, shorter first double support, longer single support, and shorter time of TO (see **Table 22**).

Statistically significant differences between independent samples of ND cadence in relation to hip flexors spasticity, and between independent samples of stride length in relation to ankle plantar flexors spasticity were found (see **Table 23**). Higher ND cadence was related to lower hip flexors spasticity. Longer stride length was related to lower ankle plantar flexors spasticity.

Statistically significant differences between independent samples of ND cadence and gait speed in relation to hindfoot deformity were also found (see **Table 23**). Varus in prone was related to higher ND cadence, and valgus in standing was related to slower gait speed. No relationship was found between ST parameters, and contractures and pROM outcomes.

Table 22. Significant correlation coefficients between spatiotemporal parameters and quantitative clinical outcomes

	Spatiotemporal parameters						
Clinical outcomes	**ND cadence**	**Stride length (m)**	**Step width (m)**	**Gait speed (m/s)**	**First double support (%)**	**Single support (%)**	**Time of toe off (%)**
GMFM-66 (score)	-	0.776**	-0.586**	0.683**	-0.581**	0.549*	-0.568*
GMFM-88-E (%)	-	0.756**	-0.639**	0.715**	-0.616**	0.584**	-0.610**

ND, non-dimensional; GMFM-66, Gross Motor Function Measure 66; GMFM-88-E, Gross Motor Function Measure 88 dimension E (walking, running, jumping). * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Own elaboration.

Table 23. Significant relationships between spatiotemporal parameters and qualitative clinical outcomes

	Significant ANOVA statistic			Significant Kruskal-Wallis statistic			
Clinical outcomes	**ND cadence**	**Stride length (m)**	**Step width (m)**	**Gait speed (m/s)**	**First double support (%)**	**Single support (%)**	**Time of toe off (%)**
Hip flexors spasticity	6.157**	-	-	-	-	-	-
Ankle plantar flexors spasticity	-	3.713*	-	-	-	-	-
Hindfoot deformity (unloaded)	7.177*	-	-	-	-	-	-
Hindfoot deformity (loaded)	-	-	-	6.912*	-	-	-

ND, non-dimensional. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Own elaboration.

4.4. Clinically relevant spatiotemporal parameters

From the results of studies 1 (systematic review) and 3 (correlational study), a list of ST parameters that are clinically relevant, that is, responsive to treatments, and related to impairments (interpreted as outcome measures of gait pattern) and/or activity limitations (interpreted as outcome measures of walking) was defined (see **Table 24**).

Other types of gait parameters (kinematic, kinetic and sEMG data) showed responsiveness to treatments in study 1. However, their relationships with impairments and activity limitations were not evaluated in study 3; therefore, they were not included in the list. Further research is needed to complete the set of clinically relevant gait parameters in children with bilateral spastic CP.

Table 24. Clinically relevant spatiotemporal parameters

Spatiotemporal parameters	Responsiveness to treatment	Relationship	
		Impairment	Activity limitation
Cadence	Orthosis, strength, balance, gait	Hindfoot deformity (unloaded), hip flexors spasticity	
Stride length	BoNT-A, orthosis, strength, balance, gait	Ankle plantar flexors spasticity	GMFM (total, E)
Gait speed	BoNT-A, orthosis, strength, balance, gait	Hindfoot deformity (loaded)	GMFM (total, E)
Single support	Casting		GMFM (total, E)
Time of toe off	Balance		GMFM (total, E)

BoNT-A, botulinum neuro-toxin A; GMFM, Gross Motor Function Measure; E, dimension E (walking, running, jumping).

Own elaboration.

5

Discussion

5. DISCUSSION

5.1. Study 1: Gait parameters in children with bilateral spastic cerebral palsy: a systematic review of randomized controlled trials

This work presents a literature review of 21 RCT, published in English between the years 2000 and 2016, which used the IGA to obtain ST, kinematic, kinetic, and sEMG outcome measures. We identified the gait parameters used to evaluate gait disorders in children with bilateral spastic CP and analyzed their responsiveness to clinical interventions.

