PhD thesis

The use of instrumented gait analysis in interdisciplinary interventions for children with cerebral palsy

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1. Preface

The idea to complete the studies that constitute this thesis originated from a proposal by orthopaedic surgeon Niels Wisbech Pedersen to develop a stronger collaboration between the Motion Analysis Laboratory at Odense University Hospital and the Danish Cerebral Palsy follow-Up Program (CPUP), with the purpose of implementing three-dimensional instrumented gait analysis children with cerebral palsy followed in CPUP.

His initiative led to my first meeting with Anders Holsgaard-Larsen, head of research in the Motion Analysis Laboratory at Odense University Hospital, and subsequently to our drafting of a project protocol entitled "The effect of a specific treatment plan based on clinical gait analysis in the cerebral palsy follow-up program" in early March 2011. After many challenges, and meetings, methodological discussions with Søren Overgaard and others, and a huge effort by Anders Holsgaard Larsen, the project "Individually defined multidisciplinary interventions for children with cerebral palsy – The impact of three-dimensional gait analysis on gait and functional mobility" was approved as the basis for a PhD study in late summer 2012.

The thesis is based on work carried out in the Orthopaedic Research Unit at the Department of Orthopaedic Surgery and Traumatology, Odense University Hospital, and at the Department of Clinical Research, University of Southern Denmark. It is based on three clinical studies described in four scientific papers, of which two have been published and two have been submitted to peer-reviewed journals.

Acknowledgements

First of all, a very big thank you goes to the children and their families who kindly participated in the research. I am truly indebted and grateful for their involvement and for making the process so enjoyable. Their courage, strength and stories are truly inspiring and motivate me to hopefully make a difference in this challenging but incredibly satisfying field. Also, a very big thank you to all of the participating paediatricians, orthopaedic surgeons and physiotherapists who have helped with the recruiting of participants and who have been involved in the interdisciplinary interventions with the participants.

I thank my main supervisor Associate Professor Anders Holsgaard Larsen for always knowing how to motivate me to work harder and learn more, and my co-supervisors Clinical Associate Professor Niels Wisbech Pedersen MD for believing in me and trusting me to meet the challenges of the world of clinical gait analysis and Professor Søren Overgaard MD for welcoming me into his research unit and letting me learn that clinical research can be very diverse.

To all of my colleagues, fellow students and the staff in the Gait Analysis Laboratory at Odense University Hospital and the Orthopaedic Research Unit, I thank them for their support, advice and encouragement. Furthermore, I give a special thanks to Dennis Brandborg Nielsen, Lotte Slot Jensen, Rasmus Sørensen, Maria Thorning, Line Kiilerich and Christina Fonvig for their help in the data collection.

I also give a very special thanks to Maria Thorning and Anders Holsgaard Larsen for taking excellent care of the projects and participants during my maternity leave. They made it possible for me to be introduced to the challenge of balancing work life and family life in a very safe and caring way.

I acknowledge the support of the University of Southern Denmark, an Odense University Hospital Research grant, a Region of Southern Denmark Research grant and a PhD grant, the Physiotherapy Practice Foundation, the Ludvig and Sara Elsass Foundation, the Linex Foundation and the Danish Physiotherapy Research Fund. None of the supporters played a role in the study designs, collection, analysis or interpretation of data; nor in the writing or decision to submit the manuscripts for publication.

Finally, a deep and warm thanks to my son Jonas and my partner Anders, as well as extended family and friends, for reminding me that life is much more than a research education.

Abbreviations

The following abbreviations are used in text or legends in the thesis.

BL	Bilateral spastic cerebral palsy
CI	Confidence Interval
CP	Cerebral palsy
CPUP	Cerebral Palsy follow-Up Program
FMS	Functional Mobility Scale
Gait analysis	Three-dimensional instrumented gait analysis
GDI	Gait Deviation Index
GMFCS	Gross Motor Function Classification System
GMFM	Gross Motor Function Measure
GPS	Gait Profile Score
GVS	Gait Variable Score
ICC	Intra-class Correlation Coefficient
ICF	International Classification of Function
IQR	Interquartile range
PEDI	Pediatric Evaluation of Disability Inventory
PedsQl	The Pediatric Quality of Life Inventory
PODCI	Pediatric Outcome Data Collection Instrument
SD	Standard Deviation
UL	Unilateral spastic cerebral palsy

List of papers

The thesis is based on the following three studies and four papers. They will be referred to in the text by their Roman numerals and, where relevant, the letters, as indicated below.

Study / paper	Name and reference
I	Test-retest Rasmussen HM, Nielsen DB, Pedersen NW, Overgaard S, Holsgaard-Larsen A. Gait Deviation Index, Gait Profile Score and Gait Variable Score in children with spastic cerebral palsy: Intra-rater reliability and agreement across two repeated sessions. Gait & Posture. 2015;42(2):133-7.
IIa	Randomised controlled trial protocol Rasmussen HM, Pedersen NW, Overgaard S, Hansen LK, Dunkhase-Heinl U, Petkov Y, Engell V, Baker R, and Holsgaard-Larsen A. The use of instrumented gait analysis for individually tailored interdisciplinary interventions in children with cerebral palsy: a randomised controlled trial protocol. BMC Pediatrics. 2015;15(1):202.
IIb	Randomised controlled trial Rasmussen HM, Pedersen NW, Overgaard S, Hansen LK, Dunkhase-Heinl U, Petkov Y, Engell V and Holsgaard-Larsen A. The use of instrumented gait analysis for individually tailored interdisciplinary interventions in children with cerebral palsy: a randomised controlled trial. [Submitted to Development Medicine & Child Neurology, October 2017].
III	Cross-sectional study Rasmussen HM, Svensson J, Christensen MT, Pedersen NW, Overgaard S, Holsgaard-Larsen A. Threshold values of ankle dorsiflexion and gross motor function in children with cerebral palsy – a cross-sectional study [Re-submitted to Acta Orthopedica, November 2017].

2. Introduction

This thesis focuses on younger children with spastic cerebral palsy who walk unaided. They comprise more than half of all children with cerebral palsy. The vast majority of the ambulatory children with cerebral palsy experience an altered gait pattern or other walking difficulties and are dependent on healthcare interventions throughout their childhood.

The idea to explore the use of three-dimensional instrumented gait analysis (gait analysis) in individually defined interdisciplinary interventions for gross motor function emerged from experience in clinical practice and a critical appraisal of the scientific literature, which showed that evidence for the effectiveness of gait analysis was lacking for the patient group of interest.

In this introduction, the diagnosis and clinical characteristics of ambulant children with cerebral palsy are presented in terms of its effect on body functions and structures as well as activity and participation. Furthermore, a thorough description of the current healthcare and interdisciplinary interventions and gait analysis are outlined.

2.1. Cerebral palsy: The clinical signs and their impact on walking

Cerebral palsy is a diagnosis that includes a range of conditions caused by a non-progressive brain injury occurring in the developing foetal or infant brain. Although the brain injury is non-progressive, the neuro-musculoskeletal and movement-related functions may deteriorate and cause activity limitation [1].

According to the Surveillance of Cerebral Palsy in Europe the definition of cerebral palsy must include the following five key elements:

> *"Cerebral palsy is a group of disorders;*
> *- It is permanent but not unchanging;*
> *- It involves a disorder of movement and/or posture and of motor function;*
> *- It is due to a non-progressive interference/lesion/abnormality;*
> *- This interference/lesion/abnormality is in the developing/immature brain"* [1a]

Cerebral palsy is the most common congenital motor disability in childhood with a prevalence of 1.5-3.0/1000 live births (95% CI: 1.32 – 1.68 and 2.69 – 3.31) in Europe [1]. The latest published prevalence for a Danish cohort is 2.4 per 1000 live births (95% CI: 1.8 – 3.2) for children born from 2003 to 2008 in the Region of Southern Denmark [2].

The diagnosis of cerebral palsy can be categorised into four subtypes: spastic (unilateral or bilateral), dyskinetic, ataxia, and mixed form [1]. The subtype is supplemented with a classification of gross motor function using the Gross Motor Function Classification System (GMFCS) [3]. The GMFCS is an ordinal scale with five levels of function, representing clinically meaningful distinctions in motor function. Children at level I are the least disabled, although they may have limitations in advanced motor skills. Children at level V have the most severe motor disability. Approximately 65% of all children with cerebral palsy walk independently without aids and are consequently classified at GMFCS level I or II [4].

The clinical signs of cerebral palsy gradually develop during the first years of life and become visible as the child grows and the central nervous system matures. The first signs of cerebral palsy may be early development of hand dominance in grasping, around 3 to 6 months of age or delayed development of unsupported walking, around 18 to 24 months of age [5]. The most common clinical signs of spastic cerebral palsy are muscle weakness and muscle imbalance across joints, altered muscle tone, reduced passive range of motion, and deformity of bones and joints [1, 6, 7], which often lead to an altered gait pattern, such as stiffness of the knee in the swing phase of gait, excessive hip and knee flexion (crouch gait), intoeing and equinus [8]. Furthermore, the children experience activity limitations (e.g. in dressing, feeding and functional mobility) and restricted participation (e.g. when playing or participating in social, school and community activities), compared with their typical peers [9].

The development of gross motor function is often delayed and some functions may never be achieved. The children walk independently later than their peers, they walk at a slower pace and with an increased energy consumption [10]. According to the GMFCS, walking performance in children at GFMCS levels I and II after 6 years of age can be described as walking without limitation (GMFCS level I) and walking with limitation (GMFCS level II) [3]. Most children at GMFCS level I walk independently on all surfaces at 5, 50 and 500 meters, corresponding to walking at home, at school and in the community, according to the Functional Mobility Scale (FMS). However, some children can only walk independently on even surfaces and a few use sticks at 500 meters. The degree of independence in mobility is more diverse among children at GMFCS level II. The majority are independent on even surfaces, some use sticks, a walking frame (5, 50 and 500 meters) or a wheel chair (500 meters) for independent mobility [4].

When the children and their parents are asked to identify factors that adversely affect health-related quality of life, the amount of gait pathology has been shown to play an important role [11]. Furthermore, children, parents and healthcare professionals identify impairments in body function and structure as well as gross motor skills as domains they would like to see impacted by interventions [12].

2.2. Healthcare and interdisciplinary interventions

People in Denmark have universal and free access to health care. The responsibility for healthcare is shared between regions and municipalities. The municipalities are responsible for interventions by orthotists, physiotherapists and occupational therapists. The regions are responsible for the hospitals and thus, interventions such as spasticity management and orthopaedic surgery handled by orthopaedic surgeons and paediatricians [13]. Guided by the problems faced by each child, interventions are individually planned

to help the child and family to achieve their goals [14].

The healthcare professionals offer standardised clinical examinations throughout childhood using the Cerebral Palsy follow-Up Program (CPUP) developed in Sweden more than 20 years ago [13]. The use of the surveillance program and the associated national clinical quality database is designed to lead to early detection of complications, such as hip dislocation, scoliosis, and muscle contracture as well as to improvements in the quality of healthcare [13, 15]. The CPUP uses threshold values and three categories inspired by traffic light signals on passive range of motion and migration percentage of the hip joint to guide clinical decisions. For children on GMFCS levels I to III, the threshold values of passive range of motion are set to ensure that the patient is able to dorsiflex adequately in the stance and swing of walking [16]. The CPUP uses the following interpretation for the three categories of passive range of motion:

> *"Green means "clear" and that no indication of deterioration was noted during assessment, yellow indicates that vigilant observation or potentially treatment is recommended, and red indicated "alert" and that treatment is urgently needed (assuming no specific contra-indications)" [17a].*

The current interdisciplinary interventions offered by the municipal and regional healthcare providers to children with cerebral palsy at GMFCS levels I and II, are described below. The interventions have been offered to participants in the experimental and the control group in Study II.

Municipal healthcare
In the municipalities, physiotherapists responsible for interventions are affiliated with a range of different institutions, such as rehabilitation centres, nurseries, special needs schools, and independent clinics [13]. The physiotherapeutic interventions aim to prevent deterioration in, or to improve, body functions and structures and enhance the child's ability to perform activities and participate in social roles. A large variety of interventions are used depending on the problems faced by the individual child, and the clinical expertise and facilities available. An experience-based list of the interventions used within the framework of the International Classification of Function (ICF) is shown Table 1.

Orthopaedic surgeons and paediatricians prescribe orthoses that subsequently are financed by the municipalities under social legislation. Private companies provide the orthoses, based on the defined aims, the described impairments and the family's wishes. The orthotics are primarily aimed at the joints in the ankle and foot to support stability or mobility of the joints, or to support muscle function [18]. The most commonly used orthoses are the ankle/foot orthoses, insoles/foot orthoses and the dictus band/ankle strap.

The organisation of healthcare in Denmark, and the diverse geographic location across 23 municipalities of the 60 participants in Study II, has led to 58 physiotherapists and a large number of prosthetics being involved in the interventions offered to the participants.

Regional healthcare
The paediatric departments offer interdisciplinary consultations, where children, parents, and the local healthcare team consisting of professionals from the municipal and regional healthcare systems meet and agree on future surveillance, coordinate common goals and plan interdisciplinary interventions for the child [13].

Paediatricians and orthopaedic surgeons are responsible for spasticity management. The most frequently used intervention is injection of Botulinum toxin type A in hyperactive muscles in the lower extremities, most often the Gastrosoleus muscle [19].

Treatment in the form of orthopaedic surgery is performed at highly specialised centres.

Table 1. The most common interventions used by physiotherapists in Denmark

ICF dimensions	Name of intervention	Description
Body functions and structures	Fitness training	Planned structured activities involving repeated movement of skeletal muscles that result in energy expenditure.
	Strength training	Training with the use of progressively more challenging resistance to movements to improve muscle function.
	Stretching	Use of an external passive force exerted upon the limb to move it into a new and lengthened position.
Activity (Motor activities)	Functional training	Task-specific practice of functional tasks.
	Goal-directed training	Specific practice of child-set goal-based tasks.
	Hippo-therapy	Therapeutic horse riding to practise postural control, balance and symmetry.
	Home programs	Practice of tasks by the child, led by the parent or other adult and supported by the therapist, in the home or school environment.
	Hydrotherapy	Aquatic-based exercises.
	Neurodevelopmental therapy (NDT, Bobath)	Direct, passive handling and guidance to improve performance.
Participation	Assistive technology	Equipment or devices to improve independence e.g. walking frames and wheelchairs.

Abbreviations: ICF: International Classification of Function.

Some of the most common surgeries are tendon transfers, muscle tendon lengthening, rotational osteotomy and stabilisation of joints. The surgeries aim to restore joint mobility, muscle function, stability and lever arm function [20].

In total, six paediatric departments and two departments of paediatric orthopaedic surgery were involved in the healthcare of children with cerebral palsy in Study II.

2.3. Gait analysis

The purpose of gait analysis is to record biomechanical data on the movements and forces on the body segments during gait [21]. Since the introduction of gait analysis laboratories in the early 1980s, the objective biomechanical measurements during gait have played a major role in the development of surgical interventions used in the treatment of children with cerebral palsy [22]. Today, gait analysis has developed into an essential part of research in, and clinical practice for, ambulant children with cerebral palsy [21].

