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Pain and health-related quality of life in children and adolescents with cerebral palsy

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“To affect the quality of the day, that is the highest of arts.”

Henry David Thoreau

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PREFACE

I Acknowledgements

First, I would like to thank all children with cerebral palsy (CP), their parents and caregivers for their time and the opportunity to learn from their experiences. I hope the study findings will contribute to improved care and surveillance of CP.

This PhD project was carried out at the Division of Paediatric and Adolescent Medicine, Oslo University Hospital in the period 2019-2022, thanks to a PhD grant from the Norwegian Dam Foundation (number 2019/FO235195) supported by the Norwegian CP Association.

I am grateful to all health care providers in the habilitation units across Norway who had collected data for the Norwegian Quality and Surveillance Registry for Cerebral Palsy (NorCP) and the opportunity to use the data for research. Special thanks also to Guro L. Andersen, MD, PhD, and Reidun B. Jahnsen, PT, PhD, professor emerita, and to Sandra J. Hollung, PhD, at the NorCP and thanks to Vegard Håvik at the Norwegian Directorate of Health for assistance with data files. Thanks also to Oslo University Hospital for statistical service through Oslo Center for Statistics and Epidemiology. I would like to thank Anette Ramm-Pettersen, PhD, professor at University of Oslo and the Head of Department for Child Neurology for her support towards this project.

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Selma Mujezinović Larsen Oslo, 12.05.2022

At the submission in May 2022, two of four papers in this thesis were available online. The last two papers were under review. One is now available online, and the other has been accepted:

Health-related quality of life in adolescents with cerebral palsy; a cross-sectional and longitudinal population-based study. Larsen SM, Terjesen T, Jahnsen RB, Diseth TH, Ramstad K. *Child: Care, Health and Development.* https://doi.org/10.1111/cch.13055

Daytime contacts and general practitioner consultations, and pain as a reason for encounter in children with cerebral palsy; a Norwegian national registry linkage study. Larsen SM, Eide TB, Brunborg C, Ramstad K. *Scandinavian Journal of Primary Health Care. (Accepted for publication on October 16th 2022)*

Two of 13 approvals listed in chapter 10 Appendices are attached in the printed thesis. The remaining 11 approvals had been submitted to University of Oslo only.

Selma Mujezinović Larsen Oslo, 23.10.2022

II Abbreviations

BPI	Brief Pain Inventory
CFCS	Communication Function Classification System
CHQ	Child Health Questionnaire
CP	Cerebral Palsy
CPCHILD	Caregiver Priorities & Child Health Index of Life with Disabilities
CPOP	Cerebral Palsy Follow-Up Program, part of NorCP since late 2020
CP QOL	Cerebral Palsy Quality of Life Questionnaire
CPRN	Cerebral Palsy Registry of Norway, part of NorCP since late 2020
GMFCS	Gross Motor Function Classification System
GP	General Practitioner
HRQoL	Health-Related Quality of Life
ICD-10	International Statistical Classification of Diseases and Related Health Problems, 10th Revision
ICD-11	International Statistical Classification of Diseases and Related Health Problems, 11th Revision
ICF	International Classification of Functioning, Disability and Health
ICF-CY	International Classification of Functioning, Disability and Health – Children and Youth Version
ICHI	International Classification of Health Interventions
ICPC-2	International Classification for Primary Care
ITB	Intrathecal Baclofen Therapy
KUHR	Norwegian Directorate of Health's database for the control and reimbursement of health expenses (Kontroll og Utbetaling av HelseRefusjoner)
MP	Migration Percentage in hip
NorCP	Norwegian Quality and Surveillance Registry for Cerebral Palsy (from late 2020)
NRS	Numeric Rating Scale
OSF	Open Science Framework
OUH	Oslo University Hospital
QoL	Quality of Life

PedsQL	Pediatric Quality of Life Inventory
PRO	Patient- (Person) Reported Outcome
PROM	Patient- (Person-) Reported Outcome Measure
RFE	Reason for Encounter
SCPE	Surveillance of Cerebral Palsy in Europe
UN	United Nations
VAS	Visual Analogue Scale
WHO	World Health Organization
WHO-FIC	WHO Family of International Classifications
WONCA	World Organization of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians; short name World Organization of Family Doctors

III Summary

Background: Cerebral palsy (CP) is the most common disorder of movement and posture in childhood, often accompanied by secondary challenges in cognition, epilepsy, and pain. Reports show that up to 75 % of all children with CP have pain, and that pain is often undertreated. Thus, pain has been considered a major challenge in care for children with CP since it influences health-related quality of life (HRQoL) negatively. The knowledge base on pain in children with CP is constantly increasing. Still, longitudinal studies on pain and HRQoL are scarce. Many different health care professions are involved in care for children with CP. Still, it is unknown if children with CP encounter a general practitioner (GP), or if they seek GP advice when in pain.

Aims: The overall aim of this PhD thesis was to investigate pain and pain management in children with CP outside hospital. We investigated possible changes in pain, hip pain and HRQoL and relevant factors that could be associated with these variables, in a cohort of children, now youth with CP who were dependent on waking aid and who followed national CP surveillance program (Paper I-III). We also investigated if a diagnosis of CP in children (0-17 years) influenced the frequency of daytime contacts and consultations with a GP, and the frequency of pain as a reason for consultation (Paper IV).

Methods: Papers I-III are based on a follow-up study with both cross-sectional and longitudinal design. All non-ambulatory children registered in Norwegian Quality and Surveillance Registry for Cerebral Palsy (NorCP) with bilateral CP, GMFCS levels III to V, born 2002-2006, living in South-Eastern Norway were invited to participate. Two identical data collections were performed five years apart, in childhood (7-12 years) and adolescence (12-17 years). One primary caregiver responded on behalf of each participant at both time points. Pain last four weeks was assessed using questions on pain frequency and intensity from Child Health Questionnaire (CHQ), a body map to localize pain sites and two questions on pain interference with activities of daily living and sleep from the Brief Pain Inventory (BPI), and an interview on pain, hip pain and the use of first-line analgesics. Hip displacement was measured on radiographs of the pelvis taken through NorCP. HRQoL was assessed using five of six CPCHILD domains. Paper IV is based on a registry study of GPs' daytime contacts available from the Norwegian Directorate of Health's database for the control and reimbursement of health expenses. All daytime contacts with regard

to type of contact and reason for encounter (RFE), in period 2006-2018 were analyzed for persons born in 1996 -2012. Linkage to NorCP identified children with CP. Comparison was performed between children registered in NorCP and children not registered in NorCP.

Results: Papers I-III: Pain and hip pain were assessed twice in 67 children. The prevalence of recurrent pain, number of pain sites, pain intensity and frequency, and pain interference with activities of daily living, all increased from childhood to adolescence, while pain interference with sleep was unchanged. The presence of moderate or severe pain, or marked increase in pain severity, did not necessarily result in use of first-line analgesics in adolescence. Hip pain prevalence increased from childhood to adolescence. Severe hip subluxation (hip migration percentage 50-89%) and high motor impairment were independent risk factors for hip pain. Proxy-reports on HRQoL were collected for 64 adolescents, of whom 58 had available proxy-reports from childhood. From childhood to adolescence, the mean CPCHILD domain scores worsened slightly in *General Health* and remained unchanged in the other four domains. In adolescence, severe motor impairment was associated with low scores in the HRQoL domains *Personal Care, Positioning, Comfort and Emotions,* and *General Health*, but not in the domain *Overall Quality of Life*. Severe pain was associated with low scores in *Positioning, Comfort and Emotions, General Health,* and *Overall Quality of Life,* but not in the domain *Personal Care.* In all domains, low domain score in childhood was associated with low score in the corresponding domain in adolescence. Paper IV: Children with CP did not meet GPs more often, but GPs reported more administrative work for children with CP than for children in the general population. GPs coded pain as a RFE more seldom in consultations with children with CP than in children in the general population.

Conclusions: Systematic assessment of all pain and of HRQoL through CP surveillance programs might contribute to a more efficient communication on pain management. When encountering a child with CP, health care professionals, both in primary and specialist care, should ask for pain even if the patient (child or parent) does not address pain. Information on pain prevention and pain treatment should be given repeatedly to primary caregivers and their child during the CP surveillance.

IV Summary in the Norwegian language (Norsk sammendrag)

Bakgrunn: Cerebral parese (CP) er den vanligste bevegelsesforstyrrelsen hos barn og er ofte fulgt av nedsatt kognisjon, epilepsi og smerte. Opptil 75 % av barna med CP har smerte, og smerte er ofte underbehandlet. Smerte oppfattes som en stor utfordring i omsorgen for barn med CP da den påvirker helserelatert livskvalitet (HRQoL) negativt. Kunnskapsbasen om smerte hos barn med CP vokser stadig, men longitudinelle studier som fokuserer på smertestatus hos samme individer på to tidspunkter er sjeldne. Mange medisinske profesjoner er involvert i oppfølging av barn med CP, men det er ukjent i hvilken grad barna kontakter fastlege, og om de gjør det for smerte.

Mål: Den samlede målsetningen var å øke innsikten i hvordan smerter hos barn med CP forløper og blir håndtert og om den påvirker HRQoL samt diskutere bruk av helsetjenester i lys av eksisterende teoretiske rammer. Vi undersøkte vi om det var endring over 5 år i forekomsten av smerter generelt, hoftesmerter, og HRQoL i en kohort av barn med CP, nå ungdom som hadde store gangvansker og som hadde fulgt det nasjonale oppfølgingsprogrammet for CP (Artiklene I-III). Vi undersøkte også om spesifikke faktorer kunne være assosiert med smerter, hoftesmerter og HRQoL i ungdomstid. I en annen barnepopulasjon med CP (0-17 år) undersøkte vi om CP diagnosen påvirket frekvensen av kontakter på dagtid med fastlege og om den påvirket hyppigheten av smerter som årsak til konsultasjon hos fastlege (Artikkel IV).

Metode: Artiklene I-III er basert på en oppfølgingsstudie som har både tverrsnitts- og longitudinell design. Alle barn som var registrert i NorCP med bilateral CP, GMFCS III-V, født 2002-2006 fra sør-øst Norge ble invitert til å delta. To innholdsmessig identiske data innsamlinger ble foretatt med fem års mellomrom, i barndom (7-12 år) og ungdomstid (12-17 år). En primær omsorgsgiver besvarte spørreskjema og et strukturert intervju på vegne av sitt barn ved begge tidspunkter. Smerte de siste fire uker ble kartlagt ved hjelp av spørsmål om hyppighet og intensitet fra CHQ, kroppskart for smertelokalisasjon og to spørsmål om smertens påvirkning på daglige aktiviteter og søvn fra BPI, samt et intervju om smerte, hoftesmerte og bruk av smertestillende medikamenter. Hofteledds dislokasjon ble målt på røntgenbilder av bekkenet samlet gjennom NorCP. HRQoL ble kartlagt ved fem av seks CPCHILD domener. Artikkel IV er basert på en registerstudie av kontakter med fastlege på dagtid (data fra Helsedirektoratet). Tidsrommet 2006-2018 ble analysert for type og årsak for kontakt for

personer født 1996-2012. Kobling til NorCP data ble foretatt for å identifisere barn med CP. Resultater for disse ble sammenliknet med resultatene for personer som ikke var registrert i NorCP.

Resultater: Artiklene I-III: Rapporter om smerter og hoftesmerter (Artiklene I-II) var tilgjengelig for 67 deltagere, en fra barndom og en fra ungdomstid. Prevalens av smerter, antall smertesteder, smerte intensitet og frekvens, samt smertens påvirkning på daglige aktiviteter økte, mens smertens påvirkning på søvn var uendret. Moderate eller sterke smerter, eller høy økning i smerte resulterte ikke nødvendigvis i inntak av første-linje smertestillende medikamenter. Prevalens av hoftesmerter økte også. Alvorlig hofteledds subluksasjon (migrasjonsprosent 50-89 %) og betydelig redusert motor funksjon (GMFCS V) var uavhengige risiko faktorer for hoftesmerter. I Artikkel III hadde vi 64 foreldre rapporterte om ungdommens HRQoL, hvor av 58 rapporterte i barndom også. Det var ingen signifikant endring i domeneskårene fra barndom til ungdomstid, med unntak av forverring i domenet *Generell Helse* grunnet økning i antall medikamenter. Betydelig redusert motorisk funksjon (GMFCS V) var assosiert med lave skårer i domenene *Personlig stell, Stilling, Forflytting og Mobilitet, Velvære & Følelser* and *Generell Helse,* men ikke domenet *Barns Generelle Livskvalitet*. Sterk smerte i ungdomstiden var assosiert med lave skårer i alle domener unntatt *Personlig stell*. I alle domener, var lav domeneskåre i barndom assosiert med lav skåre i tilsvarende domene i ungdomstiden. Artikkel IV: Barn med CP møtte ikke fastlegen oftere på dagtid enn barn i den generelle befolkningen. Fastlegene kodet smerte sjeldnere i konsultasjoner med barn med CP enn i den generelle barnebefolkningen. Konklusjon: Systematisk kartlegging av smerte og helserelatert livskvalitet gjennom oppfølgingsprogram for CP vil kunne bidra til mer effektiv kommunikasjon om behandling av smerte hos barn. I møte med kronisk syke barn, inkludert CP, bør helsearbeidere alltid spørre om smerter, også når smerter ikke nevnes av barnet eller foreldre. Informasjon om forebygging og behandling av smerter bør gis kontinuerlig til pårørende og barnet deres under oppfølgingen for CP.

V List of papers included in the thesis

Paper I

Larsen SM, Terjesen T, Jahnsen RB, Ramstad K. Recurrent pain in adolescents with cerebral palsy: a longitudinal population-based study. *Developmental medicine and child neurology. 2022;64(3):357-63.*

Paper II

Larsen SM, Ramstad K, Terjesen T. Hip pain in adolescents with cerebral palsy: a population-based longitudinal study. *Developmental medicine and child neurology.2021;63(5):601-7.*

Paper III

Larsen SM, Terjesen T, Jahnsen RB, Diseth TH, Ramstad K. Health-related quality of life in adolescents with cerebral palsy: a cross-sectional and longitudinal population-based study. *Submitted March 25th 2022 to Child: Care, Health and Development (status: under review).*

Paper IV

Larsen SM, Eide TB, Brunborg C, Ramstad K. Frequency of general practitioner consultations and pain as a reason for encounter in children with cerebral palsy: a Norwegian national linkage study. *Submitted March 15th 2022 to Scandinavian Journal of Primary Health Care (status: under review).*

VI Papers at the glance

Paper I

Title: Recurrent pain in adolescents with cerebral palsy: a longitudinal population-based study

Aims: To investigate pain characteristics, pain interference with daily life and use of analgesics in adolescents with cerebral palsy (CP) and to compare the results with findings five years earlier.

Methods: Sixty-seven adolescents, GMFCS levels III-V, participating in a CP surveillance program, were assessed on pain twice five years apart. Primary caregivers marked recurrent pain sites and graded pain interference with daily activities and sleep. Pain severity was obtained through the two questions from the Child Health Questionnaire (CHQ), transformed to a pain score scaled 0-100, where 100 represents no pain. Use of short-acting analgesics was recorded.

Results: Over five years, the prevalence of recurrent pain, number of pain sites, pain intensity and frequency all increased significantly. The most frequent pain sites were hip/thigh in GMFCS level V and knee in level III. Median CHQ pain score decreased from 60 to 40 ($p<0.001$). Pain interference increased for daily activities ($p=0.011$), but not for sleep. Twenty-eight of 54 participants with moderate or severe pain (CHQ pain score ≤ 60) received no short-acting analgesics.

Interpretation: In adolescents with CP, pain increased over five years despite follow-up in a surveillance program. An algorithm on pain management has been proposed to be included in surveillance programs.

Paper II

Title: Hip pain in adolescents with cerebral palsy: a population-based longitudinal study

Aims: Aims of the study were to investigate the prevalence, characteristics and risk factors of hip pain in adolescents with cerebral palsy (CP), and compare the findings with those of the same individuals five years earlier.

Methods: Sixty-seven adolescents (28 females), enrolled in a CP surveillance programme, with bilateral CP, Gross Motor Function Classification System (GMFCS) levels III-V, were assessed on hip pain. Their caregivers responded to the questions on the intensity and frequency of hip pain from Child Health Questionnaire (CHQ), (transformed to CHQ hip pain score; 100 indicates no pain). Interference of hip pain with daily activities and sleep was recorded on numeric rating scales. Hip displacement was measured radiographically by the migration percentage (MP).

Results: Twenty-eight participants had 44 painful hips. Their mean CHQ hip pain score was 40 (SD 21.4, range 10-80). Independent risk factors for hip pain, low CHQ hip pain score, and interference with sleep, were severe hip subluxation (MP 50-89%) and GMFCS level V. MP 50-89% was the only independent risk factor for interference with daily activities. Over five years, the number of participants with hip pain had increased from 18 to 28, while the mean MP of the most displaced hip was unchanged.

Interpretation: Our CP hip surveillance programme did not protect the participants against increasing prevalence of hip pain during adolescence. We suggest that surveillance programmes for CP should include guidelines for characteristics and management of hip pain.

Paper III

Title: Health-related quality of life in adolescents with cerebral palsy: a cross-sectional and longitudinal population-based study

Aims: The aims of this population-based cross-sectional and longitudinal study were to investigate different aspects of health-related quality of life (HRQoL) in adolescents with cerebral palsy (CP), to define possible changes from childhood to adolescence, and to identify factors associated with low HRQoL in adolescence.

Methods: Proxy-reports of 64 adolescents, aged 12-17 years, with bilateral CP in GMFCS levels III-V participating in a surveillance program, included five of the six domains from the HRQoL instrument Caregiver Priorities & Child Health Index of Life with Disabilities (CPCHILD): (*1) Activities of Daily Living and Personal Care, (2) Positioning, Transfer and Mobility*, (3) *Comfort and Emotions*, *(5) General Health* and *(6) Overall Quality of Life*, and the two questions on pain from the Child Health Questionnaire (CHQ). Fifty-eight participants (91%) took part in the longitudinal study.

Results: From childhood to adolescence, the mean CPCHILD domain scores decreased slightly in *General Health* and remained unchanged in the other four domains. In the domain *General Health*, the number of medications increased, which was the reason for the score decrease. Pain severity increased significantly. Severe motor impairment was associated with low scores in domains *1, 2, 3* and *5*, and more severe pain with low scores in domains *2, 3, 5* and *6*. A low domain score in childhood was associated with a low score in each corresponding domain in adolescence.

Conclusion: An assessment of HRQoL should be included in CP surveillance programs because this could identify needs for interventions in individuals with severe CP. This study indicates the importance of improved pain management in both children and adolescents with severe CP.

Paper IV

Title: Frequency of general practitioner consultations and pain as a reason for encounter in children with cerebral palsy: a Norwegian national linkage study

Aims: The aim was to compare the frequency of daytime contacts, and pain as a reason for encounter (RFE) with a general practitioner (GP), in children with cerebral palsy (CP) to that of the general paediatric population.

Method: The study investigates daytime contacts in the period 2006 to 2018 using the Norwegian Directorate of Health's database for the control and reimbursement of health expenses. Children with CP were identified using linkage to the Norwegian Quality and Surveillance Registry for Cerebral Palsy (NorCP). All children born 1996 to 2012 who contacted a GP were included. Children with CP registered in NorCP were cases and children not registered in NorCP were controls. Frequencies of all daytime contacts, including consultations and administrative contacts were analyzed. International Classification for Primary Care was applied for RFE. Frequencies of consultations with pain as a RFE were analyzed.

Results: Cases accounted for 0.46% of all daytime contacts and 0.27% of all daytime consultations, the latter corresponding with the estimated national prevalence of CP. GPs registered more administrative contact and coded pain as a RFE less frequently in consultations with cases (6%) than with controls (12%).

Conclusion: Children with CP did not consult a GP more often than the general paediatric population did. In consultations, GPs should ask for pain even if the child with CP or parent does not address pain. The local multidisciplinary team should encourage the family to consider consulting a GP if the child is in pain.

1 INTRODUCTION

This thesis addresses pain and management of recurrent pain in the care for children with cerebral palsy (CP). “Care” is defined as “the process of protecting someone and providing what that person needs” according to the Cambridge Dictionary (1). “Process” is defined as “a series of actions that one takes in order to achieve a result” (1), which implies that a certain period of time is required. “To protect someone” means “to keep someone safe from injury, damage or loss” (1). Children with CP encounter many care providers in the process of care, including daily contact with primary caregivers and teachers to occasional contact with health-care providers in the health care services. Pain management requires time because it consists of several actions: assessment, evaluation of possible causes and suitable treatment, and evaluation of the given treatment. In medical research on pain in children with CP, focus has most often been on pain prevalence, often assessed in cross-sectional studies as a snap shot, and not longitudinally addressing changes in pain characteristics such as pain severity and pain interference with daily activities and sleep. Still, changes over time could be of more interest to patients and their caregivers. For primary caregivers (parents and staff in medical homes), there are several management alternatives for observed pain in CP: 1) Treat pain, 2) Contact a general practitioner (GP) for advice, or 3) Save the concerns for the annual appointment in the specialist care. Each time a caregiver acts on pain, either by taking care of it, or seeking advice from health care providers, represents a potential opportunity to learn more about pain. This is also an opportunity for a child to learn self-care. The question is if the health care system provides a framework which contributes to empower primary caregivers and children with CP by providing enough information on pain management to enable them to act and to seek advice when needed.

This thesis will focus on pain in children with CP in the Norwegian context, which is based on the independency to make one’s own decisions and on equality for all. Study results on pain and health-related quality of life (HRQoL) in non-ambulatory children with CP, and on GPs’ involvement in care for children with CP at all disability levels, will be used to bring recommendations for improved pain management in CP a step forward.

2 BACKGROUND

2.1 Theoretical frameworks

This thesis is based on different aspects of pain and pain management that require not only one, but several, theoretical frameworks to be addressed. I will start with the bio-psycho-social model of understanding of disease defined by Dr. Engel (2), address its role in the development of classification defined by the WHO, and continue with the model on utilization of medical care by Andersen and Newman (3).

