

More than a foot: gait, gross motor skills, neurodevelopmental difficulties and health-related quality of life in children with idiopathic clubfoot



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Stockholm 2019

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Published by Karolinska Institutet.

Printed by Eprint AB 2019, Stockholm, Sweden.

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ISBN 978-91-7831-301-3

MORE THAN A FOOT: GAIT, GROSS MOTOR SKILLS, NEURODEVELOPMENTAL DIFFICULTIES AND HEALTH-RELATED QUALITY OF LIFE IN CHILDREN WITH IDIOPATHIC CLUBFOOT

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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“Once we accept our limits, we go beyond them”

Albert Einstein

ABSTRACT

Introduction: Idiopathic clubfoot (IC) is one of the most common congenital musculoskeletal deformities and can affect one or both feet of the child. However, knowledge beyond the structural deformity is still limited. This thesis aimed to evaluate unexplored fields by including measures that might affect the children's overall health. This included evaluation of gait, gross motor skills, neurodevelopmental difficulties (NDD), and health-related quality of life (HRQoL).

Methods and participants: An explorative cross-sectional research approach of four studies divided into two parts was used. In part one, gait and gross motor skills were evaluated in 59 and 47 children with IC, respectively, born in 2005–2008 and treated in Stockholm County (mean age 5.4 ± 0.5 years). Gait was evaluated using three-dimensional gait analysis, and gross motor skills were evaluated using the Clubfoot Assessment Protocol. For comparison, 28 typically developing (TD) children were recruited (mean age 5.5 ± 0.6 years). In part two, NDD and HRQoL were surveyed in children with IC born in 2004–2007 in Stockholm and Skåne counties. Parents to 106 children with IC (mean age 9.4 ± 0.6 years) answered the Five to Fifteen questionnaire and Royce's Disease-specific instrument to operationalise NDD and satisfaction of the clubfoot treatment outcome, respectively. The children answered the generic HRQoL questionnaire EQ-5D-Y. A general population sample of 109 community schoolchildren (mean age 9.5 ± 0.6 years) was used for comparison.

Results: Children with IC were found to have significant gait deviations, gross motor deficits and asymmetries at five years of age. No differences were found in bilateral and unilateral IC with the main concerns regarding decreased dorsi-plantar flexion range and ankle power generation in gait in both groups, compared with the TD children. In terms of gross motor skills, one-leg hop and stand deviated in 85 and 87% of the children, respectively. Associations between gross motor skills and passive range of motion of the foot, gait, and initial clubfoot severity were generally poor. The contralateral leg in children with unilateral IC showed no discrete gait or gross motor deficits; however, global gait measures revealed gait modifications. In nine-year-old children with IC, significantly more NDD were found in comparison with the general population, and group differences were evident in the domains of motor skills, perception, and language and in the subdomains of gross and fine motor skills, relation in space, comprehensive, and expressive language skills. Thirty-one per cent of the children in the IC sample were defined as experiencing NDD of clinical relevance. In this subgroup, parents reported significantly lower satisfaction of the clubfoot treatment outcome. In the overall IC sample of nine-year-old children, the children reported a satisfying overall health status despite more HRQoL problems, mainly regarding pain and discomfort. Neither being born with one or two affected feet nor sex affected NDD or HRQoL, however NDD negatively affected HRQoL.

Conclusions: Children with bilateral and unilateral IC have similar marked gait and gross motor deficits on the affected side, thus indicating similar clubfoot severity and development. Nonetheless, awareness of foot involvement is important because of pronounced asymmetries in children with unilateral IC. Gross motor skills are not related to several foot measures and should be considered a different outcome entity in the evaluation of IC. Therefore, gross motor assessment as well as pain management should be emphasised in the follow-up of children with IC. Finally, health care providers should be attentive to NDD in children with IC appearing more often than would be expected by chance, especially since NDD negatively affect clubfoot treatment outcome and HRQoL.

LIST OF SCIENTIFIC PAPERS

- I. **Lööf E**, Andriess H, André M, Böhm S, Broström EW. Gait in 5-year- old children with idiopathic clubfoot: A cohort study of 59 children, focusing on foot involvement and the contralateral foot. *Acta Orthopaedica*. 2016, 87: 522-28
- II. **Lööf E**, Andriess H, André M, Böhm S, Iversen MD, Broström EW. Gross motor skills in children with idiopathic clubfoot and the association between gross motor skills, foot involvement, gait and foot motion. *Journal of Pediatric Orthopaedics*. 2017, Feb 24. doi: 10.1097/BPO.0000000000000964
- III. **Lööf E**, Andriess H, Broström EW, André M, Bölte S. Neurodevelopmental difficulties in children with idiopathic clubfoot. *Developmental Medicine & Child Neurology*. 2019, 61: 98-104
- IV. **Lööf E**, Andriess H, Broström EW, André M, Böhm S, Bölte S. Neurodevelopmental difficulties negatively affect health-related quality of life in children with idiopathic clubfoot. *Acta Paediatrica*. 2018, Dec 27. doi: 10.1111/apa.14709

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LIST OF ABBRIVATIONS

3DGA	Three-Dimensional Gait Analysis
ADHD	Attention-Deficit/Hyperactivity-Disorder
ANOVA	Analysis of Variance
ASD	Autism Spectrum Disorder
BOT	Bruininks-Oseretsky Test of Motor Proficiency
CAP	Clubfoot Assessment Protocol
CI	Confidence Interval
DCD	Developmental Coordination Disorder
DSI	Disease Specific Instrument
DSM	Diagnostic and Statistical Manual of Mental Disorders
FTF	Five to Fifteen
GDI	Gait Deviation Index
HRQoL	Health-Related Quality of Life
IC	Idiopathic Clubfoot
ICF	International Classification of Functioning, Disability and Health
ITW	Idiopathic Toe Walking
LMIC	Low-income and Middle-Income Countries
MABC	Movement Assessment Battery for Children
MANOVA	Multivariate Analysis of Variance
MQ	Motion Quality
NDD	Neurodevelopmental Difficulties
Nm/kg	Newton-meter per kilogram
PDMS	Peabody Developmental Motor Scale
PROM	Patient-Reported Outcome Measure
SD	Standard Deviation
SF-36	36-Item Short Form Health Survey
TD	Typically Developing
VAS	Visual Analogue Scale
W/kg	Watts per kilogram

THESIS AT A GLANCE

Study	Aim	Methods	Results	Conclusions
I	To evaluate gait in children with IC with extra focus on foot involvement (bi- and unilateral IC) and the contralateral leg, in comparison with TD children.	Gait was evaluated in 59 children with IC and 28 TD children using 3DGA, including discrete gait parameters, GDI, and GDI-Kinetic.	Similar gait deviations were found in bi- and unilateral IC in comparison with TD legs, with decreased foot motions and lack of ankle power as the main concerns. The contralateral leg showed no deviations in discrete gait parameter compared with TD legs, but global gait modifications to the affected clubfoot side were found in GDI/GDI-Kinetic.	Bi- and unilateral IC show the same gait deviations and can be clustered as one uniform group when evaluating gait. However, in children with unilateral IC gait deviations might be perceived as poorer due to asymmetries. The contralateral leg should not be used as a reference in gait.
II	To evaluate gross motor skills in children with IC compared with TD children. Additionally, to explore the impact of foot involvement and associations between gross motor skills, gait, passive foot motion, and initial clubfoot severity.	Gross motor skills were evaluated using the MQ-domains from CAP in 47 children with IC and in 28 TD children. GDI and GDI-Kinetic were calculated from 3DGA. The Dimeglio classification scale defined initial clubfoot status before treatment.	Poorer gross motor skills, gait, and passive foot motion as well as gross motor asymmetries were found in children with IC compared with TD children. One-leg stand and one-leg hop deviated in the majority of the children with IC regardless of foot involvement. Contralateral legs showed similar gross motor skills as legs of TD children. Gross motor skills correlated poorly to moderately with GDI, GDI-Kinetic, passive foot motion, and initial clubfoot status.	Gross motor deficits and asymmetries are present in children with both bi- and unilateral IC. Gross motor skills seem to represent a different outcome entity in regards to traditional outcome measures such as passive foot motion and should be evaluated in the follow-up of IC.
III	To examine NDD in a cohort of children with IC compared with the general population.	NDD were evaluated in 106 children with IC and 109 age-, sex-, and residential parallellised community schoolchildren using the FTF questionnaire.	Group differences were found with more difficulties in the IC sample in the total FTF and the domains of motor skills, perception, and language; and the subdomains of gross and fine motor skills, relation in space, comprehensive, and expressive language skills. Thirty-one per cent of the children with IC showed clinically significant NDD. In this subgroup parents reported lower satisfaction of the clubfoot treatment outcome.	Increased prevalence of NDD in children with IC together with less satisfaction of the clubfoot treatment showed that NDD should be considered in the clinical practice of IC.
IV	To survey HRQoL in a cohort of children with IC in comparison with a general population sample, and the influence of sex, foot involvement, and NDD on HRQoL.	HRQoL was evaluated in the same participants as in Study III using the questionnaire EQ-5D-Y. FTF was collected to operationalise NDD.	Children with IC reported similar overall health status despite more problems in the domains of mobility, doing usual activities, and having pain/discomfort compared with the general population sample. Foot involvement and sex did not affect HRQoL, but NDD affected HRQoL negatively.	Children with IC experience satisfying overall health status despite higher reports of mainly pain/discomfort. HRQoL seems to be substantially affected by coexisting NDD in children with IC, thus health care providers should be attentive to both HRQoL and NDD in children with IC.

PREFACE

Clubfoot, and the management of clubfoot, has been known since the first documents of clubfoot from the 12th century B.C. in Egypt.¹ Idiopathic clubfoot has gone from a fairly severe condition causing disability and social unacceptance¹ to a condition hardly noticed in today's society if treated correctly. Still, there remains a lack of knowledge regarding several aspects of the condition beyond the structural deformity.

In the clinic, parents with an infant with idiopathic clubfoot often inquire if the child will experience pain, be able to walk, run, play with friends, and have “a normal life”. Some parents also wonder if it matters whether the child was born with one or two clubfoot deformities. Some questions can be answered from clinical knowledge and previous research, but there is still insufficient evidence to answer all of these questions. Furthermore, in clinical work a suspicion of additional difficulties in children with idiopathic clubfoot, apart from the musculoskeletal deformity, has been raised. Difficulties such as problems with attention and language, which cannot be explained by the status of the foot, question the notion of idiopathic clubfoot being an isolated musculoskeletal deformity. This thesis aimed to explore some of these questions, to broaden our understanding, and to fill the gaps of knowledge regarding children with idiopathic clubfoot. Finally, by studying these questions, the thesis aimed to look at idiopathic clubfoot from a wider perspective – to see the child, not just a foot.

The foundation of the thesis is four studies concerning different aspects of children with idiopathic clubfoot, and these are presented and discussed both individually and joint together with the intention to give an explicit understanding of the findings. Hopefully, at the end, this thesis will have taken us one step further and stretched the boundaries in the research and knowledge of children with idiopathic clubfoot.

Stockholm, 8 January 2019



Elin Lööf

1 INTRODUCTION

To date, most research in children with idiopathic clubfoot (IC), one of the largest patient groups in paediatric orthopaedics, has focused specifically on the structural deformity. This has given us valuable knowledge about the deformity itself as well as about important treatment factors. Thus significant improvements in the treatment of IC have emerged in recent decades, for example, the worldwide recognition of the Ponseti treatment method.²⁻⁴ However, knowledge beyond the structural deformity is still limited. The intention with this thesis was to stretch our knowledge beyond the musculoskeletal structure of the deformity. The International Classification of Functioning, Disability and Health (ICF) model inspired the conceptual framework of the thesis that included several measures beyond those of structural impairments/outcome measures. With the inspiration of the ICF, the intention was to study unexplored fields within IC that might affect the children's health status. Consequently, the studies within the thesis start with exploring the essentials of gait and gross motor skills in children with IC. Thereafter, exploratory studies follow regarding concerns about neurodevelopmental difficulties (NDD) and the effects on health-related quality of life (HRQoL) when being born with IC.

1.1 CLUBFOOT

Clubfoot, sometimes referred to as talipes equinovarus, is a complex deformity of the foot and lower leg (Figure 1) that can be detected already in utero.⁵⁻⁷ Clubfoot can be divided into two subtypes with various names:

Idiopathic/isolated/non-syndromic clubfoot, indicating that the deformity is an isolated deformity without other known abnormalities or causalities.

Syndromal/syndromic clubfoot, indicating that the clubfoot occurs together with other abnormalities, such as a part of genetic syndromes, neurological disorders, or with additional malformations, which is the case in about one quarter of children with clubfoot.⁸⁻¹⁰

Finally, *congenital* is often used as a prefix to stress that the child is born with the deformity. This thesis discusses the first subtype of clubfoot, and the term *idiopathic clubfoot (IC)* will be used in conjunction with the overall term *clubfoot* when the subtype is not specified.



Figure 1. Baby with bilateral clubfoot before treatment.

1.1.1 Incidence

Clubfoot is one of the most common musculoskeletal deformities and the most common foot deformity at birth.^{9,11} The reported incidence of clubfoot varies between 0.6 and 6.8 of every 1,000 new-borns¹⁰⁻¹⁴ depending on ethnic group and different inclusion criteria of the clubfoot subgroups. In the Scandinavian countries, the incidence of clubfoot has been reported to be 1.1-1.4 of every 1,000 live births.¹⁵⁻¹⁷

1.1.2 Aetiology

The aetiology of clubfoot is still unknown, but it is believed to be multifactorial with a combination of environmental and genetic factors.^{10,18} For environmental factors, maternal smoking has been identified as the most robust and consistent risk factor.^{9,10,14,17-20} Other environmental factors such as parental age and education level, parity, maternal anxiety and depression, body mass index, alcohol, coffee drinking, selective serotonin-reuptake inhibitor consumption, season of birth, and population density are inconclusive.^{10,11,15-18,20-23}

Genetic factors are probably of great significance in clubfoot, with approximately one quarter of the cases being familial.^{9,18,24} Moreover, the genetic contribution is also reinforced by the sex discrepancy found in clubfoot.²⁵ Not only are males affected about two to three times more often by clubfoot,^{10,11,15,16,21} affected females seem to carry a higher genetic load and will transmit the deformity to their offspring to a greater extent than males.²⁵ The fact that clubfoot has an innate heterogeneity, with children being born with bi- or unilateral clubfoot in half of the cases, respectively, underpins the genetic factor. Although variants in different gene clusters have been shown to be associated with the deformity, the mechanism of the genetic variations and how their interactions contribute to clubfoot remain to be defined.^{10,18,26}

1.1.3 Pathology

The development of the foot begins with the lower limb bud that is first seen in gestational week four, and at week eight the lower limbs have rotated 90 degrees medially.²⁷ At the same time, the feet can be observed in an equino-varus-adductus position.²⁸ This position decreases gradually, and at the end of week 11 the feet have reached an almost neutral position regarding those components.²⁸ In clubfoot, the earliest reported prenatal ultra-sonographic findings have been reported from week 12 of gestation, and today clubfoot is generally detected prenatally.^{5,29}

The pathology of clubfoot is complex and is characterised by several components. The main components are equinus, hindfoot varus, forefoot adductus, cavus, and supination of the foot.³⁰ Structural abnormalities include a medial tilt and shift of the calcaneus, a somewhat abnormally shaped talus, and a medial displacement of the navicular.³¹⁻³⁴ Commonly reported abnormal soft tissue structures include an increase of collagen fibres, contractures of the medial and posterior musculature, muscle hypoplasia and atrophy, and abnormal muscle activity.^{26,32,35-39} Abnormalities such as shortness of the foot and leg length discrepancy,^{40,41} as well as increased joint laxity and peroneal nerve dysfunction have been described.⁴²⁻⁴⁷

1.1.4 Clubfoot severity

Clubfoot presents with different levels of severity at birth depending on factors such as the mobility and morphology of the foot. In order to establish severity, a classification system is most often used.⁴⁸⁻⁵⁰ Some evidence has been presented of a link between initial severity and treatment factors such as number of casts, the need for extensive surgery, and the risk for relapse.⁵¹⁻⁵⁵ However, some studies have opposed these results, and the relation between initial severity, treatment, and outcome factors is still debated.⁵⁶⁻⁶¹

Analogously, possible relations between clubfoot severity, number of affected feet, and sex are still controversial with some studies suggesting that bilateral clubfoot and females might represent a more severe clubfoot phenotype and thus be harder to treat.^{25,62-64} However, several studies have found contrasting results.^{52,59-61,65} Nonetheless, females with clubfoot have stated lower HRQoL,^{66,67} and parents to girls with clubfoot have reported subjectively worse treatment outcomes in comparison with males.^{68,69} Because of the notion of differences in clubfoot severity due to foot involvement (defined as being born with one or two affected feet) and sex (referring to biological sex⁷⁰), extra emphasis was put on these factors throughout this thesis. It is worth noting that bilaterally affected feet and clubfoot in plural are both referred to as IC/clubfoot in the thesis because the word “clubfeet” would be a misrepresentation of the name of the diagnosis.

1.2 MANAGEMENT OF CLUBFOOT

Several treatment methods to manage clubfoot have been described in the literature, from gentle serial manipulation and strong bandaging to maintain the correction as described in 400 B.C. by Hippocrates (and which is notably similar to today’s conservative treatment methods) to drastic surgeries and “clubfoot machines”.^{1,71,72} With the introduction of anaesthesia and aseptic techniques in the 19th century, clubfoot treatment became radical with surgery aiming to obtain a “perfect” foot.⁷¹ However, long-term outcomes were poor, and today conservative treatment is recognised to be superior to surgery.⁷³⁻⁷⁶

1.2.1 Conservative treatment and the Ponseti method

Different conservative treatment methods include the Kite technique, the French physiotherapy method, the Copenhagen method, and the Ponseti method.^{7,30,77-82} Today the Ponseti method is probably the most practised treatment method worldwide and could be considered the gold standard.^{2-4,83-90} The Ponseti method can be described in two phases –the initial correction phase and the maintenance phase (Figure 2). In the initial correction phase, the clubfoot is manipulated with weekly serial castings for the first weeks of life. To fully correct the foot, an Achilles tenotomy is most often required (a minor procedure thus not being referred to as a surgical method). In the maintenance phase, the corrected clubfoot is kept in a foot-abduction brace to prevent relapse, first for 23 hours a day for three months and then during the night and naps until the age of four to five years.^{30,87,90}



Figure 2. The two phases in the Ponseti method. In the initial correction phase, long leg casts are weekly applied to correct the clubfoot. In the maintenance phase, the foot-abduction brace is used during night and naps until four to five years of age to hold the corrected clubfoot and prevent relapse. Both feet are braced, i.e. also the contralateral foot in children with unilateral clubfoot.

1.2.2 Relapse

Relapses, i.e. a regression of one or several components of the deformity,⁹⁰ are still common with reports varying from 7% to as many as 68% of the patients treated with the Ponseti method.^{2,38,55,90-94} The great disparity of relapse rates is probably due to different definition criteria, follow-up periods, and inconsistency to the Ponseti protocol.⁹⁵⁻⁹⁷

In cases of relapse, casting and bracing is most often introduced again, sometimes followed by soft tissue surgery such as tibialis anterior tendon transfer as a part of the Ponseti protocol.^{55,94,98} Noncompliance with the bracing regime is the major and consistent risk factor reported for experiencing relapse.^{55,59,60} Other factors such as sex, number of affected feet, parental material status and educational level, cultural origin, and family income seem not to affect the relapse rate,^{55,59} although the role of the parents' educational level has been inconclusive.⁶⁰

Because adherence to the brace is the single most important factor to prevent relapses, emphasis has been on increasing compliance through different brace designs, protocols, and educational interventions.⁹⁹⁻¹⁰⁹ Nevertheless, adherence to the brace regime can be perceived to be difficult, and one study using wireless sensors showed that the braces were only being used for 62% of the recommended time.¹¹⁰ Furthermore, questions about wearing the braces might feel judgemental and therefore be answered vaguely or incorrectly by the families.¹⁰⁹ At the same time, clinicians are sometimes poorly equipped to handle non-compliance.¹¹¹

1.2.3 Clubfoot treatment in Sweden

In Sweden, children with clubfoot are treated free of charge in centralised public hospitals as a part of the Swedish national health insurance. A conservative treatment approach in line with the Ponseti method was gradually introduced mainly in the early 2000s. However, considerable regionally modifications existed, for example, in Stockholm and Skåne counties with the use of synthetic soft casts and knee-ankle-foot orthoses (Figure 3). From the 2010s, a strict Ponseti treatment protocol has been adopted in several counties in Sweden.



Figure 3. An example of a knee-ankle-foot orthosis typically used in Stockholm and Skåne counties before the introduction of a strict Ponseti protocol using the foot-abduction brace (orthosis of TeamOlmed AB).

1.2.4 Evaluation of treatment outcomes

Untreated clubfoot might cause decreased mobility, pain, and threaten potential productivity.^{112,113} The goal with the treatment of clubfoot has been described as to correct the foot to a “functional, pain free, plantigrade foot with good mobility and without calluses, and that the patient does not need to wear modified shoes” (Ponseti 1992).³⁰

In the evaluation of treatment outcomes, several concerns have been raised.^{2,68,84,114,115} First, research on the treatment outcomes in patients with clubfoot has historically mainly focused on radiological and morphological outcomes assessed by the orthopaedic surgeon.^{68,114} However, it has been emphasised that outcome measures should also include functional status and patient-reported outcome measures (PROMs) to best reflect the patients’ perspective.^{68,84,114} Second, traditional outcome measures might not be the main concern for the patients. As an example, radiographic data have failed to correlate significantly with PROMs such as reported satisfaction and function.^{68,116} Third, although the Ponseti method can be considered the gold standard treatment method⁸⁸ there is still a lack of well-designed randomised controlled trials to assess the best treatment option.⁸⁴ Finally, despite the fact that clubfoot can be either bi- or unilateral, with concerns about different disease severity burden,^{62,64} most previous studies have clustered all affected feet as one homogenous group.