Referral to gait analysis is dependent on institutional guidelines or the clinical reasoning of the individual paediatrician or orthopaedic surgeon [21], as there is no international consensus on referral criteria.

In clinical practice, gait analysis is used for the diagnosis between disease entities, the assessment of severity, the extent or nature of the disease, the monitoring of progress and the prediction of outcomes of the intervention [21].

Studies have shown that gait analysis affects the decisions regarding orthopaedic surgical interventions [23-25], and that good agreement can be obtained between recommendations based on gait analysis and the surgery performed [25-28]. Furthermore, gait analysis has been used in research to evaluate interventions, such as selective dorsal rhizotomy [29, 30], orthopaedic surgery [31], botulinum toxin [32] and different types of physiotherapy [33-35].

Data collection in clinical practise

The methods currently used to perform gait analysis in children with cerebral palsy at GMFCS levels I and II at the Gait Analysis Laboratory at Odense University Hospital are described below. Some of the methods have been applied to participants in Study II, as outlined in detail in chapter 4 in section 4.3 Outcome measures and 4.4 Interventions.

Typically, the examination of a child consists of functional tests, measurement of body segments, recording and processing of gait, and a physical examination [21]. The individual parts of the examination are often adapted to the individual child, based on a weighing up of the possible gains relative to the expected time consumption in an extensive examination [36].

To support the interpretation of the biomechanical data, functional tests are used to establish the gross motor capacity of the child [37]. Non-standardised tasks, such as standing on one leg, toe walking or different kinds of jumping; and standardised measures of gross motor capacity, such as the Gross Motor Function Measure [38] and 1-minute walk test [39] are used in the interpretation of the examination.

Measurement of the child's height, leg length, joint width and body weight are taken [36].

Data are typically collected while the child walks the length of an approximately 10-meter walkway a minimum of 10 times during the examination [21]. The central measurement in gait analysis is the recording of data on the movement of the body segments in three dimensions with an optoelectronic tracking system using reflective markers placed on the skin over bony landmarks. The data allows the quantification of joint movement (joint kinematics). The joint kinematics are supplemented with data from multicomponent force plates recording the position of the ground reaction forces, as the child walks. The recordings are used to calculate the moments that the muscles and other soft tissues are exerting at the joint (kinetics). Besides kinematic and kinetic data, temporal-spatial data are collected, mainly walking velocity, steps per minute, step and stride length and step width [21].

A thorough physical examination is conducted for comparison with the biomechanical data [36]. Muscle weakness, altered muscle tone, reduced passive range of motion and deformities are the common clinical manifestations of cerebral palsy and are measured using standardised methods [37].

Interpretation, recommendations and dissemination
Although data from gait analyses are objective, the interpretation of data, recommendations of interdisciplinary interventions and dissemination of recommendations are, to some extent, subjective. Studies have documented large discrepancies in physicians' interpretations of data when identifying soft-tissue problems and bone deformities of the lower limb [40], poor agreement between specific surgical recommendations across surgeons and institutions [41] and large variation in the compliance between guideline recommended surgery and performed surgeries [26, 27, 42].

The approach called Impairment-Focused Interpretation is based on the principles that the process and the resulting report should be relevant, succinct, evidence-based, transparent, within the competence of the authors and time-efficient [36]. The overall aim is to identify and report the impairments that are affecting an individual's gait. The method does not consider or report on other factors, such as institutional resources or preferences of the child and family, which might influence clinical decisions about interventions [43]. The clinimetric properties of the method have not been reported.

In the report, the impairments that are affecting the child's gait pattern are described by body part (such as bone or muscle) and what is wrong with it (such as altered muscle tone, contracture, deformity or weakness). Furthermore, the underlying features in the gait data displayed in the graphs and supplementary data (e.g. physical examination and gross motor function performance), that identify the impairments are well documented [36]. The method is carried out in four parts: 1) orientation, 2) mark-up, 3) grouping and 4) reporting, as displayed in Table 2 [36].

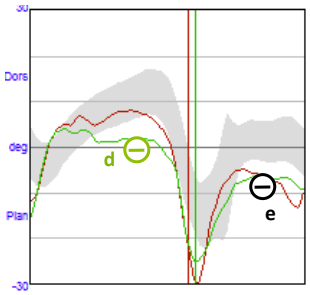
Textbooks on clinical interpretation of gait analysis have proposed guidance on the choice of treatment recommendation [37, 44]. Miller (2007) presents a description of segments and joint compensations and proposes the use of gait treatment algorithms based on the cerebral palsy subtype, the child's age and the movement features affecting

Table 2. Impairment focused interpretation
Description of the four parts of the Impairment-Focused Interpretation and examples of how the information is disseminated in the report.

1) Orientation

Review information about	*Example: Informations in the report*
• Background and diagnosis	• *Spastic unilateral cerebral palsy*
• Classification of gross motor function and performance	• *GMFCS level II - FMS 6 – 6 – 1. 1-min walk: 82.5 meter*
• Patient-reported function	• *PODCI Global Functioning Scale: 72*
• Current and past interventions	• *Past interventions: Physiotherapy*
Walking pattern and gait data	
• Visual observation of gait (video)	• *Overall Gait Deviation Index: 90.6*
• Summary scores of gait	• *Walking speed 1.18 m/s (96% of normal)*
• Temporal-spatial parameters	
• Check consistency of gait data	
• Selection of one representative trial	

2) Mark-up

Marking features	*Example: Gait Data - ankle dorsiflexion*
• Marking features on gait graphs using symbols, colours (side) and letters. See example of dorsiflexion	
List the features	*d Too little right dorsiflexion in stance*
• Type of symbol, side, variable (graph) and timing	*e too little dorsiflexion in swing.*

3) Grouping

Group and describe	*Example: Impairment*
• Group features and supplementary data	*Impairment: Left plantar flexor spasticity Documented with feature d and e; and spasticity and normal passive range of motion in the physical examination.*
• Describe: evidence (Clear, Probable, Possible), effect on walking (minor, moderate, major) and features not grouped.	*Evidence: Clear - Effect: Moderate.*

4) Reporting

Finish the report	
• Write other comments to the interpretation, if relevant (e.g. warnings, uncertainty).	

Abbreviations: Gross Motor Function Classification System (GMFCS), Pediatric Outcomes Data Collection Instrument (PODCI), Functional Mobility Scale (FMS),

the child's gait [37]. It is recommended that the formal treatment recommendations are made by healthcare professionals with relevant specific backgrounds, i.e. only an orthopaedic surgeon should make recommendations about orthopaedic surgery [36].

The results and recommendations for interventions are typically presented in a report that is distributed to the referring physician [27], but discussion of the recommendations with the surgeon who will perform the operation has also been proposed [25].

2.4. Summary – Motivation for the studies

Gait analysis has become an important and reliable method of clinical assessment of gait in ambulant children with cerebral palsy [22, 45, 46]. Nevertheless, the referral to gait analysis is dependent on institutional guidelines or the clinical reasoning of the individual paediatrician or orthopaedic surgeon[21]. The CPUP ensures continuous surveillance of all children with cerebral palsy with the same standardised assessments throughout childhood and, thus, is a common basis for decisions about interdisciplinary interventions. In CPUP, overall gross motor function and functional mobility are evaluated by standardised classification systems and measures [13]. However, the gait pattern, i.e. the manner of walking used by the child is not evaluated. Hence, the idea of combining the CPUP with the use of gait analysis in the interdisciplinary interventions for children with cerebral palsy emerged when the implementation of CPUP in Denmark was initiated.

A literature search showed that gait analysis has primarily been investigated as a measurement method. Furthermore, a few studies reported its effectiveness for evaluating outcomes of the types of orthopaedic surgical interventions used [23-25], of orthopaedic surgery of the lower limb [42] and of individualised physiotherapy [34, 35].

Thus, the research question for this thesis emerged from experience in clinical practice and a critical appraisal of the scientific literature, revealing unknown effectiveness of the use of gait analysis in interdisciplinary interventions for children with cerebral palsy.

In the planning of Study II, we became aware that the clinimetric properties of the Gait Deviation Index, a summary measure of overall gait, had only partly been described in the literature, which is the motivation for carrying out Study I.

The interpretation of the gait analysis from the baseline assessment revealed some children with severely reduced passive range of motion (corresponding to the red values in the traffic light signal used by the CPUP) were walking with only minor deviation in their gait measured with the Gait Deviation Index, which encouraged the completion of Study III.

3. Study aims and hypotheses

The overall aim of the thesis was therefore to investigate the use of gait analysis in individually defined interdisciplinary interventions for children with cerebral palsy. The specific study aims are listed below.

3.1. Study I. Test-retest

The aim of this study was to investigate the intra-rater reliability and agreement of the most common gait summary measures: the Gait Deviation Index, the Gait Profile Score and the Gait Variable Score in children with cerebral palsy across two repeated sessions.

3.2. Study II. Randomised controlled trial

This study aimed to determine if individually tailored interdisciplinary interventions with gait analysis lead to greater improvements than individually tailored interdisciplinary intervention without gait analysis in overall gait pathology, walking performance and patient-reported outcome measures of function, disability and health-related quality of life.

The predefined hypotheses were:

H1) The use of gait analysis in the planning of individually tailored interdisciplinary interventions would be superior in improving overall gait pathology (evaluated by the Gait Deviation Index (primary outcome)) compared with 'usual care' in children with cerebral palsy at GMFCS levels I and II.

H2) The use of gait analysis in the planning of individually tailored interdisciplinary interventions would be superior compared with 'usual care' in improving walking performance (1-min walk test) and patient-reported outcomes of functional mobility (Pediatric Evaluation of Disability Inventory), overall health, pain and participation in normal daily activities (Pediatric Outcomes Data Collection Instrument) as well as health-related quality of life (Pediatric Quality of Life Inventory Cerebral Palsy Module) in children with cerebral palsy at GMFCS levels I and II.

3.3. Study III. Cross-sectional study

The aim of this study was to investigate the threshold values used by the CPUP by testing the hypothesis that passive range of motion in ankle dorsiflexion is associated with gross motor function and that gross motor function differs between the groups of participants in each category. Gross motor function is measured by various methods describing the overall gross motor capacity, the ankle-specific gait capacity, and the use of gross motor skills in everyday life.

4. Methods

4.1. Study outline, registration and ethics

The thesis is based on the above three studies with the following methodological design:
Study I Intra-rater reliability and agreement study
Study II Randomised controlled trial
Study III Cross-sectional study

Study registration
The studies have been reported to the Danish Data Protection Agency (2008-58-0035). ClinicalTrials.gov have been used for study registration (NCT:02160457, Registered 09.06.2014) and the information on the site has been updated throughout the study (Updated 17.07.2015, 17.07.2016 and 20.07.2017), including the statistical analysis plan (Uploaded 25.07.2017).

Ethics
Ethics approval was obtained from the Committee for Medical Research Ethics in the Region of Southern Denmark (S-20120162) and the studies were conducted in accordance with the Declaration of Helsinki.

Children and parents were given verbal and written information about the study, experimental procedure and potential risks, such as discomfort when the patches with the reflective markers were removed and fatigue during the examinations. Furthermore, children and parents were informed that participation was voluntary and that, at any stage in the study, they could decide to discontinue participation without giving any reason and without it having consequences for their further treatment. Informed consent to participate was obtained verbally from the children, and in writing from the parents.

4.2. Participants and sample size
The number of participants, age, sex, cerebral palsy subtype and gross motor function of the participants are outlined in Table 3.

Reference group
The three studies investigated gait in children with cerebral palsy using gait summary measures that calculated the deviation from the gait of a reference group of typically developing children, preferably collected in the same gait analysis laboratory.
The Gait Deviation Index and Gait Profile Score are speed-dependent [47, 48], which can be managed by using a reference group with a walking speed similar to the study group.

The existing reference data used at our centre were from 15 children aged 7 to14 years. To mimic the age and thereby also the height and walking speed of the participants in the three studies, we supplemented the existing reference group with gait data from an additional 15 children aged 5 to 10 years without gait impairment. Thus, a reference group of 30 typically developing children aged 5 to 14 years was used to calculate the gait summary measures in the three studies.

Participants for the reference group were recruited from September 2012 to February 2013 by the research unit and through personal networks.

Study I. Test-retest
Through e-mail and an oral presentation at a national conference, the principal investigator (HMR) invited physiotherapists and medical doctors affiliated with our institution to participate in the recruitment of participants. The healthcare professionals encouraged children and their parents to participate in the study by contacting the principal investigator (HMR). Children were enrolled after screening for eligibility, and were tested and retested from March to October 2013. Eligibility criteria were age of 5 to 12 years, a diagnosis of spastic cerebral palsy at GMFCS levels I or II and could coorporate to complete the gait analysis. Exclusion criteria were: orthopaedic surgery or injection with botulinum toxin type A within 6 or 3 months prior to baseline assessment, respectively.

To mimic clinical practice and the sampling of data for the planned RCT study (Study II), three teams of two assessors conducted the data collection at the Motion Analysis Laboratory at Odense University Hospital.

Sample size
The sample size of the study was determined with an expected Intra-class Correlation Coefficient (ICC) of 0.89 for the Gait Deviation Index (primary outcome of the RCT), as reported by Miller et al. [49] and a 95% confidence interval (CI) of ± 0.1, resulting in a sample of 18 children.

Study II. Randomised controlled trial
Children registered in the CPUP in the Region of Southern Denmark and the North Denmark Region were screened for eligibility and invited to participate in Study II. Eligibility criteria were age of 5 to 8 years and a diagnosis of spastic cerebral palsy at GMFCS levels I or II. Exclusion criteria were: orthopaedic surgery or injection with botulinum toxin type A within 52 or 12 weeks prior to baseline assessment, respectively. Furthermore, the children schould to be able to participate in the examination and their parents needed to speak and understand Danish. Participants were recruited from June 2014 until June 2016 and data were collected from August 2014 to July 2017. Questionnaires were mailed to the parents prior to the examination at the Motion Analysis Laboratory at Odense University Hospital.

Sample size
The sample size for this study was based upon the Gait Deviation Index (primary outcome), collected in Study I, which included a comparable group of children with cerebral palsy (mean Gait Deviation Index 79.3, SD 12.0). A minimum clinically important difference in the Gait Deviation Index has been defined as 7.9 points by the current group of

Table 3. Participants in the studies

	Reference		Study I		Study II-III	
Number, n	15		18		60	
Age, mean (SD)	6 y 10 m	(1 y 8 m)	8 y 0 m	(2 y 1 m)	6 y 10 m	(1 y 3 m)
Sex, boys/girls, n (%)	7/8	(47/53)	12/6	(67/33)	21/39	(35/65)
CP subtype, UL/BL, n (%)		-	10/8	(56/44)	43/17	(72/28)
GMFCS I / II, n (%)		-	9/9	(50/50)	42/18	(70/30)

Abbreviations: BL: Bilateral spastic cerebral palsy; CP: Cerebral palsy; GMFCS: Gross Motor Function Classification System; SD: Standard deviation; UL: Unilateral spastic cerebral palsy (UL).

authors a priori, which is equivalent to an improvement of 10%, as suggested by Swartz et al. [30]. A minimum of 29 subjects in each group (n = 58) was required with alpha = 0.05 and 80% power. Following these estimations, it was decided to include 60 children in total (30 participants in each group), allowing for a dropout rate of 5%.