2.1.1 Bio-psycho-social model

Professor of psychiatry and medicine George Engel presented a bio-psycho-social model (Fig. 1) and advocated for a holistic approach to health problems (2), suggesting that all aspects of a health problem should be addressed during assessment and treatment. This model is more than four decades old, but its message remains important: Care for a whole person.

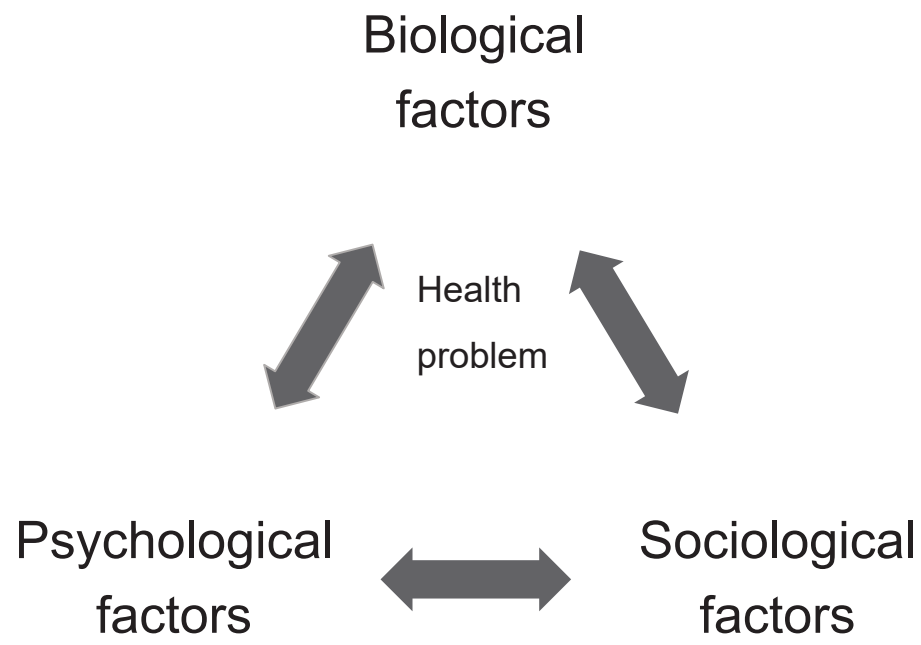

Figure 1. Dr. Engels' Bio-Psycho-Social Model (2). Adapted.

2.1.2 The World Health Organization Family of International Classifications (WHO-FIC)

The concept of WHO-FIC has been created to give a common framework and language to report, compile, use, and compare, health information at the national and international level. Norwegian health professionals follow the WHO-FIC (4) (Table 1).

Table 1. WHO-FIC (In italics, classifications applied in the data collection, and/or discussed in this thesis). Adapted from WHO web-page

Related Classifications	Reference Classifications	Derived Classifications
International Classification of Primary Care, Second Edition (ICPC-2)	***International Classification of Diseases (ICD) Version 10 (ICD-10)***	International Classification of Disease for Oncology, Third Edition (ICD-O-3)
International Classification of External Causes of Injury (ICECI)		The ICD-10 Classification of Mental and Behavioural Disorders
The Anatomical, Therapeutic, Chemical (ATC) classification system with Defined Daily Doses (DDD)	***International Classification of Functioning, Disability and Health (ICF)***	Application of the International Classification of Diseases to Dentistry and Stomatology, Third Edition (ICD-DA)
ISO 9999 Technical aids for persons with disabilities – Classification and Terminology	**International Classification of Health Interventions (ICHI) *under development***	Application of the International Classification of Diseases to Neurology (ICD-10-NA)
International Classification for Patient Safety (ICPS)		*International Classification of Functioning, Disability and Health, Children & Youth Version (ICF-CY)*
International Classification of Nursing Practice (ICNP)		

WHO-FIC brings together different classifications dealing with various dimensions of health and health care in order to present a more comprehensive picture of a health system. The three reference classifications are:

1. The International Classification of Diseases version 10 (ICD-10) (5) explains a health condition (i.e. diagnosis), and focuses on the cause of disease. ICD-10 is used in Norwegian specialist care and national registries (Papers I-IV).

2. The International Classification of Functioning, Disability and Health (ICF) (6), which applies the bio-psycho-social model as the basis, was adopted in 2001 by the WHO. The ICF is a scheme that is meant to comprehensively classify the functioning and health of individuals, and it complements the ICD coding scheme (7). ICF aims to measure health and disability, as well as the consequences of a health condition on function, activities of daily living, and participation. ICF introduced a shift of focus from the cause of a disease to the impact of a disease, asking professionals to find solutions by adapting the environment to the person. ICF classifies bodily functions and structures, activities and participation, and various environmental factors that restrict or allow person to function in an array of everyday activities, all aspects addressed in a non-hierarchic structure with an aim to enhance body function, activity, participation and ultimately HRQoL (Figure 2). There is also a derived version for Children and Youth (ICF-CY) (8) published in 2007, which is designed to record characteristics of the developing child and the influence of environmental factors that surround the child .

   Part 1 of the ICF Functioning and disability, has two components (7):

   - *Body functions and structures. Body functions* refer to the physiological and psychological functions of the body systems. Impairments describe alterations from the norm in the functioning of these systems. *Body structures* refer to the anatomical parts of the body, and may be differentiated from the disease or health condition.
   - *Activities and participation. Activity* refers to the execution of a particular task or action, whereas these tasks can then be grouped within particular life situations or roles, referred to as *participation*. Activity limitations are the challenges and difficulties that an individual may experience in performing particular tasks. Participation restrictions refer to challenges in the ability to be involved or engaged in particular life roles, such as, learning and applying knowledge, mobility in different environments or interpersonal interactions and relationships.

   Part 2 of the ICF Contextual factors which constitute the background within which an individual functions has two components (7):

- *Environmental factors* include the physical and social environment, but also attitudes surrounding the individual.
- *Personal factors* are features of the individual that are not part of their health condition or health status, and include demographic characteristics such as age, sex and ethnic origin, but also lifestyle preferences and habits, upbringing, education, coping style, motivation and other personality traits. Of notice, personal factors are not classified in the ICF, but their contribution is recognized as part of the framework.

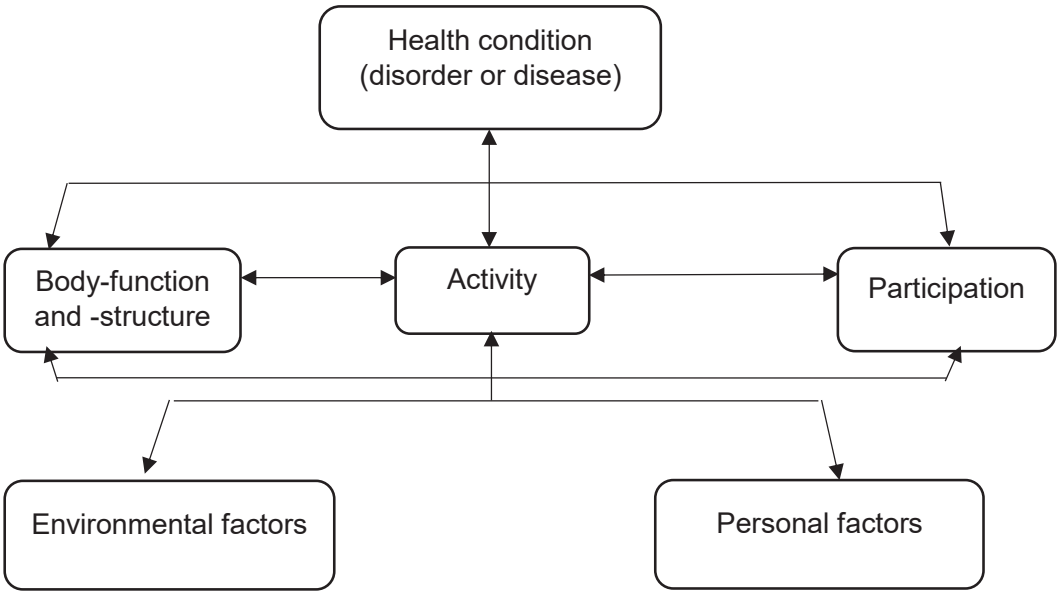

Figure 2. ICF model. Adapted from WHO webpage

3. The International Classification of Health Interventions (ICHI), released recently, is to be a common tool for reporting and analyzing health interventions for clinical purposes (9). The classification is built around three axes: Target (the entity to which the Action is carried out), Action (a deed done by an actor to a Target) and Means (the processes and methods by which the Action is carried out). ICHI covers interventions carried out by a broad range of providers across the full scope of health systems including interventions on diagnostic, medical, surgical, mental health, primary care, allied health, functioning support, rehabilitation, traditional medicine, and public health. ICHI has not yet been applied in research on CP.

Additionally, a related classification, the International Classification of Primary Care version 2 (ICPC-2) (10) developed by World Organization of Family Doctors (WONCA) for coding of reason for encounter (RFE) in primary care (accepted by WHO as classification in primary care), is of relevance (Paper IV). ICPC-2 consists of 17 chapters on organ systems. Each chapter includes codes for symptoms and complaints (numbers 01 to 29), process codes (numbers 30 to 69) and disease codes (numbers 70 to 99).

2.1.3 Health services use and healthcare seeking

Despite several differences in funding of health care in Norway and the United States of America, a behavioral model of medical care utilization in US developed by Andersen and Newman (3, 11) is useful in identifying the factors that influence individual decisions to use medical care. The model suggests that use is dependent on predisposing and enabling factors as well as on the level of illness. All children and persons with disabilities are dependent on others to act on their behalf when they need health services. Seeking healthcare is also dependent on the patients' (and caregivers') expectations towards the GP (12). Healthcare seeking is addressed in Paper IV.

Predisposing	**Enabling**	**Illness Level**
Demographic	Family	Perceived
Age	Income	Disability
Sex	Health Insurance	Symptoms
Marital Status	Type of Regular Source	Diagnoses
Past Illness	Access to Regular Source	General State
Social Structure	Community	Evaluated
Education	Ratios of Health Personnel and Facilities to Population	Symptoms
Race	Price of Health Services	Diagnoses
Occupation	Region of Country	
Family Size	Urban-Rural Character	
Ethnicity		
Religion		
Residential Mobility		
Beliefs		
Values Concerning Health and Illness		
Attitudes toward Health Services		
Knowledge about Disease		

Figure 3. Individual Determinants of Health Service Utilization. Adapted from Andersen and Newman (3).

2.2 Patient Reported Outcomes (PRO)

For decades, the effect of medical treatment has been reported only by medical staff. Lately, the concept for looking at health has evolved to also include patient reported outcomes (PRO). The term patient- (or person) reported outcome is used when people (including children and parents) reflect directly on their life experience in relation to a health condition and its treatment, without any interpretation by healthcare professionals or others (13). A measure used to evaluate PRO is called a patient reported outcome measure (PROM). Also ICF encourages healthcare providers to recognize the biopsychosocial dimensions of health, beyond the level of disability and to address the experiences and views of patients and their closest relations.

In paediatric populations with chronic neurological conditions, the PROM concept has also been accepted and includes both self- and proxy-report, when choosing potential interventions or evaluating their impact (14). Self-report on PROM is important. The ability to communicate on pain, localization, intensity, frequency and duration of pain, is reduced in many individuals with chronic conditions, in children especially, and reporting on outcome measures is often dependent on a proxy-report from those responsible for a person's daily care.

2.2.1 Pain

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" by the International Association for the Study of Pain (IASP), (15, 16). In 2019, IASP Task Force was to review comments on a proposed new definition of pain as "An aversive sensory and emotional experience typically caused by, or resembling that caused by, actual or potential tissue injury", adding in accompanying notes that "Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human or a non-human animal experiences pain." This note is important because it is a reminder to take into account a person's ability to share their condition with others.

Pain can also be a relevant PRO in relation to a condition, its treatment or a lack of it. A new ICD-11(5) includes diagnosis of pain, and additional coding on chronicity (chronic when lasting more than 3 months), severity, distress and interference (graded mild-moderate-severe), and temporal pattern (intermittent, persistent, persistent with overlaid attacks). Further, there is no

international consensus on how pain should be reported on in research. Most research on pain reports on prevalence, while in the clinical assessment focus is on intensity, frequency, quality, location and temporality. Pain intensity may be reported on a visual analogue scale (VAS) or a numeric rating scale (NRS). Pain in a non-verbal person may be reported through the observation of pain behavior (17). The Child Health Questionnaire (CHQ) (18), a generic instrument developed to evaluate functional status, well-being, and health outcomes in children, includes items on pain intensity and frequency combining them into pain severity score. Also the Health Utilities Index 3 (HUI-3) includes a pain variable, assessing the presence and severity of pain in relation to limitations of normal daily activities (19).

Research on pain in the general paediatric population has been conducted either by survey in schools (20), or by geographical cohorts using linkage of health system databases (21), both showing that pain is a frequent reason to seek health care in children. Still, the true prevalence of pain is difficult to define in children.

2.2.2 Quality of Life and Health-Related Quality of Life

Quality of life (QoL) is defined by the WHO as an individual's perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards and concerns (22). QoL incorporates the persons' physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to environment. The term QoL originates from the field of oncology, where "the gap theory" refers to the gap measured between the hopes and expectations of the individual and that individual's present experience (23). One definition of HRQoL is "an individual's perception of various aspects of their lives that they think is affected by a particular medical condition or treatment" (24). There are several instruments developed to investigate QoL and HRQoL in a paediatric population. I will discuss relevant instruments in the General Discussion below.

2.3 Cerebral Palsy (CP)

CP is listed as a diagnosis in ICD-10 (5) in Chapter IV with codes G80.0-G80.9 *Cerebral palsy* as a condition of the nervous system. CP describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-

progressive disturbances that occurred in the developing fetal and infant brain (25). The definition of CP leans heavily on the ICF and assumes activity limitation and participation restriction. Further, the motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behavior, by epilepsy, and by secondary musculoskeletal problems. Cerebral palsy is a lifelong condition since there is no cure for CP. In Norway, the prevalence of CP is calculated to 2.5 (95% CI 2.4-2.7) per 1,000 (26).

2.3.1 Classification of CP

Communication about patients with CP had been improved after the introduction of several classification systems, which complement ICD-10 (5) by providing a common ground when communicating in clinical practice, research, teaching and administration. The following three classifications are relevant in the thesis:

The Surveillance of Cerebral Palsy in Europe (SCPE) (27) which classifies CP according to the most predominant neurological symptoms of abnormal pattern of movement and posture defining following CP subtypes:

(i) Spastic CP (bilateral and unilateral spastic) is characterized by increased tone, pathological reflexes resulting in abnormal pattern of movement and posture

(ii) Dyskinetic CP (dystonic and choreo-athetotic) is characterized by involuntary, uncontrolled recurring, occasionally stereotyped movements, varying muscle tone and predominating primitive reflex patterns.

(iii) Ataxic CP is characterized by loss of orderly muscular coordination, so that movements are performed with abnormal force, rhythm and accuracy.

The Gross Motor Function Classification System (GMFCS) (28) which classifies gross motor performance in children with CP in five levels (here adapted for age 6-12 years):

Level I The child walks without limitations, but speed, balance and coordination are limited

Level II The child walks in most settings, and climbs stairs holding onto a railing. The child may experience difficulty walking long distances and balancing on uneven terrain, inclines, in crowded areas or confined spaces. The child may walk with physical assistance, a handheld

mobility device or use wheeled mobility over long distances. The child has only minimal ability to perform running and jumping.

Level III The child walks using a hand-held mobility device in most indoor settings. They may climb stairs holding onto a railing with supervision or assistance. The child uses wheeled mobility when traveling long distances and may self-propel for shorter distances.

Level IV The child requires physical assistance or powered mobility in most settings. The child may walk for short distances at home with physical assistance or use powered mobility or a body support walker when positioned. At school, outdoors and in the community child is transported in a manual wheelchair or uses powered mobility.

Level V The child is transported in a manual wheelchair in all settings. The child is limited in her/his ability to maintain antigravity head and trunk posture and control leg and arm movements.

The Communication Function Classification System (CFCS) (29) which evaluates if the person consistently and effectively alternate sender and receiver roles in communication with familiar and unfamiliar communication partners, defines five levels:

Level I The person is effective Sender and Receiver with unfamiliar and familiar partners

Level II The person is effective, but slower-paced Sender and/or Receiver with unfamiliar and familiar partners

Level III The person is effective Sender and effective Receiver with familiar partners

Level IV The person is inconsistent Sender and/or Receiver with familiar partners

Level V The person is seldom effective Sender and Receiver with familiar partners

2.3.2 Pain

Pain in children with CP has been investigated in several cross-sectional studies (30-33) by addressing prevalence. Two systematic reviews estimated prevalence to vary between 14 and 76 % depending on the inclusion criteria for populations regarding factors such as age and CP severity (34, 35). In the young population with severe CP, musculoskeletal pain has been

recognized as the most dominant type (36). Higher pain prevalence in the foot, ankle and leg was reported in children with lower motor impairment, while hip pain was more frequent in children with higher motor impairment (33). Several researchers have advocated that high prevalence of pain could be a result of inadequate approach to pain management (37-39). Despite the high pain prevalence in CP, there are only few previous studies on pain characteristics such as pain intensity, frequency, and pain interference with daily activities and sleep (30, 31, 40). Still, longitudinal population-based studies are scarce. We addressed these issues in Paper I.

A new classification of pain in children with CP that is aligned with new mechanisms of pain has recently been proposed (41), as the Cerebral Palsy Pain Classification (CPPC). Its aim is to optimize both the registration and assessment of pain conditions, and thus ensure common language on pain in CP. This classification addresses pain classification as defined in the ICD-11. However, Norwegian health system still uses ICD-10 version.

2.3.3 Hip pain

Historically, hip dislocation has been recognized as one of the main causes of pain in non-ambulatory children with CP (42). The high prevalence of hip dislocation in this population was the main reason to initiate CP surveillance programs (43). A decreasing prevalence of hip dislocation has been seen as an indicator for the efficiency of surveillance programs (43, 44). Even though population-based research has become standard in several countries, hip pain has been addressed only in studies with cross-sectional design (45-47). Longitudinal studies on hip pain have the potential to contribute to enhanced knowledge of the natural course of hip pain, but we found no such studies. We have addressed these issues in Paper II.

2.3.4 Quality of Life and Health-related Quality of Life in CP

The SPARCLE studies on children with CP had shown that pain influences negatively on both QoL and participation (30, 31, 48-52). Previously, HRQoL has been investigated in relation to surgical interventions such as hip and spine surgery, and ITB (53, 54) and hip displacement (55) in children with CP. However, there are no longitudinal studies on HRQoL in children with CP who followed a CP surveillance program. We have addressed HRQoL in non-ambulatory adolescents and possible changes in HRQoL from childhood to adolescence in Paper III.

2.4 The Norwegian healthcare system

In order to set the stage for this study, I will briefly describe the healthcare system in Norway, and the context in which this PhD project took place.

The government is responsible for the organization of health care ensuring availability, accessibility, acceptability and quality in the medical services to all inhabitants. Even though the health care system provides a right to health, each person has a choice to use this right or not. Children are in a vulnerable position when seeking health care because they are dependent on others to assess their health issues and to seek help accordingly. Thus, the caregivers must learn to understand the specific needs of their child as well as how the health care system functions.

The Norwegian healthcare system consists of primary and specialist health care. The primary care is present in all local communities, and usually includes GP, physical therapist (PT), and nurse (and occasionally other health care providers). The specialist care in Norway most often takes place in hospitals and includes all medical professions.

2.4.1 Primary health care

The general assumption in the medical community is that structured follow-up can contribute to an early detection of health issues, better health, and early treatment. Norwegian health authorities have started with surveillance of child development through “Health stations” in 1939. Health stations are a regular part of the care of newborns, pre-school and school children, focusing on general development, growth and vaccines. All other health issues are tasks for a regular GP. In 2000, a reform of the primary health care introduced a new GP system, called “Fastlegeordningen”, in which all inhabitants of Norway get appointed one GP who can be contacted for regular visits, including acute and chronic health issues. The system defined the GP as a cornerstone of the health-care system, thus ensuring the continuity in health care. This GP system is under constant evaluation but has not been evaluated in relation to children with disabilities who also receive follow-up in the specialist health care as a supplement to the primary health care. The paediatric population with CP receives follow-up most regularly from physical therapists in the primary health care.

2.4.2 Specialist health care

The frequency of follow-up in specialist care depends on the complexity of the medical condition. In the late 1990s, Norwegian health authorities saw the need to organize follow-up of children with disability in separate out-ward clinics called “habilitation units”, as an addition to already existing specialist care at general paediatric clinics, health stations and GP’ services in primary health care. For many children with chronic conditions, referral and further follow-up at “habilitation units” starts at an early age, and lasts up to 18 years of age.

The primary and specialist care have organizational differences, but I choose to mention a few facts that are relevant for this thesis. While each contact with a GP (primary health care) is usually initiated by a patient when a health issue occurs, the first contact with specialist care (i.e. habilitation units) is dependent on a primary referral, either from a neonatal unit (or paediatric department), a GP, or a Health station. All further follow-up in the habilitation units is dependent on the severity of a condition, which also influences the frequency of appointments. The contact may be more frequent for certain conditions such as complicated forms of epilepsy, progressive encephalopathies or other rare conditions. In the habilitation units, a child with CP usually meets a multidisciplinary team.

2.5 National databases

A unique identification number, introduced in the 1960s ensured unique identification of each person living in Norway, and is used in all national databases. This is very useful in research, as it makes both the linkage and the national statistics studies possible. A description of two databases that are relevant for this thesis follows.

2.5.1 Norwegian Quality and Surveillance Registry for Cerebral Palsy (NorCP)

Organized CP surveillance in Norway started in 2006 after a Swedish model with CPUP (56), which showed reduced rates of hip dislocation in the paediatric population with CP (43, 44). Two national databases for paediatric population with CP, the National Register for CP (CPRN) and Cerebral Palsy Follow-Up Program (CPOP) (57) were joined in NorCP in 2020 (58). The aim of NorCP is to procure research-based knowledge on causes and occurrence of CP, as well as health, function, participation, QoL, and medical treatment of persons with CP (58). NorCP

follows the CP definition suggested by Rosenbaum et al. (25) and the diagnosis listed in ICD-10 (5). There are approximately 2,400 individuals registered in the NorCP per December 31st 2021. NorCP is based on written informed voluntary consent signed by parents. There are three registrations in NorCP, the first at diagnosis (usually at age 0-3 years), the second at the age of 5 years when a CP diagnosis is confirmed, and the third at the age of 15 years (58). The Norwegian surveillance protocol includes a traffic-light system for when to act based on findings on radiographs of hips and measurements of the range of joint motion. There are two questions on pain: if pain was present and where it was located (59). The surveillance protocol is registered annually, and biannually in children with severe CP and all pre-school children. The work on best practice guidelines for management has been initiated in the fall of 2021.