Moreover, several studies have included both the right and left foot in individuals with bilateral involvement.^{115,117} By including both feet as independent measures, without making statistical compensation, the results might be misleading.¹¹⁸ Not only are the right and left feet related in all individuals, in other words, they are not independent of each other, it has been shown that in bilateral clubfoot both feet are highly correlated with each other in regards to several parameters.¹¹⁵

1.3 GAIT

Measuring gait, i.e. the quality of the walking pattern, has been stated to be useful in obtaining data on the level of limitations due to pathology in both patient follow-ups and in the evaluation of interventions.¹¹⁹ Gait can be measured with technical instruments such as three-dimensional gait analysis (3DGA) systems that provide information on gait kinematics (joint and segment angles), kinetics (joint moments and power), and spatiotemporal parameters.^{120,121} In the progress of expanding outcome measures from static to dynamic outcome measurements in IC, gait analysis has been found to be useful in patients with clubfoot.^{114,122}

To date, most studies of gait in individuals with IC have mainly focused on gait in the evaluation of different treatment methods. Thus, the Ponseti method has been found to be superior to surgical treatment,¹²³⁻¹²⁹ whereas the findings in comparison with the French physiotherapy method have been inconclusive.^{58,124,128,130}

Despite the progress made in conservative treatment methods, gait alterations are common in individuals with IC. Frequently reported kinematic gait deviations in children with IC are decreased dorsiflexion of the foot, internal foot progression (internally rotated foot in relation to the gait direction), and hyperextension of the knee in comparison with control subjects.^{58,100,122,124-126,130-132} In terms of kinetic parameters, the main findings have been decreased ankle moments and decreased power generation in the ankle.^{100,124-126,131,132}

Because large quantities of data can be obtained from 3DGA, summary measures can be useful tools to objectively quantify the degree of gait deviations in comparison to a control sample.¹¹⁹ Several summary measures exist, among them is the Gait Deviation Index (GDI), a generic multivariate measure developed to provide a global measure of gait pathology.¹³³ Although gait summary measures should be used in conjunction with discrete gait parameters, the ease of interpretation and the generic nature of GDI have yielded great attention of the index since it was developed ten years ago.^{119,133} Thus, the index has been widely adopted and used in both children and adults with various disorders.^{119,134} In children with IC, the GDI had been used in one publication prior to the conduction of the gait study in this thesis. In this, Duffy et al. showed that children with Ponseti-treated clubfoot had a global gait pattern closer to those born without the deformity compared to a surgically treated group, although gait in both groups still deviated from the control group.¹²⁶

Noteworthy in prior studies of gait in IC is that only the affected legs have been included, i.e. only half of the child (one leg) in cases of unilateral IC.^{58,122,124-126,130-132} Accordingly, the

contralateral leg is rarely included, although it has been shown that the contralateral foot should not be referred to as normal or used as a reference regarding step initiative, foot pressure, and force when analysing gait.¹³⁵⁻¹³⁷ Additionally, the contralateral foot has been shown to have significant flatfoot deformities and adaptations in tiptoe raising,^{138,139} possibly affecting the gait pattern. Moreover, in previous gait studies bi- and unilateral clubfoot have been clustered as one uniform group without knowledge of whether they experience the same gait pattern or not.^{58,122,124-126,130-132} With the notion that bilateral clubfoot might represent a more severe clubfoot phenotype, this questions the accuracy of these findings. Finally, most studies have included both legs in bilateral cases as independent measures.^{58,122,124-126,130-132} Consequently, when considering these limitations the validity of previous gait findings in children with IC can be questioned. Thus, gait in children with IC including the impact of having one or two affected feet seems to be an unexplored field.

1.4 GROSS MOTOR SKILLS

Gross motor skills are coordinated body movements, including locomotor and balance skills, that are described as the building blocks for overall fundamental motor skills.¹⁴⁰ According to Shumway-Cook and Woollacott,¹⁴¹ body movements emerge from an interaction of the individual, the task, and the environment (Figure 4). Individual factors include sensory/perceptual, cognitive, and motor/action systems,¹⁴¹ and the structural deformity of IC, as a part of the biomechanical system, may be primarily placed in the latter. Factors associated with the task are mobility, postural control, and upper extremity function, referring to different demands of the task. Finally, regulatory and non-regulatory features of the environment include attributes such as the flat floor in a laboratory milieu and background noise, respectively (Figure 4). Subsequently, according to the model an interaction between the above-mentioned factors are essential to create body movements and thus are necessary in the performance of gross motor tasks.

Development of locomotor rhythms starts already in utero.¹⁴¹ After birth, development continues as the child reaches gross motor milestones such as crawling, standing, walking, and jumping.^{141,142} Further development of gross motor skills enables the child to perform and participate in everyday functions such as putting on clothes (standing on one leg), playing with friends on the playground (e.g. skipping), and moving around in society (e.g. standing up and maintaining balance on the bus). Thus, experiencing gross motor deficits has been connected to reduced physical activity, increased body weight, reduced self-esteem, and negative psychosocial outcomes and school performance.¹⁴³⁻¹⁴⁶

Several instruments have been used to measure gross motor skills, movement, and function in children.¹⁴⁰ As noted, different terms have been used due to inconsistent definition and terminology within the field. In this thesis, the term gross motor skills refers to locomotor and balance skills. Furthermore, if not exclusively specified of cited authors, the term fundamental motor skills¹⁴⁰ is used when considering both gross motor and objective/manipulation skills. Finally, the term motor skills is used as an umbrella term.

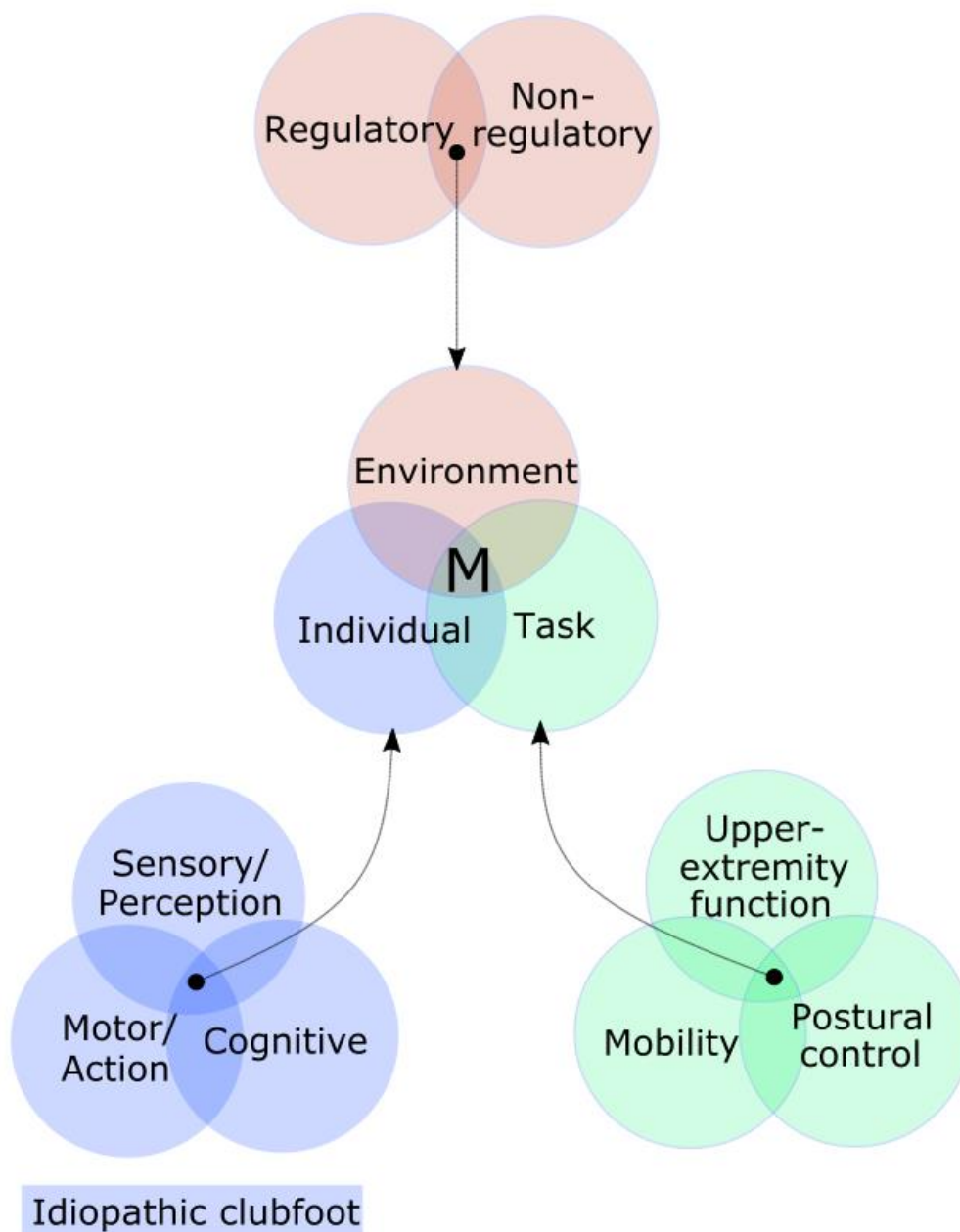


Figure 4. Body movement (M) as an interaction between the individual, the task and the environment. Within the individual, the structural deformity of idiopathic clubfoot may be primary placed within the motor/action system. Adapted from Shumway-Cook and Woollacott.¹⁴¹

1.4.1 Gross motor aspects in children with idiopathic clubfoot

Studies of gross motor development in babies and toddlers with IC have revealed delays in achieving gross motor milestones, mainly regarding later debut of independent walking.^{142,147} Consequently, children with IC start to walk independently at a mean age of 14 months, which is approximately two months later than children born without the deformity.^{142,147,148} Rates of attained gross motor milestones have been found not to relate to foot involvement, sex, treatment method (Ponseti or French treatment methods), brace compliance, number of casts, the need for tenotomy, or family history of clubfoot.^{147,148} However, the relation between initial severity of the clubfoot and independent walking is inconclusive.^{147,148} Still, children experiencing an early relapse of the deformity seem to achieve a significantly later walking debut.¹⁴⁸ Because of the early gross motor delay with weak associations to clubfoot factors, it has been suggested that clubfoot might be a marker of an underlying mild motor developmental dysfunction or other inherent associated factors.¹⁴⁷

Fundamental motor skills have been assessed in a couple of prior studies in children with IC aged five to seven years. Karol et al. concluded that the vast majority of children with IC at the age of five years had an average gross motor function using the Peabody Developmental Gross Motor Scale (PDMS).¹⁴⁹ Despite this, 14% of the children had rankings interpreted as below average or poor. Furthermore, the gait disturbances found in the same sample of children with IC did not to interfere with gross motor function.¹⁴⁹ In contrast, Andriessse et al. concluded that children at age seven with IC had an increased prevalence of motor impairment, with no clear correlation to the clinical status of the IC, compared to normal references using the Movement Assessment Battery for Children (MABC).¹⁵⁰ Both studies included areas apart from the feet and legs such as aiming, catching, and object manipulation.^{140,149,150} Similar to the findings in toddlers, no relationships were found between the motor findings and the status of the clubfoot, foot involvement, the extent of foot surgery, or the treatment method used.^{149,150}

At the age of nine to ten years, children with IC have been found to have fewer total daily steps and 79% of the walking capacity compared with norm references.^{131,151} Nonetheless, similar athletic ability as healthy peers have been reported in the same age group of children with IC.¹⁵² Neither walking capacity nor athletic ability were influenced by the child being born with one or two affected feet.^{151,152}

In summary, studies of gross motor aspects of children with IC have yielded diverse conclusions. Still, there seems to be some consistency in that motor deficit might not be directly related to the structural abnormalities (e.g. status of the clubfoot or number of affected feet) and/or treatment method. This is in line with our observation at the physiotherapy clinic that children with well-corrected feet also sometimes struggle with gross motor tasks such as keeping balance and skipping. Notwithstanding these studies, gross motor skills in children with IC have been remarkably unexplored.

1.5 NEURODEVELOPMENTAL DIFFICULTIES

Neurodevelopmental disorders include a range of conditions with onset in the developmental period, usually manifesting before the child enters school, and they are typically persistent.^{153,154} The developmental challenges can vary from specific limitations to global impairments affecting personal, social, academic, or occupational functioning.¹⁵³ Examples of neurodevelopmental disorders are attention-deficit/hyper-activity disorder (ADHD, including difficulties such as impulsivity, disorganisation, inattention, and hyperactivity), autism spectrum disorder (ASD, including difficulties regarding social interaction, communication, and restricted repetitive behaviours), and developmental coordination disorder (DCD, concerning difficulties in performing and coordinating motor skills).^{153,154} The aetiologies of neurodevelopmental disorders are better known in some disorders, while others are less known, but there is commonly a multifactorial underpinning in which strong genetic as well as environmental factors seem to contribute.¹⁵³⁻¹⁵⁵ Just as in clubfoot, several neurodevelopmental disorders have been reported with a skewed sex ratio towards males as well as an apparent heritability.¹⁵⁴⁻¹⁵⁶ The reported prevalence of ASD, ADHD, and DCD varies between roughly 1% and 6% of children in the general population.^{153,157,158}

When assessing neurodevelopmental disorders, multiple domains are evaluated with the consideration of atypical behaviour or developmental delays in areas such as behaviour, cognition, language, and motor skills.¹⁵⁴ A summary assessment from a multidisciplinary team based on patient history, clinical assessment, and test results from screening instruments makes up the foundation for the child to be diagnosed with a neurodevelopmental disorder.¹⁵⁹ Numerous of instruments have been developed for this purpose such as the Five to Fifteen (FTF), the Child Behavior Checklist, and the Developmental Coordination Disorder Questionnaire.¹⁵⁹⁻¹⁶²

In this thesis, neurodevelopmental *difficulties* (NDD) are defined as symptoms and traits indicative of neurodevelopmental *disorders*.

1.5.1 Neurodevelopmental difficulties and idiopathic clubfoot

To the best of our knowledge, neurodevelopmental disorders or NDD have never been studied exclusively in individuals with IC. However, in a sub analysis of children at an orthopaedic ward used as a control group in a study of childhood stroke, seven out of thirteen (54%) patients with clubfoot were found to have ADHD or ADHD traits.¹⁶³ In children with idiopathic toe walking, i.e. toe walking without any other known pathology, an increased incidence of NDD has been reported with respect to a normative reference material of children.¹⁶⁴ Moreover, children with ASD and language disorders have a well-known association with increased prevalence of toe walking.¹⁶⁵⁻¹⁶⁸ However, the aetiology of the association remains unknown.^{165,166} Prior studies of toe walking and the high incidence of ADHD in children with IC found by chance¹⁶³ indicate a possibly higher prevalence of NDD in children with musculoskeletal foot deficits.

In addition, at the physiotherapy clinic when working with children with IC, an observation has been that advanced difficulties such as hyperactivity, problems with concentration, body control and language are common. Such difficulties are hardly explained by the structural musculoskeletal deformity of clubfoot. In the same manner, in the aforementioned studies of gross motor aspects in children with IC, other explanations beyond the clubfoot deformity such as focusing problems or an underlying mild motor development dysfunction have sometimes been proposed.^{147,150}

Altogether, there seem to be indications of a possible link between NDD and distal musculoskeletal deficits, including IC. Early diagnosis of neurodevelopmental disorders is essential to provide treatment and support for the child and family.¹⁵⁴ In children with IC, it is necessary to explore a possible connection to NDD, to identify NDD, and to provide early treatment and support. Not least because the latter might affect the treatment of the clubfoot.

1.6 HEALTH-RELATED QUALITY OF LIFE

Quality of life is a broad term involving the sense of well-being, happiness, and satisfaction of life.¹⁶⁹ In order to stress the physical and mental aspects in relation to quality of life, the term health-related quality of life (HRQoL) is often used.¹⁶⁹ As such, HRQoL can be defined as “perceived physical and mental health”.¹⁷⁰ HRQoL is commonly assessed with self-reported disease-specific or generic questionnaires such as the EQ-5D instrument and the 36-Item Short Form Health Survey (SF-36).^{169,171,172} In children, proxy versions are sometimes used, i.e. answered by a parent or someone else close to the child. However, the validity of proxy reports of HRQoL have been questioned in both studies of children with congenital musculoskeletal deficits and children with mental and behavioural disorders.¹⁷³

HRQoL has been found to be negatively affected in children with chronic conditions such as neurodevelopmental disorders,¹⁷³⁻¹⁷⁵ thus highlighting the importance of assessing and targeting treatments in relation to HRQoL in paediatric patients.^{174,175} Moreover, physical measures alone seem insufficient to evaluate the impact of a specific health condition on an individual’s life.¹⁷⁶ Correspondingly, it has been emphasised that HRQoL measures should be included in the evaluation of clubfoot.^{84,114} Still, only a few studies of small cohorts evaluating HRQoL exist within the field of clubfoot research, mainly in individuals treated with surgical management and as a secondary outcome measure. In children with IC, two studies including HRQoL measures have been identified in the literature, both evaluating HRQoL using proxy-reports and evaluated as secondary outcome measures. In those studies, both yielded similar high HRQoL in comparison with norm material at the age of four to five years of age.^{68,177} However, a serious ceiling effect was also noted, thus questioning the validity of the findings.⁶⁸ A third study including “happiness” found that parents of children treated with the Ponseti method reported lower happiness in their children compared with reports of parents to children treated with the French physiotherapy method or surgery.¹⁴⁹ The authors considered the prolonged use and struggles of night-time bracing to be a reason for their findings.¹⁴⁹

In adolescents with clubfoot, comparable HRQoL results have been found using the Child Health Questionnaire compared with an age-matched control group.¹¹⁶ However, one exception was found in the domain General Health with significantly lower scores for the clubfoot population.¹¹⁶ In adults with clubfoot, HRQoL has been inconclusive when using the SF-36 in comparison with norm material. Dobbs et al. and Smith et al. reported lower SF-36 scores,^{127,178} while Hsu et al. reported higher scores in adults with clubfoot compared with the norm material.¹⁷⁹ Moreover, two Nordic studies have suggested that female patients with clubfoot have lower HRQoL than their male counterparts and norm materials, respectively.^{66,67}

Finally, in the evaluation of children with IC, HRQoL might not just be a measure of the clubfoot treatment outcome. HRQoL measures might also create a platform for communication with the child and family and thus help to identify areas of interest and to facilitate futures studies and interventions where appropriate.¹⁷⁶

1.7 RATIONALE

In the evaluation of IC, we ought to consider the deformity from a wider perspective, not just the foot. Even so, knowledge beyond the structural musculoskeletal deformity of IC is still limited. The outline of this thesis was to study previously unexplored fields by including measures that might affect the children's overall health condition. Not only will this provide new knowledge and understanding of children born with IC, it could possibly provide a foundation for further treatment development and support within the field of IC. The obtained knowledge might eventually not only benefit the child, but also the affected family and the community as a whole.

2 AIMS OF THE THESIS

The overall aim with the thesis was to evaluate gait, gross motor skills, NDD, and HRQoL in children with IC.

The specific aims of the studies were as follows:

Study I

To evaluate gait in children with IC with particular focus on foot involvement (bi- and unilateral IC) and the contralateral leg (in children with unilateral IC) in comparison with TD children.

Study II

To evaluate gross motor skills in children with IC compared with TD children. In addition, to explore the impact of foot involvement on gross motor skills and to examine the associations between gross motor skills, gait, passive foot motion, and initial severity of the clubfoot.

Study III

To examine NDD in a cohort of children with IC compared with the general population.

Study IV

To survey HRQoL in a cohort of children with IC in comparison with the general population and the influence of sex, foot involvement, and NDD on HRQoL in children with IC.

3 RESEARCH APPROACH

To answer the research aims, an exploratory quantitative research approach of four individual studies was conducted, divided into two parts (Figure 5):

- Part one evaluated gait and gross motor skills (Studies I and II), comprising motion data and linking to the end of the primary treatment period.
- Part two explored NDD and HRQoL (Studies III and IV), comprising survey data in the follow-up period.

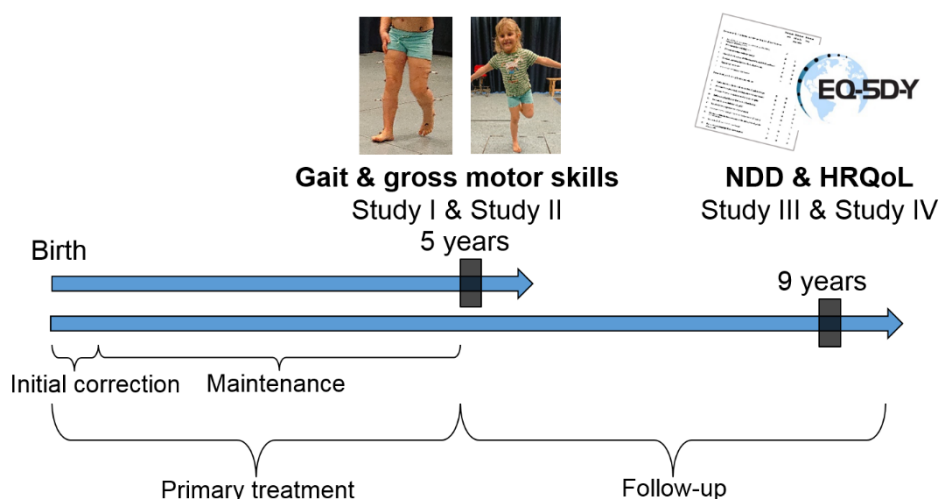


Figure 5. Schematic timeline of the studies within the thesis in relation to the children's ages and treatment. *NDD* neurodevelopmental difficulties; *HRQoL* health-related quality of life.