A total of 89 gait parameters were statistically analyzed in the included studies. ST parameters were the most frequently used (18 included studies) followed by kinematic (15), kinetic (five), summary indexes (five), and sEMG data (four). If the parameters are analyzed individually, gait speed, stride length, and cadence were the most frequently used (in 17, 17, and 15 studies respectively), while the rest of parameters were used only in one study (47% of the gait parameters), two studies (31%), or between three and six studies (15%). It should be studied why kinetic and sEMG data are not usually used in intervention studies although they are considered necessary to clarify the gait patterns commonly seen in individuals with CP and plan an appropriate intervention (83).

Fifty-six gait parameters showed significant results. Kinematic were the type with more responsive parameters (38) followed by sEMG (seven), ST (five), kinetic (four) and summary indexes (two). Eighty-one per cent of responsive kinematic parameters were joint angles (ankle, knee, or hip) and 79% were from sagittal plane. This makes sense since the widest movements involved in gait are ankle plantarflexion/dorsiflexion, and knee and hip flexion/extension. Most of the gait pattern classifications are based on sagittal plane kinematics (173) and many gait deviations observed and treated in children with CP occur in the sagittal plane (263). However, deviations in the transverse and frontal planes are also considered important in clinical decision-making and intervention planning, and analyses in these planes could improve content validity of gait classifications (251).

The selection of an appropriate outcome measure depends on many factors including the type of intervention (87). Responsiveness is intervention-specific so we analyzed the gait parameters that showed significant results for each type of intervention. Gait speed, cadence, and stride length showed to be responsive to the majority of interventions or, analyzed from another point of view, the majority of interventions had an effect on them. On the other hand, from the number of gait parameters with significant results, we observed that some

interventions had their main effect at a certain level: BoNT-A plus casting and orthopedic devices on the ankle, surgery on the knee, and gait programs on the hip. The studies included in this review were not selected for the analysis of the relationship between gait parameters and interventions, and a rigorous scientific methodology to statistically analyze this relationship was not followed. Therefore, these results should be considered only as additional observations that could inspire new hypotheses and future research studies on this field.

There is no consensus on the relevant gait parameters for each clinical problem (218). Only three included studies specified the parameters selection criteria (288,292,296) (based on the expected changes or a study of the literature), so the selection probably could have been done subjectively in all cases. From the 15 studies that used kinematic and/or kinetic data, 13 analyzed specific gait parameters and two analyzed the full time-series through the Gait Variable Score (also called Movement Assessment Profile) (279,281). There are two main risks when using scalar gait parameters: 1) the rationale behind the selection of the gait parameters is often unclear. Reducing the large amount of data subjectively may introduce post hoc regional focus bias (type I or type II error resulting from expanding or reducing the scope of the clinical hypothesis after seeing the data) and potential clinically relevant parameters could be omitted (218,220,302); and 2) there exist covariance among vector components of multidimensional kinematic and kinetic data. Conducting scalar statistical testing on multiple dependent gait parameters may introduce intercomponent covariation bias (type I or type II error resulting from the failure to consider the covariance among vector components), especially in small sample sizes (218,302,303).

Some solutions have been proposed to avoid these risks. First of all, a clear hypothesis should be stated a priori and an adequate statistical approach should be selected in accordance to this hypothesis (218). In case of non-directed hypotheses (302), statistical methods such as the Bonferroni correction are often applied to deal with the risk of detecting a false positive when testing a large number of dependent gait parameters, but some of them can increase the probability of obtaining a false negative result (218,221). The statistical parametric mapping, which belongs to full gait curves analysis, is a promising statistical alternative to scalar gait parameters analysis with regard to the interpretation of multidimensional biomechanical data (218,220,302). Statistical parametric mapping is able to perform hypothesis testing on kinematic and kinetic data in a continuous manner, avoiding the need for subjective a priori data reduction, and it also takes into account the dependency between different time instances of the gait cycle (218). So, statistical parametric mapping overcomes both bias sources (302). In case of directed hypotheses (302), performing a scalar gait parameters analysis overcomes the risk of bias (220,302).