2.5.2 Database for the control and reimbursement of health expenses (KUHR)

The Norwegian primary health care receives governmental support. The Norwegian Directorate of Health and the Norwegian Medical Association defined reimbursement codes for GPs in primary care. All Norwegian GPs who take part in "Fastlegeordningen" send a monthly report to the Database for the control and reimbursement of health expenses (KUHR) at the Norwegian Directorate of Health, thus applying for reimbursement of health expenses. The reimbursement codes are used together with ICPC codes for RFE. In Norway, use of ICPC codes started in 1998, and use of ICPC-2 version started in 2003. All GP reports on work with patients are saved in the KUHR database. Over the last decade, several research projects have used data from KUHR (60-63).

3 AIMS

The overall aim of the thesis was to study pain and HRQoL in children with CP. The specific aims were:

1. To investigate the variables listed below in a cohort of non-ambulatory adolescents with CP, possible changes from childhood to adolescence, and relevant factors that could be associated with:
   - pain (Paper I)
   - hip pain (Paper II)
   - HRQoL (Paper III)
2. To compare the frequency of daytime contacts, consultations, and pain as a RFE with a GP in children with CP to that of the general population of the same age (Paper IV)

The hypotheses in Papers I-III were:

- Prevalence of pain and severity of pain do not change from childhood to adolescence.
- Prevalence of hip pain does not change from childhood to adolescence and severe motor impairment is associated with hip pain.
- HRQoL domain scores do not change from childhood to adolescence and severe pain is associated with low HRQoL domain scores.

The hypotheses in Paper IV were:

- The frequency of daytime consultations is not affected by a diagnosis of CP.
- The frequency of daytime consultations related to pain is not affected by a diagnosis of CP.
- The frequency of daytime consultations related to musculoskeletal pain is not affected by a diagnosis of CP.

4 METHODS

4.1 Study design, study populations and enrollment of participants

Papers I-III are based on a follow-up study and have both a cross-sectional and longitudinal population-based study design. Children (now adolescents) with CP, born 2002-2006, living in South-East Norway, with bilateral CP and ambulatory function GMFCS level III-V registered in NorCP were invited to participate. An invitation to 139 eligible children was sent in 2013-2014, of whom 77 participants in the first data collection in childhood (46, 55). In 2019, letters of invitation were sent to 71 (of 77) children who participated in the first data collection (Figure 4).

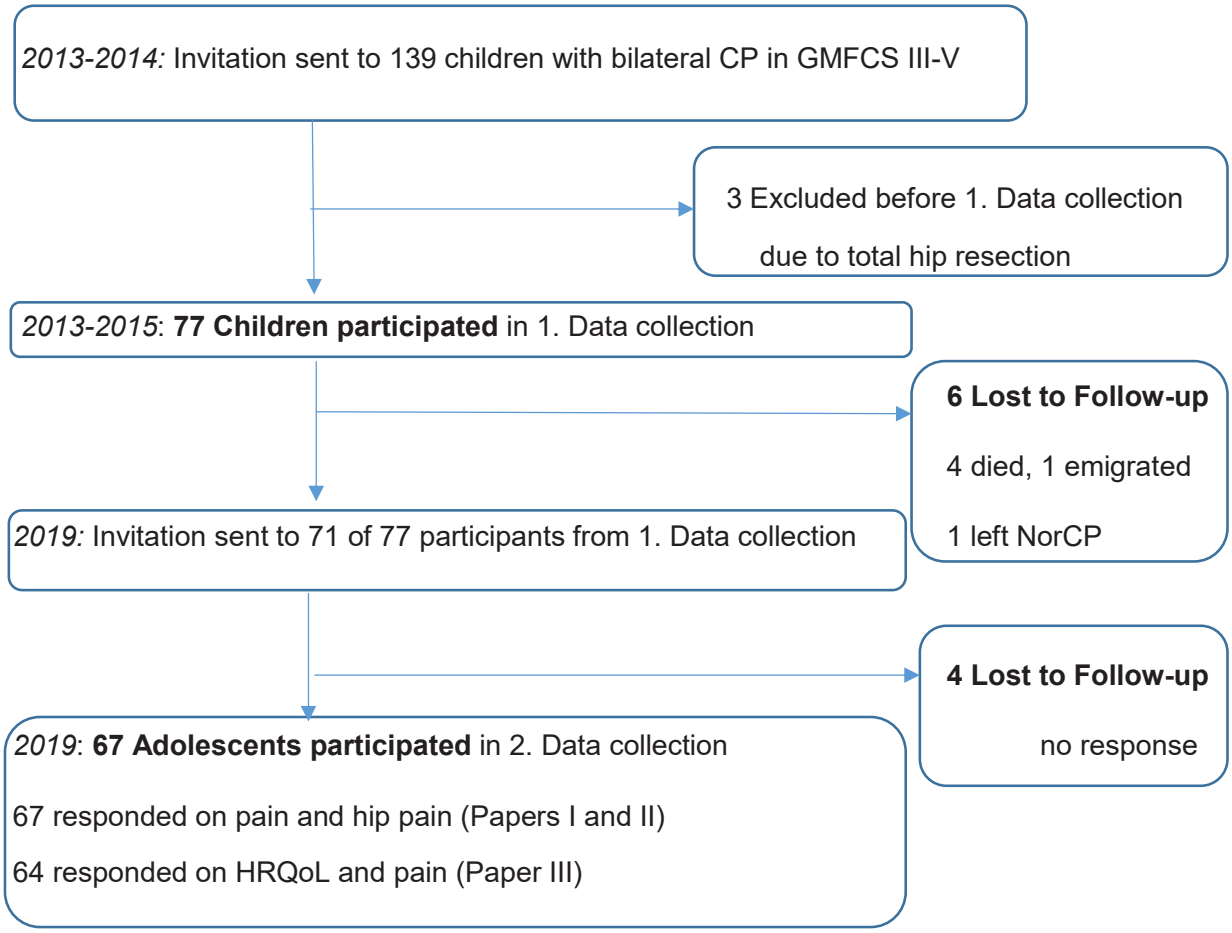

Figure 4. Flow-chart on participants in Papers I-III

Paper IV is based on a national study of daytime contacts with GPs in the time period 2006-2018. The study population was all children (0-17 years) born 1996-2012 registered in KUHR. A linkage between KUHR and NorCP was performed, and comparisons were made between those registered in NorCP (cases) and those not registered in NorCP (controls).

4.2 Collection of data

In Papers I-III, primary caregivers responded to research materials consisting of questionnaires on pain and HRQoL and a structured telephone interview. A copy of the content of an envelope sent to participants is available in Appendix A. The interview protocols for the first and second data collection are available in Appendix B. In Paper IV, data on age, type of daytime contact, and RFE a GP, were retrieved from KUHR.

4.3 Measures

Psychometric theory is the science of assessing the measurement properties of a tool, and its key concepts are reliability and validity. Several measures in this thesis have psychometric properties, and these were commented on in further text when appropriate.

Outcomes

- ***Recurrent pain*** (Paper I) was assessed by asking primary caregivers to respond to the question "Does the participant have recurrent pain?" where "recurrent" was defined as 4 weeks or more. Pain was recorded as a dichotomous variable.
- ***Locations of recurrent pain*** (Paper I) were obtained from the body outline (anterior and posterior view) from Brief Pain Inventory (BPI), Norwegian version (64). In order to compare with other pain studies, instructions were provided to record all pain sites with recurrent pain.
- ***Pain intensity and frequency*** (Paper I) was assessed by asking primary caregivers to respond to the two questions on pain from the Child Health Questionnaire CHQ (18), which is a generic instrument for the assessment of health status in children. It has been translated, cross-culturally adapted, and evaluated according to international guidelines for use in Norway and other countries (65). The two questions asked from CHQ were on (a) pain intensity (raw score 1-6): "During the past 4 weeks how much bodily pain or

discomfort have your child had," with the response alternatives "none, very mild, mild, moderate, severe and very severe," and (b) pain frequency (raw score 1-6): "During the past 4 weeks how often did your child have bodily pain or discomfort," with the response alternatives "none of the time, once or twice, a few times, fairly often, very often and every day or almost every day," respectively. Reliability and validity of CHQ questions on pain have been found satisfactory in children with CP (66).

- An algorithm for transforming and summing of scores on intensity and frequency, into a ***pain severity CHQ pain score*** in 0-100 scale was applied (18) (Paper I). A CHQ pain score of 100 indicates no pain. The CHQ pain score had been applied in pain research earlier (46, 67). We categorized CHQ pain score 0-30 as severe, 40-60 as moderate, and 70-90 as mild pain. Changes in CHQ pain scores of 20 and less were considered as no change in pain, while a change of 30 or more was regarded as less or more pain.
- ***Interference of pain*** (Paper I) was reported by primary caregivers. The impact of pain was assessed with selected items from BPI (64). It measures the level of pain interference with function using 0 (no interference) to 10 (complete interference) on a numerical rating scale. Two items were chosen, ***activities of daily living and sleep***, and the time span was modified from pain experienced during the last 24 hours to pain experienced the last four weeks.
- ***Recurrent hip pain*** (Paper II) was assessed by asking primary caregivers to respond to the question "Does the participant have hip pain lasting four weeks or longer?" Hip pain was recorded as a dichotomous variable.
- ***Hip pain intensity and frequency*** (Paper II) were not categorized in hip pain literature earlier. The same pain questions from CHQ were used to ask about hip pain (18). Hip pain intensity and hip pain frequency combined defined hip pain severity, which was presented as CHQ hip pain score (Paper II).
- ***Interference of hip pain with activities of daily activities and sleep*** (Paper II) was assessed with selected items from BPI (64). Hip pain interference had not been investigated earlier using the two BPI questions with a numerical rating scale. The time span was modified from pain experienced during the last 24 hours to pain experienced the last four weeks.

- ***HRQoL*** in participants was assessed using the questionnaire Caregiver Priorities Child Health Index of Life with Disability (CPCHILD) (68) (Paper III) and included 5 of 6 domains (36 items): (1) *Activities of Daily Living and Personal Care* (9 items); (2) *Positioning, Transfer and Mobility* (8 items); (3) *Comfort and Emotions* (9 items); (5) *General Health* (3 items); and (6) *Overall Quality of Life*. Domain (4) Communication and Social Interaction (7 items) was excluded because it was excluded in the previous study (55). CPCHILD focuses on measuring caregivers' perspectives of the activity limitations, health status, well-being, and ease of care. Items are rated on degree of difficulty ('no problem' to 'impossible') and level of independence ('independent' to 'total assistance'). The instrument has sound psychometric properties (69). CPCHILD is one of recommended instruments for paediatric population with severe CP (70). The Scandinavian version of the CPCHILD has proven to be a valid and reliable proxy measure for HRQoL (71).
- ***Frequency of daytime contacts*** with a GP (Paper IV) was measured by the frequency of the KUHR codes for consultations (2ad, 2ae, 11ad), simple contacts (1ad, 1bd, 1be), interdisciplinary interaction between GPs and other professionals in the primary health care (1f, 14), referrals without consultation (1h), and prescriptions (1i), all listed in the excerpt from the code list of "Normaltariffen" (Appendix C).
- ***Reasons for encountering (RFE)*** a GP were assessed by the ICPC-2 codes registered in KUHR. ICPC-2 codes regarded relevant for pain were collapsed and labelled "pain codes" before the frequencies were analyzed (Paper IV). Also the frequency of ICPC-2 code (10) used for CP as a RFE in primary healthcare (*N99 Neurological disorder, other)*was investigated in cases.

Explanatory variables

- ***CP diagnosis.*** In both studies (Papers I-IV), all participants were registered in NorCP (58), and had a CP diagnosis confirmed through NorCP guidelines and in accordance to ICD-10 (5). Data on CP diagnosis (in NorCP) were confirmed prior to invitation to the data collection in adolescence (Papers I-III).

- ***Predominant movement disorder*** was recorded according to the classification suggested by SCPE (27), and was retrieved from the NorCP (Papers I-III). Data was collected prior to invitation to the data collection in adolescence.
- Functional effect of motor impairment was recorded as ***gross motor performance*** according to the GMFCS (28) and was available from NorCP (Papers I-III). Information was collected prior to data collection in adolescence, even though GMFCS is usually stable after the age of 5 years in more severe forms of CP (72).
- Functional effect of the impairment in communication was recorded as ***communication performance*** according to the CFCS (29) and collected from NorCP (Papers I and III).
- ***Hip displacement*** was measured by migration percentage (MP) (Paper II) by Reimers' method (73). The following categorization was performed: Normally positioned hips MP<33, hip displacement MP 33-89, and hip dislocation 90-100. Date of radiographs was available from NorCP (former CPOP), and consent allowed contact with a local hospital for import of radiographs.
- ***Type of hip surgery*** (Paper II) was recorded from NorCP as bony surgery and soft-tissue surgery according to the classification generally accepted by orthopaedic surgeons (Terje Terjesen, personal communication). All information on surgery was confirmed by a primary caregiver through the interview.
- ***Parental relation*** between a participant and a person who responded was registered during the interview, and according to CPCHILD (Papers I-III).
- ***Confirmation of identity of informant*** in the longitudinal design was secured through questions on date of birth and sex of informant available in CPCHILD (Papers I-III).

4.4 Statistics

The statistical analyses were performed using Statistical Product and Service Solutions (SPSS) software, versions 26-27 (IBM, Armonk, New York, USA) in Papers I-III and STATA version 16 (Stata Corp LLC, Texas, USA) in Paper IV. Oslo University Hospital and University of Oslo provided the license for use.

Papers I-III: Data were presented either as frequency, percentage, proportion, and described with mean and standard deviation (SD) for continuous variables, or median and range if continuous

variable had skewed distribution. Correlation between ordinal variables was explored calculating Spearman's correlation coefficient (significant when $p < 0.05$ and coefficient > 0.30) (Paper I). Categorical variables were analyzed with the Pearson chi-square test (Papers II), while Fisher's exact test was applied for small samples (Papers II and III). Continuous variables were analyzed with Student's t-test, analyses of variance with Scheffe's post hoc test (Paper II). Non-parametric statistics (Mann-Whitney U test) was applied for ordinal variables and skewed continuous variables (Paper I). In longitudinal analyses, proportions were analyzed with McNemar's test (Papers I and II), continuous variables with paired samples t-test (Papers I-III) and ordinal variables with Wilcoxon Signed Ranks test (Paper I). Regression analyses were applied for analyses of factors that could be associated with dependent variables, linear regression if dependent variable was continuous (Papers I-III) and logistic regression (Paper II) if dependent variable was categorical. In regression analyses, variables were included in multivariable linear regression analyses if $p < 0.1$ in univariable analyses (Paper I-III). Normality of residuals was tested to explore the fit between models and observed data. All tests were 2-sided. Differences were considered significant if $p < 0.05$. Participants with missing values were excluded from analyses, imputation was not performed. A priori sample size calculation was not performed prior to the second data collection in adolescence due to the predefined study population from childhood.

Paper IV: Data were presented as the number of age specific contacts (%) and frequency of chosen ICPC-2 codes. Risk ratio (RR) with 95 % confidence interval (CI) was calculated using a calculator for cohort studies. Risk ratio below one meant that cases had lower risk than controls, and above one that cases had higher risk than controls.

4.5 Ethics

The studies were approved by the Regional Committee for Research Ethics, Papers I-III: 2012/2258 and Paper IV: 2018/1250 (Appendix D, in Norwegian language).

The Commissioner for the Protection of Privacy in Research at OUH approved data storage in all studies.

Papers I-III: A parent or legal guardian provided signed written informed consent to participation in 2013-2014, which covered the two data collections. An invitation to participate in the second data collection was sent to the home address of the participants who participated in the first data collection only. We included the questionnaires, a time-table for scheduling a convenient time for a telephone interview and a prepaid return envelope in the letter. Prior to sending the letter, we checked that the participant was alive through NorCP. Around 15% did not respond for four weeks, and got one reminder invitation with the same questionnaires.

Paper IV: As mentioned earlier in the Background, legal guardians of all children registered in NorCP have signed an informed consent which allows linkage to other registries without obtaining a new consent. KUHR database was not specifically mentioned as one of the registers. Still, Regional Committee for Research Ethics considered this database to be similar to other listed registries and allowed linkage without a new consent since the results could benefit the population with CP. The study was exempt from consent for controls because data on age, sex, place of living and ICPC-2 code only, would not violate the privacy. Further, for each case we would need at least five controls, and asking for consent among controls could have caused a selection bias. For data on individuals living in a community with less than 1,000 inhabitants, information on place of living was removed by a KUHR official.

5 RESULTS

Study population, responders and non-responders in Papers I-III

This population based study assessed participants in childhood and adolescence. There were no changes in variables predominant movement disorder and GMFCS level between childhood and adolescence, which allowed for longitudinal comparison. In childhood, there were no significant differences in distribution for sex and GMFCS between responders and non-responders (46). In adolescence, there were no significant differences between responders and non-responders with regard to sex, predominant movement disorder and GMFCS (Table 2).

Table 2. Comparison between responders and non-responders in adolescence (12-17 years)

		Responders	Non-responders	Responders	Non-responders
		Papers I-II		Paper III	
N (%)	136 (100)	67 (49)	69 (51)	64 (47)	72 (53)
Sex					
Boys	83 (61)	39 (58)	44 (64)	38 (59)	45 (63)
Girls	53 (39)	28 (42)	25 (36)	26 (41)	27 (38)
p-value		0.506		0.709	
Predominant movement disorder (CP type)					
Spastic	101 (74)	53 (79)	48 (70)	50 (78)	51 (71)
Dyskinetic	32 (24)	14 (21)	18 (26)	14 (22)	18 (25)
Ataxic	3 (2)	0 (0)	3 (4)	0 (0)	3 (4)
p-value		0.167*		0.318*	
Gross Motor Function Classification system (GMFCS)					
Level III	32 (24)	15 (22)	17 (25)	13 (20)	19 (26)
Level IV	34 (25)	17 (25)	17 (25)	16 (25)	18 (25)
Level V	70 (51)	35 (52)	35 (51)	35 (55)	35 (49)
p-value		0.953		0.679	
Statistics: Pearson chi square. *Fisher exact test.					

In adolescence, among non-responders there were four participants who died. Due to lack of consent, we do not have information on deaths among non-responders in first data collection.

Proxy-reports on pain for 67 children/adolescents in GMFCS levels III-V were collected twice, in childhood and adolescence. Median age in adolescence was 14 years, 4 months. The median time between the two data collections was 5 years, 2 months (range 3:8 to 5:11 years:months).

Paper I Recurrent pain in adolescents with cerebral palsy: a longitudinal population-based study

In adolescence, pain prevalence was 93 % and mean CHQ pain score was 40. The most frequent pain sites were the hip/thigh in participants in GMFCS level V, hip/thigh and lower leg/foot in GMFCS level IV and knee in GMFCS III. The prevalence of abdominal pain was highest in GMFCS level V. Longitudinal comparison in 67 participants, showed increase in pain prevalence of recurrent pain (45 to 62), mean number of pain sites (1 to 3), pain intensity, frequency and pain interference with activities of daily living, while pain interference with sleep was unchanged. Pain severity increased (mean CHQ pain score decreased from 60 to 40), pain severity increasing in all GMFCS levels from childhood to adolescence. Presence of moderate (CHQ pain score 40-60) or severe pain (CHQ pain score 0-30), or marked increase in pain severity (40 points or more) between childhood and adolescence did not necessarily result in use of first-line analgesics. Ten of 15 participants receiving ITB received first-line analgesics. Their mean pain score was 30 (range 10-100) and categorized as severe pain.

Paper II Hip pain in adolescents with cerebral palsy: a population-based longitudinal study

In adolescence, 28 of 67 participants had hip pain, in 44 hips. Their mean CHQ hip pain score was 40 (SD 21.4). Number of participants with hip pain increased from 18 (in childhood) to 28 (in adolescence). Number of painful hips increased from 22 to 44. The mean migration percentage of the most displaced hip was unchanged from childhood to adolescence. In adolescence, independent risk factors for hip pain and hip pain interference with sleep were severe hip subluxation (migration percentage 50-89%) and GMFCS level V. Severe hip subluxation was the only independent risk factor for interference with activities of daily living.

Paper III Health-related quality of life in adolescents with cerebral palsy: a cross-sectional and longitudinal population-based study

Proxy-reports on HRQoL for 64 adolescents, in GMFCS levels III-V, and who followed a CP surveillance program, were collected at mean age 14 years and 6 months (range 12-17 years). Fifty-eight of 64 participants had proxy-reports collected in childhood (age 7-12 years), thus comprising a longitudinal sample in adolescence. Mean CPCHILD domain scores varied from 43 (*Personal Care*) to 76 (*Comfort and Emotions*). Participants in GMFCS level V had slightly

better scores (7-8 points higher) than the scores given in the CPCHILD manual (68). There were no significant differences in domain scores whether or not the participants in GMFCS level V had ITB treatment. There were no significant changes in the HRQoL mean domain scores between childhood and adolescence, except for domain *General Health* which worsened from 70 to 65, due to increase in number of medications. In adolescence, severe motor impairment was associated with low scores in domains *Activities of Daily Living and Personal Care*, *Positioning, Transfer and Mobility*, *Comfort and Emotions* and *General Health* but not in domain *Overall Quality of Life*. Severe pain was associated with low scores in all domains except *Activities of Daily Living and Personal Care.* In all domains, a low domain score in childhood was associated with a low score in the corresponding domain in adolescence.