3.1 STUDY DESIGN

An explorative cross-sectional study design was used in all four studies, two based on motor assessments of the children and two on survey data.

3.2 SAMPLE SIZE AND STATISTICAL POWER

Regarding gait data (Studies I and II), a difference of five GDI points was considered to indicate a clinically relevant difference based on prior pilot data and research on the index.¹⁸⁰ Thus, prior power calculation revealed that a sample size of 25 participants in each group was required to reach a statistical power of 0.8, with an alpha level of 0.05, to detect group differences.

In the survey-based studies (Studies III and IV), no prior power calculations were done. However, post-hoc power analysis (based on sample size and an alpha level of 0.05 using parametric statistics) revealed a statistical power for between-group effects of 0.55 for small, 0.90 for medium, and 0.96 for large effects.

3.3 PARTICIPANTS

A total sample of 302 children participated in the four studies, of whom 165 were children with IC. An overview of the participants can be found in Table 1. Details of the sample characteristics can be found in the individual papers. Furthermore, details of sociodemographic parameters for the participants in Studies III and IV can be found in the appendix.

Table 1. Participants included in Studies I-IV.

Study	Participants	County catchment-area	Data collection period	Mean (SD) age	Boys % (n)	Bilateral IC % (n)
I+II	59* children with IC	Stockholm	2009-2013	5.4 (0.5)	69 (41)	51 (30)
	28 TD children	Stockholm	2013-2014	5.5 (0.6)	64 (18)	NA
III+IV	106 children with IC	Stockholm & Skåne	2014-2016	9.4 (0.6)	73 (77)	49 (49)
	109 schoolchildren	Stockholm & Skåne	2015-2016	9.5 (0.6)	73 (79)	NA

*12 children with IC were excluded in Study II from the original 59 children participating in Study I. *IC* idiopathic clubfoot; *TD* typically developing; *NA* not applicable.

3.3.1 Studies I and II

Studies I and II included children with IC from Stockholm County born between the years 2005 and 2008. The inclusion criterion, except for these basic prerequisites, was an age of 4.5 to 6.5 years at the time of the data collection. In total 122 children were identified as being born with IC in the medical records during the included time span. Of those, 44 children were excluded due to missing gait analysis data ($n = 29$) or no written consent ($n = 15$). Moreover, 19 children were excluded due to the following reasons: clubfoot treatment performed by other professionals than orthopaedic surgeons ($n = 7$), suspicion of IC not being the primary diagnosis ($n = 5$), outside the age range ($n = 5$), and developmental dysplasia of the hip ($n = 2$). For Study II, another 12 children were excluded due to missing gross motor data. Thus 59 and 47 children with IC were included in Studies I and II, respectively (Figure 6).

For comparison material, 28 TD children in the same age span were included in Studies I and II. TD children were defined as children from the general population without any known disorder or diagnosis that would affect gait. The TD children were recruited through advertising posters at preschools in Stockholm as well as at Karolinska Institutet and Karolinska University Hospital.

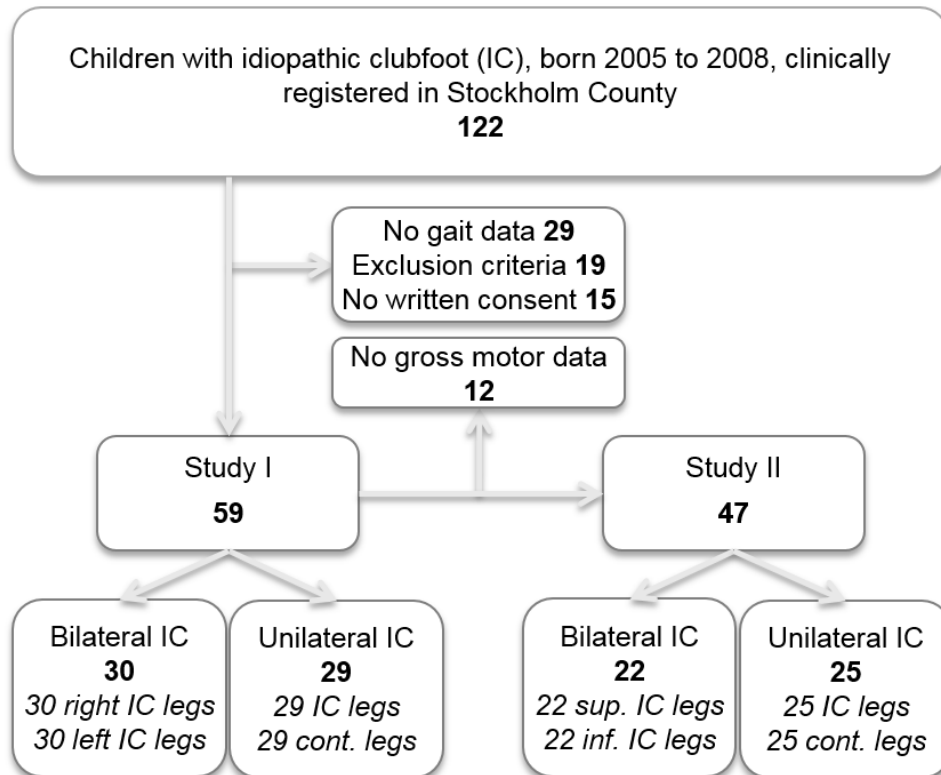


Figure 6. Flowchart of the children with idiopathic clubfoot in Studies I and II including divisions of the legs within the studies. *Cont.* contralateral; *Sup.* superior; *Inf.* inferior.

3.3.2 Studies III and IV

Studies III and IV consisted of four annual cohorts of children with IC from Stockholm and Skåne counties born in the years 2004 to 2007. For these studies, 182 children with IC were identified from the medical records from the two counties, which gave an incidence of 1.1/1000 of the 160,114 live births during these years.¹⁸¹ Seven children were excluded because they had moved abroad or had protected personal data. Consequently, 175 children with IC and their parents were invited to participate. Of those, 116 returned the questionnaires, which gave a response rate of 66%. However, ten children had to be excluded due to incomplete responses or because IC was found not to be their primary diagnosis. Thus, for Studies III and IV 106 children with IC were included (Figure 7).

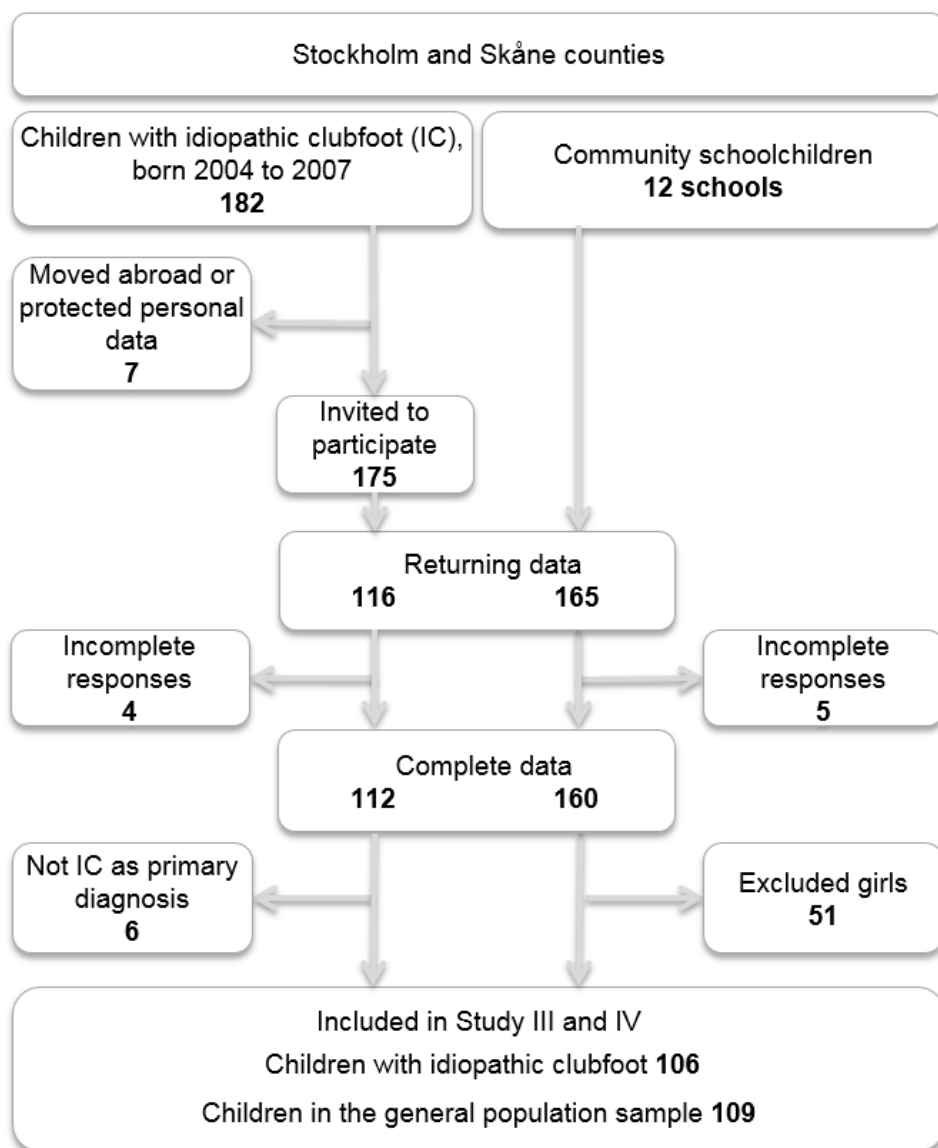


Figure 7. Flowchart of the children with idiopathic clubfoot and the community schoolchildren for the general population sample in Studies III and IV.

For comparison material, a general population sample was recruited from randomly selected schools within the same county areas. In total 23 schools were approached and 12 schools (eight from Stockholm and four from Skåne) chose to participate. In total 160 children in the same school grades as the children from the IC sample and their parents returned completed questionnaires. However, due to the uneven sex distribution in the IC sample, a greater portion of the girls were randomly excluded. Consequently, the general population sample comprised 109 community children, parallelised for residential area, age, and sex (Figure 7).

3.4 DATA COLLECTION

3.4.1 Motion data

Data regarding gait and gross motor skills in Studies I and II were collected at the Motion Laboratory at Karolinska University Hospital, Solna, Sweden. In children with IC, data were collected in a clinical setting as a part of the clubfoot follow-up programme at the hospital, while data for the TD children were collected solely for research.

In order to collect reliable data, every effort was made to make the child and family comfortable and to follow standardised procedures at the laboratory. To do so, the child and family were first introduced to the laboratory and the procedure in order to become familiar with the environment and the equipment. Thereafter, a physical examination was generally performed followed by placement of the motion markers. Next, the child was instructed to walk barefoot approximately 10–20 times on a 10-metre pathway at a self-selected speed. Soft toys were used at the ends of the pathway to encourage, attract attention, and guide direction (Figure 8). The parents were placed alongside the pathway, and all children walked by themselves. However, in some cases the parents had to encourage the child by walking next to the pathway. Finally, the children were instructed to perform the tasks of running, walking, toe and heel walking, one-leg stand, and one-leg hop, all of which are items included in the Clubfoot Assessment Protocol (CAP).¹⁸² One-leg stand and hop were performed for both legs. In a few cases, the parents supported the child by performing the same task by the side of the pathway. If the child did not understand or had trouble performing the task, he or she was encouraged to try again. The visit normally lasted for one to two hours.

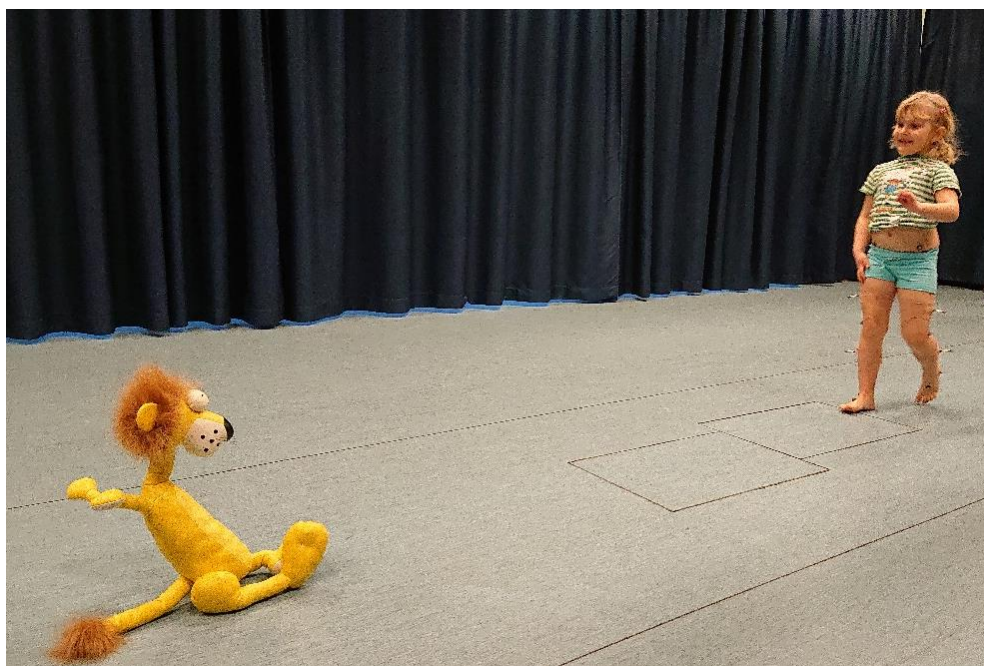


Figure 8. Walking on the pathway at the Motion Laboratory with motion markers placed on the pelvis and legs.

3.4.1.1 Physical examination

A goniometer was used to obtain information on passive range of motion of the joints of the lower extremities. All measurements were collected with the child in a supine position, except for hip rotations and tibia torsion that were assessed in a prone position. Anthropometric measures were additionally noted as a part of the standardised gait analysis procedure.

3.4.1.2 Three-dimensional gait analysis

Gait data were collected using a 3DGA system consisting of eight motion cameras (Vicon® Motion Systems Ltd, Oxford, UK) and two force plates (Kistler®, Winterthur, Switzerland). The system makes it possible to obtain detailed information from the child's gait pattern regarding kinematics and kinetics in the sagittal, frontal, and transversal planes as well as spatiotemporal parameters.^{120,121} To collect data from the lower extremities and pelvis, 16 passive reflective motion markers were placed on pre-defined anatomical landmarks on the child.¹²⁰ Seven segments were defined according to the Vicon's Plug-In Gait model consisting of the pelvis, two thighs, two shanks and two feet. The pelvis segment and the foot progression angle were defined in a global mathematical reference system, whereas the rest were defined from the proximal segments, e.g. the ankle angles were defined relative to the position of the shank segment.

To acquire data from the individual child's gait, three representative gait trials including gait kinematics and spatiotemporal parameters were subjectively selected by the author. Due to difficulties in obtaining clean force strikes for the children, only two representative trials of gait kinetics were selected. Thereafter, custom-made templates in the software program MATLAB® R2014a (The MathWorks Inc., Natick, MA, USA) were used to extract data from the trials and to calculate the GDI/GDI-Kinetic scores. Finally, an average of the trials was calculated to obtain one single value for each leg for every child.

3.4.1.3 Gross motor data

Gross motor data were obtained from the videotapes recorded in the frontal plane of the children when performing the gross motor tasks. To quantify the motion quality of the gross motor tasks, five assessors individually rated the tasks from the videotapes using the CAP instrument. Children with IC were randomised together with the TD children. The assessors had information on the child's age, but no other information was provided, i.e. they were blinded to whether the child had IC or not. The assessors were instructed to view the videotapes three times at most without stopping or slowing down the tape. Finally, the median scores of the ratings were used to operationalise the children's gross motor skills.

3.4.2 Survey data

The survey data for Studies III and IV were collected during the spring terms when the children were supposed to attend their second or third school grade according to the Swedish school system, i.e. eight to ten years of age. Information about participation, including the questionnaires, was sent to the home addresses of the children and addressed to the parents. In the general population, some schools chose to give the letters directly at school or to send the information only by emails or newsletters. The parents were instructed that the questionnaire EQ-5D-Y was to be answered by the child and the rest by the parents. The families were informed that they could answer the questionnaires either on paper with a pre-paid return envelope or online on the Internet. To answer online, the families were provided with an individual passkey. The homepage was exclusively designed for Studies III and IV, and the forms were constructed to visually look like and to be answered in the same manner as the paper and pencil versions. Before answering the questionnaires on the Internet, the parents had to approve participation by reading the provided information and giving consent. One reminder was sent including the questionnaires, and another was sent later with only information on the homepage. No reminders were sent to the general population.

3.5 OUTCOME MEASURES

An overview of outcome measures and data sources used in each study is provided in Table 2.

Table 2. Summary of outcome measures and data sources used in Studies I-IV.

Outcome measures	Data source	Study I	Study II	Study III	Study IV
Gait parameters	3DGA	x			
GDI	3DGA	x	x		
GDI-Kinetic	3DGA	x	x		
Passive range of motion	Physical examination	x	x		
Dimeglio classification scale	Medical records	x	x		
MQ-CAP	Videotapes		x		
Sociodemographic parameters	Survey data			x	x
FTF	Survey data			x	x
Roye's DSI	Survey data			x	x
EQ-5D-Y	Survey data				x

GDI Gait Deviation Index; *MQ-CAP* Motion quality domains from the Clubfoot Assessment Protocol; *FTF* Five to Fifteen; *DSI* Disease specific Instrument; 3DGA three-dimensional gait analysis.

3.5.1 Gait parameters

The included discrete gait parameters in Study I were subjectively chosen with the consideration of clinical importance and previous research.^{58,124-126} The standardised terminology of the gait cycle was used, consisting of the stance phase (typically the first 60%) and the swing phase (the remaining 40%) with further subdivisions (Figure 9).¹²¹

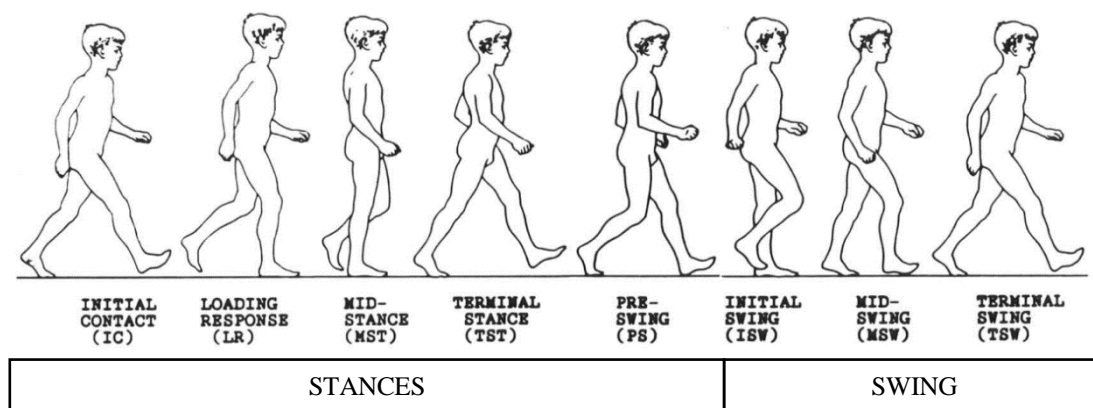


Figure 9. The gait cycle (reprinted with permission),¹⁸³ with the stance and swing phases.

The kinematic parameters were as follows (the percentage refers to the defined data collecting sections of the gait cycle):

- At initial contact: foot flexion and hip rotation (0-2%)
- At mid-stance: maximal dorsiflexion and mean hip rotation (12-31%)
- In stance: mean foot progression (10-50%) and maximal knee extension (25-60%)
- At pre-swing: maximal plantarflexion (50-70%)
- At mid-terminal swing: mean flexion of the foot (75-100%)
- Complete gait cycle: dorsi-plantar flexion range (0-100%)

Internal moments were accordingly selected:

- Maximal dorsi- and plantarflexion moments (0-100%)
- Maximal knee flexion moment in stance (25-60%)
- Maximal hip abduction moment in early stance (0-32%)

Finally, power generation parameters were chosen to reflect the concentric muscle actions:¹⁸³

- Maximal ankle power generation (0-100%)
- Maximal ankle to hip power generation ratio (0-100%)

Furthermore, because walking speed might affect gait parameters^{184,185} both walking and non-dimensional speed were evaluated to rule out potential speed differences between the groups.