There is another handicap related to scalar gait parameters: they are usually defined on the basis of normal kinematic and kinetic curves and they can be difficult to extract from pathological gait curves (304). Furthermore, the definitions of scalar gait parameters are often unclear, making it difficult for researchers to reproduce or confirm results (218). Statistical parametric mapping could be a solution since it avoids the need to define gait parameters. Otherwise, a clear definition of the scalar gait parameters (like the one proposed in this review) could help clinicians to understand, interpret, reproduce, and compare results.

The IGA is expensive, complex, and time-consuming to learn and to use in real practice (52). Consequently, it is not always accessible for clinicians (99,305). The quotidian application of expensive healthcare technologies cannot be justified until the evidence unequivocally demonstrates its utility (52). Conclusions about the usefulness of the IGA can only come from multiple high quality scientific studies free from bias (175). However, these studies are scarce (174,176). Our review provides evidence from RCT supporting the responsiveness of the gait parameters to interventions. Our results may also guide clinicians and researchers to select the most relevant gait parameters according to the clinical hypothesis and the treatment selection.

5.2. Study 2: Gait event detection using kinematic data in children with bilateral spastic cerebral palsy

We compared two different thresholds of Ghoussayni's algorithm (Gho05 and GhoWS) with the gold standard gait event detection method (GRF) in order to validate them as alternative gait event detection methods in children with bilateral spastic CP. Ghoussayni's algorithm (210) is based on kinematic data, so it can be applied in severely involved or very young patients with small steps, when the assessment with GRF cannot be done, or on treadmills where force plates were not build in. Gho05 had already shown good performance in children with CP (212,213). However, no statistical results about GhoWS had been published before the present study (212).

Ninety-eight valid gait events from 16 children with bilateral spastic CP were detected. This number was conditioned by the gold standard event detection method. In optimal conditions (healthy gait pattern and force plates configuration adapted to stride length), it would have been possible to obtain a maximum of 4 gait events per trial (right FS, left FS, right TO and left TO). We collected 62 trials, so that would have resulted in 248 gait events. The pathological gait of children with CP (short, irregular, slide and drag steps) reduced the applicability of force plate data and we actually detected 98 gait events, a 39.5% of all potential events. This result reinforces the need to develop alternative methods to GRF based on kinematic data, such as Ghoussayni's algorithm. Moreover, methods based on kinematic data are not conditioned to the number of force plates and all the gait events occurring within the measurement volume can be detected (210).

Our results indicated that both Gho05 and GhoWS were significantly close enough to GRF (in terms of equal means) in the detection of FS, but only Gho05 was significantly close enough to GRF in the detection of TO, so our hypotheses were rejected. These results are consistent with those reported by Gonçalves et al. (213), who validated Gho05 for children with unilateral or bilateral spastic CP. However, they are not aligned with those of Bruening and Ridge (212), who found that GhoWS improved Ghoussayni's algorithm accuracy. Our results also indicated better performance of Ghoussayni's algorithm for FS than for TO. These results are also in agreement with those reported by Ghoussayni et al. (210), who showed smaller average differences between GRF and the automated algorithm in relation to FS (within 1.5 frames) than to TO (between 9 and 10 frames). Inaccuracies in TO detection could be improved by using a Hallux marker, but its placement presents some problems depending on the CP gait pattern (212).

The new adaptation of Ghoussayni's algorithm for the detection of FS in children with CP made it possible to distinguish the way each child performed each FS. This is an advantage over the method used by Gonçalves et al. (213), who detected FS using the heel marker in all cases, although some children perform FS with the toe. It is also an advantage over the method used by Bruening and Ridge (212), who first classified children into different gait patterns, and then detected FS using the toe or heel marker according to this classification, without taking into account that some children do not perform all FS in the same way.

ST parameters are calculated from gait events. Focusing on the methods' mean bias, Gho05 showed a negative difference both for FS and TO, so it tends to delay the gait events in comparison to GRF. GhoWS showed a positive difference for FS and a negative difference for TO, so it tends to advance FS and delay TO in comparison to GRF (the same was observed in comparison to Gho05). This fact could result in bigger differences between GRF (or Gho05) and GhoWS in terms of ST parameters such as first double support, single support, and time of TO, which are calculated from FS to TO, or vice versa. When comparing ST parameters calculated from Gho05 and GhoWS, statistically significant differences were found in the three mentioned ST parameters. Our results reinforce the thought that, in IGA, careful consideration should be given when comparing ST parameters obtained using different methods (210).