Paper IV Frequency of general practitioner consultations and pain as a reason for encounter in children with cerebral palsy

Daytime contacts with GP were analyzed in children born 1996-2012 in period 2006-2018. Comparison was performed between children with CP registered in NorCP (cases) and those not registered in NorCP (controls), and for the three age groups: 0-5, 6-11 and 12-17 years. There were 23,616,791 daytime contacts, 108,413 (0.46%) in cases, and 23,508,378 (99.54%) in controls. The cases accounted for 0.27% of all 16,057,216 consultations. This corresponds with national prevalence of CP of 2.5 per 1000 (95% CI 2.4-2.7) (74). Thus, frequency of daytime consultations is not affected by the CP diagnosis. Pain was more often registered in consultations with controls than in consultations with cases in all three age groups. Thus, the frequency of daytime consultations related to pain is affected by a diagnosis of CP. Musculoskeletal pain was more often registered in consultations with controls than in consultations with cases in age groups 6-11 and 12-17 years, while there was no difference in age group 0-5 years. Thus, the frequency of daytime consultations related to musculoskeletal pain is affected by a diagnosis of CP in older children.

Summary of main results in Papers I-IV is available in Table 3.

Table 3. Summary of main results, Papers I-IV		
Variable	Result	Reference to paper in this thesis
Longitudinal comparison in same population 5 years apart, childhood (7-12 years) and adolescence (12-17 years)		
Pain prevalence Neck pain Back pain Pain in upper limbs Hip/thigh pain Knee pain Abdominal pain	Increased (below if increase significant) Increased Unchanged Unchanged Unchanged Increased Unchanged	Paper I
Number of pain sites	Increased	Paper I
Pain interference with daily activities sleep	 Increased Unchanged	Paper I
Pain characteristics Intensity Frequency Severity (CHQ pain score)	 Increased Increased Increased	Paper I
Prevalence of hip pain	Increased	Paper II
Factors associated with hip pain	Severe motor impairment Migration percentage 50-89%	Paper II
Mean Migration percentage in worst hip	Unchanged	Paper II
HRQoL domains in CPCHILD 1 Personal care 2 Positioning 3 Comfort and Emotions 5 General Health 6 Overall Quality of Life	 Unchanged Unchanged Unchanged Decreased (due to increased number of medication) Unchanged	Paper III
Factors associated with low HRQoL domains scores in adolescence	Severe motor impairment More severe pain Low scores in corresponding domain in childhood	Paper III
Comparison between the children with CP (cases) and the children in general population (controls)		
Frequency of GP consultations	No difference between cases and controls	Paper IV
Pain as a RFE in GP consultations	Cases had lower risk than controls	Paper IV
Musculoskeletal pain as a RFE in GP consultations	Cases had lower risk than controls except for in age group 0-5 years, in which there was no difference	Paper IV

6 GENERAL DISCUSSION

I will now address ethical and methodological considerations, followed by a discussion on the results in each of the four publications. I will also discuss how our findings may fit in existing classifications and theoretical frameworks, especially with an aim to facilitate development of recommendations for pain grading, assessment, and management within a CP surveillance program. Finally, I will address implications for clinical work, surveillance protocols and national guidelines, and touch upon plans for future research.

6.1 Ethical considerations

The project followed the principles for medical research involving human subjects defined in the Helsinki Declaration (HD) (75). I will address the following ethical aspects defined by Emanuel (76) and referring to the HD principle(s) when appropriate: *Collaborative partnership, Social value, Scientific validity, Fair participant selection, Benefit/Risk Ratio, Independent review, Informed consent*, *Respect for participants and Vulnerable population in research*.

Collaborative partnership: The involvement of representatives from the research population and from patient organizations has become the golden standard in medical research because it secures focus on the aspects of health that are most important for the particular patient population. This project was fully supported by the Cerebral Palsy Association of Norway. Study findings have been disseminated in fora of the CP association during the last three years.

Social value: A study on paediatric CP from the USA revealed that parents, patients and medical professionals consider pain to be the top priority domain treatment outcomes (77). Pain in children with CP is therefore a research topic with acknowledged social value.

Scientific validity: Principle 21 in HD states that "Medical research involving human subjects must conform to generally accepted scientific principles, be based on thorough knowledge of the scientific literature, other relevant sources of information". All choices made with regard to the method are addressed in the section Methodological considerations, and this research conforms to scientific principles applying all relevant sources of information including the scientific literature and official websites available in English and Scandinavian languages.

Fair participant selection: The registration in NorCP is based on a generally accepted scientific principle of inviting everyone with the relevant medical characteristic. All eligible participants were invited to participate in 2013-2014 (Papers I-III). Paper IV included information on the paediatric population of Norway that contacted regular GPs in "Fastlegeordningen".

Benefit/Risk Ratio: Principle 17 in HD states that "All medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or groups affected by the condition under investigation. Measures to minimize the risks must be implemented." On benefits, research on vulnerable groups and their use of health services can contribute to improve the care not only for the group but for the general population as well (Paper IV). On risks, the radiation caused by radiographs in the surveillance program has been weighed against the benefits of the surveillance. We used radiographs taken through a hip surveillance program (Paper II). Questionnaires on pain and HRQoL (Papers I-III) include many items on highly sensitive issues that might have caused emotional pain in the caregivers. The fact that we ask about pain without offering any cure for the pain creates a possibility that some parents may get false expectations about the effects of the project for their child. However, all participants had clinical follow-up in their respective habilitation units. None of the participating children got better merely by participating in the study on pain, since the study was observational and did not involve intervention. One could argue that inquiries about pain could initiate reflection on pain and initiate seeking advice and managing pain, thus becoming a benefit of participation in the study. The research entailed no risk to participants, and minimal burden, such as time and reflection on health, for the primary caregivers.

Independent review: Principle 23 in HD states that "The research protocol must be submitted for consideration, comment, guidance and approval to the concerned research ethics committee before the study begins." The studies have been approved by the Regional Committee for Research Ethics, and relevant ethical considerations, including relevant protocols, were provided before the start of the studies.

Informed consent: Principle 28 in HD states that "For a potential research subject who is incapable of giving informed consent, the physician must seek informed consent from the legally authorized representative." Invitation to participate was sent to primary caregivers of children in the age group 7-12, and consent was obtained from the legally authorized representative (Papers I-III). Due to low age, the consent was collected from guardians only. Linkage study (Paper IV) was exempt from the consent requirement, because the consent for NorCP (58) allowed linkage to other national registries.

Respect for participants: Principle 24 in HD states that "Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information." We followed national standards for data storage, which secured privacy and confidentiality.

Vulnerable population in research: Principle 20 "Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research." We believe that this research was responsive to the health needs and priorities of this group. The studies intended to promote the health of the paediatric population with CP and could not be performed with other participants. Principle 13 in HD "Groups that are underrepresented in medical research should be provided appropriate access to participate in research." This principle was the corner stone of this project since we focused also on a population with severe CP.

6.2 Methodological considerations

The ultimate goal of all research is to extend the knowledge base in the field studied using a valid, precise and reliable method. Below are considerations with regard to the choices made on study design, costs, internal validity, bias, random errors, associations, external validity, and choice of variables.

6.2.1 Study design

Papers I-III are prospective observational population-based studies with both cross-sectional (adolescence) and longitudinal design (comparison childhood and adolescence). Papers I-III had a descriptive and analytic approach. We wanted to explore associations between parameters in a

cohort of non-walking children with CP without doing interventions besides standard treatment ensured through the surveillance program. Thus, an observational study with longitudinal design was considered appropriate. Paper IV is a retrospective linkage study of two registries. The major strength of these two studies is that both studies are population-based. Paper IV had a descriptive and analytic approach. We wanted to compare the daytime contact with a GP between a cohort included in a CP surveillance program, and children in the general population. Thus, a linkage of two national databases was considered appropriate.

6.2.2 Internal validity and reliability

The accuracy of results is determined by the degree of systematic variation from the true value (validity) and the degree of absence of random variation (precision). The term internal validity encompasses how accurately a study describes what it aims to measure.

Validity refers to the extent to which a tool is measuring what it is designed to measure. *Content validity* is usually evaluated by the judgement of several experts (real life experts and professionals) within the field of interest. *Construct validity* refers to the consistency of the concepts that are being measured. *Predictive validity* refers to the correlation between the measure and a clinically relevant criterion standard in future. *Discriminant validity* demonstrates the predicted behavior in differentiating groups of individuals with high and low scores in known groups. *Reliability* estimates the extent to which the scores produced are free from random errors and are stable and accurate, i.e. consistent. There are three important types of consistency: over-time (test-retest reliability), across items (internal consistency), and across different researchers (inter-rater reliability). The risk for random errors decreases with an increasing sample size.

In Papers I-III, we collected data using proxy-reports. If we had chosen to collect data using self-reports (15), we would probably have encountered difficulties in interpreting results in relation both to the true value and the precision (78), due to high percentage of participants with communication and cognition impairment in our research population. Since our focus was on possible change over the period of five years, we strived to collect proxy-reports from the same caregiver, thus satisfying the internal validity in longitudinal design. However, in a few adolescents who lived in care homes, we could not ensure the same respondent since their primary contact can change over a period of five years. We have not tested over-time reliability in this thesis, but we chose instruments with high reliability in studies on their psychometric

measures (CPCHILD and CHQ). There were significant correlations between all the HRQoL domains (data unpublished) confirming satisfying internal consistency. There was also significant correlation between pain variables (Paper I). In longitudinal studies, which may involve several data collectors, one has to pay attention to random sampling variation and broad distribution due to individual variation and measurement errors, which could decrease the precision. The collection of data (including interviews) involved two researchers (Papers I-III), each researcher performing one data collection alone. The preparation of the research material was conducted together with the researcher who was responsible for the inclusion of participants and the first data collection in childhood in order to avoid systematic differences in the two data collections and further compromise the reliability of longitudinal comparison. The researchers defined the following instructions on the sampling procedure: a) The questionnaires on pain and HRQoL were sent by surface-mail and were followed by a structured interview on telephone, to confirm the responses, and provide new information on hip pain; b) The content of the interview procedure on pain and hip pain performed in childhood was followed in adolescence; c) The order of data collection sequences made it possible to ensure that the prevalence of pain and hip pain were not compromised by the order in data collection. We agreed that each interview would consist of asking predefined questions only. We asked for date of birth of all primary caregivers, thus ensuring a confirmation of identity for primary caregivers. Further, one third of the primary caregivers chose to give all answers during the interview only. Still, the aforementioned procedure was followed. Also, the measurements on all radiographs of pelvis were performed by the same researcher at both data collections (Paper II). The sample size in Papers I-III was limited due to the longitudinal design.

In Paper IV, data registered by a GP and sent to KUHR was motivated by a reimbursement of health expenses, which requires one single ICPC-2 code to be generated. A Norwegian study on correctness of ICPC-2 codes (63) found the coding of RFE satisfactory in consultations, which supported our choice to perform analysis on RFE in consultation only. The sample size was large, which decreased random errors and increased reliability.

6.2.3 Bias

There are several threats to internal validity in both studies, and bias is discussed here. Bias is a result of trends in the process of selection of participants or data collection that can lead to conclusions that are systematically different from the true ones.

Selection bias may occur if participants are not randomly selected from the target population of interest. This can make the study sample less representative and a generalization of results to the target population may not be valid.

In Papers I-III, the comparison of non-responders and participants (46) showed that there were no significant differences in age, sex, and ambulation according to GMFCS. Due to the content of the consent, only parameters available in NorCP were analyzed. Since information on socio-economic measures in non-responders was unavailable, a selection bias might have occurred. We collected proxy-reports only, because we expected that many participants in GMFCS level V would also be in CFCS levels IV and V, and therefore not be able to self-report. To include only children able to self-report might also have resulted in a selection bias. Boys were overrepresented in our population (58 % in Papers I-II and 59 % in Paper III, Table 2), which is in line with the previous Norwegian study on prevalence of CP in the paediatric population (26).

Paper IV included all contacts with a GP who received governmental reimbursement. The study did not include contacts with fully private medical centers. Due to the tax-funded health care in Norway, we assume that the number of contacts with such centers is very small and that restriction to contacts registered in KUHR does not cause a selection bias.

Information bias, also called observation or measurement bias refers to systematic errors between groups that arise during data collection, recording and handling of data as well as due to missing data.

The precision of responses for each pain site, marked on a body map (Papers I and II), was ensured through additional questions during an interview with open response. We asked only primary caregivers to respond on CHQ questions on pain (Papers I-III), and did not strive to collect information from others who might have observed the child during school hours. Further, in longitudinal design, in order to avoid systematic errors and information bias, the respondent should be the same person in all data collections. This was satisfied in Papers I-III.

In Paper IV, information bias should be considered. The informants were GPs who had a reimbursement agreement for health expenses. One single code generates reimbursement. A recent study confirmed that Norwegian GPs strive to use ICPC-2 codes correctly (63). Still, patients with chronic conditions might encounter a GP with more than one RFE, and even though the software registration system allows several ICPC-2 codes to be registered, GPs might have omitted relevant RFE due to their busy practice.

Collection of data on events in the past can cause *a recall bias*. In Papers I-III, the CHQ questions on pain referred to the last four weeks prior to the data collections. A shorter recall time might ensure more precise responses, but the period of four weeks allowed for the use of the adjective "recurrent" on pain, which was the main focus of the study. The use of proxy-reports, instead of self-reports, probably reduced recall bias because children with severe CP might have a disturbed understanding of the time frame and also the grading of pain. Several studies on pain support the use of proxy-reports in children with severe developmental disabilities because children often have limited abilities in communicating their pain precisely in time (78-80). When Benini et al. (80) asked children with developmental disability to self-report on the location and intensity of pain following immunization, only half of them were able to give self-reports that were fitting despite an hour of instruction on how to use the self-report tools.

In Paper IV, recall bias may be less relevant since GPs strive to register RFE at the end of each consultation or the same working day. We cannot exclude the possibility that some GPs register later than this.

Reporting bias occurs when some outcomes are not selected for publication. This can be addressed either by openness or pre-registration of chosen outcomes. Outcomes that did not change during the observation period might be considered as "not interesting". However, we included results on all variables (Papers I-III) that we collected. Paper IV is the first in a series of several planned publications.

The *Hawthorne effect* refers to a change in behavior or performance due to an awareness of being observed. The first interview with primary caregivers might have initiated additional contacts with health care providers to assess and manage pain prior to the second data collection (Papers I-III). Such action would not violate the study results since the study aim was to quantify pain in children with CP at two time points regardless of interventions given. Further, GPs were

not aware that a linkage study (Paper IV) would be performed, and such information would hardly influence GPs' coding.

6.2.4 Associations vs. causal relationship

The scope of this thesis was not to investigate causal relationships since this research does not address exposure and outcome which can be best addressed in randomized control trials.

Papers I-III had observational design, and causality cannot be determined in studies with such a design. The scope of Papers I-III was to investigate factors that could be associated with pain, hip pain and low HRQoL domain scores. We investigated possible associations between dependent variables (pain, hip pain and HRQoL) and relevant independent variables (sex, age, predominant movement disorder, GMFCS level) addressed in earlier research (46, 50, 81). In paper III, we also investigated possible associations between HRQoL domain scores and pain severity in adolescence, similarly to a study in adults (82), and between HRQoL domain scores in adolescence corresponding domain scores in childhood (50). In Paper II, the association between migration percentage in the most displaced hip and both hip pain and CHQ hip pain score as dependent variables was investigated, similarly to previous studies on hip pain (45, 46). Paper IV does not address causality.

6.2.5 External validity

External validity concerns generalizability, i.e., the ability to apply a conclusion from a source population to the more general target population (83). All conclusions depend on the design, population, and statistical model used in a study.

The study population in Papers I-III consisted of children with different ethnic origins living in South-Eastern Norway, diagnosed with CP following international standards on diagnosing CP through NorCP (58). This increases the external validity of the study. Further, comparisons on distribution of sex, predominant movement disorder and level of motor impairment between responders and non-responders were performed twice, not showing differences between the groups (Table 2). However, information on socio-economic background and place of living (urban vs. rural) was lacking and therefore not included in the comparison. External validity of a longitudinal study depends also on the number of participants lost to follow-up. In Papers I-III, this number was low, which increases the generalizability. Our study population was limited to

participants in GMFCS levels III-V, which implies that our conclusions can be applied only to similar populations with CP.

Paper IV includes contacts with GPs who received governmental reimbursement. The Norwegian welfare system (tax-funded medical services) differs from countries that base their medical services on medical insurance. Our findings are comparable to other countries with a strong welfare system.

6.2.6 Choice of variables

The study was planned as both cross-sectional and longitudinal from the start in 2012 (Papers I-III). The longitudinal design required use of the same questionnaires on pain and HRQoL, validated for a population with severe CP and age groups 7-12 and 12-17 years. Also, the chosen instruments had to be available in the Norwegian language.

Pain severity can be graded using VAS and NRS. Still, information on the frequency and temporality of pain, and on pain interference, adds to the overall understanding of pain. There were also several measures for the grading of pain severity such as the pain module in the CHQ (18) and Health Utilities Index 3 (HUI-3) (19). Several studies have applied HUI3 pain score as a pain variable, thus assessing the presence and severity of pain in relation to limitations of normal daily activities (84, 85). However, normal daily activities would differ greatly due to the variety of motor disability in our target population with CP, ranging in GMFCS from level III (able to move on their own with walking aid) to level V (bound to wheel chair). We believed that the grading of pain severity should be independent from daily activities because the reference frames for daily activities would differ greatly (Papers I-III). Questions on pain from CHQ were used in previous research in children with CP (46, 50, 81), and recently in treatment evaluation in the children with juvenile idiopathic arthritis (67).

There were several both generic and condition-specific measures for QoL and HRQoL described in the international knowledge base (70): the CHQ, PedsQL, and KIDSCREEN as generic instruments for QoL, and CP QoL-Child, the CPCHILD, the PedsQL-CP, and DISABKIDS as condition-specific instruments. Since the aim was to collect reports on HRQoL in a target population with more severe forms of CP, a condition-specific instrument with the items adapted for the target population using proxy-reports was preferred. The PedsQL-CP uses two versions for the chosen age groups (7-12 years and 12-17 years). The Norwegian version of

DISABKIDS was not validated for CP. The measure CPQoL still awaits validation in Norway. Thus, the chosen instrument was the CPCHILD (68, 69). In a study on content comparison of HRQoL measures for CP based on the ICF, the CPCHILD showed a unique pattern by covering a variety of activity and participation categories from the chapters on communication, mobility, self-care, major life areas and community, social and civil life (86).

In the study on HRQoL (Paper III), we should have included CPCHILD's domain *Communication and Social interaction.* The items in this domain were regarded as less relevant in the preparatory phase of the first data collection (55), but the authors reconsidered its importance after comparing results to a study by Jung (87). In adolescence, information on the domain *Communication* would ensure results on a complete HRQoL measure.

With regard to time frames, we used the CHQ question to assess pain in the last four weeks (18) (Papers I-III) and CPCHILD to assess HRQoL in the last two weeks (68) (Paper III). We believe that this difference in time did not have significant influence on results. Further, we did not ask for the duration of pain episodes. Such information could have contributed to the understanding of choices made with regard to pain management (Papers I-II).

6.2.7 Statistical considerations

In Papers I-III, the number of available participants was fixed, and we could not increase it due to the study design. The sample size was relatively small as it varied from 64 to 67. A type II error is more likely to occur when the sample size is too small, the true difference (or effect) is small and when variability is large. A small sample size could be a reason for not being able to confirm an association between hip pain and presence of femoral deformity or presence of a femoral plate. A small sample size was a reason to be cautious when interpreting our results. The small sample size might explain the high standard deviation (SD) for several variables. In Paper I, the number of factors used in the association analysis was limited by the size of the population. Further, we chose pain severity in adolescence and not change in pain severity because we did not want to complicate the statistical analysis. However, we could have focused on the correlation between the change in pain severity and the change in HRQoL domain scores, but this would also require a more intricate statistical analysis. In Paper I, we provided a table on the frequency of the response alternatives for pain intensity and frequency, but in Paper II the similar variables for hip pain were described with mean (SD). Since these variables are ordinal we

should have used the frequency table as we did in Paper I. In Paper III, data on HRQoL was missing only in a few participants, and mostly on two questions concerning emotional health. However, the total number of participants did not enable us to pursue this finding further.

In the preparatory phase of our linkage study (Paper IV), we considered using five controls per each case after an a priori sample size calculation, but abandoned the procedure because the process of picking controls would be costly and time-consuming. We included therefore all children who were in contact with a GP in the period 2006-2018, and treated "cases" and "controls" as groups. Thus, we did not provide the exact numbers of individuals considered as "cases" and "controls". The majority of our results were presented as risk ratios between cases and controls using a calculator for cohort studies. Due to the limitation in the software (maximum N=10,000,000), we chose to present risk ratios for the three age groups, 0-5, 6-11 and 12-17 years.

6.3 Results

Longitudinal population-based studies on pain and HRQoL in children with CP remained scarce, while studies on their contact with a GP remained absent. Thus, the comparison of our findings to other studies was challenging both due to the lack of such studies but also due to differences in study design in the few existing studies.

Pain

Several studies claim that pain in a paediatric population with CP is increasing with age because pain prevalence was higher in older age groups (31, 33). Beside pain prevalence, changes in pain can be measured comparing the number of pain sites, pain frequency, pain intensity, pain severity and pain interference with activities of daily living and sleep. However, we found no longitudinal studies on pain in children with CP in GMFCS levels III-V, with standardized observation time to support the claim that pain increases. In our study of 67 young people with CP, the number of participants with pain increased from 45 to 62 from late childhood (7-12 years) to adolescence (12-17 years) (Paper I). Paper I is the first to show that pain prevalence increased from childhood to adolescence, and during a time interval of five years. The observation time of five years was in accordance with SPARCLE studies (31, 48). The inclusion

of participants from age 7 to 12 years only at the first data collection, and age 12 to 17 years at the second data collection, ensured comparison of pain status at two developmental time points, “childhood” and “adolescence”. Christensen et al. (84) addresses change in pain status. However, the observation time was not standardized, and one could question whether the study design was truly observational. The latter might be explained by the inclusion of pain assessment by a physician in their study design. In cases of pain, the physician would be obliged to provide treatment for pain which in turn interferes with an observational study design.