3.5.1.1 Gait Deviation Index

The GDI and the GDI-Kinetic were used in Studies I and II to quantify the overall global gait pattern. GDI comprises kinematic gait curves from the pelvis and hip in all three planes, the knee and ankle in the sagittal plane, and the foot progression in the transversal plane (Figure 10).¹³³ The kinetic equivalent, GDI-Kinetic, consists of kinetic gait curves including internal moments from the hip, knee, and ankle in the sagittal and frontal plane and the total joint power from the hip, knee, and ankle (Figure 10).¹⁸⁶ Both indices are designed to quantify how far the nine kinematic/kinetic gait curves are from a representative control sample in order to provide an overall score for each leg. In this thesis, the 28 TD children from Studies I and II were used to embody the GDI/GDI-Kinetic reference norms (Figures 10). GDI/GDI-Kinetic scores of 100 or more represent a gait without pathology, and every ten-point reduction equals one standard deviation (SD) from the typical gait, indicating gait pathology.^{133,186} Several clinical studies of both healthy children and in individuals with gait pathology, including children with IC, support the validity of the GDI.^{100,119,126,187} However, studies using the GDI-Kinetic are still rare.¹¹⁹

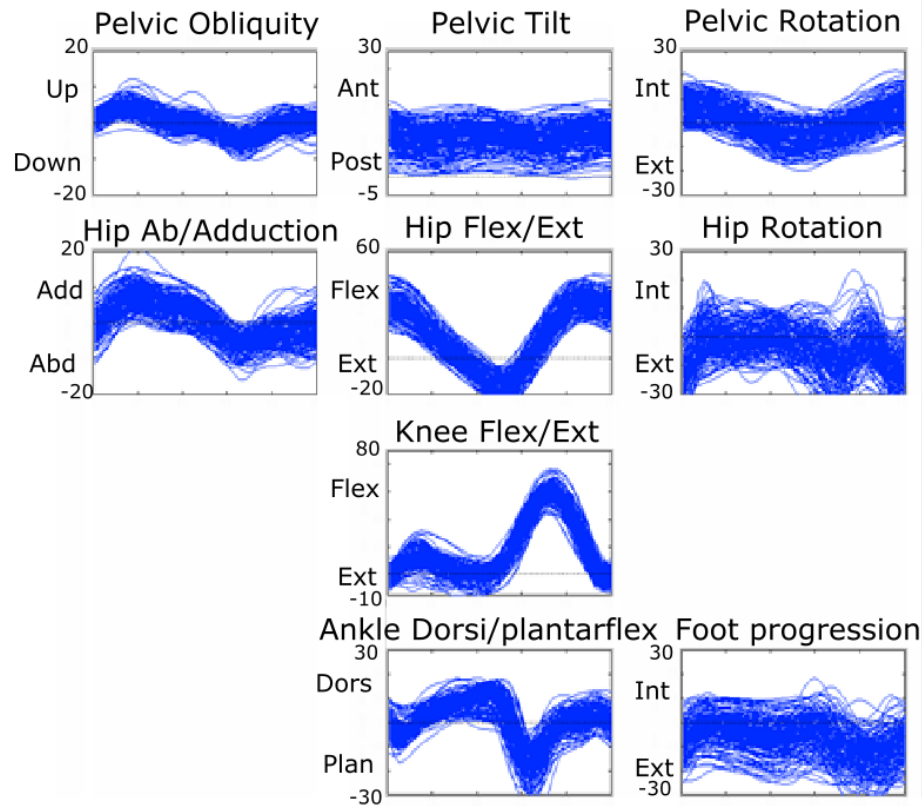
3.5.2 Passive range of motion

Passive range of motion of the foot, knee, and hip were obtained from the physical examination at the Motion Laboratory in Studies I and II.

3.5.3 Clubfoot Assessment Protocol

For Study II the Motion quality (MQ) domains from the CAP were used to evaluate gross motor skills. The CAP is an assessment instrument developed for use in a clinical setting to standardise the follow-up procedure in children with clubfoot.¹⁸² The instrument consists of 19 items divided into five domains: Passive mobility (seven items), Muscle function (two items), Morphology (four items), and MQ I (four items) and MQ II (two items). For Study II only the MQ domains were used wherein the assessor rates the quality of running, walking, toe and heel walking, and one-leg stand and hop. An ordinal scale is used from 0 (cannot) to 4 (within normal) with standardised pre-defined criteria for every level. As an example, the item one-leg stand is rated as very deviant if “*the child needs help to find the balance position; no alignment of upper body; needs to work a lot with arms and legs to keep standing on one leg*”.¹⁸⁸ The child is assessed in the frontal plane, and each leg is rated separately. The CAP has been found to be a valid instrument to use in daily clinical practice in children with clubfoot, with good reliability and responsiveness in methodological studies of the instrument.^{182,189}

Gait Deviation Index (GDI)



GDI-Kinetic

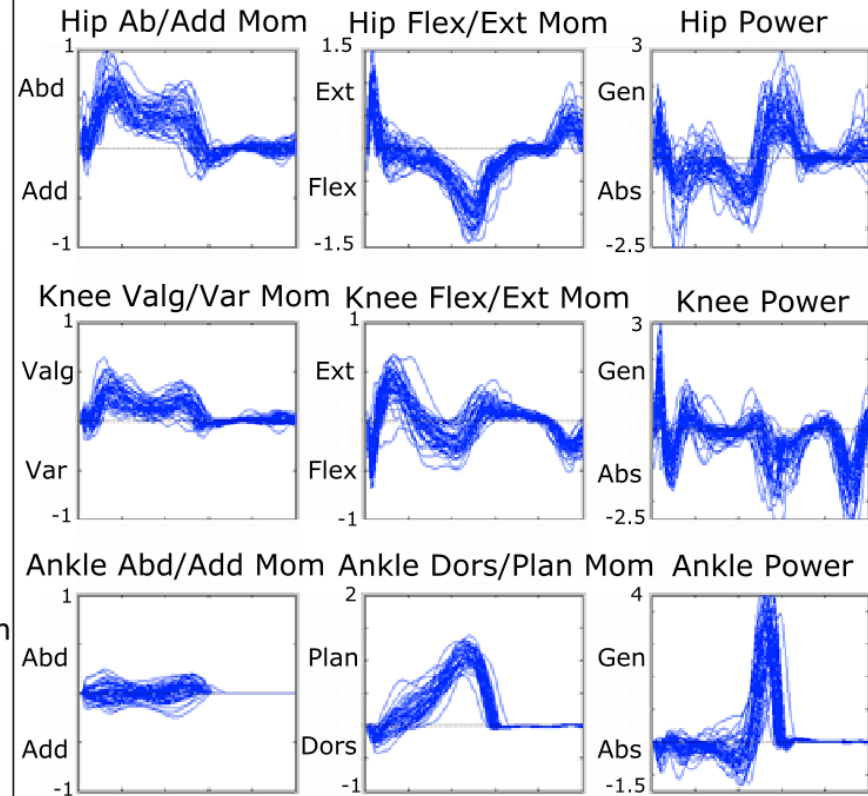


Figure 10. Gait kinematics of the pelvis, hip, knee, and ankle included in the GDI and gait kinetics of the hip, knee, and ankle included in the GDI-Kinetic. Every blue line represents one gait cycle of one leg from the typically developing children that embodied the reference norm values of the GDI and GDI-Kinetic.

3.5.4 Dimeglio classification scale

In Studies I and II, the initial severity of the clubfoot was obtained from the medical records. In all cases except for one child with missing data, the Dimeglio classification scale had been used to quantify clubfoot severity prior to treatment. In accordance with the instrument, the clubfoot was scored on a four-point scale concerning mobility of the following four parameters: equinus in the sagittal plane, varus in the frontal plane, derotation of the calcaneo-forefoot, and adductus of the forefoot relative to the hindfoot in the horizontal plane.⁴⁸ Additional points might be given for medial or posterior crease, cavus, and poor muscle condition. Consequently, the clubfoot can be classified as mild, moderate, severe, or very severe with higher scores indicating a more severe deformity.⁴⁸ The instrument has been found to be reliable, easy to apply,¹⁹⁰⁻¹⁹² and valid to be used for the follow-up of clubfoot.¹⁹³ Thus, the Dimeglio classification scale is recommended to be used before any treatment in clubfoot,^{83,87} and is widely used both in clinic practise and in research.¹⁹²⁻¹⁹⁴

3.5.5 Patient-reported outcome measures

3.5.5.1 Sociodemographic questionnaire

The parents answered a checklist with information regarding several sociodemographic parameters such as age, sex, siblings, special teaching/pedagogical support, school grade, cohabiting parents, residential area, and leisure/sports activities of the children. Moreover, parents answered an open question if the child had any disorders or disabilities. Finally, the parents were asked about their educational level, profession, birth country, and relationship to the child. In addition, parents to children with IC were inquired about number of affected feet.

3.5.5.2 Five to Fifteen questionnaire

The FTF Nordic questionnaire for evaluation of development and behaviour in children and adolescents was used to explore NDD. The instrument has been developed to be used in children aged 5 to 15 years in both clinical settings and in research to screen for developmental and behavioural difficulties such as NDD.^{161,195,196} The parent-based questionnaire comprises 181 items within eight domains (motor skills, executive functions, perception, memory, language, learning, social skills, and emotional/behavioural problems) and 20 subdomains.¹⁶¹ The items are scored in three levels; ‘does not apply’ (0), ‘applies sometimes or to some extent’ (1), or ‘definitely applies’ (2). No single value can be obtained from the whole FTF, however mean item scores can be calculated for each domain and subdomain.¹⁶¹ Moreover, domain scores can be used to obtain a profile of strength and difficulties across the eight domains.¹⁹⁶ To identify children at risk, a cut-off level of scores above the 90th percentile in any domain is considered an indication of concern for developmental disorders.¹⁹⁵ Studies of psychometric properties of the instrument have demonstrated good reliability and reproducibility.^{161,197} Clinical and population-based studies have supported the validity of the instrument.^{161,164,195,196,198-201}

3.5.5.3 *Roye's Disease-specific instrument*

Roye's Disease-specific instrument (DSI) was used as a measure of clubfoot treatment outcome, as perceived by the caregivers. The parent-reporting instrument was designed to measure treatment outcome regarding satisfaction and function.⁶⁸ Ten items, also including appearance, pain, and physical limitations, are rated on a four-point ordinal scale. Each item can be presented individually, and an overall score can be calculated ranging from 0 (low) to 100 (high satisfaction/function).^{68,202} Previous reports on the instrument have shown high internal consistency and sensitivity to change.²⁰² Moreover, Roye's DSI has been found to correlate with objective treatment outcome measures such as passive range of motion of the foot.⁶⁸ The instrument has been found to be useful in the follow-up of patients with clubfoot and has been used in several clinical studies.^{2,85,98,101,114,116}

3.5.5.4 *EQ-5D-Youth*

To measure HRQoL, the generic EQ-5D-Y (youth) questionnaire was used. The EQ-5D-Y was developed in 2009 from the EQ-5D designed for adults by the EuroQol Group.²⁰³⁻²⁰⁷ In the child-friendly version, children aged eight or older self-report their HRQoL regarding the five dimensions of 'mobility (walking about)', 'looking after myself', 'doing usual activities', 'having pain or discomfort', and 'feeling worried, sad or unhappy' without the need of a proxy.²⁰⁴ The dimensions are scored on a three-point scale of severity as no problems (1), some problems (2), or a lot of problems (3).²⁰⁴ From the answers, a five-digit EQ-5D-Y health profile can be derived. As an example, the profile 11111 would represent full health with no problems, whereas 11123 would represent some problems in the dimension 'having pain or discomfort' and a lot of problems in 'feeling worried, sad or unhappy'. In addition, the child is asked to rate their current overall health status on a Visual Analogue Scale (VAS) ranging from 0 (worst) to 100 (best).²⁰⁴ The EQ-5D-Y has demonstrated sufficient feasibility, reliability, and validity in studies of the instrument's psychometric properties.^{204,205,207} Several clinical studies have supported the EQ-5D-Y's validity, and population-based studies have used the instrument to screen for population health.²⁰⁸⁻²¹³ In Sweden, the instrument has been validated in children and adolescents with motor, orthopaedic (including clubfoot), and medical disabilities in comparison with children from the general population.²¹⁴ Moreover, the feasibility and validity of using the EQ-5D-Y as a web-based questionnaire have been confirmed.²¹⁵

3.6 STATISTICAL METHODS

An overview of statistical methods used in the thesis is provided in Table 3, and detailed information can be found in the individual papers. All statistical analyses were performed in IBM SPSS software (IBM Corporation, Armonk, NY, USA). An alpha level of <0.05 was applied for all analyses.

Table 3. Overview of statistical methods used in Studies I-IV.

	Study I	Study II	Study III	Study IV
ANOVA	x		x	
Chi-square test	x		x	x
Confidence interval (95%)	x			
Descriptive statistics	x	x	x	x
Eta-squared			x	
Fisher's exact test				x
Independent t-test			x	
Intraclass Correlation Coefficient ^{2,1}		x		
Kruskal–Wallis test	x	x		
Linear mixed-model	x			
Mann–Whitney U-test	x	x	x	x
MANOVA			x	
Sign test		x		
Spearman's rho		x		

ANOVA analysis of variance; *MANOVA* multivariate analysis of variance

3.6.1 Ensuring statistical independency between the legs

In Studies I and II, an effort was made to ensure the statistical accuracy of the legs because the right and left leg are dependent on each other. Moreover, because one of the research aims was to consider foot involvement, both studies were designed to include both feet/legs. To be able to do so, the children were divided into groups (Bilateral IC, Unilateral IC, and Control) and legs into side/units (right/left, superior/inferior, or unilateral IC/contralateral). Figure 6 shows a schematic overview of the divisions.

In Study I, a linear mixed-model was used. In the model, the within-subject factor was side with covariance structure (compound symmetry), and the between-subject factor represented group. The Kruskal–Wallis test was used for a few parameters not displaying normal distribution. In these analyses, the means for the left and right legs were calculated in the Bilateral and the Control groups. In Study II, consisting of ordinal data, superior and inferior legs were defined depending on the total MQ-CAP scores. The Sign test was used to compare the units (superior vs. inferior) within each group of children. Thereafter, the units were compared between the groups using the Mann–Whitney U-test.

3.6.2 Analysis of survey data

In Study III, a parametric statistical approach was adapted because mean item scores were calculated for the FTF domains and subdomains in accordance with the FTF manual. By doing this, group differences on the FTF, including mean domain and subdomain scores, could be compared using simultaneous multivariate and univariate analysis of variance ((M)ANOVA). Sample membership (IC vs. general population) was set as the factor and the FTF domains/subdomains as the dependent variables. Effect sizes were calculated using eta-squared and interpreted as small = 0.01–0.05, medium = 0.06–0.13, and large > 0.14.²¹⁶ However, for single FTF items the non-parametric Mann–Whitney U-test was used to compare the results between the samples. Finally, cases of possible clinical relevance were defined as having scores above the 90th percentile in at least two domains as an alternative of only one domain as proposed by the developer of FTF.¹⁹⁵ This decision was based on the impression that the domain of motor skills might be affected by the clubfoot. The cut-off level of the 90th percentile was defined using the general population sample from Studies III and IV (Table 4).

Table 4. Percentile cut-off levels used when defining clinically relevant cases from the Five to Fifteen (FTF) questionnaire calculated from the general population sample. The cut-off levels from the FTF manual are provided as comparison.

FTF domains	General population sample	FTF manual
	Age 8.4–10.5 years	Age 9–12 years
Motor skills	0.35	0.41
Executive functions	0.88	0.92
Perception	0.33	0.33
Memory	0.46	0.54
Language	0.24	0.33
Learning	0.66	0.81
Social skills	0.26	0.35
Emotional/behavioural problems	0.33	0.30

For the EQ-5D-Y in Study IV, a binary outcome was generated by combining the severity levels of ‘some’ and ‘a lot’ of problems into one outcome called ‘any problems’. The Chi-square test was used to compare group differences. However, in cases of less than five cell counts, the Fisher’s exact test was used instead. Finally, the Mann–Whitney U-test was used to compare outcomes between the samples on the EQ VAS.

3.7 ETHICAL CONSIDERATIONS

Ethical approval for the included studies was obtained from the Regional Ethical Review Board in Stockholm (no 2012/659-31/3), and the studies were conducted in accordance with the Declaration of Helsinki. The families were given written (as well as verbal in Studies I and II) information, including information about the aim of the studies, data handling, and privacy disclaimer. Moreover, the participants were informed that their decision to participate would not affect further contact or treatment at the hospital and that they could withdraw their decision to participate at any time. Informed consent for the children to participate and for their data to be used for research purposes was obtained from the parents.

4 RESULTS AND DISCUSSION

In this section, the main findings of the four studies are summarised and discussed. With the intention to combine and to provide a coherent result in a wider perspective, the findings are presented in two parts. Part one comprises gait and gross motor skills (Studies I and II), and part two comprises NDD and HRQoL (Studies III and IV). Moreover, some additional findings not included in the papers will be presented as well as some finalising comments. Detailed outcomes from each study are provided in the individual papers.

4.1 GAIT AND GROSS MOTOR SKILLS

4.1.1 Gait pattern in affected legs with idiopathic clubfoot

The main findings from Study I revealed that children with IC exhibited gait deviations both in discrete gait parameters and in the global gait indices GDI and GDI-Kinetic on a group level. Moreover, no significant differences were detected between bi- and unilaterally affected legs. For that reason, gait findings are summarised as one uniform group regarding *legs* with IC in this section, whereas detailed information can be found in the paper. The impact of foot involvement and the contralateral leg on gait when considering the whole child will be further discussed in the coming sections.

In the legs with IC, GDI and GDI-Kinetic were found to be 90.5 (SD 9.0) and 91.2 (SD 9.2), respectively, i.e. approximately 0.9–1 SD below the global gait pattern of the TD children and thus indicating global gait deviations/pathology ($p < 0.05$). The finding of the GDI was consistent with the foregoing publication of Duffy et al. of children age five to eight years treated with the Ponseti method.¹²⁶ Similar GDI scores were also found by Manousaki et al. in children with IC age seven¹⁰⁰ and Litrenta et al. in children with clubfoot age ten years¹⁸⁷ (Figure 11). Thus, there seem to be a consistency of global gait deviations with GDI scores nearby 90 in children with IC that have been treated conservatively. However, it has been proposed that GDI scores over 80 should be considered as mild gait impairment in paediatric populations.¹⁸⁷ Besides, in comparison with other publications also using the GDI in children with various disorders, children with IC were found to have generally superior GDI scores (Figure 11). Thus, the GDI score of 90.5 might still be considered a reasonable acceptable global gait outcome on a group level. Unfortunately, GDI-Kinetic is still not commonly used, and no other publications regarding IC and GDI-Kinetic have been found.

In discrete gait parameters, central findings in IC were decreased dorsi-plantar flexion range, foot moments and ankle power generation compared with TD children. Correspondingly, decreased passive range of motion was evident in IC compared with TD feet (Table 5). This is consistent with several other studies of gait in individuals with IC.^{124-126,128,132} Problems concerning equinus and decreased dorsiflexion are in line with the pathology of the deformity and have been one of the main outcome variables in IC in general and in gait studies of IC in particular.^{114,128,217} However, decreased plantarflexion seems to be less commonly reported as

a main outcome variable in IC. Still, this was one of the main findings in Study I, with decreased plantarflexion confirmed in both passive range of motion and gait in the affected legs with IC compared with the TD children.



Figure 11. Gait Deviation Index (GDI) scores in children with idiopathic clubfoot and the typically developing children in Study I, and in comparison with other studies of children using the GDI.

*Modified Ponseti treatment method with the use of custom-made dynamic orthoses in the maintenance phase. α Arthrogyrposis Multiplex Congenita (walking with shoes). *ns* not specified; *GMFCS* Gross Motor Function Classification System. References in the figure: Duffy et al.,¹²⁶ Litrenta et al.,¹⁸⁷ Manousaki et al.,¹⁰⁰ idiopathic toe walking,¹³⁴ juvenile idiopathic arthritis,²¹⁸ Arthrogyrposis Multiplex Congenita,²¹⁹ Cerebral Palsy.²²⁰

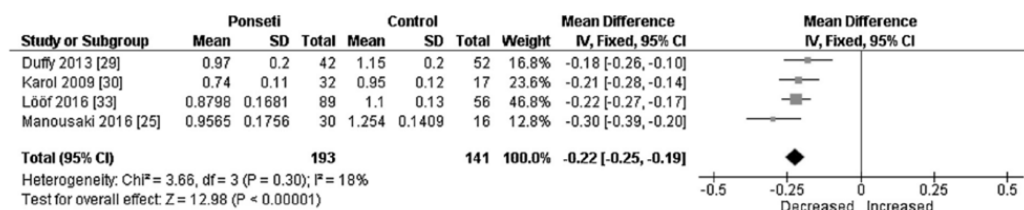
The decreased dorsi-plantar flexion range is probably one substantial reason for the reduced ankle power generation found in the IC group of 2.8 W/kg in comparison with 3.6 W/kg in the TD group ($p < 0.001$). A finding that was confirmed in a recently published meta-analysis of gait kinetics in children with clubfoot (Figure 12).¹¹⁷ In addition, a power shift was noted in the ankle/hip ratio in IC, indicating weak ankle plantar flexor muscles and compensatory hip extensor muscles. This is a compensatory mechanism previously observed in children with affected feet due to juvenile idiopathic arthritis.²¹⁸ Weakness of the ankle plantar flexor muscles has previous been described to affect gait initiation in children with IC in a study of Wicart et al.¹³⁵ In their study, the authors furthermore concluded that disturbance of sensory information due to IC might contribute to the impaired propulsion.¹³⁵ Somewhat similar, Jeans et al. suggested an inherent ankle weakness because both children treated with the Ponseti and the French physiotherapy method were found with diminished ankle power in gait and isokinetic ankle strength.¹³¹

Table 5. Passive range of motion and gait parameters in affected legs of children with idiopathic clubfoot and legs of the typically developing (TD) children from Study I. Note that IC are presented as one group, data divided into bi- and unilateral IC and the contralateral leg can be found in the paper.