5.3. Study 3: Relationship between spatiotemporal parameters and clinical outcomes in children with bilateral spastic cerebral palsy

Nineteen children with bilateral spastic CP, from 4 to 14 years of age, and with different GMFCS levels were assessed with IGA and clinical assessment. The relationships between ST parameters and clinical outcomes were studied in order to understand the links between gait disorders, impairments and activity limitations, and thus improve the clinical interpretation of ST parameters (as outcome measures of gait pattern and/or walking). We considered that gait parameters related to impairments (at body functions and structures level) provide clinical information regarding gait pattern, while gait parameters related to activity limitations (at activities and participation level) provide clinical information regarding walking (see **Figure 22**).

The main findings of the present study were the statistically significant ($p<0.01$) correlations between the dimension E (walking, running and jumping) of the GMFM-88, and six of the seven ST parameters (stride length, step width, gait speed, first double support, single support and time of TO), which confirm the link between ST parameters and walking capacity. Other studies (252–254) had already found correlations between the GMFM-88-E and stride length, gait speed and/or step width in children with CP. Some studies (252,253) also reported correlation between the GMFM-88-E and cadence, which was not found in our study.

On the other hand, we found few statistically significant ($p<0.05$) relationships between ST parameters and clinical outcomes at body functions and structures level. Regarding spasticity, we found that ND cadence and stride length were related to hip flexors and ankle plantar flexors spasticity, respectively. Desloovere et al. (243) did not find these relationships, but they found that cadence was related to knee flexors spasticity, and that stride length, gait speed and time of TO were related to hip flexors and hip adductors spasticity. Ross and Engsberg (57) reported correlations between stride length, and ankle plantar flexors, knee flexors and hip adductors aggregate spasticity. Regarding deformities, we found that ND cadence and gait speed were related to hindfoot deformity. Desloovere et al. (243) found statistically significant correlation between time of TO and femoral anteversion, which was not found in our study. Regarding contractures and pROM, we did not find any relationship with ST parameters. Conversely, Desloovere et al. (243) reported various correlations between ST parameters (cadence, stride length, gait speed and time of TO), and contractures and pROM (hip flexors contracture, hip abduction, knee flexors contracture, and ankle plantar flexors contracture).

Differences in the results of different correlation studies may be due to different causes such as participants' characteristics, normalization of ST parameters, or statistical methods. Some

studies used raw ST parameters (57,243); other studies normalized ST parameters to leg length (241,245), height (242), or percentage of age-matched normal (252); and one study only normalized some ST parameters (244); but no study justified its selection. ND normalization is used to remove systematic dependences of a parameter on relevant factors such as age, mass and leg length (231). It converts raw ST parameters into ratios, each with a function of leg length (231). However, it is not recommended to normalize parameters prior to correlation statistical analyses for the following reason: when an external covariate, for example a clinical outcome, is uncorrelated with ST parameters but is correlated with leg length, ND normalization induces spurious correlation between the ST parameters and the clinical outcome (231). In the present study, ND normalization was used after checking that no clinical outcomes were correlated with leg length (so, no spurious correlation could be induced). Partial correlation (controlling for leg length) is an alternative to ND normalization (231). However, it applies only to the statistical analysis of quantitative, not qualitative, clinical outcomes, so it was discarded for the present study.

The selection of an appropriate outcome measure depends on many factors, for example the psychometric properties (87). Clinicians and researchers need also to consider what areas of functioning, disability and health they want to study (87). The ICF-CY can help to standardize the selection of outcome measures (87). Current outcome measures in the field of CP primarily focus on assessing neuromusculoskeletal and movement-related functions (b7) (including gait pattern), and mobility (d4) (including walking) (87). Gait parameters, including ST parameters, are considered the gold standard in CP gait classification systems (60), used as outcome measures of gait pattern. The findings of the present study (relationships between cadence, stride length and gait speed, and impairments such as spasticity and deformities) support this clinical use of determined ST parameters. On the other hand, our findings (correlations between all ST parameters except cadence, and the GMFM) support the use of determined ST parameters as outcome measures of walking capacity, which is aligned with Gage et al. (49) who suggested that ST parameters may provide information regarding functional walking. This contribution is clinically relevant since the main goal of most interventions is to improve gross motor function (57). Moreover, walking is part of the brief ICF Core Set for children and youth with CP (48).