Study III. Cross-sectional study
We performed a cross-sectional study based on selected data from the baseline assessment in Study II, the randomised controlled trial.

4.3. Outcome measures

In this section, the outcome measures used in this PhD thesis are presented together with their clinimetric properties. The outcome measures are selected to cover the three individual dimensions of body function and body structures, activities and participation, and the two contextual dimensions of environmental factors and personal factors of the International Classification of Functioning, Disability and Health, version for Children and Youth (also called ICF-CY). The outcome measures, the ICF Domain they are affiliated with and their use in the studies are described in Table 4.

Diagnosis, subtype and classification of function
Date of birth and diagnosis were collected from the child's paediatrician at the initial screening for eligibility. Subtype and classification of function are used to describe participant characteristics (Studies I-III) and are used in the clinical interpretation of the gait analysis (Study II).

The GMFCS was used to classify the child's ability to perform self-initiated movements related to sitting and walking [50]. The GMFCS has strong construct validity with the Gross Motor Function Measure [51] and good inter-observer and test-retest reliability [52].

Table 4. Outcome measures

	ICF-CY Domain					Study		
	Bodyfunction and structure	Activity	Participation	Environmental factors	Personal factors	Study I Test-retest	Study II - Randomised controlled trial	Study III - Cross-sectional
Diagnosis, subtype and function								
Age and diagnosis					x	x	x	x
GMFCS		x				x	x	x
Functional Mobility Scale		x				x	x	
Instrumented gait analysis								
GMFM 66 items version		x						x
1-minute walk		x					x	x
Gait Deviation Index	x					x	x	x
Gait Profile Score	x					x		
Gait Variable Score	x					x		x
Physical examination	x							x
Patient reported outcome measures								
PEDI mobility scale		x	x	x			x	
PODCI	x	x	x				x	x
PedsQl Cerebral Palsy Module		x	x	x	x		x	x

Abbreviations: GMFCS: Gross Motor Function Classification System; GMFM: Gross Motor Function Measure; PEDI: Pediatric Evaluation of Disability Inventory; PODCI: Pediatric Outcome Data Collection Instrument; PedsQl: The Pediatric Quality of Life Inventory.

The Functional Mobility Scale was used to quantify the child's independent mobility according to the need for assistive devices in different environmental surroundings [53]. Evidence of construct validity [54], inter-rater reliability with ICCs of 0.94 to 0.95 [53] and inter-observer reliability with weighted kappa coefficients of 0.86 to 0.92 [55] have been documented.

Three-dimensional instrumented gait analysis
The gait analysis consisted of the following elements:

- Recording and processing of the gait,
- Calculation of the gait summary measures,
- Assessment of gross motor function and walking, and
- Physical examination.

All described in the following sections. The data collected during the examination were used as outcome measures in the studies and/or for clinical interpretation in Study II.

Recording and processing of the gait
As part of the gait analysis, height (centimetres), leg length (centimetres) and body weight (kilograms) were measured.

Gait analysis with three-dimensional kinematics and kinetics was performed using a 6-camera Vicon MX03 system (Study I) or an 8-camera Vicon T40 system (Study II) (Vicon, Oxford, UK) operating at 100Hz. Ground reaction forces were recorded using two force plates (AMTI, OR6-7-1000, Watertown, MA, USA), sampling at 1000Hz.

The children walked barefoot and, if relevant, also with orthotics and shoes, at a self-selected speed along a 10-m walkway until at least five acceptable trials (Study I) or ten acceptable trials (Study II) were collected for each child. Furthermore, if possible, five trials with walking speed matched to that of the baseline examination were collected (Study II). Subsequently, the parents were asked to confirm that the performance was representative of the regular gait function of their child. If not, additional trials were performed until confirmation was achieved.

The Helen Hayes marker set and corresponding Plug-in-Gait model were used to generate the kinematic data [60]. Vicon Nexus software (version 1.7.1 - 1.8.5) and Vicon Polygon software (version 3.5.2 - 4.3) were used for data processing to define gait cycles of the trials from each participant. Five trials of self-selected speed from each session were selected (Study I and Study II). Furthermore, if possible, five trials with a consistent velocity (±15%) with walking speed matched to that at baseline were also selected (Study II).

Both kinematic and kinetic data were used for the clinical interpretation (Study II) and the kinematic data were used to calculate the gait summary measures (Gait Deviation Index, Gait Profile Score and Gait Variable Score) as outcome measures (Studies I-II).

Calculation of gait summary measures
An overview of the use of gait summary measures in the studies and manuscripts is outlined in Table 5. In study III, the most affected leg was defined as the leg with the most serverly reduced range of motion in the ankle joint, i.e. the leg where one or both

measurements were classified into the red or yellow category and, if similar in range of motion, the leg with the lowest Gait Deviation Index was chosen.

Gait Deviation Index

The Gait Deviation Index is an overall quantitative index that summarises the gait pathology for each participant by comparison with a non-pathological gait. A Gait Deviation Index of 100 represents the absence of gait pathology, and each 10-point decrement below 100 indicates approximately one standard deviation from normal gait kinematics [61]. Satisfactory concurrent and construct validity of the Gait Deviation Index in children with cerebral palsy have been shown [61, 62]. Responsiveness of the Gait Deviation Index has been shown by comparing the Gait Deviation Index before and after surgical lengthening of the Gastrocnemius in children with cerebral palsy [63].

Table 5. The use of gait summary measures

	Study I	Study II	Study III
Gait Deviation Index			
Each leg	x		
Most affected leg			x
Average of both legs	x	x	
Gait Profile Score			
Each leg	x		
Overall Gait Profile Score	x		
Gait Variable Score			
Each leg	x		
Most affected leg			x

The Gait Deviation Index has been reported as a reliable measure within a single session for children with cerebral palsy [64]. Intra-tester reliability and agreement across two separate sessions have been investigated for typically developing children, demonstrating limits of agreement of ±10 points and a non-significant difference between the two sessions [64], but have not previously been investigated in children with cerebral palsy. As described in the results section of this thesis, excellent intra-rater reliability and acceptable agreement across two repeated sessions in a group of children with cerebral palsy were documented for the Gait Deviation Index in Study I [65].

Gait Profile Score

The Gait Profile Score is another overall quantitative index that, as the Gait Deviation Index, summarises the gait pathology for each participant by comparison with a non-pathological gait. It is obtained from the same gait kinematics as the Gait Deviation Index and is calculated on all gait features representing the root mean square difference between the participant's data and the average from the reference dataset [47]. Satisfactory face and criterion validity of the Gait Profile Score in children with cerebral palsy have been shown [66] and responsiveness has been documented by comparing the Gait Profile score before and after surgical lengthening of the Gastrocnemius [67].

Intra-tester reliability and agreement across two separate sessions have not previously been investigated in children with cerebral palsy. As described in the results section of this thesis, excellent intra-rater reliability and acceptable agreement across two repeated sessions in children with cerebral palsy were documented for the Gait Profile Score in Study I [65].

Gait Variable Score

The Gait Variable Score is a quantitative index in relation to Gait Profile socre, which summarises the gait pathology for each joint and is obtained from each of the gait kinematics used by the Gait Deviation Index and Gait Profile Score. It is calculated for each gait feature and represents the root mean squared difference between the participant's data and the average from the reference dataset [47]. The Gait Variable Score is illustrated by the Movement Analysis Profile (Figure 1).

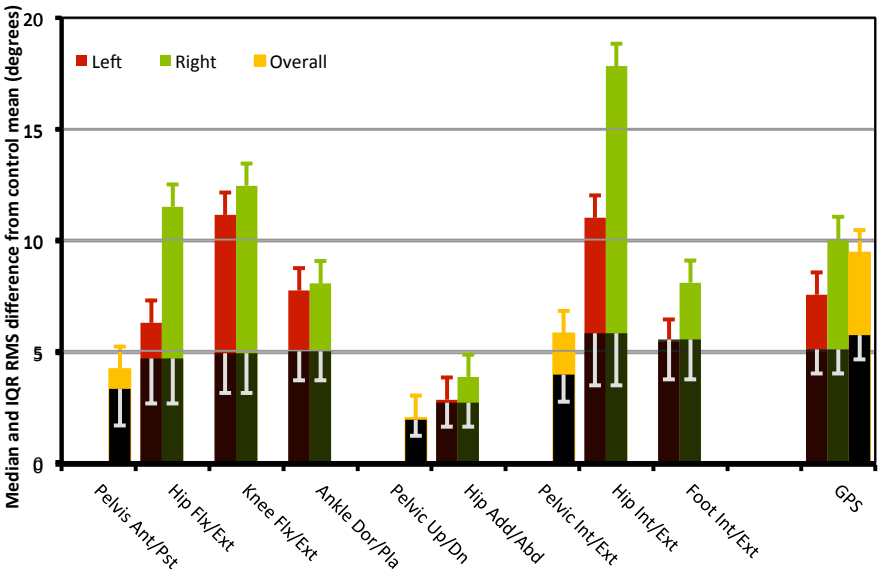


Figure 1. The Movement Analysis Profile
An example of the Movement Analysis Profile which is a graphical presentation of the scores of the 15 kinematic variables of the Gait Variable Score that together form the basis for calculation of the Gait Profile Score. The black areas are based on data from the reference group, and thus represent non-pathological gait kinematics, while the coloured areas representent the left limb, right limb and overall data from the patients being examined.

Abbreviations: Gait Profile Score: GPS, Interquartile range: IQR.

Satisfactory face validity and criterion validity of the Gait Variable Score in children with cerebral palsy have been shown [66]. Investigation of intra-session variability has suggested that the Gait Variable Score is a reliable measure within a single session [47].

Intra-tester reliability and agreement across two separate sessions have not previously been investigated in children with cerebral palsy. As described in the results section of this thesis, fair to good intra-rater reliability and acceptable agreement across two repeated sessions have been shown for the Gait Variable Score in children with cerebral palsy and were documented in Study I [65].

Assessesment of gross motor function and walking

Gross motor capacity was assessed using an experience-based selection of a minimum of 17 items from the 66-item Gross Motor Function Measure and subsequent calculation of the GMFM-66 score using the Gross Motor Function Measure Estimator software [38]. The Gross Motor Function Measure is an evaluative measure of motor function designed to document motor change in children with cerebral palsy [56]. The clinimetric properties of the measure and selected items of the measure have been extensively investigated. Excellent levels of reliability and high construct, criterion and content validity have been reported [57, 58].

Table 6. Physical examination

	Muscle function *Kendall 0-5*	**Muscle tone** *Modified Ashworth Tardieu*	**Range of motion** *Goniometer*	**Deformities** *Goniometer Observation*
Hip	Hip flexion Hip extension		Extension Abduction Intermal rotation External rotation	
Knee and tibia	Knee extension Knee flexion Quadriceps lag	Hamstring Rectus femoris	Popliteal angle Hamstring shift Knee extension Quadriceps lag Rectus femoris length	Tibial torsion Knee (valgus / varus)
Ankle and feet	Plantar flexion Dorsiflexion Inversion Eversion Confusion test	Plantar flexor	Dorsiflexion (knee 90° and 0°)	Posture of feet

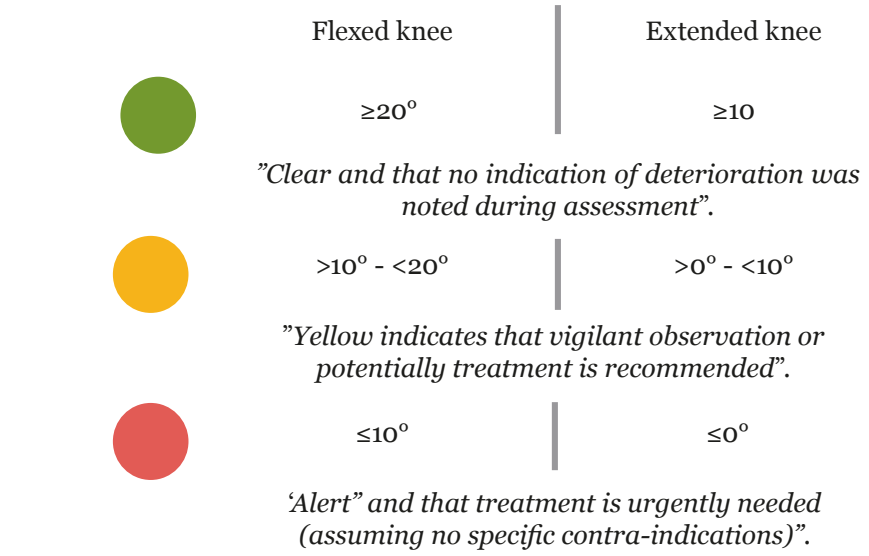


Figure 2. Ankle dorsiflexion
Clinical cut-off points, clinical interpretation for the three categories of passive range of motion and illustration of the examination of passive range of motion in ankle dorsiflexion with flexed and extended knee [16a, 17a].
Photograph used with permission from the Cerebral Palsy follow-Up Program in the Capital Region of Denmark.

Walking performance was measured with the 1-minute walk test as described by McDowell et al. [39]. Children were asked to walk as fast as possible without running on a 20-metre track for 1 minute. The test has demonstrated a high correlation with gross motor function [59] and good test-retest reliability with ICC values of 0.94 for children with cerebral palsy [39].

Physical examination

A thorough physical examination was completed after the data collection with gait analysis (Study II). The examinations were conducted as described by the CPUP [68] and Baker et al. [36] and consisted of the measures described in Table 6. The clinical examinations were used for clinical interpretation of the gait analysis, except passive range of motion in the ankle joint, which was also used in Study III.

The clinical cut-off points and clinical interpretation for the three categories of passive range of motion in ankle dorsiflexion with flexed and extended knee used in Study III, are described in Figure 2.

Patient-reported outcome measures

Pediatric Evaluation of Disability Inventory

The Mobility Scale of the original Pediatric Evaluation of Disability Inventory evaluates the child's functional mobility in everyday activities with regard to functional skills and amount of caregiver assistance [69]. A Danish version was applied as a parental questionnaire and its content and discriminative validity have been established in children with cerebral palsy [70, 71].

Pediatric Outcomes Data Collection Instrument

The Pediatric Outcomes Data Collection Instrument assesses overall health, pain and participation in normal daily activities. Concurrent and discriminant validity have been assessed by comparing the Pediatric Outcomes Data Collection Instrument with other measures of health and well-being, gross motor function and diagnostic subgroups in children with cerebral palsy [72]. Moderate to good test-retest reliability with ICC values of 0.71 to 0.97 have been reported in children with orthopaedic or musculoskeletal disorders [73].