			Idiopathic clubfoot		TD	
			Mean (SD)	n	Mean (SD)	n
PASSIVE RANGE OF MOTION	FOOT, degrees	Dorsiflexion, knee extended*	9 (7)	87	20 (4)	56
		Dorsiflexion, knee flexed*	13 (8)	89	29 (4)	56
	KNEE, degrees	Plantarflexion*	44 (12)	78	59 (7)	56
		Extension*	11 (6)	87	7 (2)	56
	HIP, degrees	Internal rotation*	52 (11)	56	58 (9)	56
		External rotation	42 (9)	56	46 (5)	56
KINEMATICS	FOOT, degrees	Max dorsiflexion	11.6 (4.6)	89	11.6 (3.1)	56
		Max plantarflexion*	12.2 (7.2)	89	17.7 (4.8)	56
		Dorsi-plantar flexion range*	23.8 (4.9)	89	29.4 (4.8)	56
		Plantarflexion at initial contact	0.6 (5.1)	89	0.6 (3.6)	56
		Mean dorsiflexion in terminal swing	3.2 (5.3)	89	3.8 (3.1)	56
		Mean foot progression in stance*	0.3 (7.6) <i>int</i>	89	4.6 (5.7) <i>ext</i>	56
	KNEE, degrees	Max extension in stance	1.4 (6.8)	89	1.7 (4.7)	56
	HIP, degrees	External rotation at initial contact	9.3 (7.8)	89	11.2 (5.8)	56
		Mean external rotation in stance	1.7 (5.8)	89	1.0 (4.9)	56
	KINETICS	MOMENTS, Nm/kg	Foot max dorsal moment*	0.12 (0.1)	76	0.17 (0.06)
Foot max plantar moment*			0.88 (0.17)	76	1.10 (0.13)	46
Knee max flexion in stance			0.20 (0.13)	76	0.25 (0.10)	46
Hip max abduction in early stance*			0.55 (0.13)	76	0.63 (0.14)	46
POWER, W/kg		Ankle max generation*	2.75 (0.76)	76	3.61 (0.75)	46
		Ratio ankle/hip generation*	1.88 (0.64)	76	2.76 (0.98)	46
SPEED, m/s	Walking Speed	1.12 (0.16)	89	1.19 (0.17)	46	
	Non-dimensional speed	0.47 (0.07)	89	0.51 (0.07)	46	

* Indicates significant differences ($p < 0.05$), further statistical details can be found in the paper. Moments refer to internal moments. *Nm/kg* Newton-meter per kilogram; *W/kg* Watts per kilogram; *m/s* meter per second; *int* internal; *ext* external.

A Ankle plantarflexor moment



B Ankle power

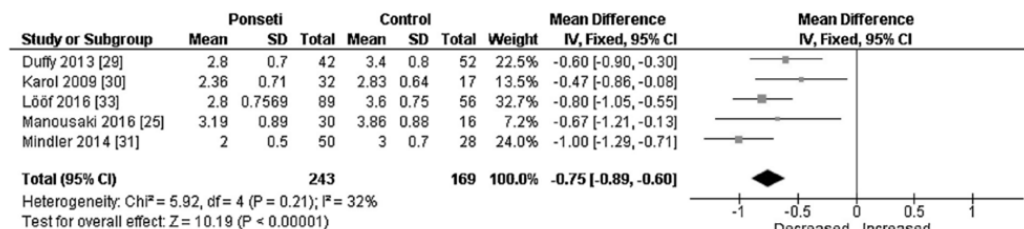


Figure 12. Meta-analyses by Tuinsma et al. comparing children that have been conservatively treated for IC with healthy controls (reprinted with permission).¹¹⁷ References in the figure refer to ^{100,124,126,132} in this thesis.

Thus, IC might be predisposed for ankle plantar flexor weakness and reduced ankle power generation. However, if this can be counteracted for with further attention on not only dorsiflexion but also plantarflexion motion and interventions to strengthen the calf muscles need to be studied. Nevertheless, the finding of 24% less ankle power generation might explain the 21% lower walking capacity¹⁵¹ and fewer total daily steps¹³¹ found in children with clubfoot compared to norm materials.

Not included in the paper but an interesting finding from Study I was that initial severity of the clubfoot did not relate to the gait deviations using the Dimeglio classification scale and GDI ($r_s = 0.104$) (Figure 13). This is consistent with Gottschalk et al.’s findings of no correlations between initial Dimeglio score and ankle motion during gait.⁵⁸ Consequently, even children born with mild IC might exhibit later significant gait deviations.

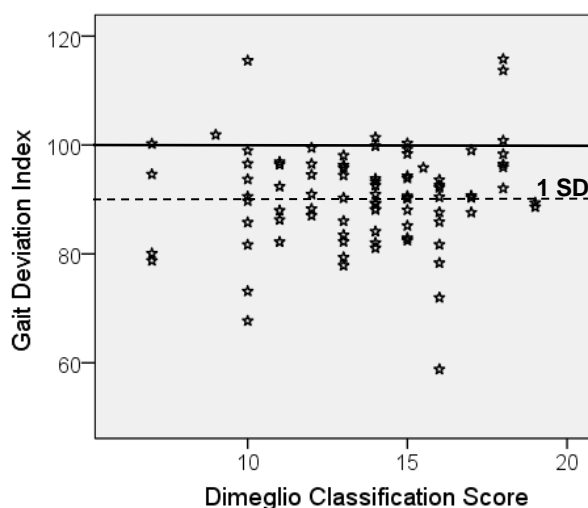


Figure 13. Initial clubfoot severity before treatment measured with the Dimeglio classification scale (higher number indicating a more severe deformity) and gait deviations measured with the Gait Deviation Index with scores below 100 indicating gait deviations.

4.1.2 Gross motor skills in children with idiopathic clubfoot

In Study II, children with IC at age five were found with gross motor deficits and asymmetries, regardless of foot involvement, in comparison with TD children. Moreover, gross motor skills correlated poorly to moderately with initial severity of the clubfoot, passive range of motion of the foot, and global gait measures, indicating a different outcome entity.

To give an overview of the gross motor findings, the sum of the inferior performing leg for each child can be used as an overall comparison, presenting a total score of 13 and 14 (depending on foot involvement) in children with IC out of the maximal score of 24. This was significantly worse than the total score of 22 in the TD children ($p < 0.05$).

In the single tasks, an MQ-CAP score of ≤ 2 was defined as deviant. Accordingly, more than half of the children with IC had deviations in toe and heel walking compared with almost none of the TD children. Even worse, a majority of the children with IC showed deviations in the tasks one-leg stand and hop compared with 32 and 43% of the TD children, respectively (Table 6). Furthermore, seven children (15%) with IC were unable to perform the one-leg hop at all on the inferior performing leg, in comparison with two (7%) in the group of TD children. Finally, one child with unilateral IC was unable to stand only on the affected leg at all in the task one-leg stand.

Table 6. Legs with gross motor deviations according to the MQ-CAP on the inferior performing leg in children from the idiopathic clubfoot (IC) and typically developing (TD) groups.

	Idiopathic clubfoot		TD n=28
	Bilateral IC n = 22	Unilateral IC n = 25	
	% (n)	% (n)	% (n)
Running	23 (5)	28 (7)	0 (0)
Walking	18 (4)	36 (8)	0 (0)
Toe walking	64 (14)	52 (13)	0 (0)
Heel walking	64 (14)	64 (16)	4 (1)
One-leg stand	91 (20)	84 (21)	32 (9)
One-leg hop	86 (19)	84 (21)	43 (12)

4.1.3 The contralateral leg

In the contralateral legs, no deviations were established in the discrete gait parameters or gross motor skills compared with the TD children. Nonetheless, global gait modifications were shown in GDI and GDI-Kinetic. This could be perceived as being contradictory; however, because GDI and GDI-Kinetic provide global measures of gait pathology having one leg experiencing gait deviations, and the other not, in the same child would be almost impossible. Nonetheless, GDI/GDI-Kinetic are designed to measure the legs independently with the ability to quantify differences and asymmetries.^{133,186} Thus, GDI-Kinetic of the contralateral leg was

found to have a lower mean score (93) than the unilateral clubfoot side (94) in Study I. Similar findings of lower GDI-Kinetic scores on the unaffected side have been shown in children with unilateral cerebral palsy.¹⁸⁶ Somewhat comparable are the findings of alterations of the contralateral side in children with IC to preserve global symmetry and equilibrium of the body in tiptoe raising and steps.^{138,221}

Nonetheless, previous findings of abnormality of the contralateral foot in discrete parameters¹³⁵⁻¹³⁷ were not replicated in our studies. Nor did it seem that the global gait modifications of the contralateral leg transmitted to gross motor skills. On the contrary, our findings suggest that the contralateral leg developed gross motor skills similar to TD legs. At the same time, because of possible gait modifications on the contralateral side, the leg should not be used as the reference in gait measurements.

4.1.4 The impact of foot involvement on gait and gross motor skills

Studies I and II both evaluated bi- and unilateral clubfoot independently of each other as well as the contralateral leg in children with unilateral clubfoot. To our knowledge, this has never been done before to this extent, thus the studies present novel findings of the impact of foot involvement on gait and gross motor skills.

In gait, mean differences of the gait parameters deviating from the group of TD children were surprisingly similar in the bi- and unilateral clubfoot groups (details in the paper). Furthermore, no differences were detected between the left and right leg in bilateral cases. Figure 14 demonstrate these findings in the parameter maximal ankle power generation in gait.

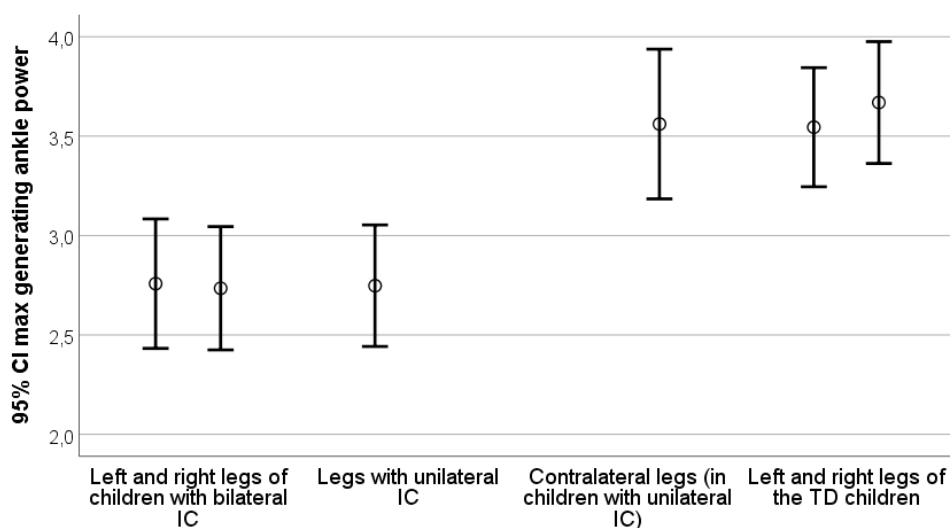


Figure 14. The 95% confidence intervals (CI) of the maximal ankle power generation (w/kg) with subdivision of the legs in children with bilateral idiopathic clubfoot (IC), unilateral IC and the typically developing (TD) children.

In Study II, also gross motor skills were found similar between bi- and unilateral IC, deviating almost equally from the results from TD children (Figure 15). These gross motor similarities are in line with research both in toddlers^{147,148} and in children five years and older.^{150-152,222,223} However, gross motor asymmetries could be detected between the inferior and superior performing legs within all groups. Not surprisingly, this was most apparent in the group of unilaterally affected children who performed significantly poorer on the clubfoot side in all items compared to the contralateral side. Somewhat more notable was that children with bilateral clubfoot also showed significant side differences in the items toe and heel walking as well as one-leg stand and hop on a group level (details in the paper). This is consistent with our clinical impression that not only children with unilateral IC, but also children with bilateral IC favour one side when performing difficult gross motor tasks. In TD children, the only asymmetry found was in the item one-leg hop (Figure 15).

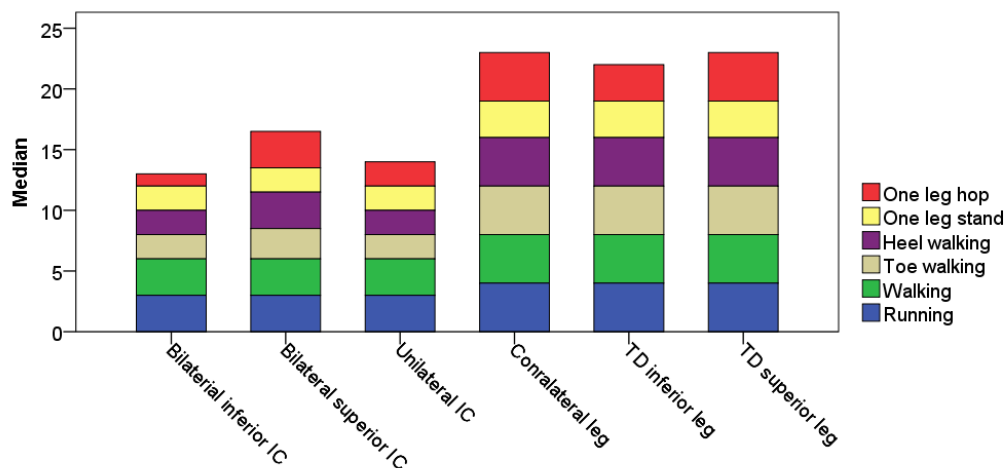


Figure 15. Median scores of the gross motor tasks divided into inferior and superior legs within the different idiopathic clubfoot (IC) and typically developing (TD) groups using the Clubfoot Assessment Protocol (CAP). In children with unilateral IC the inferior leg was always the leg with IC and the superior leg the contralateral leg.

The findings from Studies I and II dispute the theory of differences in severity between bi- and unilateral IC in relation to gait and gross motor skills. Contrary, our findings were remarkably similar between the two groups indicating both similar severities and development. For this reason, legs with bi- and unilateral IC might be combined into one uniform group in future studies of gait and gross motor skills if only the clubfoot side is assessed. If only one leg is to be selected from bilateral cases to be clustered with unilateral IC, the inferior performing leg should be the general preference. At the same time, awareness of foot involvement is important when assessing gait and gross motor skills in a clinical setting or when the whole child is considered due to the pronounced asymmetries between the legs found especially in children with unilateral IC.

4.1.5 Motor skills and development

Gross motor skills correlated poorly to global gait measures, passive range of motion in the foot, and initial severity of the clubfoot in children with IC, even if some moderate correlations were found with passive dorsiflexion and the initial severity in some MQ-CAP items (Table 7).

Table 7. Correlations between the gross motor tasks and the Gait Deviation Index, passive range of motion of the foot, and initial clubfoot severity using the Dimeglio classification scale.

	GDI	Dorsi- flexion	Plantar- flexion	Initial severity
MQ-CAP	n=69	n=69	n=64	n=68
Running	0.28	0.40	0.16	-0.22
Walking	0.31	0.43	0.22	-0.32
Toe walking	0.11	0.06	0.28	-0.31
Heel walking	-0.02	0.49	-0.05	-0.45
One leg stand	0.13	0.13	0.12	-0.24
One leg hop	0.06	0.13	0.13	-0.11
Total MQ-CAP	0.21	0.41	0.20	-0.39

GDI Gait Deviation Index; *MQ-CAP* Motion quality domains from the Clubfoot Assessment Protocol

Similar results have previously been presented in attaining early gross motor skills and in fundamental motor skills with no or weak relations to initial clubfoot severity, clinical foot status, or gait variables.^{147,149,150} In the same manner, a sub analysis from Study II (unpublished data) revealed only a poor correlation ($r_s = 0.156$) between gross motor skills and the satisfaction rate of the clubfoot treatment outcome as perceived by the parents. Indeed, it seems that gross motor skills might represent a different outcome entity that is separate from, or with a low interrelationship to, traditional outcome parameters in IC.

Since the publication of Study II, motor skills and development appear to have had an increased interest as an outcome variable in the treatment of IC with three papers published in the last year. Zapata et al. found that gross motor development in five-year-olds with IC using the PDMS 2nd edition did not differ from the norm material.²²² Still, 19% of the children with IC were found with below average or poor scores. In addition, initial clubfoot severity, foot involvement, and treatment method did not affect the gross motor development significantly. The same authors followed up their results with a study of ten-year-old children with IC, this time using the Bruininks-Oseretsky Test of Motor Proficiency (BOT) 2nd edition.²¹⁷ Again, the children with IC were found to have average scores on a group level that did not differ from the norm material. However, this time 31% of the children had scores below or well-below average for the domain Body Coordination. Once more, initial clubfoot severity did not affect the result, but surgical treatment was found to impair balance. Finally, Aulie et al. used the MABC 2nd edition to assess seven to ten-year-old children who had been treated with either

surgery or the Ponseti treatment methods.²²³ Even though no differences were detected between the treatment methods, or between bi- and unilateral clubfoot, 24% of the children were found not to have motor abilities within the defined normal range. The authors stated that they were somewhat surprised because they had suspected superior results in the Ponseti group with fewer children requiring major surgery. Consequently, they discussed how other factors might play a role, and they provided the example of how the one-leg stand requires a combination of motor control, sensory, and cognitive processes. Thus, Aulie et al. conclude that children with clubfoot should have more thorough and early neuromotor assessments.²²³

All three above-mentioned studies used instruments that assess fundamental motor skills,¹⁴⁰ contrary to our study assessing gross motor skills, and this makes it hard to make comparisons with Study II. For example, most children in our sample managed to stand on one foot/leg to some extent but had deviations in the performance of the task (e.g. with great body sway and compensating arm movements). In the PDMS, BOT, and MABC instruments, it is not the quality of the skills that is primarily rated, i.e. it does not matter if the child performs the task with a great body sway. Moreover, object-manipulation skills (e.g. throwing a ball) and tasks not including the feet (e.g. doing sit-ups) are included. Nonetheless, several similarities can be noted. First, motor skills seem to be affected in a greater proportion of children with IC compared with children without the deformity. Second, initial clubfoot severity seems not to affect motor skills significantly. Third, bi- and unilateral clubfoot appear to develop noticeably similarly. Finally, and maybe most outstanding, are the findings that treatment method or other outcome variables such as passive range of motion of the foot do not seem to affect motor skills substantially.

It has been theorised that motor development is dependent on genetic and environmental factors.^{224,225} Consequently, delays in attaining motor milestones and motor deficits might originate from genetic abnormalities as well as pre- and postnatal factors.^{224,226} For example, maternal fever and smoking during pregnancy has been associated with DCD²²⁷ and developmental (including motor) delay,²²⁸ respectively. Furthermore, in the model of body movement the motor/action system (including the biomechanical system) is just one factor within the individual.¹⁴¹ Thus other aspects, beyond the structural deformity of IC, such as genetics, prenatal, cognitive, and sensory/perceptual factors might be considered in relation to the motor deficits found in children with IC. Moreover, it is yet to be explored if additional treatment such as physiotherapy (e.g. muscle strengthening and motor training) might be beneficial in the development of gait and gross motor skills in children with IC.

4.2 NEURODEVELOPMENTAL DIFFICULTIES AND HEALTH-RELATED QUALITY OF LIFE

4.2.1 Neurodevelopmental difficulties in children with idiopathic clubfoot

To the best of our knowledge, Study III is the first study to explore NDD in individuals with IC. The major finding in this study was that children with IC, at the age of nine years, experienced more NDD compared to an age, sex, and residential area parallelised sample from the general population. This result supports our hypothesis about other difficulties in children with IC beyond the musculoskeletal deformity itself. Findings from the study have been proposed to be a novel and possibly valuable contribution to the long-term success of IC treatment.¹¹¹

By using the FTF questionnaire, significantly more difficulties were found in the domains of motor skills, perception, and language and the subdomains of gross and fine motor skills, relation in space, comprehensive, and expressive language skills (Table 8). Moreover, 26 items within all domains in the FTF except the emotional/behavioural problems domain were found with significantly more difficulties in the IC sample. For example, the items *Often has difficulty sustaining attention in tasks or play activities* and *Difficulty remembering long or multiple-step instructions* were reported to a significantly greater extent by parents to children with IC with respect to the general population sample. A full list of the 26 items is presented in the paper.

These findings support not only our hypothesis and previous indications found in the literature about IC and NDD, but also other musculoskeletal deficiencies such as idiopathic toe walking (ITW). Engström et al. surveyed 51 children with ITW with a mean age of nine years also using the FTF.¹⁶⁴ In comparison with the FTF norm material, the authors showed an increased prevalence of NDD among all domains in children with ITW with almost 25% of the children experiencing difficulties throughout the FTF. Because toe walking also has a known connection to ASD and language disorders, the authors speculate that their findings can be taken as an indicator of a common pathology.^{164,165} In comparison with the findings of Engström et al.,¹⁶⁴ the mean domain scores were found to be lower in children with IC (Figure 16). However, because the children with ITW included in the study were seeking medical advice and were referred to the orthopaedic clinic, a selection bias can be considered.^{164,229} Moreover, different methodological approaches were used in the analysis of FTF, and thus comparisons between children with IC and ITW can only be speculative. Nonetheless, looking at similarities, both studies indicate some kind of connection between distal musculoskeletal deficits and NDD in children.