5.4. Limitations

Retrospective studies have a limitation related to working with already recorded data: decision-making capacity is lost when choosing participants, materials and methods. In order to minimize this problem, a previous study with the same target population (children with bilateral spastic CP), and the same type of measurement tools (IGA, physical examination and functional assessment) as those required for the present doctoral thesis was selected. On the other hand, we had access to the previous study raw data, so we were able to calculate our own study variables.

Some limitations should be considered when interpreting the results of the study 1: 1) the scope of this systematic review was limited to English-language RCT, which might have underrepresented the set of gait parameters used worldwide, 2) only one reviewer was involved in the study selection and data collection processes, which might have increased the risk of misinterpretation, and 3) there was a big heterogeneity with regards to the selection and definition of the gait parameters, which made difficult the analysis and comparison of results.

Some limitations should be considered when interpreting the results of the study 2: 1) severely involved or very young patients walking with small steps are the target population of kinematic based event detection methods, but these characteristics do not allow comparison with the gold standard (GRF), which is the most accurate validation method; 2) the number of gait events was small due to the low percentage of valid events detected from GRF in the included CP population; 3) the walking speed used in GhoWS was calculated using FS detected from Gho05, due to the difficulty to obtain two successive FS from GRF (which only occurred in one trial); 4) the different types of FS were not equally represented: heel strike (60%), toe strike (12%), both at the same time (28%); and 5) It was not possible to calculate ST parameters from gait events detected using GRF, so we could only compare ST parameters obtained from Gho05 and GhoWS.

Some limitations should be considered when interpreting the results of the study 3: 1) relationships between ST parameters and other impairments such as muscle weakness were not studied; 2) relationships between ST parameters and walking performance were not studied; and 3) relationships between ST parameters and activity limitations and participation restrictions beyond mobility (self-care, domestic life, interpersonal interactions and relationships, major life areas, and community, social and civic life) were not studied.

5.5. Implications and future research

Having a set of clinically relevant gait parameters, that is, objective gait parameters able to identify gait disorders, detect changes in gait disorders, and relate gait disorders to impairments and activity limitations, will provide benefits at different levels: clinical, technological, and economical.

At the clinical level, gait parameters able to identify gait deviations will improve the diagnosis of children with bilateral spastic CP, gait parameters able to relate gait disorders to impairments and activity limitations will improve the clinical decision making, and gait parameters able to detect changes in gait disorders will improve the evaluation of the treatments. Therefore, the gait pattern and walking of children with bilateral spastic CP will also improve.

At the technological level, a list of clinically relevant gait parameters will define the clinical requirements for new affordable systems for the gait assessment of children with bilateral spastic CP. Affordable measurement tools will allow the IGA to be accessible to all rehabilitation centers, and consequently to more children with bilateral spastic CP. On the other hand, Ghoussayni's algorithm, including the new adaptation for the detection of FS in children with CP, will improve the data processing of the existing motion capture systems.

At the economical level, the use of objective gait parameters will help clinicians to evaluate the efficacy of treatments, to move towards evidence-based practice, and therefore to optimize the healthcare resources. On the other hand, working with a limited number of gait parameters will help to reduce the time required to interpret IGA results, and thus the cost of the IGA.

Further research is needed to: 1) determine the role of kinematic (at frontal and transverse planes), kinetic and sEMG parameters in the IGA; 2) identify the responsive gait parameters for each treatment; 3) establish the best method to detect FS in children with CP; 4) improve the detection of TO; 5) understand the links between gait parameters, and impairments, activity limitations and participation restrictions; and thus 6) complete the set of clinically relevant gait parameters in children with bilateral spastic CP.

6

Conclusions

6. CONCLUSIONS

The conclusions of the present doctoral thesis are:

1. ST parameters are the gait parameters most frequently used in the assessment of children with bilateral spastic CP (86% of studies), followed by kinematic parameters (71%). Specifically, gait speed and stride length are the most widely used (81% of studies), followed by cadence and kinematic parameters in the sagittal plane (71%). In contrast, kinetic parameters, summary indexes, and sEMG data are less used (24%, 24%, and 19% of studies, respectively).