The Pediatric Quality of Life Inventory Cerebral Palsy Module

The Pediatric Quality of Life Inventory Cerebral Palsy Module is a measure of health-related quality of life, specifically designed for children with cerebral palsy. It is based upon the parents' report and measures physical, emotional, social and school functioning. Construct validity and discriminative validity of the original version have been supported by comparing the scores from children with cerebral palsy with a generic measure of the same construct with those from children without disability. Satisfactory reliability with ICC values of 0.42 to 0.84 were demonstrated in the same study [74]. A linguistically validated Danish version was used [75].

Recommended and applied interventions

Records of the recommended and parent-reported applied interventions were used to explore the type and number of interventions in the two intervention groups with regard to the four categories: orthopaedic surgery, spasticity management, physical therapy and orthotics [14, 20]. Information about the recommended interventions was collected at the release of the gait analysis report. The applied interventions and the participants' perceived responses to the interventions were collected with a short questionnaire to the parents at 52 weeks follow-up.

Participant-perceived responses to the interventions

The parents were asked about their perception of the responses to the interventions with three clinical anchor questions by means of a 5-point Likert scale as response categories.

The question and answer categories for the anchor questions were:

> *1) "How would you describe the results of the interventions your child has participated in?"*
> *Answer categories: excellent, very good, good, fair, and poor.*
>
> *2) "In general, how would you say your child's walking ability is today compared with one year ago?"*
> *Answers categories: much better, a little better, about the same, a little worse, and much worse.*
>
> *3) "In general, how would you say your child's overall health is today compared with one year ago?" Answers categories: much better, a little better, about the same, a little worse, and much worse.*

The answers were used to determine between-group differences in the responses to the interventions and potentially also as anchor questions to determine the minimal clinically important difference [76]. Similar approaches have been used to evaluate spasticity management [77, 78] and orthopaedic surgery [79] in children and adults with cerebral palsy.

4.4. Interventions

In Study II, interventions were carried out in two study groups:
- Experimental group: Individually tailored interdisciplinary intervention based on measures performed as part of the CPUP, other clinical examinations AND gait analysis.
- Control group: Individually tailored interdisciplinary intervention based on measures performed as part of the CPUP and other clinical examinations BUT NOT gait analysis.

The two models of individually tailored interdisciplinary intervention are outlined in Figure 3.

For both the experimental and control groups, the interdisciplinary interventions addressing impairments that affect the gait are described in four categories [14, 20]: orthopaedic surgery, spasticity management, physical therapy and orthotics. The current pragmatic study design did not involve standardisation of the interdisciplinary interventions and did not provide training of the healthcare professionals in the interventions provided by the participating hospitals and municipalities.

All participants in the study continued the healthcare interventions provided by the municipalities and regions, including the yearly examinations by physiotherapists and interdisciplinary consultations.

Experimental
The experimental intervention included an individually tailored interdisciplinary intervention based on measures performed as part of the CPUP, other clinical examinations, standardised measurements of walking and recommendations from the gait analysis.

An interdisciplinary team provided recommendations for the interventions based on impairment-focused interpretation and reporting according to Baker 2013 [36]. The

data collection, interpretation, development of recommendations and dissemination of recommendations were carried out in four steps:

- Step 1: Data collection (gait analyses)
Data collection, as described in the section: gait analysis.

- Step 2 Impairment-focused interpretation
The approach 'Impairment-Focused Interpretation' [36] refers to the interpretation of the gait analysis. The principal investigator (HMR) identified and described the impairments that affected the child's gait and subsequently validated the findings with the head of the motion laboratory (AHL).

- Step 3: Recommendations for interdisciplinary interventions
The recommendations were developed to address the impairments found in the impairment-focused interpretation (Step 2) and were provided by the gait analysis team, which consisted of a neuro-paediatrician (LKH), a paediatric orthopaedic surgeon (NWP or VE), a physiotherapist (HMR) and a biomechanist (AHL).

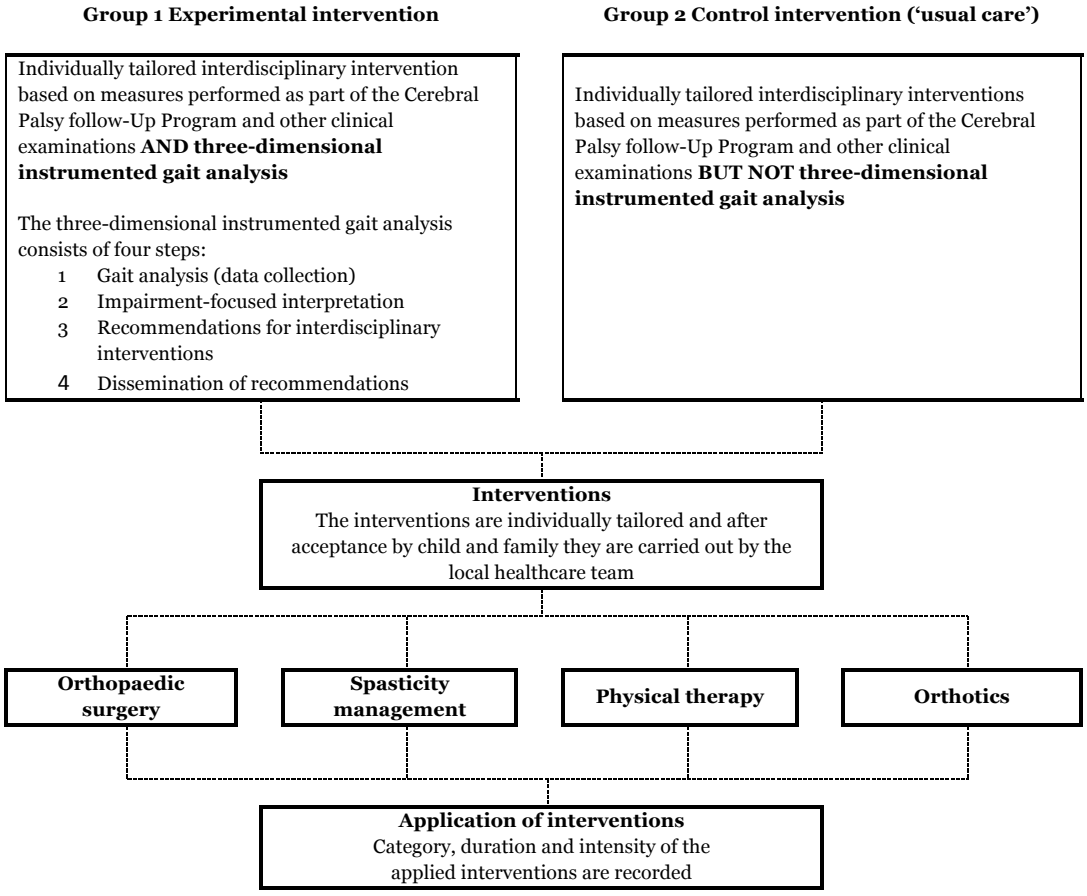


Figure 3. Interdisciplinary interventions

To facilitate an objective recommendation for treatment selection, we created a treatment algorithm, inspired by Miller 2007 [80], of the most common underlying neuro-musculoskeletal impairments of the movement features we measured. Finally, each of the recommendations for interdisciplinary interventions was based upon consensus. Otherwise, the specific interventions were not recommended.

- Step 4: Dissemination of recommendations
The parents of the child and the local healthcare team, which consisted of a paediatrician, a paediatric orthopaedic surgeon, a physiotherapist and/or an orthotist, were informed by mail about the recommendations for interventions based on knowledge from the gait analysis. The family and local healthcare teams were encouraged to contact the principal investigator (HMR) if they had any queries or uncertainties.

Adherence to the recommended interventions was not a prerequisite for participation in the current pragmatic study. As in daily clinical practice, the child, his/her family and the local healthcare team had the option to follow or to reject the recommended intervention or to choose interventions other than those recommended by the gait analysis team.

Control
The control intervention (‘usual care’) included individually tailored interdisciplinary interventions based on measures performed as part of the CPUP and other clinical examinations, but not gait analysis.

4.5. Statistical methods

An overview of the statistical methods used in each of the studies is shown in Table 7 and described briefly for each of the studies in the following sections.

Study I. Test-retest

Participant characteristics were presented with descriptive statistics. The distribution of the data was investigated using normal probability plots and the Shapiro-Wilk test [81]. Not normally distributed data were logarithmically transformed. Investigation of systematic differences was performed using the Students paired t-test and the Wilcoxon signed Ranks Test. Bland-Altman plots with 95% limits of agreement, were used to explore agreement between the two sessions [82, 83]. Reliability of each variable was quantified using ICC (two-way random effect model) and 95% CIs [82]. Agreement was assessed with the Standard Error of Measurement and absolute reliability with the Smallest Detectable Change [82].

Study II. Randomised controlled trial

The data associated with baseline characteristics were checked for completeness and their distribution was investigated using normal probability plots and the Shapiro–Wilk test [81]. Descriptive statistics were calculated with mean and standard deviation (SD), median and interquartile range (iqr) or number of patients.
Main comparative analyses between groups were performed on the full analysis set with missing data imputed using last observation carried forward. A multiple regression model with group and baseline value of the relevant variable as covariate was used to analyse between-group mean changes. The model assumptions were checked for relationship, homoscedasticity, outliers and normality of residuals. Since minor violations of the assumptions were present, the analysis was done with robust estimation.

Differences between the interventions applied and participant-perceived responses to the interventions were investigated with descriptive statistics, Pearson's chi-squared and Wilcoxon's rank-sum test.

Study III. Cross-sectional study

Participant characteristics were presented with descriptive statistics. The statistical distribution of data was investigated using normal probability plots and the Shapiro–Wilk test [81]. Scatterplots with fitted values were prepared to provide an overview of the data. Correlations were investigated with Pearson correlation coefficients or the Spearman's rank correlation coefficient.

Differences were investigated with one-way ANOVA or the Kruskal-Wallis test and, if relevant, pairwise comparisons with Wilcoxon rank sum test (Mann-Whitney).

Table 7. Overview over statistical methods

	Study I	Study II	Study III
Participant characteristics			
Descriptive statistics	x	x	x
Statistical distribution			
Normal probability plots	x	x	x
Shapiro-Wilk test	x	x	x
Transformation			
Logarithmically transformation	x		
Analysis			
Student paired t-test	x		
Wilcoxon signed ranks test	x		
Interclass correlation coefficient	x		
Standard error of measurement	x		
Smallest detectable change	x		
Multiple regression analysis		x	
Pearson's chi-squared test		x	
Wilcoxon rank sum test		x	x
Pearson correlation coefficients			x
Spearman’s rank correlation coefficient			x
One-way Analysis of variance			x
Kruskal-Wallis test			x
Graphics			
Bland-Altman plots	x		
Scatterplots with fitted values	x		x

5. Summary of results

5.1. Study I. Test-retest

Three teams of two assessors conducted the data collection from the 18 children, aged 5 to 12 years, with spastic cerebral palsy, at two sessions separated by 1 to 9 days.

No systematic bias was observed between the sessions and no heteroscedasticity was observed in Bland-Altman plots (Figure 4).

For the Gait Deviation Index and Gait Profile Score, excellent reliability with ICC values of 0.8 to 0.9 were found, while the Gait Variable Score was found to have fair to good reliability with ICCs of 0.4 to 0.7.
The agreement for the Gait Deviation Index and the logarithmically transformed Gait Profile Score, in terms of Standard Error of the Mean as a percentage, varied from 4.1% to 6.7%, whilst the smallest detectable change ranged from 11.3% to 18.5%.

For the logarithmically transformed Gait Variable Score, we found a fair to large variation in Standard Error of the Mean as a percentage, which ranged from 7% to 29% and in the smallest detectable change from 18% to 81%.

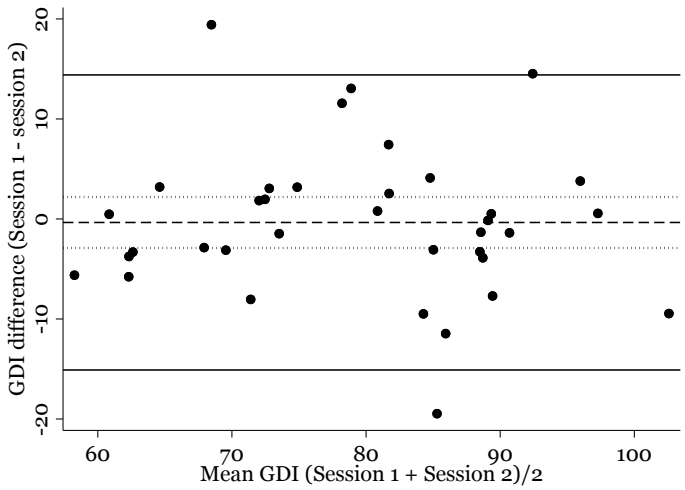


Figure 4. Example of Bland–Altman plot of Gait Deviation Index (GDI) with 95% limits of agreement (blacklines), mean difference (black dash line) and 95% CI (black dotted line).

5.2. Study II. Randomised controlled trial

In total, 160 children were invited to participate in the study. Of these, 83 children were screened for eligibility and 60 participants were randomised to either the experimental intervention (n=30) or the control intervention ('usual care') (n=30) groups. Recruitment of participants and data collection were carried out between June 2014 and July 2017. Complete assessments were available from 57 participants at baseline, 48 participants at 26 weeks follow up, and 55 participants at the primary endpoint at 52 weeks. All children received their allocated intervention of interdisciplinary interventions with or without gait analysis.

The 60 participating children had a median age of 6 years and 11 months. The full list of patient characteristics is presented in Table 1 in Paper IIb. The cerebral palsy subtype and GMFCS levels for the participants were 43 children with unilateral (experimental group / control group, n=21/n=22), 17 with bilateral (n=9 / n=8) spastic cerebral palsy, 42 children at GMFCS level I (experimental group / control group, n=20/n=22) and 18 at GMFCS level II (n=10 / n=8).

Primary outcome

At 52 weeks follow up, the mean change scores in the Gait Deviation Index for self-selected walking speed did not differ significantly between the groups (difference in Gait Deviation Index: -0.59, 95% CI; -3.9 - 2.8, Eta2 < 0.01), (Figure 5). In total, 11 participants improved more than the a priori-defined minimum clinically important difference of 7.9 on the Gait Deviation Index (experimental group / control group, n=5/n=6), resulting in a non-significant risk difference of -0.03 (95% CI; -0.23 – 0.16, Z=0.33, p=0.738).