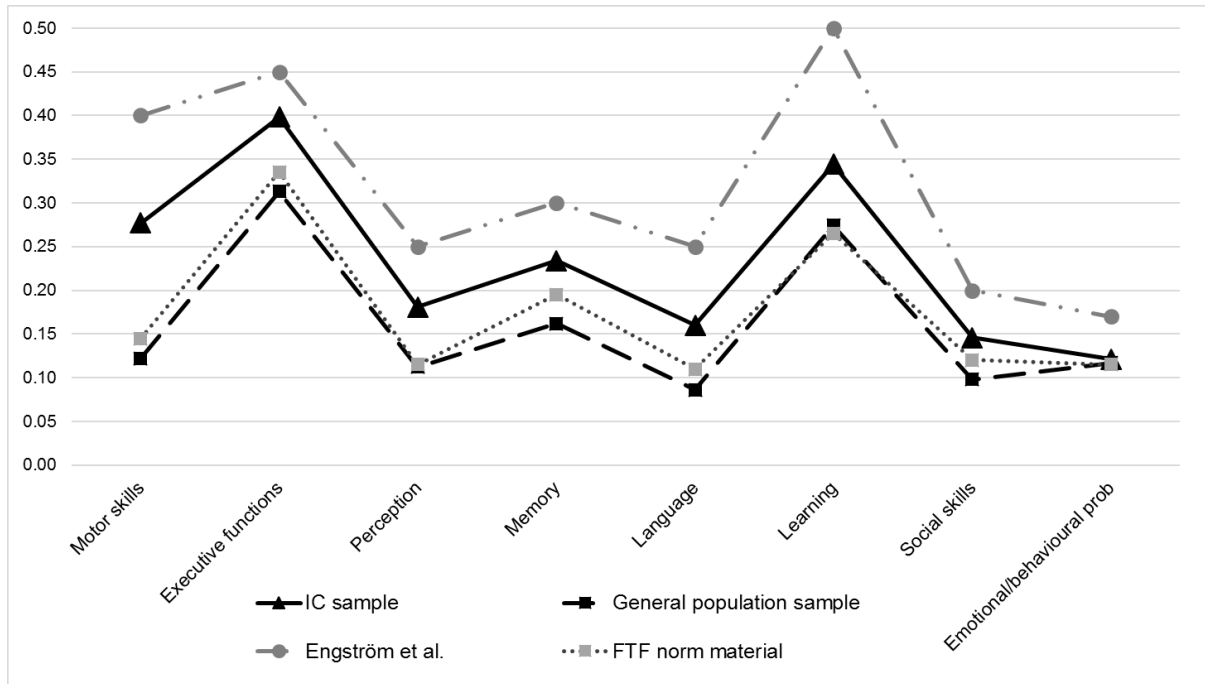


Figure 16. Mean profiles on the Five to Fifteen (FTF) questionnaire for children with idiopathic clubfoot (IC), the general population sample, the norm material from the developer of FTF age 9 to 12 years,¹⁶¹ and the result of Engström et al. study of children with idiopathic toe walking.¹⁶⁴

Because our study is the first of its kind, non-significant results might also be of interest in the generation of new knowledge and hypotheses. By exploring subdomains from the non-significant domains and raising the alpha level to <0.1 , this could give us an indication of other potential areas of interest. By doing this (unpublished data), indications of possible areas of interest were shown in the domain of memory ($p = 0.063$) and the subdomains of attention ($p = 0.074$) and hypoactivity ($p = 0.008$) from the executive functions domain, body ($p = 0.084$) and visual ($p = 0.054$) perception from the perception domain, and reading/writing ($p = 0.070$) from the learning domain (Table 8).

Table 8. Domains and subdomains from the Five to Fifteen questionnaire in children with idiopathic clubfoot (IC) and the general population sample.

	Idiopathic clubfoot n = 106			General population n = 109			Mean difference	p	Eta-squared
	Mean	SD	Median	Mean	SD	Median			
Motor skills	0.28	0.37	0.18	0.12	0.16	0.06	0.16	0.000*	0.07
Gross motor skills	0.38	0.48		0.12	0.21		0.27	0.000*	0.12
Fine motor skills	0.21	0.35		0.13	0.18		0.08	0.038*	0.02
Executive functions	0.40	0.44	0.24	0.31	0.35	0.20	0.09	0.115	0.01
Attention	0.48	0.54		0.36	0.43		0.12	0.074	0.01
Hyperactive/impulsive	0.33	0.43		0.31	0.38		0.02	0.767	0.00
Hypoactive	0.36	0.50		0.20	0.32		0.15	0.008*	0.03
Planning and organising	0.43	0.56		0.33	0.48		0.10	0.186	0.01
Perception	0.18	0.30	0.06	0.11	0.19	0.06	0.07	0.043*	0.02
Relation in space	0.17	0.35		0.08	0.21		0.09	0.019*	0.03
Time concepts	0.31	0.48		0.25	0.39		0.06	0.296	0.01
Body perception	0.17	0.32		0.10	0.22		0.07	0.084	0.01
Visual perception	0.08	0.26		0.03	0.11		0.05	0.054	0.02
Memory	0.23	0.34	0.09	0.16	0.22	0.09	0.07	0.063	0.02
Language	0.16	0.29	0.05	0.09	0.16	0.00	0.07	0.021*	0.03
Comprehension	0.24	0.43		0.12	0.27		0.12	0.014*	0.03
Expressive language skills	0.12	0.26		0.06	0.13		0.06	0.041*	0.02
Communication	0.21	0.43		0.14	0.32		0.07	0.177	0.01
Learning	0.34	0.39	0.17	0.27	0.30	0.17	0.07	0.138	0.01
Reading/writing	0.35	0.51		0.24	0.36		0.11	0.072	0.02
Math	0.25	0.47		0.20	0.39		0.05	0.410	0.00
General learning	0.16	0.36		0.12	0.29		0.05	0.284	0.01
Coping in learning	0.36	0.46		0.28	0.38		0.08	0.198	0.01
Social skills	0.15	0.31	0.00	0.10	0.22	0.00	0.05	0.193	0.01
Emotional/behavioural problems	0.12	0.19	0.05	0.12	0.21	0.03	0.00	0.891	0.00
Internalising	0.12	0.22		0.11	0.23		0.00	0.958	0.00
Externalising	0.15	0.25		0.13	0.28		0.02	0.588	0.00
Obsessive-compulsive	0.08	0.19		0.10	0.21		-0.02	0.482	0.00
Complete Five to Fifteen questionnaire								0.004*	0.10

* Indicates significant differences $p < 0.05$, and bold numbers indicate $p < 0.1$

4.2.1.1 Neurodevelopmental disorders in children with idiopathic clubfoot

Findings from Study III yield concerns of reported neurodevelopmental *difficulties*, however also a notion of increased neurodevelopmental *disorders* could be observed within the IC sample.

When analysing the FTF data, frequencies of the more severe difficulties reported by parents are also of interest, i.e. parents reporting ‘definitely applies’. For example, reporting ‘definitely applies’ in six out of the nine items in the attention and/or hyperactivity/impulsivity subdomains has been suggested to fulfil the DSM-IV criteria of ADHD.²⁰¹ In our sample of children with IC, 7.9% of the children (n = 8) fulfilled that criterion (unpublished data). This could be compared with the findings of Airaksinen et al. with 2.3% of six to eight-year-old community children fulfilling the criterion using the same method.²⁰¹ Even though this comparison is broad and without statistical power, it indicates a possibly increased occurrence of ADHD in children with IC. Moreover, these observations are in line with the increased ADHD/ADHD traits found by chance in patients with clubfoot by Max et al.¹⁶³ Lastly, the findings that 6% of the children in the IC sample were reported of the parents with, or suspected, ADHD on the sociodemographic questionnaire compared with 2% in the general population sample and 3.3% in children seven to twelve years from Stockholm County²³⁰ further support our hypothesis.

Another neurodevelopmental disorder, ASD, was found to be notably increased in our sample of children with IC, with 4% of the children reported to have the disorder by their parents. This can be compared with 1% in the general population sample and 1.7% found in children age six to twelve years in a population-based study from Stockholm County.¹⁵⁸ Finally, 3% of the children were reported to have language difficulties and 1% to have developmental delays in the IC sample, compared with 1% of the children reported to have language difficulties in the general population sample. The full list of disorders and disabilities reported of the parents can be found in the appendix.

Taken together, not only did we find increased reported neurodevelopmental *difficulties* in the IC sample, but also indications of an increased incidence of clinically diagnosed neurodevelopmental *disorders*. However, it is important to keep in mind that the FTF is a broad screening instrument and is not by itself a diagnostic tool. Furthermore, the study was not designed to evaluate neurodevelopmental disorders.

4.2.1.2 Clinically relevant cases

Our findings suggest based on the FTF questionnaire that around one third of the children with IC could have clinically significant NDD (31% in our IC sample), with a concern of developmental disorders. The estimated number was determined from having at least two domains over the 90th percentile cut-off level instead of one as defined by the developer of the FTF.^{161,195} Consequently, the result of one third of the children with IC having clinically significant NDD should not be an overestimation. There were no significant differences regarding sociodemographic parameters, foot involvement, or sex between children with IC and NDD combined and those with solely IC.

By adjusting the mean scores to the 90th percentile so that positive numbers imply mean scores above the 90th percentile cut-off level, developmental profiles of strength and difficulties can be obtained.¹⁹⁶ As seen in Figure 17, a majority of the children with IC had similar developmental profiles below the cut-off level, while children above the cut-off had greater variability.

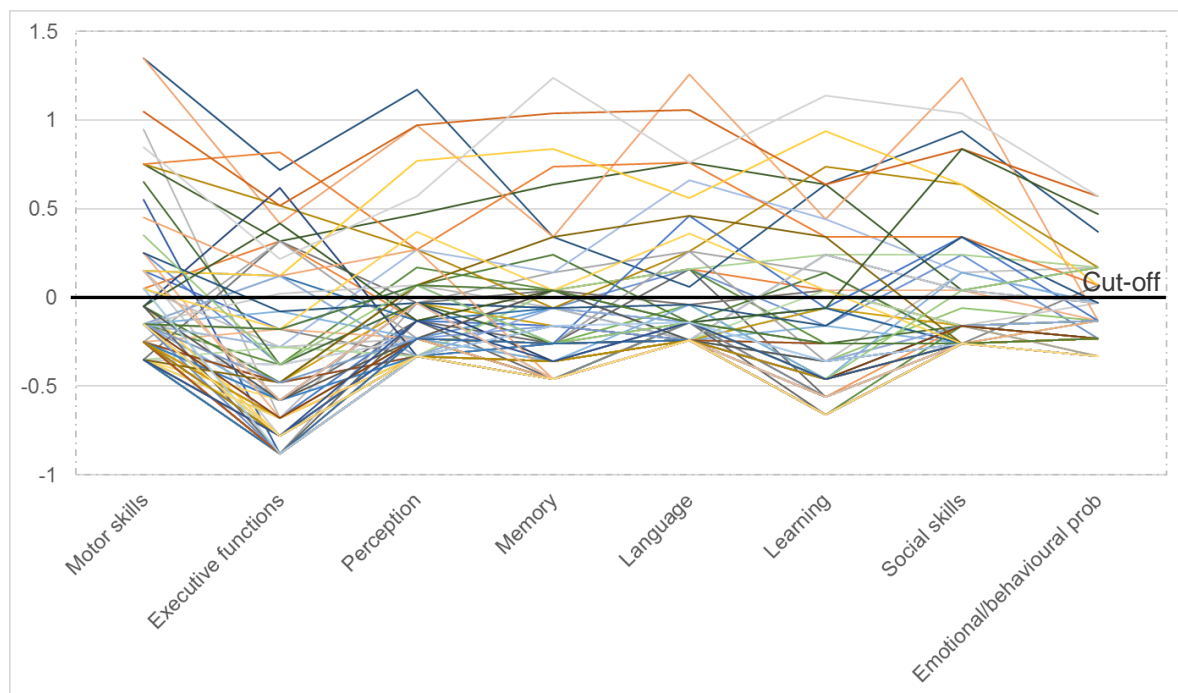


Figure 17. Adjusted mean scores according to the 90th percentile cut-off level on the Five to Fifteen questionnaire of each individual child in the idiopathic clubfoot sample. Thus, positive numbers indicate concern for developmental disorders.

4.2.1.3 Causality

Because of the cross-sectional design used in Study III, no conclusion can be drawn about the causality between IC and NDD. In conceptual models of the interrelationship of coexisting disorders, the disorders can be directly related (one disorder leading to another), coincidental (appearing independently of each other), or indirectly related (having a similar cause).^{157,231} In children with both IC and NDD, causality can only be speculated. Even so, the directly related model seems highly unlikely because that would mean that IC would cause the NDD (or the other way around). However, theories of a possible relationship between motor and language development exist, indicating a connection between motor and language impairments.²³² Theoretically, the two month's delay of independent walking in toddlers with IC^{142,147,148} might affect language development. However, the effects of attaining motor milestones, such as independent walking, on language development become smaller over time and eventually disappear as most children learn how to walk.²³³ Thus, it seems unlikely that IC by itself would cause language deficits and NDD.

Might it be possible that IC and NDD appear by chance, independently of each other, in the same sample of children? This possibility cannot be ruled out. However, given the method applied, this chance is probably low. Moreover, mothers who do not respond to follow-up are believed to exhibit factors associated with negative neurodevelopmental outcomes such as lower socioeconomic status.²³⁴ Therefore, non-responders in the cohort of children with IC in Study III are suspected to exhibit at least similar, or higher, levels of NDD.

Consequently, an indirect causality between IC and NDD might be a justified model with underlying environmental and/or genetic factors. As an example, maternal smoking is one environmental factor found to be associated with both IC and NDD.²³⁵⁻²³⁸ Moreover, genetic factors seem to contribute to the development of both IC and NDD.^{18,154,155,236,239,240} The increased prevalence of joint hypermobility found both in individuals with IC and those with NDD^{43,44,241-243} support that that a common/indirect causality may exist. However, because the cause of IC is unknown, more research is warranted within the field before any conclusions can be made.

4.2.2 Health-related quality of life in children with idiopathic clubfoot

In the final study, Study IV, HRQoL was evaluated using the EQ-5D-Y. The results showed that 51% (n = 53) of the children with IC stated full health (EQ-5D-Y health profile 11111) compared with 71% (n = 77) in the general population sample. The findings furthermore suggested more problems in children with IC regarding the dimensions ‘mobility (walking about)’ (p = 0.039), ‘doing usual activities’ (p = 0.003), and ‘having pain or discomfort’ (p ≤ 0.000, Figure 18).

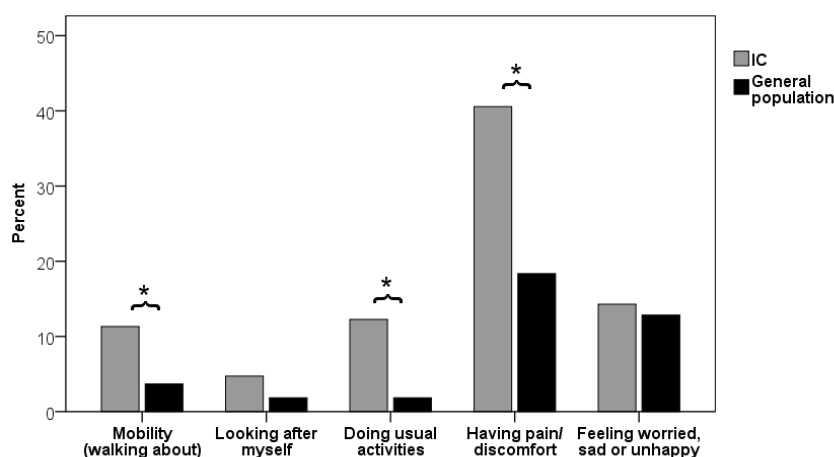


Figure 18. Percentage of the children with idiopathic clubfoot (IC) and the general population sample reporting any problems (‘some problems’ or ‘a lot of problems’) on the EQ-5D-Y dimensions. * significant differences (p < 0.05)

Despite this, the overall health status (VAS) was similar between the samples with a median of 95 in the IC sample and 93 in the general population sample (p=0.817). Furthermore, foot involvement and sex did not affect HRQoL significantly (p ≥ 0.122), contradicting previous research in IC of inferior HRQoL in females,^{66,67} but in line with previous studies of similarities between the sexes in paediatric populations.^{174,208,212,214}

The findings implied that increased problems reported in the EQ-5D-Y dimensions do not translate to lower overall health status in children with IC. Similar findings were found in Jelsma et al.’s study of children with disabilities attending special schools in comparison with children attending regular schools.²⁴⁴ In children with special needs, more problems were reported in the dimensions ‘mobility (walking about)’ and ‘looking after myself’. However, overall health status was similar to children in the regular schools.²⁴⁴ Similar patterns have been described in children with arthrogryposis and adolescents with celiac disease in Sweden.^{209,213} It seems that children are aware of their limitations, but this does not seem to affect perceived overall health status.

Children with IC in our sample were furthermore found to exhibit an overall comparable overall health status to other population-based samples of children and adolescents in Sweden.^{207,211,214} Moreover, children with IC reported better overall health status compared with children with asthma, ASD, intellectual disabilities, hearing disabilities, juvenile idiopathic arthritis, arthrogyrosis, and cerebral palsy also using the EQ-5D-Y.^{208,209,212,214} As a final point, even though significantly more problems were found on a group level, the majority of the children with IC did not report problems within the dimensions ‘mobility (walking about)’ or ‘doing usual activities’. This observation was supported by the main leisure/sport activities of the children reported by the parents (appendix). Hence, it could be argued that HRQoL seems not to be substantially affected by the diagnosis of IC in most children, with the exception of pain and discomfort.

4.2.2.1 Pain

In our sample, 41% of the children with IC reported problems concerning pain or discomfort compared with 18% in the general population sample. In the parent-reported Roye’s DSI, 58% of the parents reported that their child sometimes complained about pain in the affected foot, 60% complained when doing heavy exercise, and 26% complained when doing moderate exercise (unpublished data). Our result can be compared with the findings of Zionts et al. using the same instrument in parents to 101 children with IC with a mean age of seven years.² In their study, parents reported complaints of pain in the affected foot in 42% of the children, 48% reported pain during heavy exercise, and 35% reported pain during moderate exercise.² In another study, Hayes et al. reported that 50% of ten-year-old children with overcorrected clubfoot reported pain, while this was the case in 32% of those with corrected plantigrade clubfoot.²⁴⁵

Because we lack data on the clubfoot treatment outcome and the location of the reported pain from the children in our sample, the reason for the increased pain and discomfort can only be speculated on. However, even though treatment outcomes, including pain, have improved after the introduction of conservative treatment, pain still seems to be a major concern within the diagnosis of IC.^{75,127,129}

Chronic musculoskeletal pain can have a negative impact on physical and academic performance, sleep, and social functioning,^{246,247} and physical inactivity and overweight might also follow.²⁴⁸ At the same time, chronic musculoskeletal pain has high costs for the health care system.²⁴⁷ Therefore, pain management such as appropriate shoes and preventive education about training and overload risks should be included in the regular follow-up programs of children with IC.

4.2.2.2 The impact of neurodevelopmental difficulties on health-related quality of life in children with idiopathic clubfoot

A central finding in Study IV was that neurodevelopmental *difficulties* negatively affected HRQoL in children with IC. For example, 70% (n = 23) of the children with IC and NDD combined reported a profile of ‘any problems’ compared to 41% of those with IC and without NDD and to 29% in the general population sample.

Moreover, 25% of the children with both IC and NDD reported feeling worried, sad, or unhappy compared with 10% of the children with IC and without NDD (p = 0.038). In addition, the dimensions ‘looking after myself’ and ‘doing usual activities’ as well as overall health status were significantly diminished in children with IC and NDD combined (p ≤ 0.032, Table 9). These findings are consistent with Jonsson et al.’s review of quality of life in children with mental and behavioural disorders.¹⁷³ In their review of 41 eligible studies, the authors concluded that self-reported quality of life was significantly reduced in children with neurodevelopmental disorders compared with healthy controls.¹⁷³ These findings further support the importance of awareness of NDD in children with IC.

As a final remark, the domain ‘pain and discomfort’ did not differ significantly between those with and without NDD in the IC sample despite research suggesting that neurodevelopmental disorders such as ASD/ADHD might be connected to chronic pain in children.²⁴⁹ Thus, the increased prevalence of pain and discomfort reported in children with IC is probably more related to the IC than to NDD.

Table 9. Percentages and numbers of reported problems on the EQ-5D-Y dimensions and overall health status (VAS) in children with idiopathic clubfoot with and without neurodevelopmental difficulties (NDD).

EQ-5D-Y	NDD, n = 33	No NDD, n = 73	p
	% (n)	% (n)	
Mobility (walking about)			
No problems	81.8 (27)	91.8 (67)	0.134 ^C
Any problems	18.2 (6)	8.2 (6)	
Looking after myself			
No problems	87.9 (29)	98.6 (72)	0.032^F
Any problems	12.1 (4)	1.4 (1)	
Doing usual activities			
No problems	75.8 (25)	93.2 (68)	0.011^C
Any problems	24.2 (8)	6.8 (5)	
Having pain or discomfort			
No problems	54.5 (18)	61.6 (45)	0.491 ^C
Any problems	45.5 (15)	38.4 (28)	
Feeling worried, sad or unhappy*			
No problems	75.0 (24)	90.4 (66)	0.038^C
Any problems	25.0 (8)	9.6 (7)	
VAS median (range)	90 (40-100)	95 (50-100)	0.025^M
VAS mean (SD)	83.4 (16.8)	91.5 (11.1)	

^C Chi-square test, ^F Fisher’s Exact test, ^M Mann-Whitney U-test, *one missing answer

4.2.3 Clubfoot treatment outcome in relation to neurodevelopmental difficulties and health-related quality of life

Parents to children with IC and NDD combined were found to be less satisfied with the clubfoot treatment outcome measured with Roye's DSI, compared with those with IC alone (Median 80 vs. 87, $p = 0.03$). Similarly, parents to children with IC reporting 'any problems' on the EQ-5D-Y dimensions were found to be less satisfied compared to those with full health (Median 83 vs. 90, $p < 0.001$). These observations imply a negative relation between clubfoot treatment outcome as perceived by the parents and both NDD and HRQoL concerns (Figure 19).