2. The IGA yields responsive outcome measures for the gait assessment of children with bilateral spastic CP. Fifty-six responsive gait parameters have been identified: five ST parameters (gait speed, cadence, stride length, time of TO, and single support), 38 kinematic parameters (30 from the sagittal plane), four kinetic parameters (MAX_PlantDorsFlexMo_LR, MAX_PlantDorsFlexMo_POff, MIN_AnkleGenAbsPo_LR, and MAX_HipGenAbsPo_St; see **Table 11**), seven muscle groups (gastrocnemius, soleus, tibialis anterior, rectus femoris, lateral hamstrings, medial hamstrings, and adductor), and two summary indexes (GGI and GPS).

3. The new adaptation of Ghoussayni's algorithm for the detection of FS in children with CP distinguishes how each FS is performed (heel strike, toe strike, or both at the same time), calculating sagittal plane velocities of the two foot markers (heel and toe), and comparing the timing when each one falls below a given threshold. FS is estimated as the first frame with sagittal plane velocity of at least one of the two foot markers below the threshold.

4. Gho05 is a valid method for detecting gait events (FS and TO) in children with bilateral spastic CP, and presents better performance detecting FS than detecting TO. Conversely, GhoWS is only valid for detecting FS, so it can be dismissed as a general gait event detection method for children with bilateral spastic CP. On the other hand, GRF (gold standard) is ineffective in detecting gait events in children with bilateral spastic CP (it only detects 40% of all potential gait events).

5. Gait event detection methods have an effect on ST parameters. In our case, Gho05 and GhoWS are significantly different: Gho05 tends to delay the gait events in comparison to GRF, while GhoWS tends to advance FS and delay TO in comparison to GRF. This fact results in significant differences in some ST parameters, specifically, those calculated from FS to TO, or vice versa (that is, first double support, single support, and time of TO).

6. ST parameters are related to clinical outcomes both at body functions and structures level, and at activities and participation level. Shorter stride length, longer step width, slower gait speed, longer first double support, shorter single support, and longer time of TO are related to lower gross motor function (GMFM-66) and lower walking capacity (GMFM-88-E). On the other hand, lower cadence is related to higher hip flexors spasticity, shorter stride length is related to higher ankle plantar flexors spasticity, and slower gait speed is related to hindfoot deformity (valgus) in standing.

7. The IGA yields outcome measures able to objectively assess the two gait categories of the ICF-CY: gait pattern and walking. ST parameters related to clinical outcomes at body functions and structures level (cadence, stride length, and gait speed) have been interpreted as outcome measures of gait pattern. ST parameters related to clinical outcomes at activities and participation level (stride length, step width, gait speed, first double support, single support, and time of TO) have been interpreted as outcome measures of walking.

8. Five ST parameters (cadence, stride length, gait speed, single support, and time of TO) have been identified as clinically relevant gait parameters in children with bilateral spastic CP; that is, responsive to treatments, and related to impairments and/or activity limitations. Further research is needed to complete the set of clinically relevant gait parameters, considering other types of gait data (kinematic, kinetic and sEMG).

7

Publications

7. PUBLICATIONS

Two publications have derived from this doctoral thesis:

Gómez-Pérez C, Font-Llagunes JM, Martori JC, Vidal Samsó J. Gait parameters in children with bilateral spastic cerebral palsy: a systematic review of randomized controlled trials. Dev Med Child Neurol. 2019;61(7):770-782. doi: 10.1111/dmcn.14108.

Web of Science Journal Citation Reports Impact Factor 2019: 4.406
Pediatrics Q1 (7/128) ● Clinical neurology Q1 (38/204)

Gómez-Pérez C, Martori JC, Puig Diví A, Medina Casanovas J, Vidal Samsó J, Font-Llagunes JM. Gait event detection using kinematic data in children with bilateral spastic cerebral palsy. Clin Biomech. 2021;90:105492. doi: 10.1016/j.clinbiomech.2021.105492.