The number of pain sites also increased, showing that in CP management, attention needs to be on several body parts simultaneously. Even though our study had a relatively small sample size we could confirm an increase in the prevalence of knee pain and neck pain in GMFCS level III and level V, respectively. These findings are reminders that adjustment of walking aid and wheel chair and also the focus on day and night positioning might be of importance in pain prophylaxis.

Twenty-eight of 54 adolescents with CHQ pain score of 60 and below, defined by us as moderate and severe pain, did not receive analgesics. We have not asked about the dosage or effect of analgesics in the 26 who received analgesics. Further, we did not ask about the time of last contact with primary- or specialist health care, or if the treatment with analgesics was initiated by caregivers or prescribed or evaluated by a physician. The study design did not allow us to draw conclusions on the rationale behind treatment with analgesics, effects of such treatment, or choices made in relation to any other treatment applied by primary caregivers.

We also found that pain was present in a subgroup of participants receiving ITB. Children receiving ITB are sometimes excluded from studies on pain (45). However, ITB is directed against spasticity and dystonia, which often cause pain, but ITB does not relieve all pain. Thus, patients receiving ITB should not be excluded from pain studies.

Hip pain

Paper II is the first to report on an increase in the prevalence of hip pain over a period of five years and to report on the severity of hip pain and the interference of hip pain with activities of daily living and sleep in adolescents with CP in GMFCS III-V who followed a CP surveillance program.

The mean migration percentage (MP) in the most displaced hip had not changed over the period of five years. One explanation for this finding could be the early focus on hip surgery in

our population prior to the first data collection and hip surgery between the data collections. In the group who had hip surgery we found that hip pain occurred in cases of unsuccessful hip surgery. The presence of surgical implants showed that this could be a potential risk factor for hip pain. However, in a multivariable analysis the presence of surgical implants was not retained as an independent factor. One reason for this could be the small size of the population. Still, our findings supported our recommendation to consider presence of surgical implants as a possible cause of hip pain.

The finding of severe hip subluxation (hip MP 50-89 %) to be an independent risk factor for severe hip pain suggests that more research on early prognostic signs for hip subluxation could be warranted. Our study did not include a physical assessment or a search for other potential factors such as osteoarthritis, osteoporosis, bursitis or similar conditions, thus we cannot discuss causality. The finding of severe hip subluxation to be an independent risk factor for high interference with activities of daily living adds to the knowledge base giving prevention of hip dislocation high priority in CP surveillance. Further, we are the first to show that the majority of the hips with total dislocation (MP ≥ 90 %) were painless. Still, we have to assume that those with a total hip dislocation had hip pain while the hips were migrating.

We found that hip pain also was present in the population who received ITB. The latter is an important finding because ITB was an exclusion criteria in a previous study on hip pain (45).

HRQoL

We are the first to apply CPCHILD longitudinally in a cohort of children who were under a CP surveillance program (Paper III). Our participants received treatment as usual and continued to take part in the CP surveillance program between the two data collections. They had a high percentage of hip surgery prior to the first data collection, probably because avoidance of hip dislocation has been defined as a main focus of CP surveillance. However, hip surgery and spine surgery and ITB status prior to the first data collection was not included in the comparison with non-responders, and we do not know if our participants received more treatment than non-responders. In more detail on the 58 participants from the longitudinal sample, 38 (66%) had hip surgery prior to the first data collection, and nine underwent corrective hip surgery between the data collections, six of them for the first time. In addition, six participants had scoliosis surgery

between the two data collections, and four got started on ITB. Previous intervention studies on hip surgery (53, 88), spine surgery (88, 89), and ITB (54), confirmed the positive long term effect on HRQoL after 5 years, the largest improvement after ITB (54). We have not investigated the impact of interventions on HRQoL domains because the study design did not allow this.

Our study confirmed the discriminative validity of CPCHILD, since lower HRQoL domain scores were present in participants with increasing level of impairment. Our population in GMFCS level V had somewhat (7-8 points) higher domain scores in *Personal Care*, *Positioning* and *Overall Quality of Life*, than the population in GMFCS level V in the CPCHILD manual (68), and the Scandinavian validation study (71). One explanation could be that our participants were all adolescents, thus their scores could be more homogeneous, but also a result of longer follow-up in a CP surveillance program aimed to enhance HRQoL. We encountered difficulties when comparing our findings to those of previous studies using CPCHILD because of differences in study design (observational vs. interventional) (54, 88, 89), sampling procedures (population-based vs. at convenience) (90), and inclusion criteria for age (narrow vs. broad age range) (54, 71, 90). Our findings for GMFCS levels IV and V are similar to pre-surgery values in the studies by DiFazio et al. (53) and Miyanji et al. (89). Despite the small sample size in these studies, the effect of interventions such as hip-surgery and ITB on several HRQoL domains was confirmed. The majority of our participants had hip surgery at an early age (and prior to the first data collection). Since our findings suggest that their domain scores were unchanged over the last five years, the routines of offering hip surgery early could mean that these children might have long lasting benefits on HRQoL. The age range in our study's adolescent population was narrow, and generalizability of our findings to adolescence only, seems appropriate.

In the longitudinal analyses of five CPCHILD domains, the domain scores did not change significantly in four of five domains. The mean domain score in *General health* decreased for 58 participants. The only explanation was an increase in the number of medications between the two data collections. This means that many of our participants received more medication for their accompanying medical conditions in adolescence. Our finding of pain increase over the period of five years was not possible to trace in the domain *Comfort and Emotions* consisting of several questions on pain, and two on emotions. One explanation could be the construct of the CHQ pain score and the domain *Comfort and Emotions* in CPCHILD. In order to capture a change in the domain *Comfort and Emotions*, several of its items had to change simultaneously and in the same

direction. This is a reminder to always consider the properties of available questionnaires when deciding on which variables to include in the study design.

The finding of mainly no change in the HRQoL domain scores over the period of five years could be good news, because beside an increase in the scores, a status quo can also be considered as a desired result. The fact that four participants died between the data collections is a reminder of how vulnerable our population was and that those with severe forms of CP have a reduced life expectancy. In other words, follow-up through a surveillance program with a high focus on the need for corrective surgery, such as hip and spine surgery and ITB, could have resulted in a secondary prophylaxis resulting in unchanged HRQoL domain scores instead of a decline.

Our finding confirmed that in adolescence, a high level of motor impairment was associated with low scores in domains *Personal Care*, *Positioning, Transfer and Mobility*, *Comfort and Emotions* and *General Health*, but not *Overall Quality of Life*. The latter finding could be explained by the construct of this domain consisting of one item with no reference to disability or function. Further, low scores in several HRQoL domains were associated with severe pain, confirming the results of previous studies on children (81, 85) and adults (82). This finding confirms the importance of a continuous focus on pain in a population with CP regardless of age.

Healthcare seeking in primary care

Our findings in Paper IV are dependent on the organization of health care in Norway. Primary health-care in Norway is strong since GPs have extended authority in follow up of chronic conditions compared to other health care systems. In addition, governmental reimbursement agreements with GPs ensure a high coverage of expenses GPs have, and thus ensure that all citizens have access to care. These factors might influence the generalizability of our findings to other countries with a different organization of health care and different funding models for medical services. Still, Norwegian GPs use internationally recognized ICPC-2 codes, and a comparison to other countries using this coding system is therefore possible.

The frequency of consultations did not differ between case and control groups. This could be considered as good news since it could confirm that their needs are similar. Still, we found a higher percentage of administrative contacts in population with CP which could mean that the need for GPs' involvement is higher in the population with CP.

We found a high percentage of the ICPC-2 code N99 (17%) as the only RFE in consultations in children with CP. This disease code does not give information on which health issue was addressed in the consultation and suggests that the use of ICPC-2 codes in populations with a chronic health condition may differ compared to the use in the general population.

Children with CP met a GP more seldom for pain as a RFE than controls. However, there were no differences in pain as a RFE in the youngest age group, and differences were present in older children only. The existence of habilitation units in the specialist health care may have caused less contact with a GP for pain despite the fact that Norwegian GPs are more available, both in time and distance, than physicians in the habilitation units. Still, children with CP might have more frequent contact with other professionals in the primary health care such as physical and occupational therapists than with a GP. If we assume that children with CP truly have a lower risk for consultation with pain as a RFE, we could conclude that their needs are met elsewhere.

Also, pain severity might influence if older children and youth with CP contact a GP or not (91). One reason could be that questions on pain are saved for the next consultation in the specialist health care where they usually receive follow-up for CP. Still, postponing contact on pain causes more long-lasting pain.

6.4 Classifications and theoretical frameworks

In order to make the bio-psycho-social model work in CP, applying standardized measures on pain and HRQoL could be of high importance because such instruments address all aspects of life, ensuring more complete information and a better chance to prevent and treat pain in CP. Pain has a negative effect on mental health and social life (92), thus addressing and treating pain early might ensure better HRQoL throughout life.

When ICF-CY is applied to pain in a child with CP, the whole body might be in focus in "Body-structure/Body-Function". Research shows that pain influences negatively on "Activities of daily living" and "Participation" (51, 52). If untreated, pain could not only reduce participation, but also influence negatively on the quality, and the personal experience, of participation. A child with disability is dependent on "Environmental factors", such as the health system and family, to recognize the pain, seek help, receive treatment and evaluate the effect of the given treatment. Recurrent pain may influence negatively on several aspects of bio-psycho-

social development, and could also influence on "Personal factors", such as coping style and personality. Lack of pain management in the early age might inhibit development of the child's personal frame of reference, and decrease the chance for learning coping skills necessary to develop autonomy. Another consequence could concern the development of personality, defined as "Personal factor" in ICF. One could assume that lack of pain management could cause more serious emotional problems later in life. The ICF-CY takes into consideration that a young, developing person gradually takes independent actions on her/his health issues. Thus, "Environmental factors" such as caregivers' attitudes on pain could be one of the targets for intervention. Awareness on pain recognition can be increased if communication on pain becomes standardized. This requires standardized pain assessment. In Papers I-III, we addressed several aspects of ICF, applying standardized instruments (Table 4).

Table 4. Variables addressed in Papers (I-III) in relation to ICF for Health condition pain

Body Function	Body Structure	Activity	Participation	Environmental Factors	Personal Factors
Communication (CFCS) (I, III)	Recurrent pain* (I, III)	Pain interference with DA/sleep* (I, II)	Ambulation (GMFCS) (I-III)	Parental relation (I)	Age, sex (I-III)
	Recurrent hip pain* (II)			HRQoL* (III)	Hip surgery (II)
	Pain localization * (I)				

Note: Roman I, II and III refer to Papers I-III. DA, daily activities. * - proxy-reported

If the findings of papers I-III are to be addressed using ICHI, pain sites are *Targets*, the given treatments are *Actions*, and the process and methods for pain treatment are *Means*, Table 5. Thus, for different *Targets,* parental administration, as *Means,* seems to be of high importance if *Actions* on pain are to be effectuated. Further, if ICHI is to function, appropriate measures to define a *Target* must be applied. A thorough assessment of targets is one of the aims of CP

surveillance programs. For example, hip surveillance includes annual radiographs of hip/pelvis, but additional question on hip pain could improve *Actions* in CP surveillance (Paper II).

Table 5. Findings of this thesis applied in WHO-FIC (ICD-11, ICF and ICHI)

ICD-11	ICF	ICHI Target	ICHI Action	ICHI Means
Pain	Hip pain	Hip pain	Consider hip surgery if Hip MP ≥ 40%	Hip surgery
			Analgesics	Parental administration
	General pain	Multiple sites	Analgesics	Parental administration
	Abdominal pain	GO reflux Constipation	Reflux medication Laxantia	Parental administration
	Dystonia Spasticity	Multiple sites	Medication ITB	Parental administration ITB

In Paper I, we suggested an algorithm on pain (93) in clinical follow-up through surveillance protocols (Fig. 6). This algorithm could be useful when defining *Targets* for interventions in ICHI. The algorithm consists of three steps: 1) pain grading, 2) pain management, and 3) pain follow-up. Step 1, pain grading, is necessary if pain needing specific *Action* is to be recognized. Step 2, pain management, requires an *Action* by a physician if pain is moderate and severe, while step 3, pain follow-up, places a responsibility on the professional care-provider to see that *Action* has desired effect. This algorithm includes referral to a physician for pain management of moderate and severe pain, thus following a guideline defined by WHO (94), which supported recommendation to treat persisting pain in children.

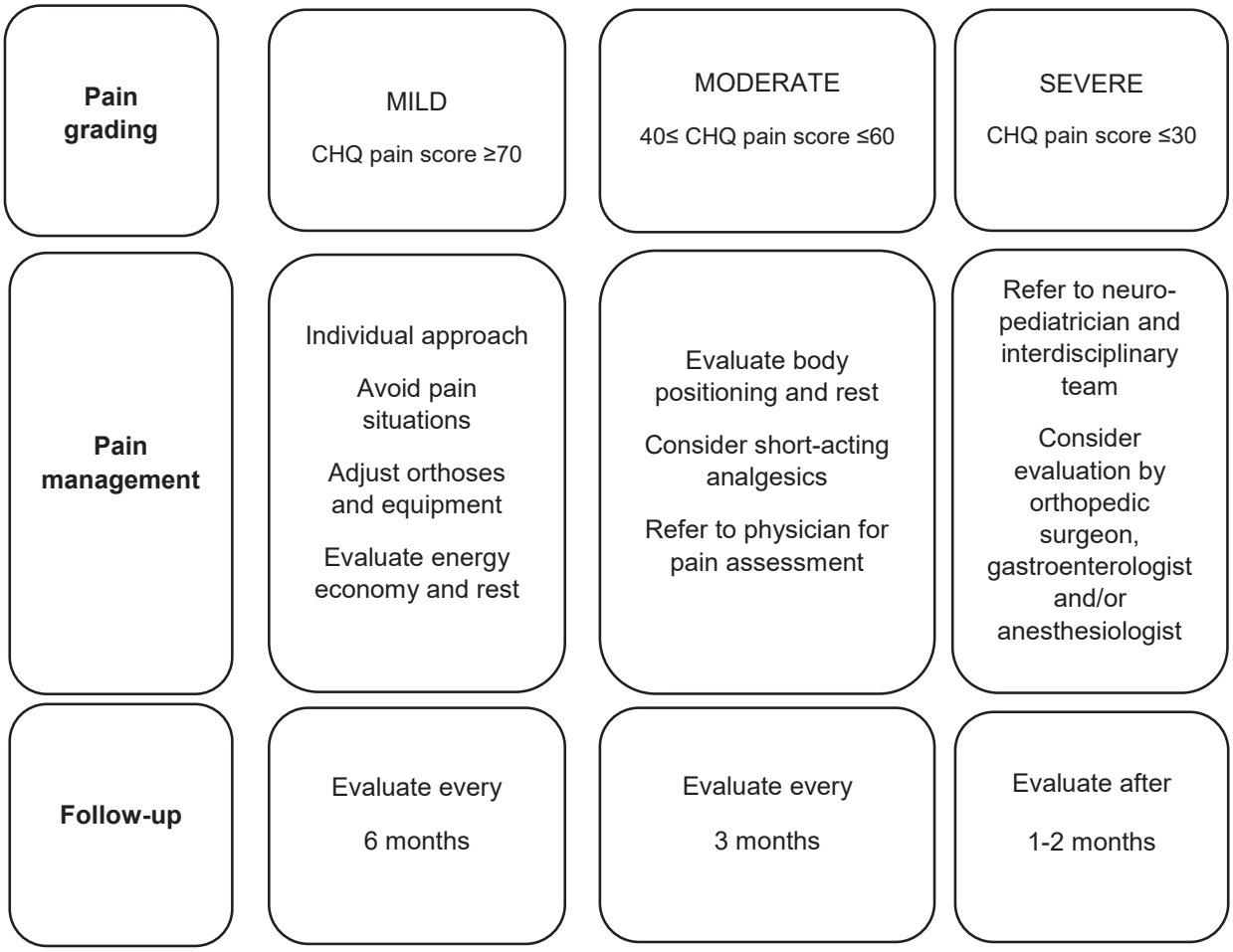

Figure 6. Algorithm on pain, adapted from Larsen et al (93).

Persisting pain (here moderate and severe pain) could be used as *Illness Level* in the Andersen and Newman model (3). A 2-color system was applied (Figure 5): 1) *green (italic)* for factors that were explained in the background information and considered satisfied, and 2) **red (bold)** for factors considered appropriate to address using the findings of the thesis. Children with CP have strong predisposing factors for the utilization of medical care, as the combination of **age (<18 years)** and **past illness (chronic disability)** suggest a more frequent contact with both primary and specialist care. When a person acquires a certain attitude or **beliefs**, it is usually through contact with health professionals with different affiliations who share their knowledge about disease, and the health system in which they work. The context in which the studies, included in this thesis, took place has been described in the section Background. In short, the tax-funded health care system in Norway ensures necessary medical services to all citizens and

prioritizes children. This suggests that *Enabling factors* in the model seem satisfied. **The level of illness** seems appropriate to combine with aforementioned **beliefs**, or more precisely attitudes and expectations towards GPs and specialist care and knowledge about disease (12). The finding of an equal frequency of consultations in children with CP and the controls suggests that enabling factors were similar. The finding of a lower frequency of pain codes as a RFE in children with CP might suggest either inequity in GPs' coding or different attitudes towards health services between the two groups. Since CP is a life-long condition, high alertness on *Facilities to Population* with disability is required to prevent and intervene on pain. Frequent **evaluation of symptoms such as pain** might ensure that illness level does not worsen. Information on pain, i.e. **knowledge about pain in CP,** could be considered as an important target for intervention when considering measures to empower children and their primary caregivers.

Predisposing	Enabling	Illness Level
Demographic	*Family*	**Perceived**
Age*	*Income**	**Disability***
(Sex)	*Health Insurance**	**Symptoms***
(Marital Status)	*Type of Regular Source**	**Diagnoses***
Past Illness*	*Access to Regular Source**	**General State***
Social Structure	*Community*	**Evaluated**
(Education)	*Ratios of Health Personnel and*	**Symptoms***
(Race)	*Facilities to Population**	**Diagnoses***
(Occupation)	*Price of Health Services**	
(Family Size)	(Region of Country)	
(Ethnicity)	(Urban-Rural Character)	
(Religion)		
(Residential Mobility)		
Beliefs		
Values Concerning Health and Illness		
Attitudes toward Health Services		
Knowledge about Disease		

Figure 5. Individual Determinants of Health Service Utilization [adapted from Andersen and Newman (3)]. Determinants in the parentheses were not addressed or discussed in this thesis.

6.5 Clinical implications

The findings in this thesis could have clinical implications for pain management in the population with CP. The findings in Papers I-III support the general concern that pain in children and adolescents with CP has not been addressed sufficiently.

- Pain should be addressed at each contact with a GP and the specialist care.
- We suggest a diary on pain as a tool of communication between the patient/caregiver and healthcare providers.
- First-line analgesics were not used in many adolescents with moderate and severe pain, thus more cooperation with and more information to primary caregivers on pain management are required.
- Hip pain in non-ambulatory children with CP requires thorough assessment because it affects many aspects of everyday life.
- Patients with hip pain and/or hip migration percentage ≥40% should be referred to a multidisciplinary team for assessment.
- A child with hip pain and normal migration percentage after hip surgery should be examined with regard to the removal of the surgical implants.
- Children with painless bilateral hip dislocation should hardly have hip surgery.
- Severe pain in adolescence was associated with a low HRQoL domain score in adolescence, thus indicating pain as the priority in care for both children and adolescents with CP.
- A low HRQoL domain score in childhood was associated with a low HRQoL domain score in adolescence, thus clinicians should also consider including a standardized measure for HRQoL in clinical follow-up at an early age. This might reveal a direction for management and provide detailed information on the health issues needing attention.

Despite equal frequency of daytime contacts with GP, the reporting on pain as RFE was less frequent in children with CP than in controls (Paper IV). In clinical work this could mean that

- Low frequency of pain as a reason for consultation might mean that pain had not been addressed as often as in the general population. Thus, GPs should be pro-active when addressing pain in the population with CP and other disabilities.
- Children with CP and their primary caregivers might have different expectations on pain management in primary health care than the general population. Thus, addressing expectation early might be useful.
- Coding on a known disease could overshadow coding for symptoms and complaints in chronic conditions.

6.6 Implications for CP surveillance protocols and national guidelines

The finding of increased pain severity (Paper I) raises some questions about pain assessment based on CP surveillance. First, bridging surveillance and management is in general a major issue. Since the Norwegian surveillance program is run by habilitation units in specialist health care, answering the questions on pain in the CP surveillance protocol might contribute to an expectation from caregivers that the specialist care is responsible for all pain management. Secondly, adjustments of the protocol itself are needed to target pain management precisely. We suggest:

- A standardized approach to pain assessment should be included in the surveillance protocol because this could improve the overall surveillance of CP.
- The surveillance protocol on pain assessment could include information on all pain sites, including the laterality of pain, characteristics of pain such as intensity, frequency, pain interference and duration of pain episodes for each pain site

Many adolescents had pain with high frequency and intensity (Paper I). We have proposed an algorithm on pain grading, management and follow-up to be included in CP surveillance programs. The algorithm goes as follows:

- Children with moderate or severe pain should be referred to a multidisciplinary team in the specialist care, and a pain management plan should be developed after a thorough pain assessment. Communication on follow-up of moderate and/or severe pain should be

established between the family and the primary and specialist health care. Children receiving ITB should also be assessed for pain in a similar manner.

- Children with mild pain should also have follow-up, because necessary steps to relieve pain should be taken with the aim to avoid pain increase.

Despite the availability of medical services, it is unclear if the Norwegian health system provides specific information about pain to those who care for children with CP. New knowledge on pain should be shared with the caregivers, since the ultimate aim of the surveillance programs must be to empower those who are closest to the child. I would recommend

- An educational course on pain to be introduced in the surveillance program, targeting both children and their parents. Telemedicine might be a tool for such a course.

The Norwegian Paediatric Association includes recommendations on pain treatment in their General Manual in Paediatrics (95). National guidelines on management of CP have been develop in the United Kingdom (96). Such guidelines have so far not been specified in Norway, but the Norwegian CP Association and NorCP have recently initiated this work.

- The findings of this thesis might contribute to the development of such guidelines on pain management in population with CP.