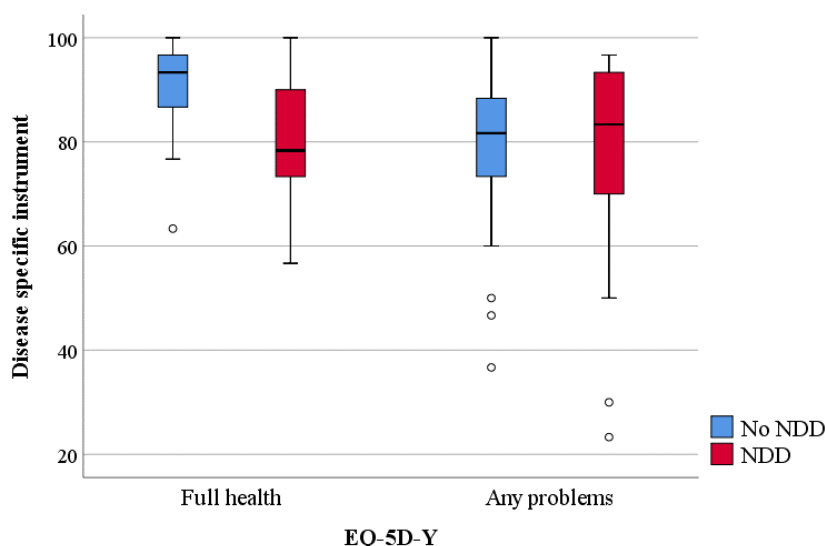


Figure 19. The parents reported satisfaction of the children's clubfoot treatment outcome using Roye's Disease specific instrument with a division of children with and without neurodevelopmental difficulties (NDD), and those reporting full health or any problems on the EQ-5D-Y.

In regards to HRQoL the result is quite straightforward because children with pain or problems with mobility are probably also those with poorer clubfoot treatment outcome according to the parents. However, several explanations could be suggested for the findings in relation to NDD. First, the group of children with both IC and NDD might have a more severe clubfoot deformity and/or be a separate subgroup in the context of clubfoot. Second, children with IC and NDD combined might be more difficult to treat for different reasons, not necessarily being of different initial severity. For example, the child might have more trouble sleeping with the brace because sleep problems and variabilities have been reported to a significant degree in children with NDD.^{250,251} Moreover, sensations related to the skin (e.g. itching or sensitivity to touch) have been related to ADHD and ASD^{153,252,253} possibly threatening brace adherence. Third, parents to children with IC and NDD combined might be harder to satisfy. If the child has NDD, and especially if these difficulties have not been revealed or properly treated/supported, the parent might connect NDD such as clumsiness with the clubfoot. Finally, because hereditary is high in neurodevelopmental disorders^{154,155} the parents might experience NDD themselves resulting in potential difficulties in handling the long and demanding treatment of clubfoot.

4.3 THE IMPACT OF FOOT INVOLVEMENT AND SEX

The impact of foot involvement and sex have been explored in all four studies of this thesis. The findings have been consistent throughout, concluding that it does not matter significantly if one is born with one or two affected feet or born a boy or girl regarding gait, gross motor skills, NDD, and HRQoL. The only exceptions were the findings of more gait and gross motor asymmetries within children with unilateral clubfoot. Taken together, these results contradict the theory of different subgroups of severity due to foot involvement or sex.

4.4 DEVELOPMENTAL CHALLENGES IN CHILDREN WITH IDIOPATHIC CLUBFOOT

In this thesis, novel developmental challenges in children with IC have been considered. Because previous research in IC has mainly been focused on traditional clubfoot treatment outcomes, the level of evidence for our findings can be considered modest because we have limited studies to compare our findings with. Nevertheless, the novel knowledge that children with IC experienced extended difficulties in areas such as language, fine motor skills, and attention together with the findings that these difficulties negatively affected treatment outcome satisfaction and HRQoL are striking. Moreover, in the work with the thesis some additional interesting observations have been made.

In an unpublished study from Sydney, Australia (A. Chivers and K. Gray, personal communication, February 15, 2018) parents of 12-month-old toddlers, 31 of whom had been born with IC and 17 without the deformity, answered the Ages and Stages Questionnaire, which is designed to screen for developmental delays. No significant group differences were observed in four of the five areas; however, significantly greater difficulties were found regarding the problem-solving domain. In this area, 32% of the toddlers with IC were reported by their parents to have increased problems compared with none of the toddlers born without the deformity.

When assessing fundamental motor skills in children with IC, Aulie et al. found that 24% of the children displayed indications of clumsiness or motor problems.²²³ Zapata et al. observed that 31% of the children were found to have below or well-below average levels of body coordination.²¹⁷ Similar findings were shown in Andriessse et al.'s study in which 35% of the children with IC were identified with motor impairment.¹⁵⁰

In the above-mentioned studies, as well as in Study III in this thesis, despite different features being studied there seems to be some consistency of additional challenges in about one third of the children with IC. Moreover, these challenges seem not to relate substantially to the status of the clubfoot (in line with Study II) or to the treatment method used. Indeed, it seems that the possible developmental challenges in about one third of the children with IC go beyond the musculoskeletal deformity itself.

In the treatment of IC, these challenges need to be considered. To begin with, developmental challenges might threaten the clubfoot treatment outcome. The most apparent risk is probably non-adherence to the brace protocol, e.g. due to sleep disturbances and skin-related problems in case of additional NDD. Knowledge of additional difficulties might make clinicians more empathetic and understanding of families who have trouble adhering to bracing.¹¹¹ Moreover, developmental challenges might be a threat to the results of extensive surgery due to relapse. For instance, if a tibialis anterior tendon transfer is performed on a child with additional challenges, it might be difficult for the child to develop a new motor strategy for the affected foot and leg thus threatening the success of the surgery.

Furthermore, when considering children with IC, the more apparent clinical problem of the clubfoot might overshadow additional difficulties and challenges. First, delays in attaining motor milestones and atypical gross motor coordination have been described as early signs of several neurodevelopmental disorders.²⁵⁴ In children with IC, those early signs might be mistakenly interpreted as part of the clubfoot diagnosis. Second, motor difficulties might be overlooked as problems due to the structural deformity when in fact they might be due to cognitive and/or sensory/perceptual factors. For example, the child might have neurodevelopmental concerns such as DCD, i.e. marked impairments in the performance of coordinated motor skills below expectations for the child's chronological age, negatively affecting academic achievements or daily activities.^{153,157} Similarly, both ASD and ADHD are associated with motor skills and coordination deficits.^{255,256} Thus by not identifying developmental challenges such as NDD, the children and families might miss out on adequate treatment and support. Third, in cases of child and/or proxy-reported lower HRQoL this might be due to NDD rather than the IC itself.^{173,175} Fourth, better motor skills have been related to health benefits,²⁵⁷ and children with suspected motor problems and low preference for active play seem to have a higher risk of physical inactivity in adolescence.²⁵⁸ Hence, additional support such as physiotherapy, including motor and achievement goal interventions,^{259,260} in children with IC might be beneficial, especially in cases of additional developmental challenges.

Finally, having a child with clubfoot has been found to negatively impact mothers' psychological well-being and to increase stress in the affected families.^{261,262} Therefore, supplementary support for the families might be required.^{261,262} In the cases of combined IC and NDD, this is probably even more vital.

For these reasons, a broad multidisciplinary approach is required to identify and care for gait, gross motor, neurodevelopmental, and HRQoL challenges within IC. Consequently, a combination of health professionals such as paediatric orthopaedic surgeons, psychologists, neurologists, and physio- and occupational therapists is warranted in the management of IC.

To put it brief, there is more than a foot to consider in the treatment and follow-ups of children born with idiopathic clubfoot.

4.5 WHAT CHARACTERISES A GOOD TREATMENT OUTCOME IN CLUBFOOT?

As a final comment, in the interpretation and discussion of the findings in the thesis, no attempt has been made to determine if the children with IC indeed had a *good treatment outcome*. Even though several traditional treatment outcome parameters are included and several comparisons have been made to the literature, the aim of the thesis has not been to judge treatment method or outcome per se. Nevertheless, the notion that the majority of children had no problems walking or running and reported no pain and full health must be considered satisfying when being born with a complex deformity.

However, in the evaluation of clubfoot, it could still be argued about what characterises a *good* outcome. No consensus exists for defining a successful clubfoot treatment.^{87,263} As an example, if the child has good range of motion of the clubfoot but is not able to hop with the foot, would that be considered a good outcome? Alternatively, what if the child reports both pain and a high overall health status (Figure 20). At the same time, NDD, and to some extent maybe even HRQoL, do not represent traditional clubfoot treatment outcomes, but rather represent a broader description of the group of children born with IC. Even gross motor skills might be part of that description. If so, the findings in this thesis might represent a cross-sectional description of children with IC and not a description of clubfoot treatment outcome.

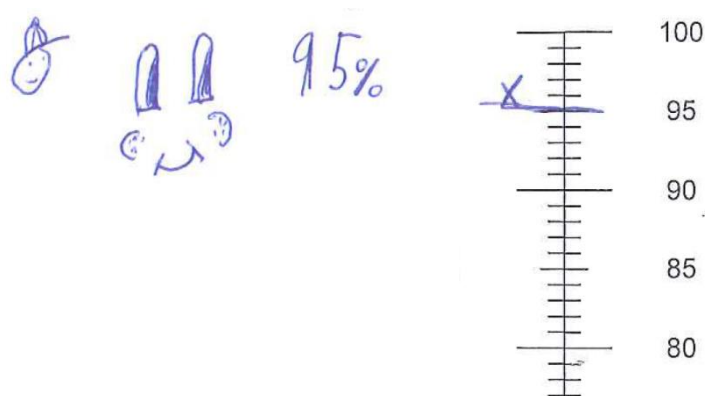


Figure 20. Child with idiopathic clubfoot reporting problems on the ‘having pain or discomfort’ dimension on the EQ-5D-Y, and an overall health status of 95 on the visual analogue scale (VAS).

4.6 METHODOLOGICAL CONSIDERATIONS

When evaluating the generalisability of findings from cross-sectional studies, as in this thesis, it is crucial to consider both internal and external validity. Because cross-sectional studies can be described as taking a “snapshot” of a group of individuals,²⁶⁴ there will always be a risk of detecting a finding by chance in that particular snapshot. Moreover, a cross-sectional design is useful to evaluate a patient group and to generate hypotheses, but it does not answer questions about causality.^{229,264} Furthermore, statistical considerations need to be weighed before conclusions can be drawn.

4.6.1 Internal validity

First, the internal validity ought to be considered because this forms the foundation for exploring external validity.

4.6.1.1 *Sample*

In Studies I and II, data were collected in a clinical setting because the children with IC were referred to the Motion Laboratory as a part of the follow-up programme at the hospital. In the programme, all children with IC should be referred to undergo a 3DGA. Even so, less than half of the eligible children with IC in Stockholm County were included in the studies, thus presenting a threat of selection bias. However, the main reason for this was due to one orthopaedic surgeon at the hospital not being aware of the referral process. For that reason, the greater portion of missing children is believed to represent a cross section of the totality because no division of severity was made between the orthopaedic surgeons. Participants in the TD control group in Studies I and II were recruited by advertising. There will always be a chance that parents answering the advertisement had children with exceptionally good or bad gross motor skills and therefore were more willing to take part in the studies. However, none of these concerns were noted.

In Studies III and IV, a great effort was made to include all children in the four annual cohorts of children with IC in the contributing counties. With the advantage of the unique personal identification numbers and the national health system in Sweden, virtually all children with IC should be included. This is supported by the identified incidence of 1.1/1,000, which corresponds to previous research.¹⁵ Nonetheless, we had no control of the non-responders in the samples, thus sampling bias cannot be ruled out. However, misclassification bias was prevented in the IC sample by validation questions regarding the child’s clubfoot and possible disabilities and diagnoses. In the general population sample, internal validity was reinforced by including families from the same county areas, during the same school terms and season, and with equivalent distribution of the sexes. Moreover, a comparison of sociodemographic variables showed no differences between the two samples. Lastly, by collecting a general population sample exclusively for the studies, internal validity was protected because the use of norm material would have introduced threats such as collection procedure, history, and age, sex, and residential area distribution.

4.6.1.2 *Study design and procedure*

In Studies I and II, some data were retrospectively collected. Because of this, some children had missing data and other measures of interest such as muscle strength were not included. Moreover, data from children with IC had been collected by several physiotherapists at the Motion Laboratory, while only a single physiotherapist (the author) collected data from the TD children. Furthermore, only the author subjectively chose the representative gait trials. This could be a threat, including measurement and selection bias and a risk of a learning curve. This threat was managed in three steps. First, a standardised procedure was used in the laboratory to collect data and to ensure consistency between the assessors. Second, in cases of uncertainties of representative gait trials, a senior physiotherapist was consulted (EB). Third, the clinical data collected by the author (about half of the IC sample) was compared with data collected by the other physiotherapists revealing no significant group differences. Two additional limitations from the 3DGA are the use of the Plug-In-Gait model with the foot as one rigid-body segment and the variability of gait in small children.^{183,265-267} However, several gait parameters such as joint angle measurements stabilises and appear adult-like at approximately four years of age.²⁶⁷ Still, not all children had sufficient kinetic data due to difficulties in making clean strikes on the force plates.

In Study II, three assessors were new to the CAP instrument, one had some experience, and one was the developer of the instrument. To rule out possible learning curves, the assessors were provided with several videotapes of children not included in the study in order to practice the procedure before assessing the children in the study. Finally, the median scores were kept in the final analysis in order to ensure a high internal validity.

In Studies III and IV, the participants answered the questionnaires at home either on paper or online. The reason for also offering online questionnaires was to improve the response rate, sample representation, and to reduce non-response bias.²³⁴ Nonetheless, by answering the questionnaires at home, we had no control of possible influences from the parents when the children were answering the EQ-5D-Y. Nor can we be entirely sure that the parents did not answer the questionnaire all by themselves. Still, psychometric analyses of the EQ-5D-Y has shown this approach to be valid.²⁰⁵ Moreover, the use of proxy reports would probably not have been representative of the child's own sense of their current HRQoL because parents might take into account aspects such as the future.¹⁷⁶ The handwriting and quite often-occurring smiley faces speak for the legitimacy of the children answering the questionnaire, even if this threat cannot be ruled out. Moreover, by using a generic questionnaire we cannot be sure the responses are related to the clubfoot. Thus, we cannot be sure that the increased reports of, for example, pain and discomfort found in the IC sample were related to the IC itself.

4.6.2 External validity

4.6.2.1 Setting

The reproducibility of a study is central in the consideration of external validity. Because Studies I and II were executed in a laboratory setting, using instruments that have been found to be valid and reliable support the reproducibility. However, the laboratory milieu and the clinical testing procedure could possibly challenge the external validity because the children might feel insecure, watched over, and uncomfortable when walking and performing the motor tasks. To reduce this threat, great effort was made to make the child comfortable at the laboratory and to encourage the child to perform their best. Moreover, the parents were sometimes consulted to inquire if they believed that the child performed differently than normally in an everyday setting. Finally, because gait trials were selected from a greater number of trials, an effort was made to select representative gait trials for each child.

4.6.2.2 Population

The children with IC in the thesis had been treated with a conservative treatment method in line with the Ponseti method. However, the modifications that were made challenge the generalisability of our findings to other populations treated with a strict Ponseti protocol. As an example, the knee-ankle-foot orthosis most often used of the children in our IC samples generally limited plantarflexion and did not brace the contralateral leg in cases of unilateral IC. This can be compared with the more flexible foot-abduction brace that also include the contralateral foot. Moreover, we had little or no information regarding traditional outcome measures such as foot mobility or the relapse rate making it hard to fully compare and explore our findings in relation to other cohorts.

The ethnicity of the included children was not considered even though some studies have proposed that ethnicity might be related to factors such as clubfoot incidence and early relapse due to communication difficulties.^{9,235,268} The only exception was questions regarding birth countries of the children and parents in Studies III and IV, which revealed no differences between the IC and the general population samples. Consequently, possible differences between different ethnic groups cannot be dismissed.

As a final remark, all studies in the thesis were conducted in a high-income country with easy and free access to treatment. Nonetheless, about 90% of all expected clubfoot cases are born in low-income and middle-income countries (LMIC). Of those, it is estimated that fewer than 15% of all children with clubfoot had access to the Ponseti treatment in the year 2015.²⁶⁹ Thus the generalisability of our findings to children with IC in LMIC is yet to be studied.

Despite these threats to external validity, the generalisability of our findings was supported by the distribution of foot involvement and sex, which corresponded with previous literature on children with IC.^{10,15}

4.6.3 Statistical considerations

In statistical hypothesis testing, there will always be a risk of making type I or type II errors. In the studies for this thesis, an alpha level of <0.05 was set in the statistical analyses, thus giving a 5% chance of discovering a false positive result. Moreover, in Study II multiple comparisons increased the risk of a type I error. Worth noticing, though, is the fact that all tests were two-tailed even though the hypotheses were that children with IC experience more problems in the included measures. Because of this, the risk of type I errors decreased. Even though the risks of type I errors could be considered the most serious, the risk of type II errors might be more predominant in this thesis because prior power calculation was conducted only for Studies I and II. However, because group differences were evident within all studies, and because a post-hoc power analysis was conducted on the survey data and revealed sufficient power, the risk of type II errors can be considered low.

In Study III, a parametric statistical approach was applied on an ordinal scale with variance heterogeneity and skewed distribution (because most parents answered 'does not apply' on the FTF), thus violating the assumption of parametric testing. Using a parametric approach with the use of M/ANOVA was motivated as follows. First, analyses of variance are considered robust against violations of parametric statistical assumptions in larger and equally sized samples, especially if the data are positively skewed as in Study III.^{216,270} As an example, violation of the normality assumption when using ANOVA should be of little concern if the sample size is 25 or more. Similarly, skewness and heterogeneous variances have been found to have little effect on the level of significance or power.²⁷⁰ Second, by using MANOVA the whole FTF could be compared between the samples in one single analysis. Thus, we could avoid multiple comparisons that would have increased the risk for type I errors. Third, the option of transforming the data would probably not have increased the statistical validity and would have been difficult to interpret.²⁷⁰ Fourth, most preceding studies using FTF and other clinical studies with similar designs as in Study III have used a parametric statistical approach, making it easier to compare our findings to other research within the area. Finally, to ensure the statistical validity of our findings in Study III a post-hoc non-parametric analysis was performed. In this analysis, the same statistical method as in Study IV was used after generating a binary outcome. Findings revealed the same significant differentiating domains as in the parametric approach.

4.7 CLINICAL IMPLICATIONS

Children with IC exhibit gait deviations and gross motor deficits at five years of age. Both children with bi- and unilateral IC favour one foot/leg when performing gross motor skills but no significant differences were evident between bi- and unilateral affected legs. However, gait and gross motor outcomes in children with unilateral IC might be perceived as worse due to pronounced asymmetries in comparison with the contralateral leg. One-leg stand and hop are two gross motor tasks that can be used in clinical practice to assess gross motor skills. Nonetheless, some children would probably benefit from a more thorough gross motor assessment as well as additional physiotherapy.

In children with unilateral IC, the contralateral leg develop discrete gait parameters and gross motor skills similar to legs of children born without the deformity. However, due to modifications to the clubfoot side in global gait measures, the contralateral leg should not be used as a reference in gait.

Initial clubfoot severity does not seem to be a strong predictor of later gait deviations or gross motor deficits. Nor can gross motor deficits be explained by the passive range of motion of the clubfoot. Thus, it appears that gross motor skills represent a different outcome entity, and other explanations such as sensory/perceptual and cognitive factors should be considered in clinical practise.

Pain and discomfort are reported by a considerable proportion of children with IC at nine years of age, and by their parents. Therefore, pain management strategies should be emphasised in the treatment and follow-ups of children with IC.

It does not seem to be substantial whether the child is born with one or two affected feet or if the child is a girl or a boy in regards to gait, gross motor skills, NDD, or HRQoL when being born with IC.

Finally, clinicians need to consider the increased prevalence of NDD found in children with IC, affecting both parent reports of clubfoot treatment outcome and HRQoL. In the presence of coexisting NDD, it might be vital to broaden and adjust the clubfoot treatment as well as adopt a multidisciplinary approach to improve support for both the children and their families. Thus, findings from the thesis should impact future follow-up programs for children born with IC in order to possible improve outcome not only with regards to gait and motor skills, but also other developmental aspects and perceived physical and mental health. The 26 items from the FTF with more difficulties within the IC sample may act as a rough shortlist to guide the clinician's attention to NDD within IC.

4.8 FUTURE RESEARCH

Future studies ought to explore if the gait and gross motor deficits persist when the children grow older and might experience more competition, higher demands, and greater awareness. Moreover, how the deficits translate to the children's everyday life, e.g. in relation to participation and self-esteem, is yet to be studied.

In future studies of gait in individuals with IC, it would be interesting to include measures such as electromyography and three-dimensional foot models such as the Oxford foot model in order to provide an explicit analysis of the gait characteristic in IC.

Future studies should explore other aspects that might possibly contribute to the gross motor deficits found in children with IC such as cognitive and sensory/perceptual factors. Moreover, because perception and relation in space were found to be associated with greater difficulties in the IC sample on the FTF, areas such as proprioception, i.e. sensing the body's position, would be interesting to explore.

The novel findings of NDD in children with IC need to be replicated in other cohorts of individuals with IC. Furthermore, future studies are needed to explore causality between IC and NDD, as well as the impact of NDD in the treatment of clubfoot. For example, one study of interest would be to investigate the connection between NDD, sleep, brace adherence, and clubfoot relapse. Moreover, exploring infant-parent attachment and the impact of the partial immobilisation during the first five years of life, would be of interest both in general when a child is born with IC and in specific cases of combined NDD.