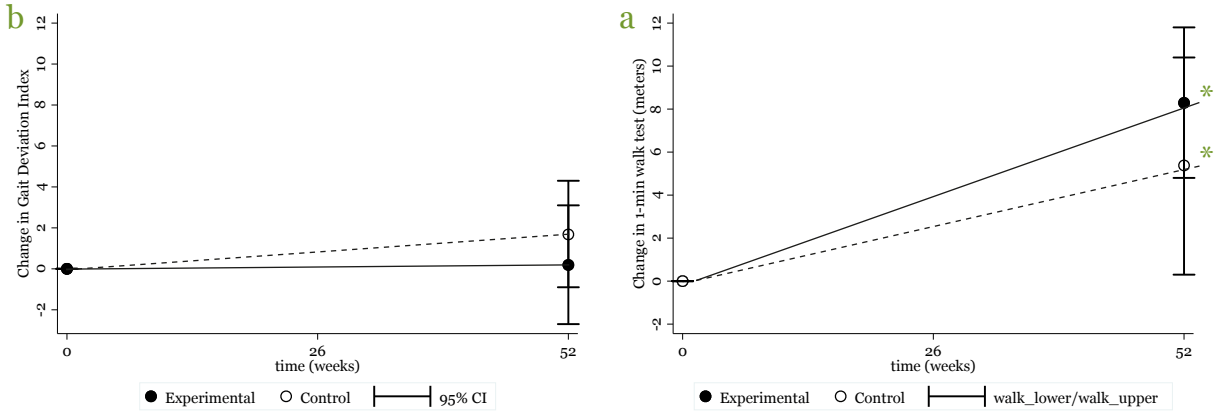


Figure 5. Within-group change from baseline in Gait Deviation Index (a) and 1-minute walk test (b)from baseline to 52 weeks.

* Statistically significant within-group change.

Secondary outcomes

No statistical significant between-group differences in change scores were observed in the 1-minute walk test (3.02 meter (-2.9 - 9.0), Eta2 = 0.02) at 52 weeks or in the patient-reported outcome measures at 26 or 52 weeks. Statistical significant and potential clinically relevant within-group improvements were seen in some of the secondary outcome measures at 26 and 52 weeks. Examples of the within-group changes are outlined in Figure 5 and Figure 6. The complete table of the within-group and between-group differences is outlined in Table 2 in Paper IIb.

Additional/tertiary outcomes

No significant difference was observed between the groups in participant-perceived responses to the interventions (p=0.19) or changes in walking (p=0.38). However, a difference between the groups was seen in overall health in favour of the experimental group (p=0.03) (Figure 7).

Interventions

The compliance with the recommended types of interventions was 24 of 28 participants for physiotherapy (% (95% CI), 86% (67 – 96), 6 of 10 participants for orthotics (60% (26 – 88)), 5 of 14 for spasticity management (36% (13 - 65)) and 0 out of 1 for orthopaedic surgery (0% (no 95% CI calculated)).

Adverse events

The participants (children and parents) did not report any serious adverse events during the study period. However, during the testing, the assessors experienced one child who did not want to wear the adhesive reflective markers at the post examination, and five children (three at baseline and two at follow-up) were too tired to complete the 1-minute walk test after the collection of gait data was completed.

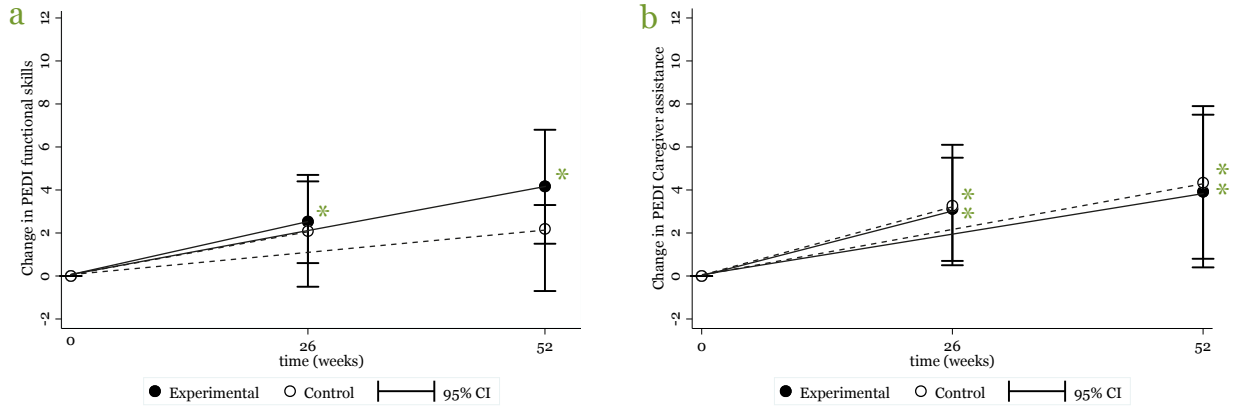


Figure 6. Within-group change from baseline in Functional skills (a) and Caregiver assistance (b) of the Mobility scale of the Pediatric Evaluation of Disability Inventory (PEDI) from baseline to 26 weeks and from baseline to 52 weeks.
* Statistically significant within-group change.

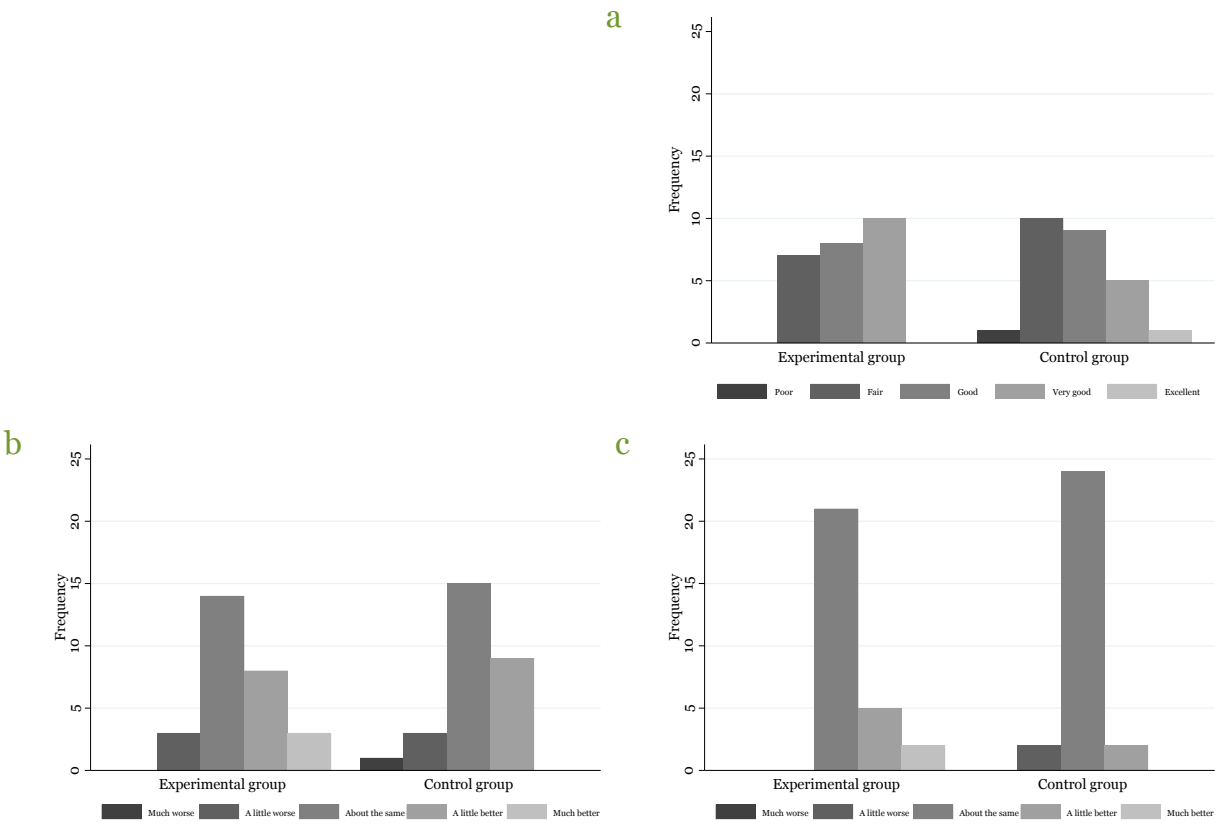


Figure 7. Bar charts illustrating the frequency of answers in each of the five categories for the participant-perceived responses to the interventions (a), changes in walking (b) and in overall health (c).

5.3. Study III. Cross-sectional

A total of 60 children with cerebral palsy participated in this study, and of these a full dataset was available for 57 participants at baseline.

Statistically significant moderate correlations were observed between the Gait Variable Score of the ankle and DF with flexed knee ($r = -0.37$, [95% CI:-0.57 - -0.13], $p<0.05$) and extended knee ($r = -0.37$, [95% CI: -0.57 - -0.13], $p<0.05$) and peak dorsiflexion and DF with flexed knee ($r = 0.49$, [95%CI: 0.26 – 0.67], $p < 0.001$) and extended knee ($r = 0.55$, [95% CI: 0.35 – 0.71], $p < 0.001$). No significant correlations between the other measures of gross motor function and passive dorsiflexion were observed. Examples of scatterplots of the correlations are outlined in Figure 8.

There were statistically significant differences in the Gait Variable Score of the ankle and peak dorsiflexion between the three groups of participants based on the categories with flexed and extended knee (Table 2 in paper III) .

For ankle dorsiflexion with flexed knee, the median Gait Variable Scores of the ankle for the red and green categories were 13.74° and 7.58°; the distributions in the two groups differed significantly ((z-score, p-value), $z = -2.63$ $p = 0.009$) and with extended knee, the median Gait Variable Score of the ankle for the red and green categories were 16.79° and 7.62°; the distributions in the two groups differed significantly ((z-score, p-value), $z = -2.43$ $p = 0.015$).

For Peak dorsiflexion, we observed a difference in red versus green and red versus yellow passive range of motion categories with flexed knee ((mean (95% CI) -9.6° (-14.4 to -4.7) and -7.9° (-13.1 to -2.6), respectively) and between red versus green and yellow versus green passive range of motion categories with extended knee (-9.57° (-15.4 to -3.8) and -7.9° (-14.2 to -1.5), respectively).

No statistically significant group-mean differences were observed between the participants classified into each of the passive range of motioncategories of passive ankle range of motion on the variables of Gait Deviation Index, 1-minute walk, Gross Motor Function Measure, the Pediatric Quality of Life Inventory Cerebral Palsy Module and Pediatric Outcomes Data Collection Instrument transfer and basic mobility scores.

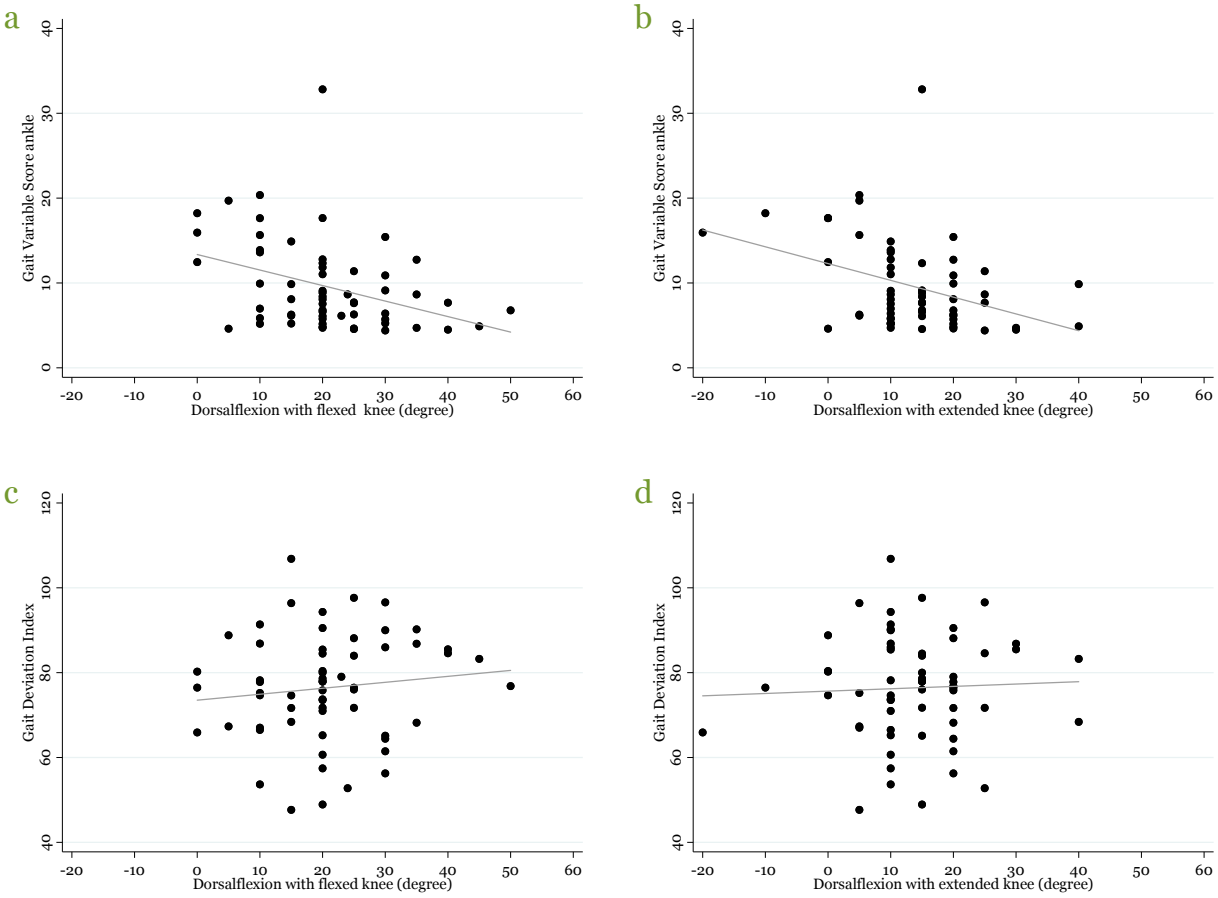


Figure 8. Examples of scatterplot of the correlation of Gait Variable Score of the ankle (a - b) and Gait Deviation Index (c - d) versus passive range of motion in dorsiflexion with flexed (a - c) and extended knee (b - d).

6. Discussion

In the following sections the methods and results are discussed and the ethical considerations are presented.

6.1. Applied methods

The overall topic of the thesis is the use of gait analysis in children with spastic cerebral palsy. The participants were not assessed by a paediatrician to evaluate and confirm the diagnosis of spastic cerebral palsy at the time of inclusion in the studies. However, the participants were recruited on the basis of their participation in the Cerebral Palsy follow-Up Program, and at all baseline assessments an experienced physiotherapist participated and confirmed the clinical signs of spastic cerebral palsy.

In the use of gait analysis, as for most outcome measures used in clinical science, one must be aware that uncertainties associated with the techniques used might lead to problems regarding the accuracy of the data collected. The Helen Hayes marker set and corresponding Plug-in-Gait model [60] used was derived from normal adults and the relationship between bones, joint centres and muscles might be different in children with cerebral palsy. Furthermore, the models depend on consistent marker placement on the participant, which sometimes is difficult due to the need for the child to stand still for long periods of time. The potential problems with marker placements was minimized by having well-trained teams of two people conducting the gait analysis and by adapting the marker placement situation to the wishes of the individual child. Furthermore, test-retest reliability in our laboratory was established on a similar patient group in study I. Thus, intrinsic and extrinsic variations of outcome measures were provided before initiation of study II.