6.7 Future research

There are still many gaps in the knowledge base on pain and pain management in children with CP. A lack of consensus on which instruments to use when grading and assessing pain, in the clinical work and research, and in CP surveillance protocols contributes to maintain the gaps. Standardization of pain grading might improve pain management, and standardization of pain diagnostics as suggested in the Cerebral Palsy Pain Classification (41) might be a valuable starting point.

Further, the knowledge on prescription of first-line analgesics in CP is scarce. Such information could be useful when introducing new guidelines. Also knowledge on prescription and use of drugs in children with severe CP receiving palliative care, could provide valuable information on existing routines and improve health care in this vulnerable population.

Frequency of consultations with GPs and frequency of pain as reason for consultation could differ in populations with CP depending on GMFCS level. Our research material makes it possible to investigate this further.

Norwegian GPs provide a broad spectrum of medical services and expect their patients to see them for both the somatic, psychological and preventive issues. Information from GPs on their management practices, attitudes and expectations could provide valuable information for facilitating shared decisions and bridging gaps in care for the paediatric population with CP.

In general, if the aim of surveillance in CP is to prevent or improve pain, more longitudinal research, including interventional studies on pain, is warranted.

7 CONCLUSIONS

The papers included in this thesis add to the knowledge base with following findings:

Over five years, in children, now adolescents, with CP in GMFCS levels III-V:

- Pain prevalence of recurrent pain, number of pain sites, pain intensity and frequency, all increased. Pain interference with activities of daily living increased, while pain interference with sleep was unchanged (Paper I).
- Prevalence of hip pain increased. Independent risk factors for hip pain in adolescence were severe hip subluxation (hip MP 50-89 %) and GMFCS level V (Paper II).
- HRQoL domain scores stayed mainly unchanged, except for the domain *General Health* which worsened due to increase in the number of medications. High motor impairment, severe pain in adolescence, and low scores in HRQoL domains in childhood were associated with low scores in HRQoL domains in adolescence (Paper III).

In comparison between children with CP (registered in NorCP, cases) and remaining children in the general population (controls) who took contact with a GP (Paper IV):

- The frequency of daytime consultations is not affected by a diagnosis of CP. Cases and controls had equal frequency of daytime consultations with GPs.
- The frequency of daytime consultations related to pain is affected by a diagnosis of CP. GPs registered pain less frequently in children with CP than in controls.
- The frequency of daytime consultations related to musculoskeletal pain is affected by a diagnosis of CP. Musculoskeletal pain was more often registered in consultations with controls than in consultations with cases in age groups 6-11 and 12-17 years, while there was no difference in age group 0-5 years.

To conclude, systematic assessment of all pain and of HRQoL through CP surveillance programs might contribute to a more efficient communication on pain management. When encountering a child with CP, health care professionals, both in primary and specialist care, should ask for pain even if the patient (child or parent) does not address pain. Information on pain prevention and treatment should be given repeatedly to primary caregivers during the follow-up.

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9 PAPERS

I

Recurrent pain in adolescents with cerebral palsy: a longitudinal population-based study

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ABBREVIATIONS

BPI	Brief Pain Inventory
CHQ	Child Health Questionnaire
ITB	Intrathecal baclofen

AIM To investigate the pain characteristics, pain interference with activities of daily living, and use of analgesics in adolescents with cerebral palsy (CP) and compare the results with previous findings.

METHOD Sixty-seven adolescents (median age 14y 4mo, range 12y 2mo–17y, 28 females, 39 males) classified in Gross Motor Function Classification System (GMFCS) levels III to V, who participated in a CP surveillance programme, were assessed on pain measures twice, 5 years apart. Primary caregivers marked recurrent pain sites and graded pain interference with activities of daily living and sleep. Information on pain severity was obtained through two questions from the Child Health Questionnaire (CHQ) and were transformed into a pain score scaled from 0 to 100, where 100 represented no pain. The use of short-acting analgesics was recorded.

RESULTS Over 5 years, the prevalence of recurrent pain, number of pain sites, pain intensity, and pain frequency all increased significantly. The most frequent pain sites were the hip/thigh in GMFCS level V and knee in GMFCS level III. The median CHQ pain score decreased from 60 to 40 ($p<0.001$). Pain interference with activities of daily living increased ($p=0.011$) but not for sleep. Twenty-eight of 54 participants with moderate or severe pain (CHQ pain score ≤60) received no short-acting analgesics.

INTERPRETATION In adolescents with CP, pain increased over 5 years despite follow-up in a surveillance programme. For enhanced management of pain, we propose that an algorithm on pain should be included in surveillance programmes.

Parents and medical professionals consider pain a highly important target for interventions in adolescents with cerebral palsy (CP).[1] A systematic review reported pain prevalence up to 75%.[2] Prevalence was higher in adolescents than in children and individuals with greater motor impairment.[3,4] Furthermore, individuals with more severe CP tended to have more intense and more frequent pain.[3] A recent cross-sectional, register-based study revealed that pain prevalence at different sites varied for different levels of motor impairment, with more hip/thigh pain in individuals with greater motor impairment, more knee pain in individuals needing walking aids, and more lower leg/foot pain in those with less motor impairment.[4] Importantly, pain influenced societal participation and quality of life negatively.[5–7] According to the National Institute for Health and Care Excellence (NICE) guidelines on CP, pain should be addressed at each clinical encounter.[8]

Longitudinal studies on pain characteristics and interference with activities of daily living in the paediatric population with CP would be useful for patient education, pain management, and improvement of surveillance programmes; however, such studies are scarce.

With regard to pain management, the use of short-acting analgesics varies from one in three to one in four patients.[7,9] In both studies, the proportion of the population with pain was greater than the proportion receiving analgesics, indicating that the full potential of analgesics might not be fully exploited. In line with this, a retrospective study confirmed that pain reported repeatedly in a CP surveillance programme was largely neglected in corresponding medical records.[10] This indicates that we need to reconsider both how we assess pain in CP surveillance programmes and bridge the assessments into pain management.

The aims of the present study were to investigate pain characteristics, pain interference with activities of daily living, and the use of short-acting analgesics in a cohort of adolescents participating in a CP surveillance programme and compare the results with findings reported 5 years earlier.

METHOD

The study had both a cross-sectional and longitudinal design. All 136 eligible adolescents, born between 2002 and 2006, living in south-eastern Norway, and enrolled in the Norwegian Quality and Surveillance Registry for Cerebral Palsy,[11] with bilateral CP and in Gross Motor Function Classification System (GMFCS) levels III to V[12] were invited to participate.[13] Data on CP type according to the Surveillance of Cerebral Palsy in Europe,[14] communication function according to the Communication Function Classification System,[15] and gross motor function according to the GMFCS[12] were retrieved from the Norwegian Quality and Surveillance Registry for Cerebral Palsy.[11]

The study was approved by the Regional Ethics Committee, REC South-East (no. 2012/2258 REK). Written informed consent was obtained for 77 adolescents (57%) in 2013 to 2014.[13] Six participants were lost to follow-up 5 years later. Thus, 71 participants received a postal invitation to the second data collection; of these, 67 (94%) participated.

Pain assessment

Data were collected through a questionnaire sent by surface mail to primary caregivers and a telephone interview. The questionnaire consisted of selected questions from the Brief Pain Inventory (BPI), Norwegian version[16] and Child Health Questionnaire (CHQ), Norwegian version.[17] The CHQ has been validated for CP;[18] the reliability of proxy reporting on pain interference in severe CP according to the BPI has been found to be satisfactory.[19]

Pain occurring for at least 4 weeks or more was defined as 'recurrent pain' and further noted as 'pain'. Pain sites with recurrent pain were marked on the BPI body outline.

Pain severity according to the CHQ was recorded for the most severe pain site (selected by the respondent). The two CHQ questions were (1) 'During the past 4 weeks, how much bodily pain or discomfort has your child had?' with the response alternatives 'none, very mild, mild, moderate, severe, and very severe', and (2) 'During the past 4 weeks, how often has your child had bodily pain or discomfort?' with the response alternatives 'none of the time, once or twice, a few times, fairly often, very often, and every day or almost every day', and were given scores from 1 to 6 respectively. These scores were transformed by an algorithm into a CHQ pain score scaled from 0 to 100, where 100 represented no pain.[20] After careful consideration and with the aim of defining a pain scoring system feasible for recommendations in a CP surveillance protocol, we categorized CHQ pain scores as 0 to 30 (severe pain), 40 to 60 (moderate pain), and 70 to 90 (mild pain). A change in CHQ pain score of 20 and less was considered as no change in pain, while a change of 30 or more was regarded as less or more pain.

The BPI questions on pain interference with activities of daily living and sleep were: 'On a scale from 0 to 10 (10=total influence), which value best describes how much pain influenced your child's 'activities of daily living' and 'sleep' respectively?' The time span was modified from 2 to 4 weeks to correspond with the CHQ.

The telephone interview started with the definition of recurrent pain and consisted of the following questions with an open response: Did your child have recurrent pain in the last 4 weeks? What are the pain sites? What relieves the pain? What increases the pain? Has your child received any medication to relieve pain (such as paracetamol, ibuprofen, or naproxen) over the past 4 weeks? Use of intrathecal baclofen (ITB) was also recorded.

What this paper adds

- Pain prevalence and the number of pain sites increased over a 5-year period in adolescents with cerebral palsy.
- Pain intensity, frequency, and pain interference with activities of daily living increased, whereas interference with sleep was unchanged.

Statistical analysis

SPSS v27 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. Data were presented either as frequency, percentage, proportion, or median with range. Correlation between variables was explored by calculating Spearman's correlation coefficient, r_s (significant when $p<0.05$ and $r_s>0.30$). Non-parametric statistics (Mann–Whitney *U* test) were applied for ordinal variables and skewed continuous variables. In linear regression, variables were included in the multivariate linear regression analyses if $p<0.1$ in the univariate analyses. Normality of residuals was satisfied. In the longitudinal analyses, proportions were analysed with McNemar's test, continuous variables with a paired samples *t*-test, and ordinal variables with a Wilcoxon signed-rank test. All tests were two-sided. Differences were significant if $p<0.05$.

Three participants (4.4%) had missing values on pain interference at the first data collection point. Imputation was not performed since this would most likely not influence the statistical analyses.

RESULTS

The characteristics of the participants are shown in Table 1. The number of participants with pain increased from 45 to 62 over the 5-year period ($p<0.001$) and the median number of pain sites in each participant increased from one (range 0–6) to three (range 0–13; $p<0.001$).

Pain prevalence increased at all sites and the increase was statistically significant in the neck and knee (Table 2). Pain prevalence increased across all GMFCS levels and the increase was statistically significant in GMFCS level III. The hip/thigh was the most common pain site in GMFCS level V, while the hip/thigh and lower leg/foot were the most common sites in GMFCS level IV and the knee in GMFCS level III. The prevalence of abdominal pain was highest in GMFCS level V.

There was a significant correlation between pain intensity and pain frequency ($r_s=0.494$, $p<0.001$). Both pain intensity and frequency increased during the 5-year period (both $p<0.001$). The median CHQ pain score decreased from 60 to 40 ($p<0.001$). Decrease across GMFCS levels

Table 1: Characteristics of the 67 participants

Characteristic	
Age, y:mo, median (range)	14:4 (12:2–17:0)
Sex	
Female	28 (42)
Male	39 (58)
Predominant movement disorder	
Spastic	53 (79)
Dyskinetic	14 (21)
Communication	
CFCS level I	7 (10)
CFCS level II	10 (15)
CFCS level III	2 (3)
CFCS level IV	13 (19)
CFCS level V	21 (31)
Unknown	14 (21)
Ambulation	
GMFCS level III	15 (22)
GMFCS level IV	17 (25)
GMFCS level V	35 (52)
Intrathecal baclofen therapy[a]	15 (22)

Data are *n* (%) unless otherwise stated. [a]Three of 17 participants in GMFCS level IV and 12 of 35 participants in GMFCS level V had intrathecal baclofen therapy. CFCS, Communication Function Classification System; GMFCS, Gross Motor Function Classification System.

Table 2: Longitudinal analysis on the prevalence of recurrent pain sites in 67 adolescents with cerebral palsy 5 years apart

Pain site	Present	Previous	*p*
Pain at any site	62 (93)	45 (67)	<0.001
GMFCS level III	12 (80)	6 (40)	0.031
GMFCS level IV	16 (94)	11 (65)	0.063
GMFCS level V	33 (94)	28 (80)	0.180
Neck pain	11(16)	1 (1)	0.006
GMFCS level III	1 (7)	0 (0)	0.334
GMFCS level IV	2 (12)	1 (6)	0.579
GMFCS level V	8 (23)	0 (0)	0.003
Back pain	12 (18)	6 (9)	0.109
GMFCS level III	3 (20)	1 (7)	0.164
GMFCS level IV	2 (12)	3 (18)	0.332
GMFCS level V	7 (20)	2 (6)	0.058
Upper-limb pain	18 (27)	10 (15)	0.152
GMFCS level III	3 (20)	1 (7)	0.334
GMFCS level IV	3 (18)	0 (0)	0.083
GMFCS level V	12 (34)	9 (26)	0.475
Hip/thigh pain	34 (51)	24 (36)	0.076
GMFCS level III	4 (27)	3 (20)	0.670
GMFCS level IV	8 (47)	6 (35)	0.431
GMFCS level V	22 (63)	15 (43)	0.070
Knee pain	31 (46)	18 (27)	0.035
GMFCS level III	9 (60)	1 (7)	0.006
GMFCS level IV	7 (41)	7 (41)	1.000
GMFCS level V	14 (40)	10 (29)	0.481
Lower leg/foot pain	21 (31)	18 (27)	0.678
GMFCS level III	6 (40)	3 (20)	0.082
GMFCS level IV	8 (47)	5 (29)	0.188
GMFCS level V	7 (20)	10 (29)	0.447
Abdominal pain	13 (19)	9 (13)	0.344
GMFCS level III	0 (0)	0 (0)	–
GMFCS level IV	2 (12)	2 (12)	1.000
GMFCS level V	11 (31)	7 (20)	0.160
Headache[a]	4 (6)	3 (4)	1.000
Other pain sites[a]	10 (15)	4 (6)	–

Data are *n* (%) unless otherwise stated. [a]Analyses for GMFCS levels not performed due to small numbers. Pain in the teeth and skin or pain localized to the respiratory or genito-urinary system was merged and labelled as 'other pain sites'. A McNemar' test was used to compare proportions. GMFCS, Gross Motor Function Classification System.

was: GMFCS level III, 100 to 40 (p=0.002); GMFCS level IV, 60 to 50 (p=0.050); and GMFCS level V, 50 to 30 (p=0.007). There were 34 (51%) participants with more pain (lower CHQ score) than 5 years before, 27 (40%) with no change, and six (9%) with less pain. In the univariate analyses, lower age and GMFCS level V were possible predictors of low CHQ score (B=7.8, 95% confidence interval [CI]=3.6–12.1, p<0.001 and B=−16.6, 95% CI=−33.1 to −0.1, p=0.049 respectively), while sex and predominant movement disorder were not (B=−5.9, 95% CI=−19.4 to 7.7, p=0.392 and B=−3.9, 95% CI=−20.4 to 12.7, p=0.643 respectively). In the multivariate analysis, younger age was the only independent predictor of lower CHQ scores (B=7.1, 95% CI=2.7–11.4, p=0.002).

There was a positive correlation between pain interference with activities of daily living and sleep (r_s=0.762, p<0.001) and negative correlations between CHQ pain score and both interference with activities of daily living and sleep (r_s=−0.521, p<0.001 and r_s=−0.370, p=0.002 respectively). Participants classified in GMFCS level III had significantly lower interference with activities of daily living (GMFCS level III vs GMFCS level IV p=0.043 and GMFCS III vs GMFCS level V p=0.001) and sleep (GMFCS level III vs GMFCS level IV p=0.009 and GMFCS level III vs GMFCS level V p<0.001) than participants in GMFCS levels IV and V. There were no significant differences between GMFCS levels IV and V regarding pain interference with activities of daily living and sleep (p=0.235 and p=0.050 respectively). Median pain interference with activities of daily living increased over the 5-year period from 1.5 (range 0–10) to 3.0 (range 0–10) (p=0.011), while median pain interference with sleep was 1.0 (range 0–10) at both data collection time points (p=0.767) in 64 participants.

The relationship between CHQ pain score and the use of analgesics is shown in Table 3. Twenty-six participants received analgesics and 41 did not. Their median CHQ pain score was 20 (range 0–60) and 50 (range 10–100) respectively (p<0.001). Regarding changes in pain, 18 of 34 participants with more pain did not receive analgesics and neither did 8 of the 12 participants with a pronounced pain increase (CHQ score decrease ≥60). There was a positive correlation between the use of analgesics and pain interference with activities of daily living and sleep (r_s=0.682, p<0.001 and r_s=0.415, p<0.001 respectively).

The median CHQ pain score was 30 (range 10–100) in the 15 participants receiving ITB. Ten of 15 participants receiving ITB received analgesics and five did not. Their median CHQ pain score was 20 (range 10–60) and 70 (range 30–100) respectively.

Longitudinal data on pain characteristics and interference are available in Figure S1 and Table S1 (online

Table 3: Caregiver-administered short-acting analgesics during the last 4 weeks in relation to pain severity at the two data collection points

	Present		Previous	
Pain score	Medication *n*=26	No medication *n*=41	Medication *n*=12	No medication *n*=55
CHQ 100	0	8	1	20
CHQ 70–90	0	5	1	10
CHQ 40–60	11	16	7	20
CHQ 0–30	15	12	3	5

Medication consisted of short-acting analgesics (paracetamol/ibuprofen/naproxen). CHQ, Child Health Questionnaire.

supporting information). Caregiver experiences on factors that increased and relieved pain are shown in Table S2 (online supporting information).

Forty-five caregivers gave a written response to the BPI and CHQ and were interviewed, while 22 caregivers responded to the BPI and CHQ during the telephone interview. Responders (87% parents, 85% female) were the same 61 caregivers as 5 years earlier as well as six new primary caregivers in the home care facility. The mean time between the two data collection points was 5 years 1 month (median 5y 2mo, range 3y 8mo–5y 11mo).

DISCUSSION

The main findings of this study were that the prevalence of recurrent pain was high in adolescents with CP and that pain prevalence, the number of pain sites, pain severity, and pain interference with activities of daily living all increased over a period of 5 years despite follow-up in a CP surveillance programme.

Pain prevalence was higher (93%) than in previous studies (37–77%).[2,3] One reason could be that we recorded pain regardless of pain severity or level of pain interference. Also, our population was restricted to ages 12 to 17 years and GMFCS levels III to V, a group with expected high pain prevalence.[4] The increase in pain prevalence was statistically significant only in GMFCS level III, which could be attributed to weight gain, extensive physical strain, and increasing contractures.[21]

Pain prevalence at each site was higher than reported by Eriksson et al.,[4] possibly due to a narrower age range in our study population. In line with previous studies, the most frequent pain site was the lower limbs.[3,4] A trend of most frequent pain in the abdomen and hip/thigh in GMFCS level V and most frequent knee pain in GMFCS level III was supported.[4] Furthermore, increasing frequency of neck pain in GMFCS level V and knee pain in GMFCS level III was reported. Our data on neck pain must be taken with caution since this group consisted of only 11 participants. Nonetheless, positional factors such as lack of adjustment of the wheelchair and prolonged sitting or lying without support are potential causes. An increase in knee pain could be caused by increased crouch gait and lack of correct adjustment or omitted use of orthoses, which is common in adolescents in GMFCS level III.[22]

Our participants had moderate-to-severe pain (60%) and daily pain (40%) more often than previously reported by Parkinson et al.[3] (37% and 11% respectively), which is probably explained by the inclusion of only GMFCS levels III to V in the present study. The finding of younger age as a predictor of more severe pain within the 12 to 17 year age group is not in agreement with the study by Eriksson et al.[4] One reason could be the narrow age range. We found no significant difference in pain severity between participants with spastic and dyskinetic bilateral CP.

Pain interfered with activities of daily living, thus adding to the knowledge base that pain in CP has a negative impact on daily life.[4,7,23] The finding of higher pain interference with activities of daily living in GMFCS levels IV and V was in line with the study by Christensen et al.[24]

Longitudinal studies are useful to evaluate the natural history of pain and the effects of treatments and interventions. Our study had an observation time of 5 years, which ensured a comparison between childhood and adolescence in the same individuals. Two longitudinal studies previously reported changes in pain in a paediatric population with CP.[24,25] These studies reported no significant change in mean pain scores. In contrast, we found a more adverse pain development, with an increase in pain and pain interference with activities of daily living over 5 years. Comparing the results is difficult because of differences in study population (population- vs hospital-based), age (mean=14y 7mo vs 8y 8mo vs 8y 6mo), age range (12y 2mo–17y vs 3–16y vs 3–18y), time span between data collection points (mean=5y 1mo vs 2y 4mo vs 1y), and inclusion of GMFCS levels III to V only versus including all GMFCS levels.[24,25]

Factors that aggravated pain (Table S2) were in line with a previous report.[3] The most prevalent factor was staying in the same position over time. This information should be discussed with primary caregivers to secure 24/7 positioning strategies. Passive muscular stretching both relieved and increased pain. Other actions that most often relieved pain were rest, change of position, and use of analgesics. In line with the study by Tedroff et al.,[9] who reported a positive correlation between the frequency of use of analgesics and pain interference, we found positive correlations between the use of analgesics and both pain interference with activities of daily living and sleep. Although the number of participants receiving analgesics increased over 5 years, 28 out of 54 participants with moderate or severe pain did not receive analgesics. This suggests that the pain-relieving potential of analgesics was not fully exploited. Nonetheless, the use of analgesics should be based on individual preference and potential side effects as well as pain severity and interference. We have not been able to find studies on pain and the use of analgesics in children with CP receiving ITB. The finding that most had moderate or severe pain and received analgesics indicates the need for close follow-up of pain even if ITB is used.