Longitudinal studies are required to explore if it is possible to identify children early who are at risk of later gait and gross motor deficits, NDD, and HRQoL problems, i.e. identify predictive factors of later developmental challenges. Longitudinal studies would also be able to explore if multidisciplinary approaches would be advantageous in the treatment and care of children with IC.

The findings from this thesis might act as a platform of knowledge for designing interventions. An example of a possible intervention is a designed physiotherapy-training programme to study training capacity in children with IC.

To get a better understanding and deeper knowledge from the children with IC and their families' perspective, a qualitative research approach would be of interest. For example, focus groups or individual in-depth interviews with the families concerning questions such as how they handle the bracing regime or talk about the IC at home could provide valuable insights.

Finally, future research of children with IC should preferably include both objective and subjective measures of both structural and global contexts in order to include aspects of the children's overall health condition. Moreover, future research ought to identify what characterises a *good* treatment outcome from the patient perspective, including individuals from low, middle, and high-income countries.

5 CONCLUSIONS

- Similar gait deviations were found in the legs with bi- and unilateral clubfoot in children with IC at five years of age in comparison with legs from TD children. Main concerns in gait were decreased dorsi-plantar flexion range, possible weak ankle plantar flexor muscles, and a 24% decrease in ankle power generation.
- Children with IC at age five were found to have gross motor deficits and asymmetries compared with TD children. Most deficits were found in the tasks one-leg stand and hop. Gross motor skills were not directly related to passive range of motion of the clubfoot, global gait measures, or initial clubfoot severity. Thus, gross motor skills might represent a different outcome entity and should be assessed in the evaluation of children with IC.
- The contralateral leg in children with unilateral IC mirrored legs of TD children in discrete gait parameters and gross motor skills, but modified to the clubfoot side in global gait measures. Subsequently, the contralateral leg should not be used as a reference when assessing gait.
- Results indicate similar clubfoot severity and development in bi- and unilateral IC in regards to gait and gross motor skills. Therefore, bi- and unilateral IC might be clustered as one uniform group in future studies using 3DGA or when assessing gross motor skills in affected legs. However, knowledge of foot involvement might be vital in a clinical setting and when the whole child is assessed due to pronounced asymmetries in children with unilateral IC.
- Nine-year-old children with IC were found to have increased prevalence of neurodevelopmental *difficulties* (NDD), especially in the domains of motor skills, perception, and language and the subdomains of gross and fine motor skills, relation in space, comprehensive, and expressive language skills compared to the general population sample. About one third of the children in the IC sample were defined with clinically significant NDD, with a risk of developmental disorders. Sociodemographic parameters, foot involvement, and sex did not differ between children with IC with or without NDD. However, parents to children with IC and NDD combined reported less satisfaction with the clubfoot treatment outcome.
- Children at age nine with IC reported satisfying overall health status despite more problems mainly regarding pain or discomfort, but also mobility and doing usual activities, compared with the general population. Foot involvement or sex did not affect the HRQoL; however, the coexistence of NDD affected HRQoL negatively.

- Health care providers should be attentive to the increased prevalence of NDD in children with IC, which probably affects both the clubfoot treatment outcome and HRQoL. This requires a broad multidisciplinary approach to improve and maximise support to children with IC and their families.

6 POPULÄRVETENSKAPLIG SAMMANFATTNING

Klumpfot (på svenska ibland även benämnd PEVA) är en deformitet av fot och underben som drabbar ca 1/1000 nyfödda barn. Man vet ännu inte vad som orsakar klumpfot men troligen är orsaken en blandning av genetiska och miljöfaktorer. När deformiteten är isolerad, dvs barnet är född med klumpfot utan annan känd skada eller syndrom, benämns detta som idiopatisk klumpfot.

Behandlingen av barn med idiopatisk klumpfot har utvecklats från krävande operationer till konservativ behandling med gipsning och skena vilket påvisat goda behandlingsresultat. Trots detta är kunskapen utöver den strukturella deformiteten begränsad. Föräldrar med ett nyfött barn med idiopatisk klumpfot ställer ofta frågor så som; spelar det någon roll om mitt barn är född med en eller två drabbade fötter, kommer mitt barn kunna gå och springa som sina kompisar och hur kommer mitt barn må av att vara född med den här deformiteten? Frågor som går att besvara till viss del utifrån klinisk erfarenhet men som det finns mycket lite forskning på. Ytterligare frågor som har väckts i det kliniska arbetet med barn med idiopatisk klumpfot är om det finns ökade svårigheter så som problem med koncentration och språk, svårigheter som inte kan anses kopplade direkt till klumpfoten. Syftet med avhandlingen var således att forska på tidigare utforskade områden som kan hjälpa till att besvara de här frågorna. Områden som skulle kunna fördjupa förståelsen för barn med idiopatisk klumpfot och barnens hälsotillstånd.

För att besvara forskningsfrågorna genomfördes fyra studier uppdelat i två delar. I den första delen undersöktes gångmönster och motorisk färdighet hos barn i femårsåldern med idiopatisk klumpfot. I den andra delen besvarade föräldrar till barn med idiopatisk klumpfot i nioårsåldern frågeformulär gällande neuropsykiatriska svårigheter och hur nöjda de var gällande resultat av barnens klumpfotsbehandling gällande funktion, smärta och utseende. Barnen fick själva skatta deras livskvalitet. Allt material jämfördes med material från barn utan idiopatisk klumpfot från den allmänna populationen.

Studierna från del ett påvisade att barn med idiopatisk klumpfot hade avvikande gångmönster samt motoriska avvikelser och asymmetrier i jämförelse med barn födda utan deformiteten. Samma typ av avvikelser sågs i de påverkade benen oavsett om barnen var födda med en eller två drabbade fötter. De huvudsakliga fynden var nedsatt fotledsrörlighet och förmåga att utveckla kraft i foten under gång. Dessutom hade åtta till nio barn utav tio avvikelser när de skulle stå eller hoppa på ett ben. De motoriska svårigheterna relaterade inte direkt till rörligheten av foten eller svårighetsgraden av deformiteten vid födseln. Det motsatta benet, hos barn med ensidig klumpfot, uppvisade inga motoriska avvikelser. Däremot anpassade sig det motsatta benet till benet med den idiopatiska klumpfoten under gång.

Studierna från del två visade att hos nioåriga barn med idiopatisk klumpfot rapporterade föräldrarna ökad förekomst av neuropsykiatriska svårigheter jämfört med barn från den allmänna populationen. Detta var tydligast inom områdena motorik, perception

(uppfattningsförmåga/varsebildning) och språk, men även områden som uppmärksamhet och minne. Ett exempel är påståendet *Har svårt att hålla kvar uppmärksamheten på uppgifter eller aktiviteter* som rapporterades till större andel hos barn med idiopatisk klumpfot jämfört med barn från den allmänna populationen. Hos ungefär en tredjedel av barnen rapporterade föräldrarna betydelsefulla svårigheter med en risk för utvecklings- eller beteendeproblem som skulle kunna kräva ytterligare utredning. Hos dessa barn var även föräldrarna mindre nöjda med resultatet av barnens klumpfotsbehandling. I den totala gruppen av nioåriga barn med idiopatisk klumpfot rapporterade barnen en generellt god upplevd hälsa idag, trots att de även rapporterade mer problem. Framförallt gällde det smärta och obehag. Det spelade ingen roll om barnen var födda med en eller två drabbade fötter, eller om de var flickor eller pojkar gällande skattad livskvalitet. Däremot påverkade den ökade förekomsten av neuropsykiatriska svårigheter hos barn med idiopatisk klumpfot livskvaliteten väsentligt negativt.

Sammanfattningsvis påvisar avhandlingen att barn med idiopatisk klumpfot bör följas upp inte enbart gällande fotens rörlighet utan även gällande gångmönster och motorisk färdighet. Två enkla test för att undersöka motorisk färdighet är förmågan att stå eller hoppa på ett ben. Eftersom motoriska svårigheter inte verkade relatera direkt till deformitetens svårighetsgrad vid födseln eller fotens rörlighet skulle troligen en del barn behöva ytterligare motorisk utredning. Detta tyder även på att svårigheterna inte alltid är direkt relaterade till den strukturella fotdeformiteten, utan att andra aspekter till de motoriska svårigheterna bör övervägas. Det motsatta benet, hos barn med ensidig klumpfot verkar utvecklas inom det normala utvecklingsspannet. Därför finns en risk att ensidig klumpfot kan upplevas som sämre än barn med två påverkade fötter. Detta trots att det inte verkar föreligga någon skillnad gällande gång och motorisk färdighet mellan enkel och dubbelsidig klumpfot. I övrigt verkar det inte spela någon större roll om barnen är födda med en eller två påverkade fötter, eller födda som pojkar eller flickor gällande de undersökta frågeställningarna. Barn med idiopatisk klumpfot och deras föräldrar bör utbildas i smärthantering eftersom problem med smärta verkar förekomma hos en stor andel av barnen. Slutligen behöver vårdpersonal som träffar barn med idiopatisk klumpfot vara uppmärksamma och medvetna om den ökade förekomsten av neuropsykiatriska svårigheter inom gruppen eftersom det tycks påverka både resultatet av klumpfotsbehandlingen och barnens skattade livskvalitet. Det kan kräva att flera olika yrkeskategorier involveras inom vården av idiopatisk klumpfot. Fynd från avhandlingen bör därför påverka framtida uppföljningsprogram för barn födda med idiopatisk klumpfot för att möjliggöra bästa möjliga vård och stöd för barn med idiopatisk klumpfot och deras familjer.

7 ACKNOWLEDGEMENTS

My doctoral studies and the work with this thesis have had its ups and downs, just as life. I could never have imagined this journey beforehand and am truly grateful to all the people that have supported, inspired, and motivated me along the way.

First, I would like to send my genuine gratitude to all of the children with idiopathic clubfoot and their families, both those participating in the studies and those I have met in my clinical work at Astrid Lindgren Children's Hospital. Thank you for your contributions, you make my work valuable.

My sincere gratitude also goes to:

My main supervisor, **Eva Broström**, for always believing in me and pushing me towards independency and to go beyond my limits. Thank you for introducing me to the world of gait and motion analysis, and science. You are an inspiration for how far a female physiotherapist can go with enthusiasm, intelligence, and hard work, but how you get your hours together is still a mystery.

Co-supervisor **Hanneke Andriesse**, for sharing your enormous knowledge and expertise within the fields of clubfoot and physiotherapy. My own early thoughts about additional challenges within children with idiopathic clubfoot would never had been realised as a research project if it were not for your contribution. Thank you for always encouraging me and giving me energy.

Co-supervisor **Mia André**, you are not just my supervisor with a careful eye for the small but important details and my boss at the clinic, you are also the one that took the leap to employ me as an inexperienced physiotherapist and as your first employee ten years ago. The support you have given me from the start, both at the clinic and as a PhD student, has been invaluable. I could not have wished for a better boss.

Co-supervisor **Stephanie Böhm**, for sharing your expertise within clubfoot and paediatric orthopaedics. I have really enjoyed having you as an instructor for how to cast clubfoot, and that you do not settle for less than perfect. Thank you for coming to the rescue when I thought I had to postpone the dissertation xx times and for introducing me to your international network.

Co-supervisor **Sven Bölte**, you became seriously involved in the project after the half-time seminar, and I could not be happier to have you as my fifth (!) supervisor. Your knowledge about research and neurodevelopmental difficulties has been vital for the latter part of the project. A special thanks for your tireless support in my statistical frustrations, improving my scientific writing, and for the precious WHY WORRY post-it note.

Karolinska Institutet, the **Department of Women's and Children's Health**, and the **Doctoral School in Health Care Sciences** for giving me the opportunity to become a PhD

student. Especially thanks to my “classmates” at **HK 12** for the support and the fun we have had together as new doctoral students.

Co-author **Maura Iversen**, Northeastern University, thank you for sharing your great knowledge in research, helping me analyse and understand the data, and for reviewing my work for Study II.

Adam Rozumalski, Gillette Children's Specialty Healthcare James R Gage Center for Gait and Motion Analysis, for the invaluable help with the GDI-Kinetic script and reviewing the first rough manuscript for Study I.

My former and present colleagues at the Motion Laboratory. **Åsa Bartonek** for your profound enthusiasm as our senior tutor at the lab, there is nothing to know about gait analysis that you do not know. **Josefine Eriksson Naili** for the fun we have had together sharing hotel rooms and fighting MATLAB. **Cecilia Lidbeck** for your willingness to share your boundless wisdom. **Marie Eriksson** for being such a source of knowledge of orthotic management and your incredible work in helping children walk. **Anna-Clara Esbjörnsson** for introducing me to clinical gait analysis and being my new ally in Lund. **Mimmi Örtqvist** for all the sensible and wise advice you have given me along the way. **Kicki Löwing** for always having time to answer my questions even though you have had a thousand and one things to do. **Lena Haggren Råsberg** for interesting discussions in the interpretation of clinical gait analyses, and for calming down my hypochondria. Finally, yet importantly, **Mikael Reimeringer**, without you there would be no thesis, no research, no gait analyses, or, I dare to say, nothing done at all that includes technical devices in the laboratory. Thank you big time for always giving me your time and your patient support!

Lanie Gutierrez-Farewik for sharing your enormous knowledge of biomechanics and being such a warm and enthusiastic person. I could not be more proud to know the first female professor of biomechanics at the KTH Royal Institute of Technology. Thanks also to all the **PhD students and research colleagues from KTH** I have met during the years who have patiently explained everything from Newton's laws to OpenSim.

Mattias Möller and **Magnus Aspdahl**, thanks for the best ever period of time working together at the clinic sharing the orthopaedic ward, laughter, frustration, candy, drinks, and fighting the red mat and dragons. Working with you has been a pure pleasure. See you at ALB finest!

All my fantastic colleagues at the **Physiotherapy department** at ALB (or whatever new name we currently go by). A special thanks to **Lotta Kaijser** and **Theresa Nagle Tsakiridis** for the support and valuable input in the clinical work with children with clubfoot. My gratitude also goes to my former colleagues, especially **Karin Thews** and **Eva Klackenberg Arrhenius**, for being my informal mentors and sharing your deep knowledge of paediatric physiotherapy, and to **Charlotta Enghag** for introducing me to the world of clubfoot.

Fellow PhD students, junior and senior researchers at the Department of Women's and Children's Health on floor seven for stimulating seminars, and discussions at lunchtime. A special thanks for the feedback in the writing of my summary thesis.

All my colleagues at the **paediatric orthopaedic clinic** at Karolinska University Hospital for always sharing your knowledge, and contributing to such an inclusive and open-minded workplace. Special thanks to those fellow PhD students in the past, **Stefan Gantelius, Marie Askenberger, Eva Bengtsson Moström, and Johan von Heideken** for doctoral drinks and showing me the way.

Per Åstrand, thank you for giving me the insight that doing a PhD is four years of education in handling frustration. Those words have actually encouraged me to continue at times when my confidence was at a low.

None-Marie Kemp and Ulrika Isaksson, for being you and always there to help. I sincerely believe there would be no research or dissertations done from floor seven without your support along the way. Thank you for everything and for always having an answer to the big and small questions.

The assessors from Study II, **Christina Orefelt, Gunnar Hägglund and Minna Petersson** for your patience and precision in assessing the children. A special thanks to Christina for sharing your clinical knowledge and supervision in my journey to become a specialised paediatric physiotherapist.

My international colleagues that I have met during my formal and informal research visits, **Jennifer McCahill** and the team at Oxford Gait Laboratory, **Denise Watson** at Chelsea and Westminster Hospital, **Kaat Desloovere** and her team in Pellenberg, KU Leuven, and **Kelly Gray** and **Alison Chivers** at Macquarie University and the Children's Hospital at Westmead in Sydney. Thank you for your hospitality and generosity in integrating me into your daily work and research groups and for sharing your great knowledge. Though probably not aware of their contribution, I would also like to send my gratitude to the children and people I have met in **Danang/Hoi An**, Vietnam and **Guangzhou**, China, for giving me perspective and for doing such important and valuable work.

All the **orthotists** I have been working with for sharing your knowledge of orthoses, always being willing to help, and for your extensive support for the children and families affected by clubfoot.

External mentor **Peter Löfmark**, the meetings were few but the words important.

Maja Petri, for creating such a lovely painting exclusively for my cover, catching everything I wanted to say with the thesis.

My **friends** in the “real life”, no one mentioned none forgotten, but you know who you are and you mean a lot to me. These years have been so intense and I hope you are still out there. I know you are still out there, let’s grab a drink and catch up!

Relatives and extended family. Especially, my grandfather **Einar**, for all the support and letting me and my family stay with you last spring. My late **grandparents**, for being such a base of support and love when growing up. The **Löfgrens**, for including me as a natural part of your family. **Sebastian** and **Poppy**, for confirming that all you need is love... and a dog.

My big and diverse family. My mother **Malin** who has taught me everything about life through highs and lows, and how a relationship can continue to grow with time. My father **Anders** who has not only given his unreserved love and support in life, but also in this thesis. Your technical support in the making of the webpage and the data collection has been priceless. My sister **Greta**, you mean a lot to me and my family; your sense of empathy for others is incredible. My brother **Gustaf**, your capacity for talking your way through everything is amazing, can you teach me some? **Anders** and **Johan**, not brothers by blood but by love, I don’t think you understand how much you have meant to me when growing up, and still mean to me. My late sister **Jenny**, you are not only my beloved sister; you are also my second mother and best friend in life. Words cannot express how much I love and miss you; see you on the other side.

Niklas, it took some years to realise why I never erased your contact details, but suddenly it was all obvious, you are the love of my life. Even though it sometimes feels like I have the worst opponent at home, you are the one that asks the most relevant questions and encourages me in everything I do. You have the biggest heart and I know that you are always there to catch me if I fall. Despite the fact that I am just your second (or third?) best friend, it seems like I hold some kind of marriage material.²⁷¹ So what do you say; is it finally time to walk down the aisle?

Finally, **Signe** and **Harald**, you are the ones that truly mean the world to me. I could not be happier having the privilege of waking up in the morning with a little foot in my back and a small arm around my neck, I love you to the moon and back. A special thanks for helping me out with the illustrations in the thesis.

Now mum’s book is finally finished, let’s go out and play in the park!

The work of the thesis was supported by grants from the Doctoral School in Health Care Science at Karolinska Institutet, Stiftelsen Frimurare Barnhuset i Stockholm, Gåvofonden för Damp-forskning vid Karolinska Universitetssjukhuset, Stiftelsen Promobilia, Sällskapet Barnavård, Sunnerdahls Handikappfond, and Stiftelsen Skobranschens utvecklingsfond.

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9 APPENDIX

Sample characteristics including sociodemographic parameters for the participants in Studies III and IV as reported of the parents.

	Children with idiopathic clubfoot n = 106	General population n = 109
Mean age (SD)	9.4 (0.6)	9.5 (0.6)
Boys, n (%)	77 (73)	79 (73)
Bilateral idiopathic clubfoot, ^a n (%)	49 (49)	NA
Unilateral idiopathic clubfoot, ^a n (%)	51 (51)	NA
Roye's Disease Specific Instrument (DSI), mean (SD)	83 (16)	NA
Children born in Sweden, n (%)	106 (100)	105 (96)
Mothers born in Sweden, n (%)	82 (77)	87 (80)
Fathers born in Sweden, n (%)	80 (76)	85 (78)
Living in Stockholm County, n (%)	79 (75)	82 (75)
Living in urban cities, ^b n (%)	52 (49)	67 (62)
Living in medium-sized cities, ^b n (%)	43 (41)	37 (34)
Living in rural county areas, ^b n (%)	10 (9)	5 (5)
Parent's education in years, ^c mean (SD)	15.3 (2.9)	15.2 (2.8)
Mothers unemployed or on sick leave, n (%)	5 (5)	1 (1)
Fathers unemployed or on sick leave, n (%)	1 (1)	0 (0)
Cohabiting parents, n (%)	91 (86)	90 (83)
No. of siblings, mean (SD)	1.7 (1.5)	1.6 (0.9)
Main sport/leisure activities of the child, ^d (%)	Soccer (44) Floorball/bandy (13)	Soccer (50) Music/choir (17)
Special teaching/pedagogical support, n (%)	5 (5)	2 (2)
One additional year in school, n (%)	1 (1)	1 (1)
Children reported with disorders/disabilities, ^e n (%)	20 (19)	13 (12)
<i>Disorders/disabilities^d</i>		
<i>Allergy</i>	5 (5)	3 (3)
<i>Asthma</i>	3 (3)	5 (5)
<i>ADHD/suspected ADHD, n (%)</i>	6 (6)	2 (2)
<i>ADD, n (%)</i>	-	1 (1)
<i>ASD, n (%)[^]</i>	4 (4)	1 (1)
<i>Dyslexia/language difficulties, n (%)</i>	3 (3)	1 (1)
<i>Not specified, n (%)</i>	2 (2)	-
<i>Hearing or vision difficulties, n (%)</i>	2 (2)	-
<i>Developmental delay, n (%)</i>	1 (1)	-
<i>Musculoskeletal problems with the lower limbs</i>	-	2 (2)
<i>Ear problems, n (%)</i>	-	1 (1)
<i>Hypothyroidism, n (%)</i>	-	1 (1)
<i>Molar-Incisor-Hypomineralization, n (%)</i>	-	1 (1)

^a foot involvement unknown in six children, ^b some missing answers in both samples, ^c for the parents answering the questionnaires, ^d open question with multiple answers possible, ^e except clubfoot. ADHD attention deficit/hyperactivity disorder; ASD autism spectrum disorder; ADD attention deficit disorder; NA not applicable.