Summary measures of gait

Summary measures of gait (Gait Deviation Index, Gait Profile Score and Gait Variable Score) were used as outcome measures in the studies. An advantage of the summary measures is that they use the gait pattern across the most important joints and movements in the lower extremities through the entire gait cycle to calculate a single score. For patients, parents, clinicians and other non-experts, a single score is more easily interpreted compared with a comprehensive report, describing all the detailed information collected during the gait analysis. However, the absolute reliability with the smallest detectable change reported in Study I meant that to accurately claim a true change in the individual child, relatively large changes in gait were necessary. Furthermore, the usability of the summary measures in the interpretation of the results of a gait analysis was limited, since the measures could not be used to identify the impairments causing the features affecting the score.

The use of a single score to evaluate changes in gait may be preferable in studies of patients, where the features impacting gait can be seen in a range of different joints and movements. This is the case in children with cerebral palsy, compared with the use of selected features from the gait cycle, such as maximal ankle dorsiflexion in stance or knee extension in initial contact. A few disadvantages in the use of summary measures as outcome measures has been reported: the lack of direction specificity which might lead to underestimation of change [84] , the distribution of the Gait Profile Score and Gait Variable Score data that is generally not considered normal [47] and the impact of gait speed [47, 48]. The disadvantages can to some extent be addressed during planning of the study, especially the impact of gait speed, which can be minimised using a speed-matched reference group. Furthermore, matching the walking speed of the participants during data collection at follow-up has been used [85]. In Study II, we planned to use this approach, but it proved impossible to instruct the children to walk at a certain walking speed.

There is growing evidence for the use of the Gait Deviation Index in children with cerebral palsy [65, 86]. However, this measure has been criticised because responsiveness has only been documented in relation to orthopaedic surgery [86]. Furthermore, a strong correlation between baseline scores and the change scores has been reported, in patient undergoing total hip artrplasty which supports a theory of a risk of ceiling effect [87].

Study I. Test-retest

Before using summary measures of gait to evaluate effectiveness in a randomised controlled trial, we documented the intra-rater reliability and agreement across two repeated sessions for the Gait Deviation Index, Gait Profile Score and Gait Variable Score. To reflect the inclusion and exclusion criteria in the intervention study, we decided on relatively narrow inclusion criteria, which might have affected the results of the study. This decision has limited the external validity of the study and might have constrained the reliability results, since the study sample was a selected group of children with cerebral palsy who were relatively homogeneous. However, the decision might have improved the possibility of achieving reasonable agreement and absolute reliability [82].

The sample size in studies of clinimetric properties of outcome measures is debated. The Guidelines for Reporting Reliability and Agreement Studies (GRAAS) [88], which we used in our planning of the study, acknowledge that the decision on sample size is not a simple one. These guidelines state that articles should explain how the sample size was chosen and state the number and characteristics of raters, subjects and replicated observations. Based on a sample size calculation, we included 18 participants and a total of 36 legs and used three assessor teams and two repeated measures of the same subject, which in the context of other studies in the field seems to be acceptable. A recent systematic review of clinimetric properties on measures of gait and walking refers to the original criteria described by Consensus-bases Standards for the selection of health status Measurement Instruments (COSMIN), that all studies with a sample size below 30 are given the methodological rating ‘Poor’ [89, 90]. The systematic review documents that only half of the studies on the subject include more than 30 participants and include studies with as few as four participants with cerebral palsy [90].

The methodologically optimal timing of the repeated sessions of gait analysis was expected to be at the same time and on the same weekday, where the child's activity levels during the days before the examination were comparable. However, to include the participants within an acceptable period of time, this was not possible. Consequently, the planning was balanced between the family's preferences, logistical constraints and the optimal timing, and the only absolute rule in the planning of the sessions was a maximum period between the sessions of 10 days.

Study II. Randomised controlled trial
The randomised controlled trial design is considered the 'gold standard' for clinical studies, and provides the most reliable evidence on the effectiveness or efficacy of healthcare interventions [91]. Study II was registered at ClinicalTrials.gov before enrolment of the first participants, the study protocol was published in an international peer-reviewed journal, the statistical analysis plan was published at ClinicalTrials.gov before unblinding of the data, and the results reported according to the CONSORT statement. Furthermore, only five participants were lost to follow-up on the primary outcome at 52 weeks, and only two participants did not complete any of the patient-reported outcome questionnaires, and thus, were completely lost at 52 weeks follow-up. These are all important requirements for a trial being rated as a high quality randomised controlled trial.

The total population of children with spastic cerebral palsy in the Region of Southern Denmark and the North Denmark Region were invited to participate in the study by their local healthcare teams in the CPUP. Together with few exclusion criteria, this strengthens the external validity and generalisability of the results from Studies II and III. Since it has been reported that the CPUP reduces the secondary consequences of cerebral palsy [92-94], the use of the surveillance program in the areas of recruitment may have reduced the proportion of children who are likely to experience severe secondary consequences of their cerebral palsy, such as reduced passive range of motion, compared with areas that do not offer a prevention program.

The relatively young age group was chosen for the study to ensure inclusion of participants at an age before the development of extensive and fixed deformities that might cause severe impairments and associated gait pathology [7]. Furthermore, the young age group was chosen for pragmatic reasons to avoid children being excluded because of earlier interventions in the form of orthopaedic surgery and to reduce the risk of participants dropping out or crossing over as part of clinical practice ('usual care'). However, this methodological decision restricts the relevance of the current findings to a relatively young age group and consequently reduces the generalisability of the results.

The decision to include children at GMFCS levels I and II was made to ensure valid data from the gait analysis to be used as the primary outcome measure. However, this may have limited the generalisability of the study results.

The sample size calculation was based on a minimum clinically important difference of 7.9 in the Gait Deviation Index, corresponding to a change of 10% as suggested by Schwartz et al. [30]. The minimum clinically important difference of 10% was used by Schwartz et al. to evaluate outcomes of orthopaedic surgery and selective dorsal rhizotomy. However, that degree of change might have been too optimistic for our study

sample and the interventions used. Furthermore, the Gait Deviation Index has recently been criticised since responsiveness has only been established in patients with cerebral palsy undergoing orthopaedic surgery [90]. The findings of the current study do not show that the experimental intervention has superior impact on the change score of the primary outcome, Gait Deviation Index - a finding that is supported by the secondary outcomes. Thus, it cannot be assumed that the missing difference on the primary outcome, Gait Deviation Index, is due to lack of responsiveness.

In the study, we used a pragmatic approach to reflect common clinical practice and ensure high external validity and generalisability of the results. This is in contrast to studies emphasising internal validity that are carried out in an 'ideal setting' with highly selected participants, practitioners and hospitals [95]. The pragmatic approach can be seen as a limitation, since reduced adherence to the recommended interventions and inconsistency in the delivery of the interdisciplinary interventions may have affected the results. One could argue that formal training in the use of the results from the gait analysis and the interventions recommended could have had an impact on the study results. A more detailed explanatory approach could have counteracted these issues but would have risked a conclusion of less value for current clinical practice, with reduced external validity and generalisability.

The use of the Impairment-Focused Interpretation approach in the interpretation of the data from the gait analysis was chosen to ensure a structured and transparent method to prepare the report. It would have been preferable if the method could have been tested in clinical practice and investigated for its ability to identify features and underlying impairments before its use in the study. However, this was not possible for our study.

A limitation in the design and outcome measures used is the lack of a standardised and detailed description of the specific interventions offered to the families, the specific applied intervention and reasons for not offering or applying interventions. This challenge is broader than the design of our study, as there are also numerous different interventions provided by medical practitioners or allied health professionals in the community and a pronounced lack of consensus about the naming of these interventions [14].

The primary follow-up period of 52 weeks was chosen to balance the desire for (i) a short follow-up for the interventions' spasticity management and physiotherapy and (ii) sufficient time for the effects of orthopaedic surgery and orthotics to be measureable, which might take as long as 24 months to emerge [96]. Based on the reported interventions applied in the study, one can speculate that a shorter follow-up (i.e. 16 weeks post release of the report) would have been more sensitive. Our study was designed to evaluate long-lasting effectiveness however, and extra follow-up at 16 or 20 weeks post start of the interventions would have been methodologically preferable but difficult to implement and not feasible for the study's sample. In addition, it could have been relevant to plan the timing of the gait analysis and the release of the report to coincide with the examinations and interdisciplinary consultations offered by the local healthcare teams. In the planning of the study, this was not considered possible, which means that for some participants, there may have been a longer period of time from the release of the report to their local healthcare team having an opportunity to discuss the recommended

interventions.

The study included a wide range of outcome measures that covered all dimensions of the International Classification of Functioning, Disability and Health [97] that seemed relevant to the participants, their parents and the healthcare professionals. As the primary outcome, we used the summary measure, the Gait Deviation Index. The properties of the measure were discussed previously in section 6.1.1. Summary measures of gait. Measures used to document the effectiveness of interventions should ideally be relevant to participants, such as survival or health-related quality of life [91]. Although it has been documented that gait plays an important role for children and their parents [11], the Gait Deviation Index must be considered as a surrogate outcome and may not be directly relevant for the participants.

6.1.4. Study II.I Cross-sectional

To investigate potential associations between outcomes of different constructs at a specific moment in time, the cross-sectional design was used. However, the study design does not allow conclusions about causality nor the extent to which the traffic light categories are able to identify children who are at risk of developing secondary consequences, such as deformities of the foot. Furthermore, the strength of our results is limited by the relatively small sample size.

The study sample of relatively young children with cerebral palsy may have reduced the number of participants with yellow and red threshold values in passive range of motion in ankle dorsiflexion, and thereby limited the strength of the results based on the groups formed by the three traffic light categories in Study III.

The rationale for the focus on the ankle joint is that reduced passive range of motion, at this specific joint, is quite common in our study sample of relatively young and well-functioning children with spastic cerebral palsy [7]. Despite the focus on joint mobility in the patients, it is well known that there is a large variability of goniometric measurements of passive range of motion [98].

6.2. Study findings and current evidence

Study I. Test-retest

The study provides evidence of the Gait Deviation Index and Gait Profile Score having excellent reliability and acceptable agreement in a group of children with cerebral palsy. However, the study also revealed a large variability in some of the Gait Variable Scores, which highlights the need for careful consideration in research and clinical practice. The study supports the use of gait summary measures in children with spastic cerebral palsy at GMFCS levels I and II at a relatively early age (8.0 ±1.2 years). The results observed in the study are comparable with the reported reliability of other outcomes retrieved from gait analysis [49, 90, 99].

Study II. Randomised controlled trial

Study II investigated the effectiveness of using gait analysis in the interdisciplinary interventions for 60 participants with cerebral palsy at GMFCS levels I or II, (median age 6 years 11months), who were randomised to the experimental or control group. No superior effectiveness in the change scores of the experimental compared with the con-

trol group were documented at 26 weeks or 52 weeks follow-up for measures of gait, health, pain, participation in normal daily activities or health-related quality of life. Thus, the study did not provide evidence for the use of gait analysis in the interdisciplinary interventions in a case-mix of children with cerebral palsy at GMFCS levels I and II, at an early age.

Our results agree with a previous randomised controlled trial on the outcome of lower extremity orthopaedic surgery with and without gait analysis [42]. The study reported lack of compliance between the recommended interventions and the interventions applied, as in our study. Several studies have reported the degree of compliance [25-28], but only a few have documented the reasons for the lack of compliance [8]. These reasons included a decision by the surgeon, a request from the patient/family and a change in patient status. The lack of compliance may also be caused by the absence of consensus about the interpretation and reporting of data, and the fact that even though the data from the gait analysis are objective, the interpretation and recommendations are to some extent subjective [40]. Lofterod et al. (2007) suggest that discussion of the recommendations with the surgeon who will perform the operation might improve the compliance [25].

In our study, the timing of the gait analysis and release of the report and recommendation to the interdisciplinary consultations offered by the paediatric departments might have improved the compliance. In practice, this could mean that the gait analysis, interpretation, recommendation and dissemination should be completed within a pre-defined time period and that the participants meet with their local healthcare team immediately after the report is available, to discuss the recommendations and decide on treatment.

An explanation for the lack of difference in the change scores between the groups may be the interventions recommended and applied. During the study, some of the healthcare professionals involved in the local teams expressed uncertainty about the recommended interventions and how they should be used in clinical practice (i.e. how the progressive resistance should be applied to improve muscle strength in the Tibialis Anterior or how often the training should be applied to be effective). This suggests that there might be a lack of common use and understanding of interventions across sectors and interdisciplinary professional groups. Furthermore, only a few studies of high quality have investigated the effectiveness of interventions to improve the impairments identified by gait analysis, making it uncertain as to what extent the applied intervention has the potential to affect the impairments [14].

Study III. Cross-sectional

This study showed that threshold values (traffic light categories) on passive range of motion in ankle dorsiflexion used by the CPUP were moderately associated with measures of gait that are specific to movement in the ankle (the Gait Variable Score ankle and peak dorsiflexion) in this sample, but not with measures of overall gait function, walking or gross motor capacity or performance. The study questions the clinical value of the categories for assessing overall gross motor function, but emphasises their value to identify isolated deviation of ankle movement during gait.

Our findings accord with the relationship between changes in passive range of motion and gait function reported in a study investigating the effects of gastrocnemius fascia lengthening in 19 children with cerebral palsy [31]. They establish a stronger association between the changes in passive range of motion in ankle dorsiflexion after surgical Gastrocnemius fascia lengthening and ankle specific gait function measured with the Gait Variable Score ankle, compared with overall gait function measured with the Gait Deviation Index [31, 63, 67].

To our knowledge, the threshold values on passive range of motion used by the CPUP have not previously been investigated as to whether they:

> *"ensure that the patient has enough passive range of motion to perform adequate dorsiflexion in walking"* [16a].

6.3. Ethical considerations

The children were included in the studies after they and their parents had given their informed consent. Their participantion were based on interest and not on a referral from their paediatrician or a paediatric orthopaedic surgeon. All participants received the results from their examinations either after their baseline assessment (Study I and the experimental group in Study II) or after their follow-up assessment (the control group in Study II). This was done since the effectiveness of gait analysis in the interdisciplinary interventions was unknown.

Very few children experienced discomfort during the assessments, but some children felt too tired to complete the entire assessment. When this happened, the child was asked if they wanted to continue the assessment, and if not, the child's choice was accepted and the healthcare team focussed on the participation in the parts of the assessment that the child had completed.

In Study II, some parents expressed that parts of the questionnaires were difficult to answer or generated reflections and thoughts about their situations. In these cases, the team explained the purpose of the questionnaires, answered any queries that had arisen or referred the parents to their local healthcare team for further discussion.

From an ethical point of view, the experiences and efforts of the participants are considered acceptable, given the purpose of the studies.

7. Conclusion

Study I. Test-retest
The Gait Deviation Index and Gait Profile Score demonstrated excellent reliability and acceptable agreement, proving that they can both be used in research and clinical practice. However, the observed large variability in some of the Gait Variable Scores requires cautious consideration when selecting outcome measures for children aged 5 to 12 years with cerebral palsy at GMFCS levels I and II.

Study II. Randomised controlled trial
This study could not confirm the hypothesis that improvement in the overall gait pathology, walking performance and patient-reported outcomes following individually tailored interventions when gait analysis is used are superior to those following 'usual care' in a case-mix of all children with cerebral palsy at GMFCS levels I and II, at an early age.