Web of Science Journal Citation Reports Impact Factor 2020: 2.063
Orthopedics Q3 (52/82) ● Engineering, biomedical Q3 (66/90) ● Sport sciences Q3 (62/88)

8

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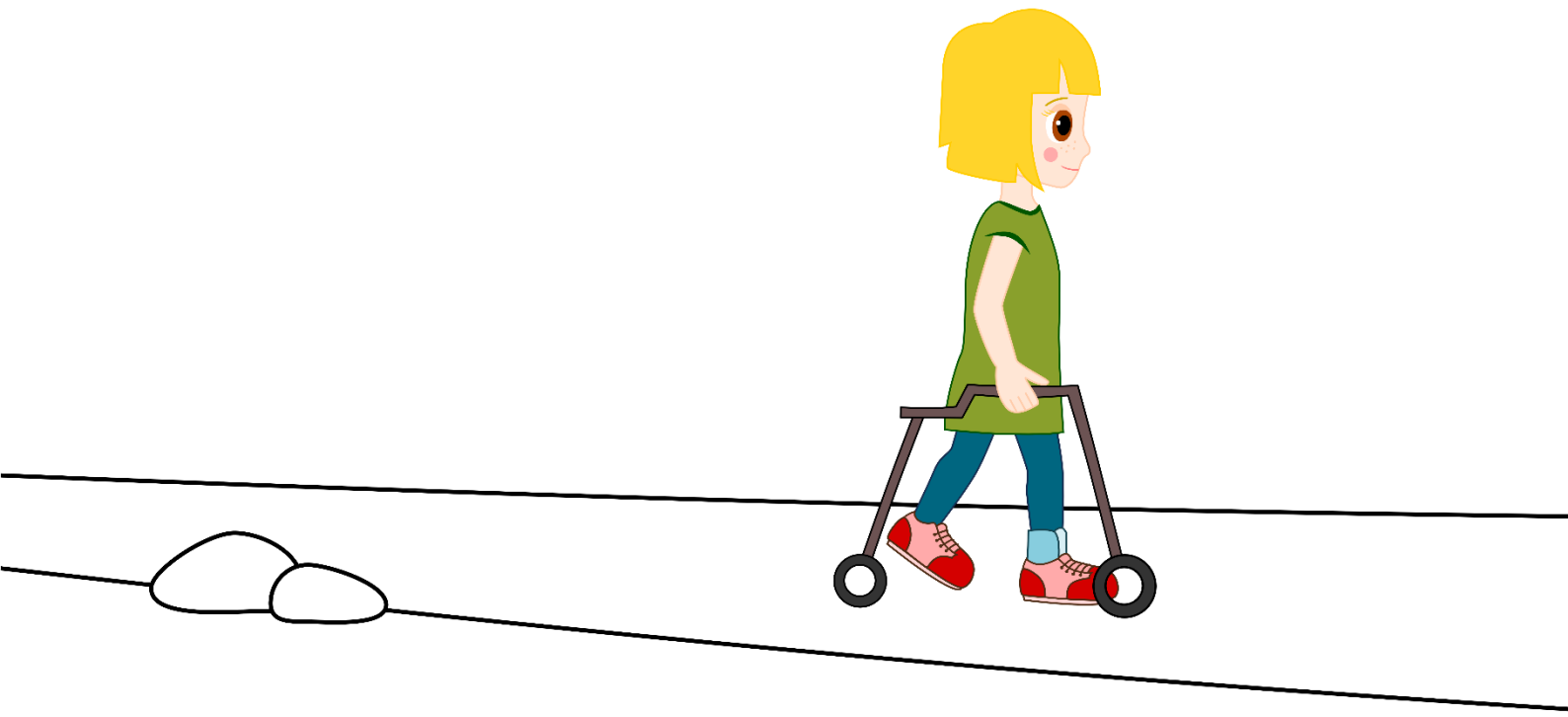
“Quan de nit,
nues i plenes de cançons,
vinguin a buscar-te des del mar
les sirenes del viatge,
no ho dubtis i emprèn el vol.
Aquí tens el meu desig.
Camina.
Camina lluny.
Camina com qui vol saber-ho tot.
Camina fins a trencar-te.
Camina.

ALGUER MIQUEL



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