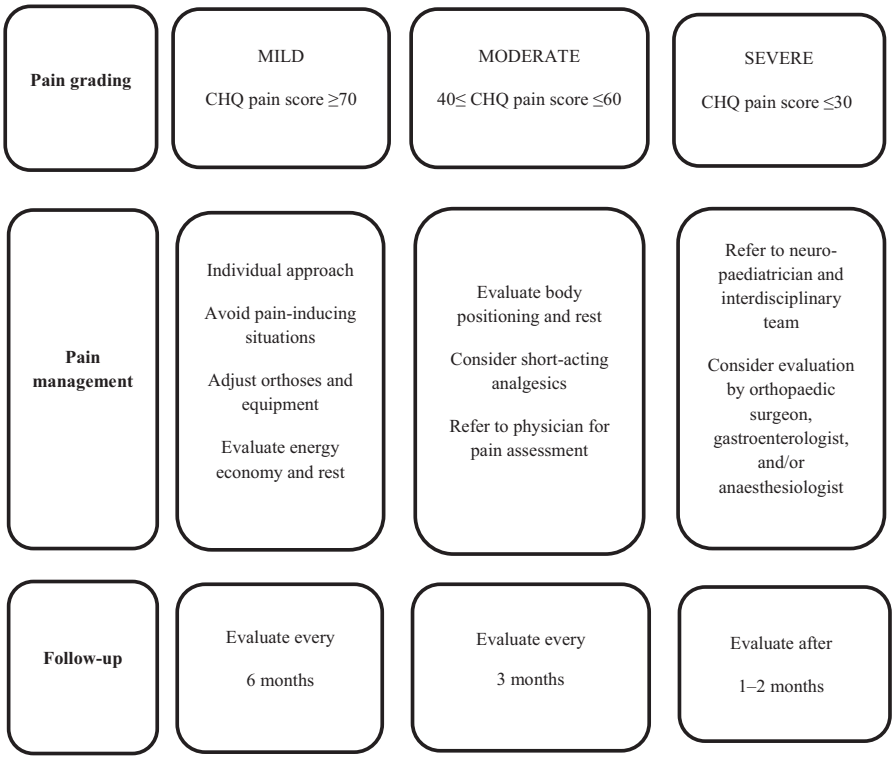

Figure 1: Algorithm on the grading, management, and follow-up of recurrent pain. The Child Health Questionnaire (CHQ) pain score was calculated according to the CHQ manual. The pain management suggested for mild pain is relevant for moderate and severe pain; the pain management suggested for moderate pain is relevant for severe pain.

Data from Sweden show that the prevalence of hip dislocation declined after the introduction of a surveillance programme that included an algorithm on hip management.[26] In contrast, the high prevalence of recurrent pain suggests that our CP surveillance programme was not helpful in initiating adequate pain management. This is in line with the study by Westbom et al.[10] After this study, the Nordic CP surveillance protocols were revised and questions on pain intensity, frequency, and interference with activities of daily living and sleep have since been included.[11] Also, the Swedish CP surveillance protocol now includes questions on pain intensity for each pain site. We support these inclusions and suggest that information on laterality of pain in the limbs and pain duration should be included. We propose that an algorithm on pain assessment and management based on the CHQ pain score should be included in the surveillance protocol (Fig. 1). One could consider differentiation in GMFCS levels in the algorithm, such as more detailed assessment of hip pain in GMFCS level V, since hip pain might be an indicator for surgical treatment of hip subluxation if the migration percentage is equal to or greater than 40%.[27] Physical assessment by a physician should be included in cases of moderate and severe pain. The local multidisciplinary team should consider all causes of pain and all available treatment alternatives and outline an action plan for each pain site. The proposed algorithm should be adjusted to the local health care system to be feasible.

This study has several limitations. First, data were based on proxy reports of pain; by definition, pain is subjective and should be self-reported whenever possible. Most of our population was in Communication Function Classification System levels IV and V; therefore, proxy reporting had to be applied to include the whole sample. Furthermore, a recent study found no significant differences in self- versus proxy-reported pain in a CP surveillance programme.[28] Second, we did not ask about the duration of pain episodes. This information could have contributed to the understanding of why some participants with moderate and severe pain did not receive analgesics. Third, the questionnaires sent out in paper form were answered during a telephone interview by one-third of primary caregivers. However, there were no significant differences in the number of pain sites or CHQ pain scores with regard to the response form. Finally, interviews were performed by a different researcher than 5 years earlier, which could challenge the reliability of longitudinal comparison.

The study has several strengths. First, it is population-based and there were no significant differences between participants and non-responders.[13] This ensured generalizability of the data. Second, the response rate at the second data collection point was high, probably because the

method included a telephone interview. Furthermore, most responders were the same person at the two data collection points, which strengthens the reliability of the comparison between the two time points.

In conclusion, pain is a considerable problem in adolescents with CP. We propose extended pain assessment and an algorithm on pain management to be included in CP surveillance programmes with the aim to bridge the gap between programmes, guidelines, and pain management.

ACKNOWLEDGEMENTS

We thank all participants and their caregivers for their time and contribution to this study. We thank statistician C Brunborg at the Oslo Center for Statistics and Epidemiology for valuable advice. The Norwegian Dam Foundation granted a PhD scholarship to S M Larsen (grant no. 2019/FO235195) supported by the Norwegian CP Association. The Norwegian South East Regional Hospital Trust partly funded K Ramstad's work (grant no. 2013083).

CONFLICT OF INTEREST

The authors have stated that they had no interests which might be perceived as posing a conflict or bias.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

SUPPORTING INFORMATION

The following additional material may be found online:

Figure S1: Longitudinal data on the number of pain sites, CHQ pain score, pain interference with daily activities and sleep, pain intensity, and pain frequency in 67 participants with CP 5 years apart.

Table S1: Longitudinal data on pain characteristics in adolescents with CP collected 5 years apart

Table S2: Proxy-reported factors which relieved and increased pain (open response)

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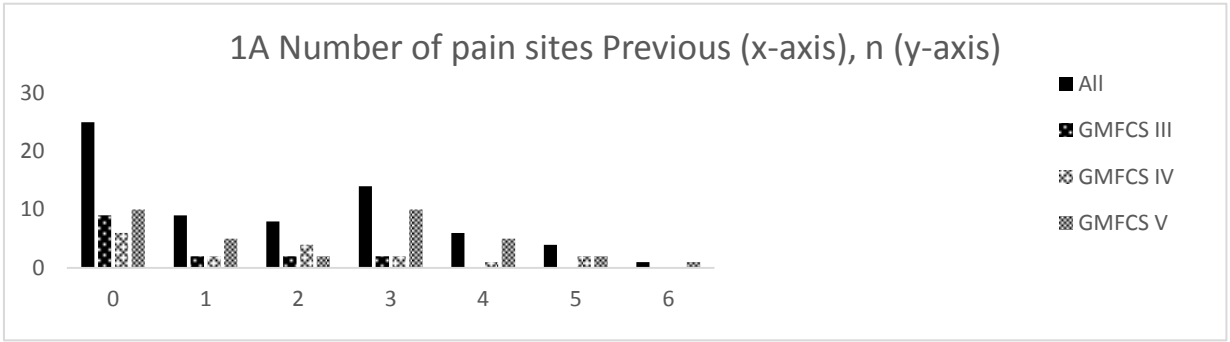
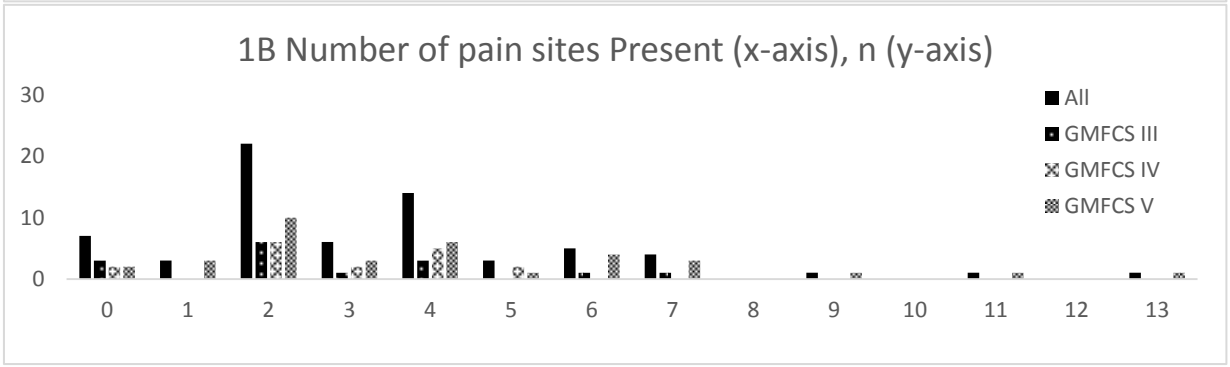
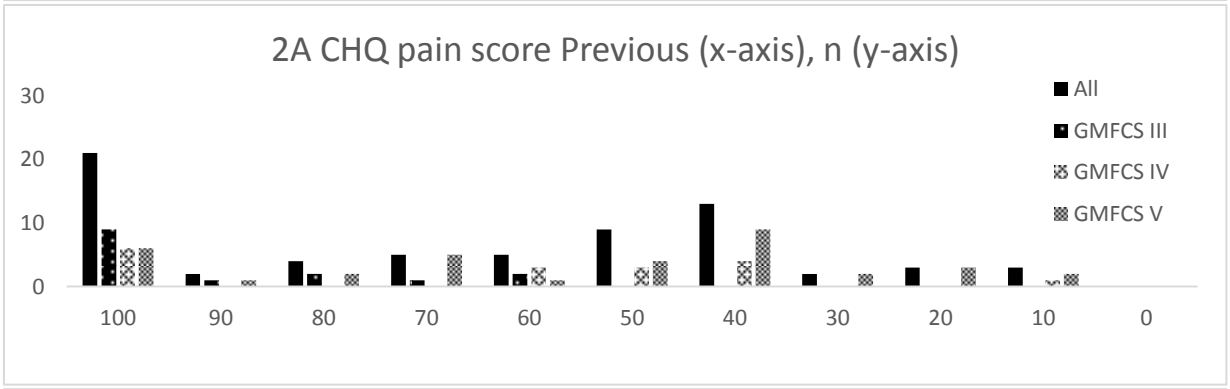
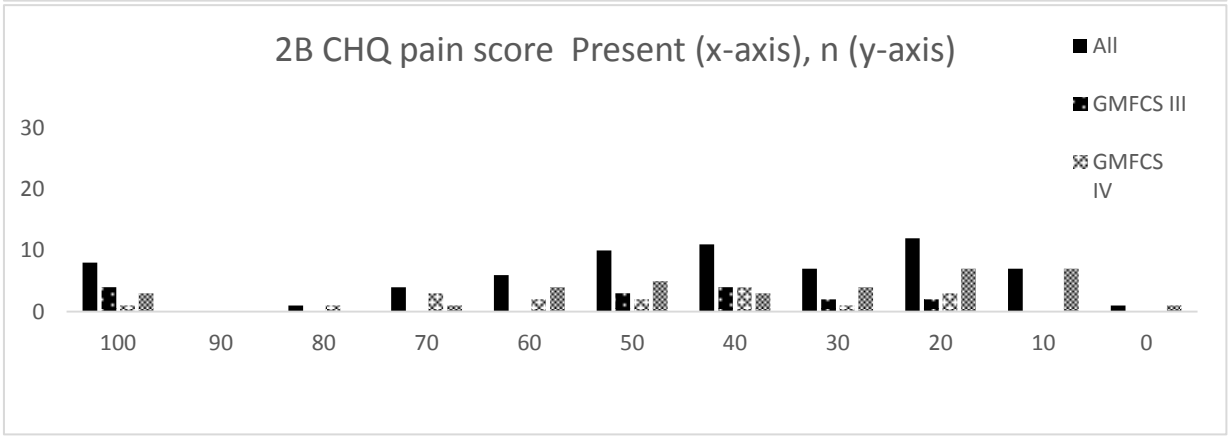
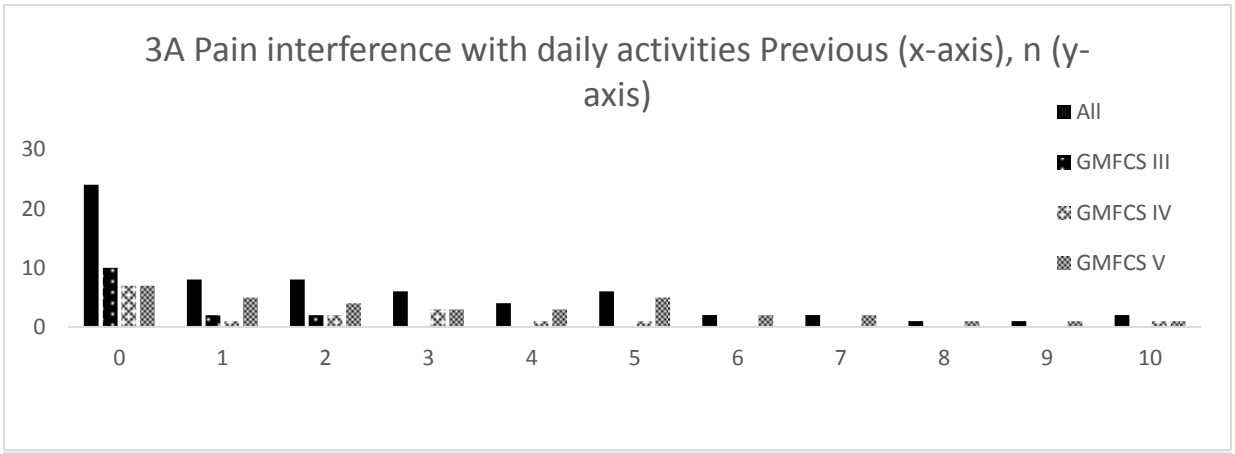
Supplementary Figure 1. Longitudinal data on number of pain sites, CHQ pain score, pain interference with daily activities and sleep, pain intensity and frequency in 67 participants with CP five years apart

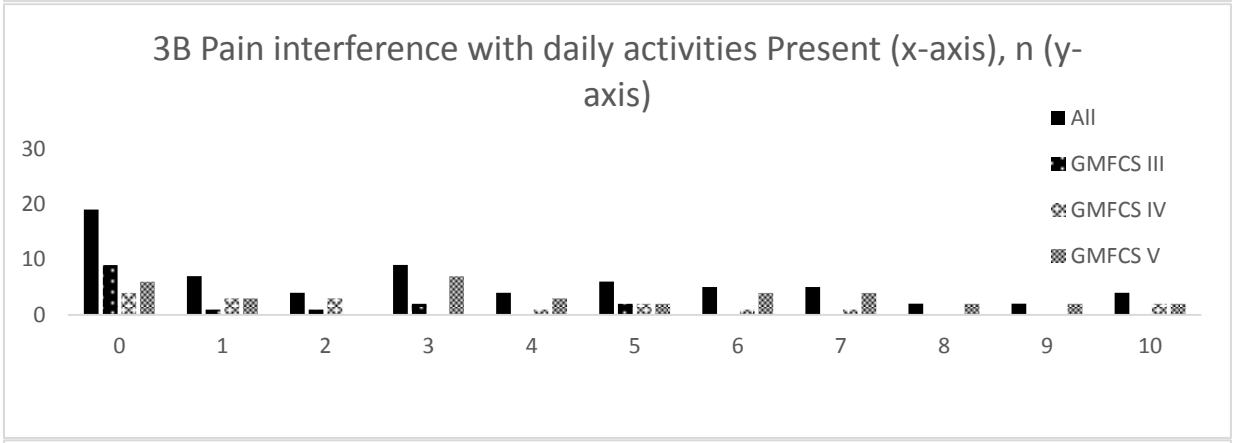


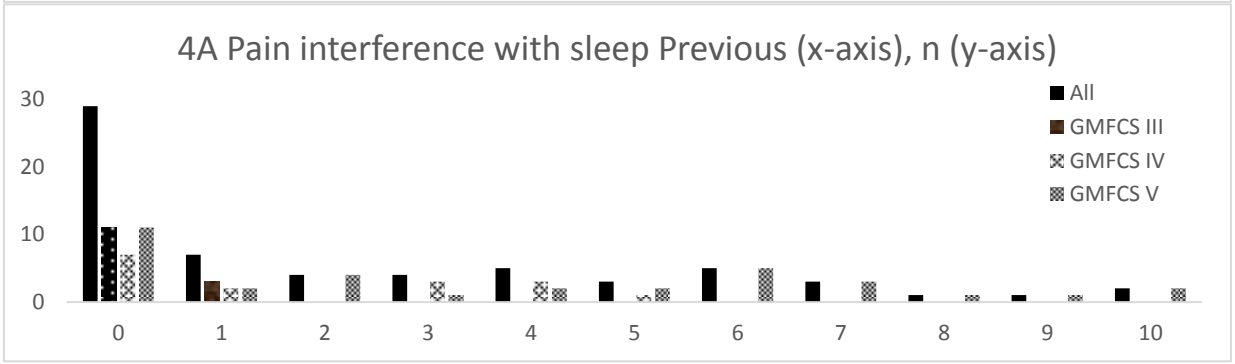







3A Pain interference with daily activities Previous (x-axis), n (y-axis)
All
GMFCS III
GMFCS IV
GMFCS V
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10


3B Pain interference with daily activities Present (x-axis), n (y-axis)
All
GMFCS III
GMFCS IV
GMFCS V
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10


4A Pain interference with sleep Previous (x-axis), n (y-axis)
All
GMFCS III
GMFCS IV
GMFCS V
30
20
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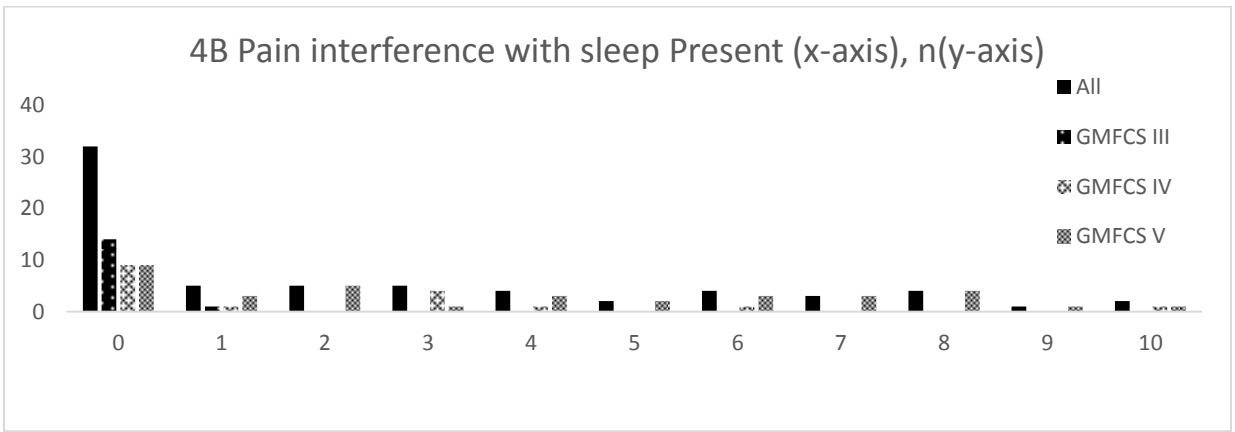
4B Pain interference with sleep Present (x-axis), n(y-axis)
All
GMFCS III
GMFCS IV
GMFCS V
40
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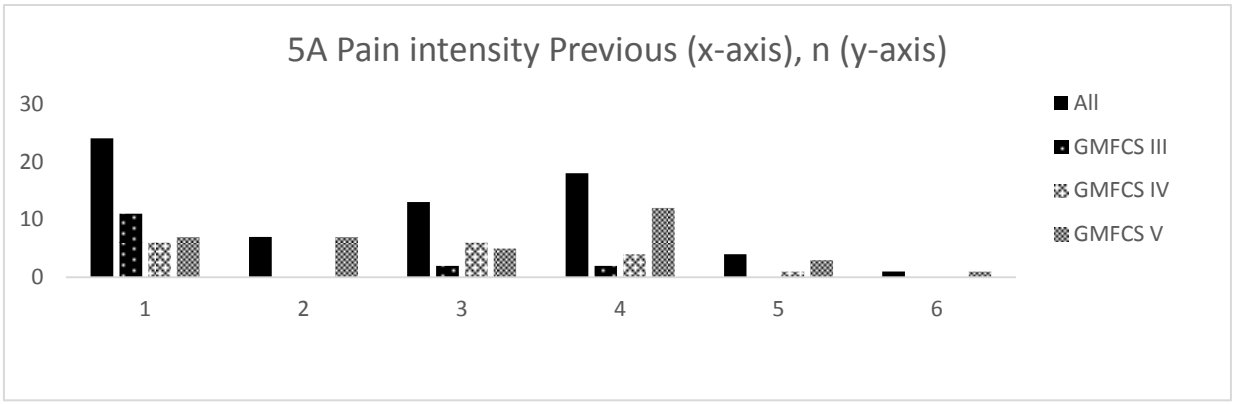