Study III. Cross-sectional
Passive range of motion in ankle dorsiflexion is moderately associated with ankle-specific measures of gross motor function (Gait Variable Score ankle and peak dorsiflexion), and the mean scores of the ankle-specific measures were different in the three categorical groups. In contrast to our hypothesis, we did not find an important relationship between pas¬sive range of motion in ankle dorsiflexion or the three related categories and overall measures of gross motor capacity or the use of gross motor skills in everyday life.

8. Perspectives

Gait analysis using the Gait Deviation Index has been used as a 'gold standard' measure of gait in children with cerebral palsy [90]. However, it is important to keep in mind that there are areas of the clinimetric properties of the Gait Deviation Index still to be investigated, such as the responsiveness of the measure and also the risk of a ceiling effect when the gait pattern is close to normal (which results in the Gait Deviation Index scoring close to 100).

The randomised controlled trial did not provide the expected evidence for the use of gait analysis in clinical practice in a case-mix of children with cerebral palsy at GMFCS levels I and II, at an early age. The highly specialised examination may still be relevant in many situations, for example, if a functional diagnosis of impairments affecting gait or documentation of changes after interventions are needed. Knowledge and evidence about which specific children with cerebral palsy may benefit from the use of gait analysis in clinical practice is lacking.

Exploratory data collected during Study II calls for further investigations that are beyond the scope of this thesis. One could have investigated differences in the change scores in the explorative outcome measures, characteristics of the responders and non-responders and to what extent the clinical examination or the patient-reported outcome measures could be used to detect children who have extensive deviations in gait who could potentially benefit from gait analysis. Furthermore, there is an obvious need to focus research on interpretation, reporting and dissemination of results and recommendations from gait analysis and on the process, where healthcare professionals incorporate the results and recommendations into clinical decision-making and thus comply with those recommendations.

The study of the clinical value of measures of passive range of motion and the three traffic light categories of dorsiflexion for indicating gross motor function in children with cerebral palsy did not have the casaulity to change clinical practice, but the study does highlight the need for further research to ensure valid tools to support clinical decision-making. Extensive validation of the follow-up program to reduce development of hip dislocation has been performed, including documentation that passive range of motion is a poor indicator of the risk of hip displacement [100]. The large amount of information in the clinical databases of the CPUP in Sweden, Norway and Denmark could be used to investigate the extent to which the measurement of passive range of motion and the three traffic light categories could be used as indicators of the development of secondary consequences, such as decreasing use of walking / standing functions or deformities in bones and joints.

9. Summary

English summary

The majority of ambulatory children with cerebral palsy experience an altered gait pattern or other walking difficulties and are dependent on healthcare interventions throughout their childhood. In the Nordic countries, a surveillance program and associated database, called the Cerebral Palsy follow-Up Program (CPUP) are used to ensure timely and consistent examinations. The interventions offered to children with cerebral palsy are based upon clinical examinations and standardised measures of overall gross motor function and functional mobility. However, the gait pattern, i.e. the manner of walking used by the child is not evaluated. This can be done with 3-dimensional instrumented gait analysis (gait analysis).

Gait analysis has been used in clinical practice and research for more than thirty years and is widely recognised as the 'gold standard' measure of gait in children with cerebral palsy. However, the potential added benefits of using gait analysis on gait, walking and patient-reported outcomes in the decision-making associated with interdisciplinary interventions to address impairments in gait have not been investigated. Thus, the overall aim of this thesis was to study the use of gait analysis in individually defined interdisciplinary interventions on gait, walking and patient-reported outcomes in children with cerebral palsy.

The starting point for the thesis was the investigation of intra-rater reliability and agreement of gait summary measures across two repeated sessions (later to be used in the randomised controlled trial). The study showed that the summary measures: the Gait Deviation Index and Gait Profile Score have excellent reliability and acceptable agreement. However, a large variability in some of the Gait Variable Scores was documented.

Having established documentation for the reliability and agreement of the Gait Deviation Index (primary outcome measure), a randomised controlled trial investigating the effectiveness of interdisciplinary interventions based on the use of gait analysis versus 'usual care' was conducted. A total of 60 children aged 5 to 8 years with spastic cerebral palsy at Gross Motor Function Classification System (GMFCS) levels I or II were randomised to the experimental or control group. No significant or clinically relevant between-group differences in the change scores of the primary outcome (Gait Deviation Index) or secondary outcome measures (1-min walk test, Pediatric Evaluation of Disability Inventory, The Pediatric Quality of Life Inventory Cerebral Palsy Module and The Pediatric Outcome Data Collection Instrument) were found at 26 weeks or 52 weeks follow-up. Showing that the addition of gait analysis in a case-mix of children with cerebral palsy at GMFCS levels I and II at an early age does not improve gait function, gross motor function and patient-reported outcome measures of disability and quality of life more than 'usual care' (without gait analysis).

Lastly, using a mechanistic approach to the data from the baseline assessment of the participants in the randomised controlled trial, we investigated the potential relationship between passive range of motion and passive traffic light categories used by the CPUP versus gait summary measures from the instruments' gait analysis, gross motor function and patient-reported outcome measures. We found that in our study sample, the range of motion in ankle dorsiflexion and the traffic light categories were correlated with measures of gait that are specific to movement in the ankle and not with measures of overall gait function, walking or gross motor capacity or performance.

In conclusion, the results of this thesis do not support the use of gait analysis in the decision-making of interdisciplinary intervention in a case-mix of children with cerebral palsy at GMFCS levels I and II, at an early age. Studies investigating which children with cerebral palsy could benefit from the use of gait analysis in clinical practice are warranted.

Danish summary - Dansk resume

De fleste gående børn med cerebral parese oplever at de bevæger anderledes and andre børn, og de vil ofte være afhængige af sundheds tilbud gennem hele deres barndom. I Danmark og de øvrige nordiske lande anvendes et opfølgningsprogram og en tilhørende database, kaldet CPOP – Opfølgningsprogram for Cerebral Parese (CPUP på svensk).

De overordnede mål med CPOP er at forbedre kvaliteten af sundhedstilbuddene til børn og unge med cerebral parese og begrænse udviklingen af sekundære følger hos det enkelte barn. Dette sker bl.a. ved at alle børn med cerebral parese tilbydes ensartede undersøgelser gennem hele barndommen. De tværfaglige indsatser til børn med cerebral parese, planlægges på baggrund af kliniske undersøgelser og standardiserede målemetoder til at vurdere grovmotorik og gang. Men barnets gangmønster evalueres ikke, hvilket kan gøres med 3-dimensionel klinisk ganganalyse.

Ganganalyse har været anvendt i klinisk praksis og forskning til børn med cerebral parese i mere end tredive år og er anerkendt som et 'guld standard' til vurdering af bevægelser under gang (gangmønstret) hos børn med cerebral parese. De mulige fordele ved at bruge ganganalyse i beslutninger om tværfaglige indsatser er ikke tidligere undersøgt. Det overordnede formål med afhandlingen er at undersøge effekterne af at anvende ganganalyse i individuelt tilpassede tværfaglige indsatser på ændringer i gangfunktionen hos børn med cerebral parese.

Første studie undersøgte pålidelighed og overensstemmelse for tre målemetoder, der beregner en samlet score for afvigelser i barnets bevægelserne under gang (Gait deviation Index, Gait Profile Score og Gait Variable Score). Resultaterne viste at de to overordnede score (Gait Deviation Index og Gait Profile Score) har en god pålidelighed og acceptabel overensstemmelse, mens en stor variation for nogle af Gait Variable Scores blev dokumenteret.

Herefter blev der gennemført et lodtrækningsstudie, hvor anvendelse ganganalyse i de tværfaglige tilbud til børn og unge med cerebral parese blev sammenlignet med det nuværende tilbud, hvor ganganalyse ikke tilbydes rutinemæssigt til alle børn. I studiet blev 60 børn med spastisk cerebral parese og gangfunktion uden hjælpemidler (GMFCS niveau I eller II) i alderen 5 til 8 år, tilfældigt fordelt mellem de to grupper. Ingen signifikante eller kliniske relevante forskelle blev dokumenteret imellem ændringerne i de to grupper ved 26 uger eller 52 ugers opfølgning. Resultaterne viser at brugen af ganganalyse til alle børn med cerebral parese og gangfunktion uden hjælpemidler (GMFCS niveau I og II) i en tidlig alder, ikke forbedrer gangmønstret eller deltagernes oplevelse af funktionsnedsættelen og livskvalitet.

Resultaterne i afhandlingen understøtter ikke brugen af ganganalyse i beslutninger om tværfaglige indsatser til alle børn med cerebral parese på GMFCS niveau I og II i en tidlig alder. Der er behov for forskningsprojekter, der fokuserer på hvilke grupper af børn med cerebral parese, der kan drage fordel af at ganganalyse anvendes.

10. References

1. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. Dev Med Child Neurol 2000, 42(12):816-824.

   [1a] Page 818 - 819.

2. Froslev-Friis C, Dunkhase-Heinl U, Andersen JD, Stausbol-Gron B, Hansen AV, Garne E: Epidemiology of cerebral palsy in Southern Denmark. Dan Med J 2015, 62(1):A4990.

3. Rosenbaum PL, Palisano RJ, Bartlett DJ, Galuppi BE, Russell DJ: Development of the Gross Motor Function Classification System for cerebral palsy. Dev Med Child Neurol 2008, 50(4):249-253.

4. Rodby-Bousquet E, Hagglund G: Better Walking Performance in Older Children With Cerebral Palsy. Clin Orthop Relat Res 2012, 470(5):11286-11293.

5. Shevell MI, Dagenais L, Hall N, Consortium R: Comorbidities in cerebral palsy and their relationship to neurologic subtype and GMFCS level. Neurology 2009, 72(24):2090-2096.

6. Wiley ME, Damiano DL: Lower-extremity strength profiles in spastic cerebral palsy. Dev Med Child Neurol 1998, 40(2):100-107.

7. Nordmark E, Hagglund G, Lauge-Pedersen H, Wagner P, Westbom L: Development of lower limb range of motion from early childhood to adolescence in cerebral palsy: a population-based study. BMC Med 2009, 7:65.

8. Wren TA, Rethlefsen S, Kay RM: Prevalence of specific gait abnormalities in children with cerebral palsy: influence of cerebral palsy subtype, age, and previous surgery. J Pediatr Orthop 2005, 25(1):79-83.

9. Imms C: Children with cerebral palsy participate: a review of the literature. Disabil Rehabil 2008, 30(24):1867-1884.

10. Liao HF, Jeng SF, Lai JS, Cheng CK, Hu MH: The relation between standing balance and walking function in children with spastic diplegic cerebral palsy. Dev Med Child Neurol 1997, 39(2):106-112.

11. Jaspers E, Verhaegen A, Geens F, Van Campenhout A, Desloovere K, Molenaers G: Lower limb functioning and its impact on quality of life in ambulatory children with cerebral palsy. Eur J Paediatr Neurol Society 2013, 17(6):561-567.

12. Vargus-Adams JN, Martin LK: Domains of importance for parents, medical professionals and youth with cerebral palsy considering treatment outcomes. Child Care Health Dev 2011, 37(2):276-281.

13. Rasmussen HM, Nordbye-Nielsen K, Moller-Madsen B, Johansen M, Ellitsgaard N, Pedersen CR, Rackauskaite G, Engberg H, Pedersen NW: The Danish Cerebral Palsy Follow-up Program. Clin Epidemiol 2016, 8:457-460.

14. Novak I, McIntyre S, Morgan C, Campbell L, Dark L, Morton N, Stumbles E, Wilson SA, Goldsmith S: A systematic review of interventions for children with cerebral palsy: state of the evidence. Dev Med Child Neurol 2013, 55(10):885-910.

15. Alriksson-Schmidt A, Hagglund G, Rodby-Bousquet E, Westbom L: Follow-up of individuals with cerebral palsy through the transition years and description of adult life: the Swedish experience. J Pediatr Rehabil Med 2014, 7(1):53-61.

16. Cerebral Parese Oppfølgingsprogram (CPOP): Alarmverdier for passive bevegeutslag 2014

    [16a] Page 1.

17. Alriksson-Schmidt AI, Arner M, Westbom L, Krumlinde-Sundholm L, Nordmark E, Rodby-Bousquet E, Hagglund G: A combined surveillance program and quality register improves management of childhood disability. Disabil Rehabil 2016:1-7.

    [17a] Page 54.

18. Morris C, Bowers R, Ross K, Stevens P, Phillips D: Orthotic management of cerebral palsy: recommendations from a consensus conference. NeuroRehabilitation 2011, 28(1):37-46.

19. Heinen F, Desloovere K, Schroeder AS, Berweck S, Borggraefe I, van CA, Andersen GL, Aydin R, Becher JG, Bernert G et al: The updated European Consensus 2009 on the use of Botulinum toxin for children with cerebral palsy. Eur J Paediatr Neurol 2010, 14(1):45-66.

20. Paul SM, Siegel KL, Malley J, Jaeger RJ: Evaluating interventions to improve gait in cerebral palsy: a meta-analysis of spatiotemporal measures. Dev Med Child Neurol 2007, 49(7):542-549.

21. Baker R, Esquenazi A, Benedetti MG, Desloovere K: Gait analysis: clinical facts. Eur J Phys Rehabil Med 2016, 52(4):560-574.

22. Gage JR: The role of Gait Analysis in the Treatment of Cerebral-Palsy. J Pediatr Orthop 1994, 14(6):701-702.

23. Deluca PA, Davis RB, Ounpuu S, Rose S, Sirkin R: Alterations in surgical decision making in patients with cerebral palsy based on three-dimensional gait analysis. J Pediatr Orthop 1997, 17(5):608-614.

24. Cook RE, Schneider I, Hazlewood ME, Hillman SJ, Robb JE: Gait analysis alters decision-making in cerebral palsy. J Pediatr Orthop 2003, 23(3):292-295.

25. Lofterod B, Terjesen T, Skaaret I, Huse AB, Jahnsen R: Preoperative gait analysis has a substantial effect on orthopedic decision making in children with cerebral palsy - Comparison between clinical evaluation and gait analysis in 60 patients. Acta Orthop 2007, 78(1):74-80.

26. Wren TA, Elihu KJ, Mansour S, Rethlefsen SA, Ryan DD, Smith ML, Kay RM: Differences in implementation of gait analysis recommendations based on affiliation with a gait laboratory. Gait Posture 2013, 37(2):206-209.

27. Wren TA, Woolf K, Kay RM: How closely do surgeons follow gait analysis recommendations and why? J Pediatr Orthop B 2005, 14(3):202-205.

28. Kay RM, Dennis S, Rethlefsen S, Reynolds RAK, Skaggs DL, Tolo VT: The effect of preoperative gait analysis on orthopaedic decision making. Clin Orthop Relat Res 2000(372):217-222.

29. Roberts A, Stewart C, Freeman R: Gait analysis to guide a selective dorsal rhizotomy program. Gait Posture 2015, 42(1):16-22.

30. Schwartz MH, Viehweger E, Stout J, Novacheck TF, Gage JR: Comprehensive treatment of ambulatory children with cerebral palsy: an outcome assessment. J Pediar Orthop 2004, 24(1):45-53.

31. Galli M, Cimolin V, Crivellini M, Albertini G: Gait analysis before and after gastrocnemius fascia lengthening in children with cerebral palsy. J Appl Biomater Biomech 2005, 3(2):98-105.

32. Baird MW, Vargus-Adams J: Outcome measures used in studies of botulinum toxin in childhood cerebral palsy: a systematic review. J Child Neurol 2010, 25(6):721-727.

33. Bandholm T, Jensen BR, Nielsen LM, Rasmussen H, Bencke J, Curtis D, Pedersen SA, Sonne-Holm S: Neurorehabilitation with versus without resistance training after botulinum toxin treatment in children with cerebral palsy: a randomized pilot study. Neuro Rehabilitation 2012, 30(4):277-286.

34. Van den Broeck C, De Cat J, Molenaers G, Franki I, Himpens E, Severijns D, Desloovere K: The effect of individually defined physiotherapy in children with cerebral palsy (CP). Eur J Paediatr Neurol 2010, 14(6):519-525.

35. Franki I, Van den Broeck C, De Cat J, Tijhuis W, Molenaers G, Vanderstraeten G, Desloovere K: A randomized, single-blind cross-over design evaluating the effectiveness of an individually defined, targeted physical therapy approach in treatment of children with cerebral palsy. Clin Rehabil 2014, 28(10):1039-1052.

36. Baker R: Measuring Walking. A Handbook of Clinical Gait Analysis, vol. 1, 1 edn. Hampshire: Mac Keith Press; 2013.

37. Miller F: Physical Therapy of Cerebral Palsy. New York: Springer; 2007.

38. Russell DJ, Wright M, Rosenbaum PL, Avery LM: Gross motor function measure (GMFM-66 & GMFM-88) User's manual, Second edition. edn. London: Mac Keith Press; 2013.

39. McDowell BC, Humphreys L, Kerr C, Stevenson M: Test-retest reliability of a 1-min walk test in children with bilateral spastic cerebral palsy (BSCP). Gait Posture 2009, 29(2):267-269.

40. Skaggs DL, Rethlefsen SA, Kay RM, Dennis SW, Reynolds RA, Tolo VT: Variability in gait analysis interpretation. J Pediatr Orthop 2000, 20(6):759-764.

41. Narayanan UG: Management of Children With Ambulatory Cerebral Palsy: An Evidence-based Review. J Pediatr Orthop 2012, 32 Suppl 2:S172-181.

42. Wren TA, Otsuka NY, Bowen RE, Scaduto AA, Chan LS, Dennis SW, Rethlefsen SA, Healy BS, Hara R, Sheng M et al: Outcomes of lower extremity orthopedic surgery in ambulatory children with cerebral palsy with and without gait analysis: results of a randomized controlled trial. Gait Posture 2013, 38(2):236-241.

43. Baker R, McGinley J, Thomason P: Impairment Focused Interpretation. In. Manchester: University of Salford; 2009.

44. Gage JR, Schwartz MH, Koop SE, Novacheck TF: The Identification and treatment of gait problems in cerebral palsy. London: Mac Keith Press; 2009.

45. Deluca PA: Gait Analysis in the Treatment of the Ambulatory Child with Cerebral-Palsy. Clin Orthop Relat Res 1991(264):65-75.

46. Thomason P, Graham HK: A systematic review of interventions for children with cerebral palsy: the state of the evidence. Dev Med Child Neurol 2014, 56(4):390-391.

47. Baker R, McGinley JL, Schwartz MH, Beynon S, Rozumalski A, Graham HK, Tirosh O: The Gait Profile Score and Movement Analysis Profile. Gait Posture 2009, 30(3):265-269.

48. Schwartz MH, Rozumalski A, Trost JP: The effect of walking speed on the gait of typically developing children. J Biomech 2008, 41(8):1639-1650.

49. Miller F CP, Richards J, Lennon N, Quigley E, Nijiler T: Reliability of kinematics during clinical gait analysis: A comparison between normal and children with cerebral palsy. Gait Posture 1996, 22:9.

50. Palisano R, Rosenbaum P, Walter S, Russell D, Wood E, Galuppi B: Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol 1997, 39(4):214-223.

51. Palisano RJ, Hanna SE, Rosenbaum PL, Russell DJ, Walter SD, Wood EP, Raina PS, Galuppi BE: Validation of a model of gross motor function for children with cerebral palsy. Phys Ther 2000, 80(10):974-985.

52. Wood E, Rosenbaum P: The gross motor function classification system for cerebral palsy: a study of reliability and stability over time. Dev Med Child Neurol 2000, 42(5):292-296.

53. Graham HK, Harvey A, Rodda J, Nattrass GR, Pirpiris M: The Functional Mobility Scale (FMS). J Pediatr Orthop 2004, 24(5):514-520.

54. Harvey A, Baker R, Morris ME, Hough J, Hughes M, Graham HK: Does parent report measure performance? A study of the construct validity of the Functional Mobility Scale. Dev Med Child Neurol 2010, 52(2):181-185.

55. Harvey AR, Morris ME, Graham HK, Wolfe R, Baker R: Reliability of the functional mobility scale for children with cerebral palsy. Phys Occup Ther Pediatr 2010, 30(2):139-149.

56. Russell DJ, Rosenbaum PL, Cadman DT, Gowland C, Hardy S, Jarvis S: The gross motor function measure: a means to evaluate the effects of physical therapy. Dev Med Child Neurol 1989, 31(3):341-352.

57. Adair B, Said CM, Rodda J, Morris ME: Psychometric properties of functional mobility tools in hereditary spastic paraplegia and other childhood neurological conditions. Dev Med Child Neurol 2012, 54(7):596-605.

58. Russell DJ, Avery LM, Rosenbaum PL, Raina PS, Walter SD, Palisano RJ: Improved scaling of the gross motor function measure for children with cerebral palsy: evidence of reliability and validity. Phys Ther 2000, 80(9):873-885.

59. McDowell BC, Kerr C, Parkes J, Cosgrove A: Validity of a 1 minute walk test for children with cerebral palsy. Dev Med Child Neurol 2005, 47(11):744-748.

60. Davis RB, Ounpuu S, Tyburski D, J.R. G: A gait analysis data collection and reduction technique. Hum Mov Sci 1991, 10(5):575-587.

61. Schwartz MH, Rozumalski A: The Gait Deviation Index: a new comprehensive index of gait pathology. Gait Posture 2008, 28(3):351-357.

62. Molloy M, McDowell BC, Kerr C, Cosgrove AP: Further evidence of validity of the Gait Deviation Index. Gait Posture 2010, 31(4):479-482.

63. Cimolin V, Galli M, Vimercati SL, Albertini G: Use of the Gait Deviation Index for the assessment of gastrocnemius fascia lengthening in children with Cerebral Palsy. Res Dev Disabil 2011, 32(1):377-381.

64. Massaad A, Assi A, Skalli W, Ghanem I: Repeatability and validation of Gait Deviation Index in children: Typically developing and cerebral palsy. Gait Posture 2014, 39(1):354-358.

65. Rasmussen HM, Nielsen DB, Pedersen NW, Overgaard S, Holsgaard-Larsen A: Gait Deviation Index, Gait Profile Score and Gait Variable Score in children with spastic cerebral palsy: Intra-rater reliability and agreement across two repeated sessions. Gait Posture 2015, 42(2):133-137.

66. Beynon S, McGinley JL, Dobson F, Baker R: Correlations of the Gait Profile Score and the Movement Analysis Profile relative toclinical judgments. Gait Posture 2010, 32:129-132.

67. Ferreira LA, Cimolin V, Costici PF, Albertini G, Oliveira CS, Galli M: Effects of gastrocnemius fascia lengthening on gait pattern in children with cerebral palsy using the Gait Profile Score. Res Dev Disabil 2014, 35(5):1137-1143.

68. Cerebral Parese Uppfölgnings Program (CPUP): Manual till CPUP - Fysioterapeuter - Pappersformulär 2017-01-01

69. Hayley SM CJ, Ludow LH, : Pediatric Evaluation of Disability Inventory (PEDI) Development, Standardization and Administration manual. Boston, MA: New England Center Hospital; 1992.

70. Christensen J: Anvendeligheden af PEDI som dansk spørgeskema. Danish. [The use of a Danish questionnaire version of PEDI]. Master thesis, Lunds Universitet; 2005.

71. Stahlhut M, Gard G, Aadahl M, Christensen J: Discriminative validity of the Danish version of the Pediatric Evaluation of Disability Inventory (PEDI). Phys Occup Ther Pediatr 2011, 31(1):78-89.

72. McCarthy ML, Silberstein CE, Atkins EA, Harryman SE, Sponseller PD, Hadley-Miller NA: Comparing reliability and validity of pediatric instruments for measuring health and well-being of children with spastic cerebral palsy. Dev Med Child Neurol 2002, 44(7):468-476.

73. Harvey A, Robin J, Morris ME, Graham HK, Baker R: A systematic review of measures of activity limitation for children with cerebral palsy. Dev Med Child Neurol 2008, 50(3):190-198.

74. Varni JW, Burwinkle TM, Berrin SJ, Sherman SA, Artavia K, Malcarne VL, Chambers HG: The PedsQL in pediatric cerebral palsy: reliability, validity, and sensitivity of the Generic Core Scales and Cerebral Palsy Module. Dev Med Child Neurol 2006, 48(6):442-449.

75. Stahlhut M, Wong CTK, Curtis D: Oversættelse af PedQL. Fag og Forskning 2010.

76. King MT: A point of minimal important difference (MID): a critique of terminology and methods. Expert Rev Pharmacoecon Outcomes Res 2011, 11(2):171-184.

77. Maanum G, Jahnsen R, Stanghelle JK, Sandvik L, Keller A: Effects of botulinum toxin A in ambulant adults with spastic cerebral palsy: a randomized double-blind placebo controlled-trial. J Rehabil Med 2011, 43(4):338-347.

78. Pascual-Pascual SI, Pascual-Castroviejo I, Ruiz PJ: Treating spastic equinus foot from cerebral palsy with botulinum toxin type A: what factors influence the results?: an analysis of 189 consecutive cases. Am J Phys Med Rehabil 2011, 90(7):554-563.

79. McMulkin ML, Baird GO, Gordon AB, Caskey PM, Ferguson RL: The pediatric outcomes data collection instrument detects improvements for children with ambulatory cerebral palsy after orthopaedic intervention. J Pediatr Orthop 2007, 27(1):1-6.

80. Freeman M: Gait. In: Physical Therapy of Cerebral Palsy. edn. Edited by Freeman M. Wilmington: Springer; 2007: 207-342.

81. S S Shapiro MBW: An analysis of variance test for normality (complete samples). Biometrika 1965, 52:591-611.

82. Lexell JE, Downham DY: How to Assess the Reliability of Measurements in Rehabilitation. Am J Phys Med Rehabil 2005, 84(9):719-723.

83. Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986, 1(8476):307-310.

84. Barton GJ, Hawken MB, Holmes G, Schwartz MH: A gait index may underestimate changes of gait: a comparison of the Movement Deviation Profile and the Gait Deviation Index. Comput Methods Biomech Biomed Engin 2015, 18(1):57-63.

85. Rosenlund S, Broeng L, Overgaard S, Jensen C, Holsgaard-Larsen A: The efficacy of modified direct lateral versus posterior approach on gait function and hip muscle strength after primary total hip arthroplasty at 12months follow-up. An explorative randomised controlled trial. Clin Biomech (Bristol, Avon) 2016, 39:91-99.

86. Cimolin V, Galli M: Summary measures for clinical gait analysis: a literature review. Gait Posture 2014, 39(4):1005-1010.

87. Jensen C, Rosenlund S, Nielsen DB, Overgaard S, Holsgaard-Larsen A: The use of the Gait Deviation Index for the evaluation of participants following total hip arthroplasty: An explorative randomized trial. Gait Posture 2015, 42(1):36-41.

88. Kottner J, Audige L, Brorson S, Donner A, Gajewski BJ, Hrobjartsson A, Roberts C, Shoukri M, Streiner DL: Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. Journal of clinical epidemiology 2011, 64(1):96-106.

89. Terwee CB, Mokkink LB, Knol DL, Ostelo RW, Bouter LM, de Vet HC: Rating the methodological quality in systematic reviews of studies on measurement properties: a scoring system for the COSMIN checklist. Qual Life Res 2012, 21(4):651-657.

90. Zanudin A, Mercer TH, Jagadamma KC, van der Linden ML: Psychometric properties of measures of gait quality and walking performance in young people with Cerebral Palsy: A systematic review. Gait Posture 2017, 58:30-40.

91. Moher D, Hopewell S, Schulz KF, Montori V, Gotzsche PC, Devereaux PJ, Elbourne D, Egger M, Altman DG: CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ 2010, 340:c869.

92. Hagglund G, Alriksson-Schmidt A, Lauge-Pedersen H, Rodby-Bousquet E, Wagner P, Westbom L: Prevention of dislocation of the hip in children with cerebral palsy: 20-year results of a population-based prevention programme. Bone Joint J 2014, 96-B(11):1546-1552.

93. Hagglund G, Andersson S, Duppe H, Lauge-Pedersen H, Nordmark E, Westbom L: Prevention of dislocation of the hip in children with cerebral palsy - The first ten years of a population-based prevention programme. Journal of Bone and Joint Surgery-British Volume 2005, 87B(1):95-101.

94. Hagglund G, Andersson S, Duppe H, Lauge-Pedersen H, Nordmark E, Westbom L: Prevention of severe contractures might replace multilevel surgery in cerebral palsy: results of a population-based health care programme and new techniques to reduce spasticity. J Pediatr Orthop B 2005, 14(4):269-273.

95. Zwarenstein M, Treweek S, Gagnier JJ, Altman DG, Tunis S, Haynes B, Oxman AD, Moher D, group C, Pragmatic Trials in Healthcare g: Improving the reporting of pragmatic trials: an extension of the CONSORT statement. BMJ 2008, 337:a2390.

96. Thomason P, Baker R, Dodd K, Taylor N, Selber P, Wolfe R, Graham HK: Single-Event Multilevel Surgery in Children with Spastic Diplegia A Pilot Randomized Controlled Trial. J Bone Joint Surg Am 2011, 93A(5):451-460.

97. World Health Organization: International Classification of Functioning, Disability and Health: Children & Youth Version: ICF-CY. Geneva; 2007.

98. McDowell BC, Hewitt V, Nurse A, Weston T, Baker R: The variability of goniometric measurements in ambulatory children with spastic cerebral palsy. Gait Posture 2000, 12(2):114-121.

99. McGinley JL, Baker R, Wolfe R, Morris ME: The reliability of three-dimensional kinematic gait measurements: a systematic review. Gait Posture 2009, 29(3):360-369.

100. Hagglund G, Lauge-Pedersen H, Wagner P: Characteristics of children with hip displacement in cerebral palsy. BMC Musculoskelet Disord 2007, 8:101.