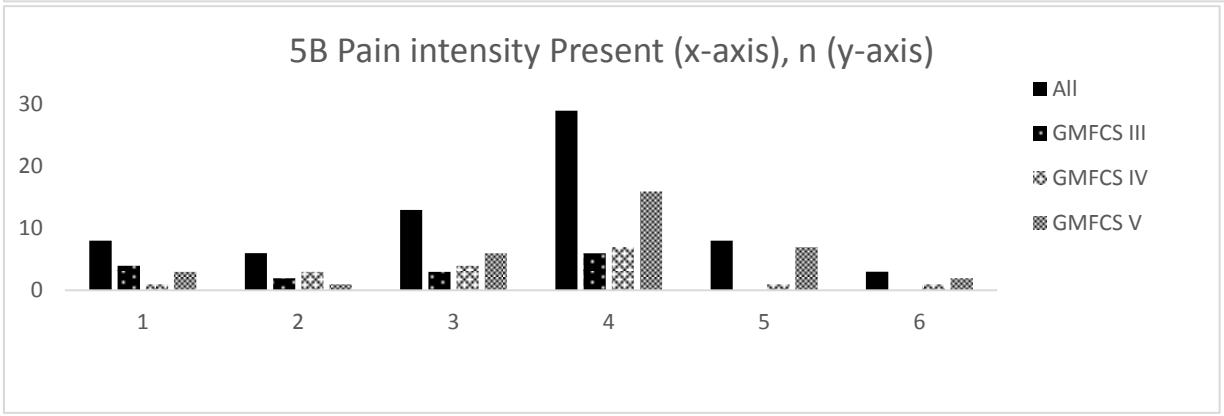

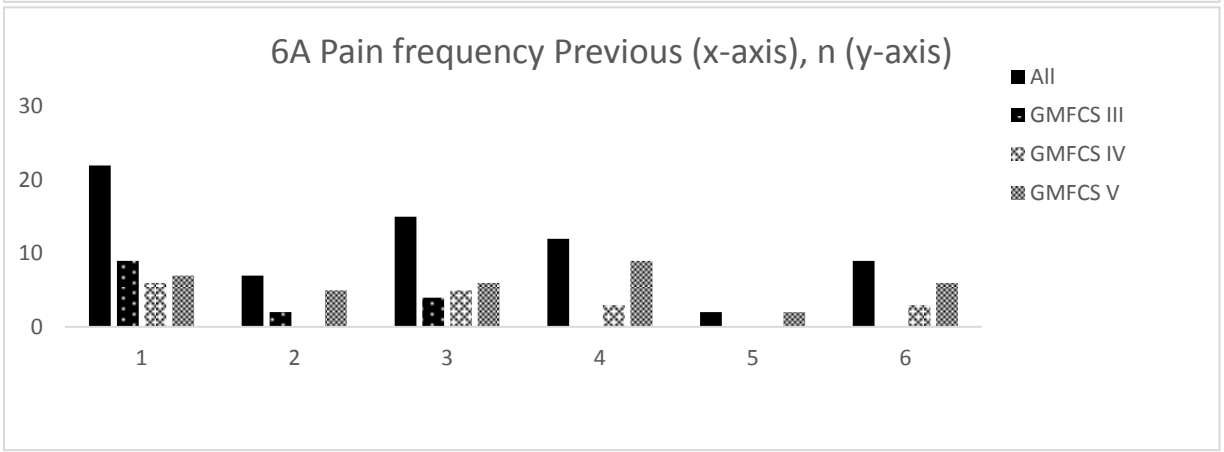

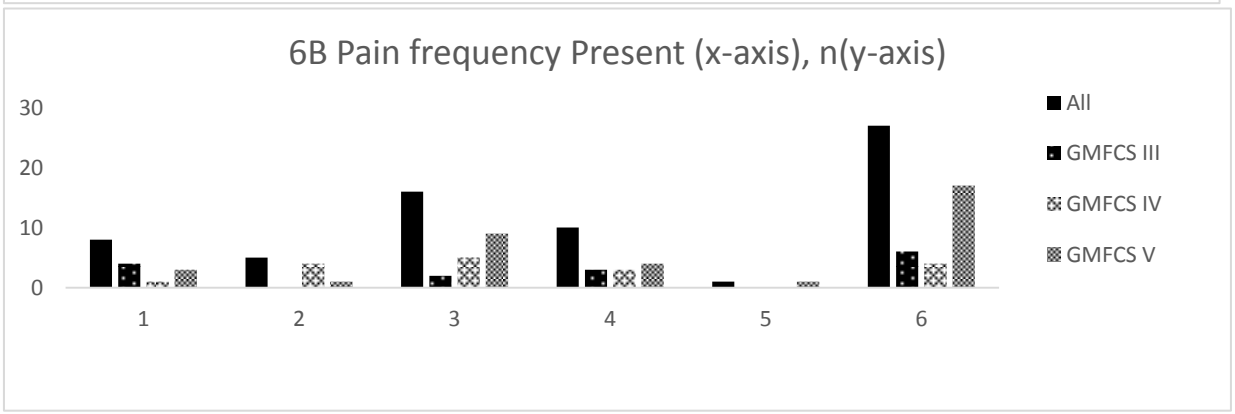

In 1A and 1B data are number of participants with 0,1,2,…,13 pain sites. In 2A and 2B CHQ pain score scaled 100-0, where 100 represents no pain. In 3A, 3B, 4A and 4B: Pain interference (with daily

activities/sleep) based on BPI scale 0-10, 0 represents no interference, 10 complete interference (3 missing values in 3A and 4A). In 5A and 5B Pain intensity (x-axis): 1 none, 2 very mild, 3 mild, 4 moderate, 5 severe, 6 very severe). In 6A and 6B: Pain frequency (x-axis): 1 none of the time, 2 once or twice, 3 a few times, 4 fairly often, 5very often, 6 every day or almost every day

1A, 2A, 3A, 4A, 5A, 6A at previous data collection, 1B, 2B, 3B, 4B, 5B, 6B at present data collection.

GMFCS, gross motor function classification system. CHQ, Child Health Questionnaire. BPI, brief pain inventory.

Table S1. Longitudinal data on pain characteristics collected 5 years apart

Pain characteristics	Data collection		
	Previous	Present	p-value
Number of pain sites, all	1 (0-6)	3 (0-13)	<0.001
GMFCS level III	0 (0-3)	2 (0-7)	0.003
GMFCS level IV	2 (0-5)	3 (0-5)	0.046
GMFCS level V	3 (0-6)	3 (0-13)	0.005
CHQ pain score, all	60 (10-100)	40 (0-100)	<0.001
GMFCS level III	100 (50-100)	40 (20-100)	0.002
GMFCS level IV	60 (10-100)	50 (20-100)	0.050
GMFCS level V	50 (10-100)	30 (0-100)	0.007
Pain interference with daily activities*	1.5 (0-10)	3 (0-10)	0.011
GMFCS level III	0 (0-2)	0 (0-5)	0.136
GMFCS level IV	1.5 (0-10)	2.0 (0-10)	0.098
GMFCS level V	3 (0-10)	4 (0-10)	0.133
Pain interference with sleep*	1 (0-10)	1 (0-10)	0.767
GMFCS level III	0 (0-1)	0 (0-1)	0.157
GMFCS level IV	1 (0-5)	0 (0-10)	0.720
GMFCS level V	2.5 (0-10)	3 (0-10)	0.875
Pain intensity, all			<0.001
GMFCS level III			0.045
GMFCS level IV			0.053
GMFCS level V			0.013
Pain frequency, all			<0.001
GMFCS level III			0.004
GMFCS level IV			0.322
GMFCS level V			0.016

Data are median (range) for 67 participants (15 in GMFCS level III, 17 in GMFCS level IV and 35 in GMFCS level V). *Data on pain interference are available for 64 participants (14 in GMFCS level III, 16 in GMFCS level IV and 34 in GMFCS level V). Data on pain intensity and frequency are available in Supplementary Figure 1. Statistics: paired samples t-test for number of pain sites and CHQ pain score and Wilcoxon Signed Rank test for pain interferences, pain intensity and pain frequency.

Table S2. Proxy-reported factors which relieved and increased pain (open response)

Pain sites	What did relieve pain?
Abdominal	first-line pain medication (4), enema (4), laxantia (2), hip flexion prior to flatulence (2), meal (1), correct infusion rate in gastrostomy (1), flatulence (1), defecation (1)
Musculoskeletal	pain medication (first-line paracetamol/ibuprofen) (26), stretching/end stretching (12/21), rest (16), positioning (11), massage (7), being careful (4), use of personal lifter (2), careful clothing (1), assist at spasm attacks (1), morphine (1), clonidine (1), cream (1)
Neck	physical therapy (1), neck support with pillow (1), derive (1), correct position (1)
Back	back stretching (2), tilt back wheel chair (1), rest with pillow (1), move hips (1)
Lower limbs	change of position (11), avoid/end physical activity (6), warm-up movements (3), warm bath/shower (2), warmth (2), joint-support when stretching (1), compression stocking (1), get shoes on (1)
Pain sites	**What did increase pain?**
Abdominal	constipation (2)
Musculoskeletal	same position over longer period of time (20), stretching/too much stretching (7/7), abrupt and/or extreme movements (13), any movement (6), extensive physical activity (4), cold weather (4), incorrect position over longer time (3), lack of support under position change (3), lack of assistance (3), lack of physical activity (2), lack of stretching (2), lack of orthopedic devices (2), inexperienced assistant (2), stress (1), weight bearing (1), incorrect stretching (1), use of devices (1), use of shoes (1), lack of rest (1), asymmetry (1), noise (1), epileptic seizures (1)

Data are number of participants in parenthesis (n). Pain localized in neck, back and limbs was defined as musculoskeletal pain. Abdominal pain was attributed to gastro-esophageal reflux, gastrostomy, flatulence and/or constipation.

II

Hip pain in adolescents with cerebral palsy: a population-based longitudinal study

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ABBREVIATIONS

CHQ	Child Health Questionnaire
CPOP	Cerebral Palsy Follow-Up Program
ITB	Intrathecal baclofen

AIM To investigate the prevalence, characteristics, and risk factors of hip pain in adolescents with cerebral palsy (CP) and compare the findings with those of the same individuals 5 years earlier.

METHOD Sixty-seven adolescents (28 females, 39 males; mean age 14y 7mo; SD 1y 5mo; range 12–17y) with bilateral CP, in Gross Motor Function Classification System (GMFCS) levels III to V enrolled in a CP surveillance programme were assessed for hip pain. Their caregivers responded to the questions on the intensity and frequency of hip pain from the Child Health Questionnaire (CHQ) (transformed to CHQ hip pain score; 100 indicates no pain). Interference of hip pain with daily activities and sleep was recorded on numeric rating scales. Hip displacement was measured radiographically by the migration percentage.

RESULTS Twenty-eight participants had 44 painful hips. Their mean CHQ hip pain score was 40 (SD 21.4; range 10–80). Independent risk factors for hip pain, low CHQ hip pain score, and interference with sleep were severe hip subluxation (migration percentage 50–89%) and GMFCS level V. A migration percentage of 50% to 89% was the only independent risk factor for interference with daily activities. Over 5 years, the number of participants with hip pain increased from 18 to 28, while the mean migration percentage of the most displaced hip was unchanged.

INTERPRETATION Our CP hip surveillance programme did not protect the participants against increasing prevalence of hip pain during adolescence. We suggest that surveillance programmes for CP should include guidelines on the characteristics and management of hip pain.

Seventy-five percent of children and adolescents with cerebral palsy (CP) have pain, most frequently located in the lower limbs.[1,2] In a hospital-based study, physicians identified hip displacement as the most frequent primary source of severe pain in children and adolescents with CP. This accounted for 24% of the causes of pain that had prevented participation in activities, confirming the clinical significance of hip pain.[3] In accordance with this, several countries have developed surveillance programmes for children with CP, aiming to monitor hip displacement, avoid hip dislocation, and prevent hip pain.[4,5]

Hip displacement is usually measured radiographically by the migration percentage.[6] A few studies have explored the association between hip pain and increasing migration percentage in CP, but different age groups and strategies to assess hip pain make comparison of the results difficult.[7–10] In non-ambulatory young adults, the prevalence of hip pain increased with increasing migration percentage.[7] In a study of non-ambulatory children aged 7 to 12 years, hip pain was found to be significantly associated with severe hip displacement, while mild and moderate displacement did not influence the occurrence of hip pain. Hip pain occurred in 60% of hips with a migration percentage of ≥50%.[10] Another study of children aged 4 to 16 years confirmed an association between hip pain and hip displacement.[11] However, no association between hip pain and migration percentage was found in 18 participants aged 2 to 21 years.[9] Thus, further studies on the relationship between hip pain and hip displacement are warranted.

A Swedish register-based study on pain in children and adolescents with CP found that pain, even when repeatedly reported during follow-up, was largely neglected in the corresponding medical records.[12] This indicates that there is a knowledge gap between recording pain and providing adequate pain management in CP-surveillance programmes.

The aims of this study were to assess the prevalence of hip pain over a 5-year period in a population-based cohort of adolescents with CP and to investigate the characteristics and risk factors of hip pain and the interference of such pain with daily activities and sleep.

METHOD

The present study is a longitudinal, population-based study of non-ambulatory adolescents, enrolled in the Norwegian

Cerebral Palsy Follow-Up Program (CPOP),[13] born from 2002 to 2006, with bilateral CP and living in south-eastern Norway. Data on CP diagnosis[14] according to the Surveillance of Cerebral Palsy in Europe[15] and ambulation according to Gross Motor Function Classification System (GMFCS)[16] was retrieved from CPOP.

The study was approved by the Regional Ethics Committee, REC South East (reference 2012/2258 REK). Informed written consent was obtained for 77 participants recruited to the previous study in the period 2013 to 2014.[10] Six participants were lost to follow-up: four had died, one had moved out of Norway, and one had left the CPOP. Thus, 71 participants received a postal invitation to participate in the present data collection during 2019, of whom 67 participated (94%).

Assessment

Information on hip pain was collected from primary caregivers during a structured telephone interview performed by one of the authors (SML). Hip pain was recorded as a dichotomous variable: no pain or pain. If hip pain was present, laterality was noted. Caregivers were asked: 'What is the reason that you believe your child has pain?' The circumstances of hip pain were explored by asking: 'In which situations does hip pain occur?' with an open response, which we classified in pain linked to position (long time in the same position, change of position, during personal care), provoked pain (muscle stretching, palpation, weight bearing on lower limb), and spontaneous pain (at night, dependent on temperature), as proposed by Hodgkinson et al.[7]

The questions on pain from the Child Health Questionnaire (CHQ, Norwegian version)[17] were applied for (1) pain intensity: 'During the last 4 weeks how much hip pain or discomfort has your child had?' with the response alternatives 'none, very mild, mild, moderate, severe, and very severe'; and (2) pain frequency: 'During the last 4 weeks how often did your child have hip pain or discomfort?' with the response alternatives 'none of the time, once or twice, a few times, fairly often, very often, and every day or almost every day' respectively scored 1 to 6. Scores were transformed by an algorithm into a 0 to 100 scale, where 100 indicates no pain.[18] For the purpose of the present study, we categorized hip pain scores 10 to 30 as severe, 40 to 60 as moderate, and 70 to 90 as mild hip pain.

To assess the interference of hip pain with daily activities and sleep, the Brief Pain Inventory (Norwegian version) was utilized.[19] The Brief Pain Inventory uses a numeric rating scale from 0 to 10 for pain interference with function, where 0 indicates no interference. The questions were modified into asking for pain interference over the last 4 weeks.

Caregivers responded if the participant was on intrathecal baclofen (ITB) therapy and other medication for spasticity and pain over the last 4 weeks, and whether hip surgery had been performed. Further details on hip surgery were available from the CPOP.

The latest radiograph of the pelvis and hip joints, taken for CPOP, were transferred to Oslo University Hospital's Picture Archiving and Communication System (PACS; Sectra, Linköping, Sweden) after the interview. If the latest radiograph was taken before 2017, the respondent was asked to permit a new radiograph to be taken. The radiographs were enlarged for better visualization of the landmarks, and measurements were performed digitally by one of the authors (TT). Migration percentage was measured in both hips using Reimers' method.[6] Depending on their migration percentage, the hips were categorized as normal (migration percentage <33%), subluxated (migration percentage 33–89%), or dislocated (migration percentage ≥90%).[13] Further, hip subluxation was categorized as mild (migration percentage 33–39%), moderate (migration percentage 40–49%), and severe (migration percentage 50–89%). Pelvic obliquity was measured as the angle between the horizontal line and the line between the lowest points of the pelvic bones on the right and left side.[20] Further, the presence of deformities of the proximal femur (flattening or deformity of the femoral head and marked shortening or pronounced varus of the femoral neck) was assessed. Sixty-one participants had available radiographs. Three participants had complete hip dislocation on older radiographs. As dislocation is a permanent condition when left untreated, and no hip surgery had been performed, these participants were included in the radiographic evaluation. Three participants had ended the hip surveillance programme. Thus, the radiographic evaluation included 64 of the 67 participants. The median time between radiograph and interview was 5 months before the interviews (range 26mo before the interview to 6mo after the interview on hip pain).

What this paper adds

- Hip pain prevalence increased in adolescents over a 5-year period in a cerebral palsy surveillance programme.
- Risk factors for hip pain were Gross Motor Function Classification System level V and severe hip subluxation.

Statistics

SPSS version 26 (IBM, Armonk, New York, USA) was used for the statistical analysis. A comparison of proportions was analyzed using McNemar's test. Categorical variables were analysed with the Pearson χ^2 test and logistic regression, while continuous variables were analysed with Student's *t*-test, analyses of variance with Scheffe's post hoc test, and with linear regression. For the evaluation of risk factors for hip pain and low CHQ hip pain score, each variable was initially assessed in univariable analyses. Then variables significant at the 0.05 level were included in a multivariable regression analysis. Paired sample *t*-test was used for longitudinal analysis of migration percentage of the most displaced hip. All tests were two-sided. Differences were considered significant when $p<0.05$.

RESULTS

Sixty-seven adolescents (28 females, 39 males; mean age 14y 7mo; SD 1y 5mo; range 12–17y) with bilateral CP,

participated in the study. Fifty-three participants (79%) had a predominant spastic movement disorder, while 14 had dyskinetic CP. GMFCS level distribution was: GMFCS level III 15 (22%), GMFCS level IV 17 (25%), and GMFCS level V 35 (52%). Thirty-two participants were receiving medication for epilepsy and 15 were receiving ITB. Hip surgery had been performed in 47 participants; soft-tissue releases in 21, and bony procedures in 26.

Hip pain was reported in 28 participants and in 44 hips. Pain was bilateral in 16 participants and unilateral in 12. Caregivers reported that 24 participants were able to self-report on pain verbally, 31 participants expressed pain with special sounds and gestures, and 12 caregivers based their answers on observation of behavior during daily routines. Two caregivers were not able to localize pain, and their responses were noted as 'no hip pain'.

There was no significant difference between the prevalence of pain in hips with normal migration percentage and hips with mild or moderate subluxation: 31% and 21% respectively (Table 1). However, the prevalence was significantly higher (p=0.004) in the group of eight patients with severe subluxation (migration percentage 50–89%), where pain was present in eight of the nine subluxated hips. Five of these patients had unilateral severe subluxation (migration percentage 52–75%), unilateral pain in the subluxated hip, and pronounced pelvic obliquity ranging from 5° to 22° with the subluxated side highest (Fig. 1). In the eight hips (five patients) with complete dislocation, hip pain was present in only one hip. Three of these patients had bilateral, painless dislocation, and pelvic obliquity was <6° (Fig. 2).

Patient-related risk factors for hip pain are shown in Table 2. When parameters associated with hip pain were tested in multivariable logistic regression, GMFCS level V was statistically significant, whereas age was not. Migration percentage could not be computed because one of the categories contained no hips. Deformities of the proximal femur were found in 18 of the 128 hips. The plate used for fixation of femoral osteotomy had not been removed in 25 hips. Both femoral deformity and the presence of a femoral plate were significantly associated with hip pain (p=0.006 and p=0.023 respectively). When both these variables were analyzed together with migration percentage and GMFCS in multivariable logistic regression, GMFCS level V and migration percentage 50% to 89% remained as independent risk factors.

Table 1: Association between hip pain and hip migration percentage in 128 hips of 64 adolescents with cerebral palsy

		Hip pain		
Migration %[a]	Number of hips	No hip pain	Hip pain	*p*
All hips	128	86	42	
<33	97	67	30	0.004
33–39	9	7	2	
40–49	5	4	1	
50–89	9	1	8	
90–100	8	7	1	

[a]Three patients did not have available pelvic radiographs.

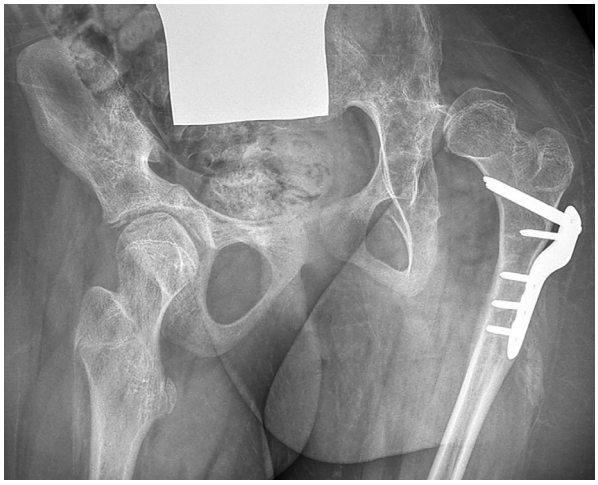

Figure 1: Radiograph of a 14-year-old female with bilateral spastic cerebral palsy in Gross Motor Function Classification System level IV, showing severe subluxation and femoral head deformity of the left hip and marked pelvic obliquity. She had unilateral severe pain in her left hip (Child Health Questionnaire hip pain score 20).

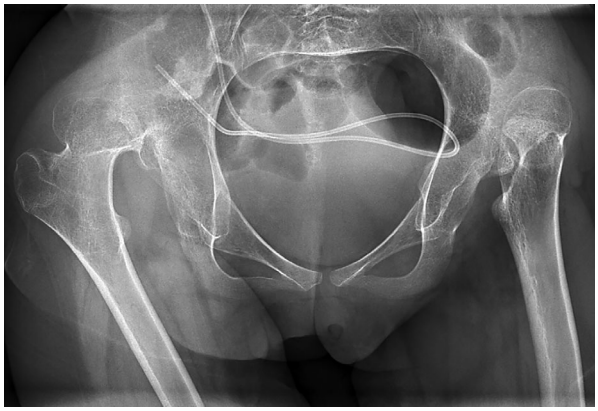

Figure 2: Radiograph of a 14-year old female with bilateral spastic cerebral palsy in Gross Motor Function Classification System level V, with painless bilateral complete hip dislocation, deformity of the right femoral head, and no pelvic obliquity.

In the 28 participants with hip pain, the mean CHQ hip pain intensity score was 3.8 (SD 0.8, range 2–6) and mean frequency score was 4.3 (SD 1.6, range 2–6). Their mean CHQ hip pain score was 40 (SD 21.4). Severe hip pain (score 10–30) was present in 13 patients, whereas 10 had moderate hip pain (score 40–60) and five had mild hip pain (score 70–90). Parameters significantly associated with low CHQ hip pain score were GMFCS level V and migration percentage 50% to 89% (Table 3). In multivariable linear

Table 2: Association between hip pain and possible risk factors for hip pain in 67 adolescents with cerebral palsy

Risk factor	No hip pain	Hip pain	Univariable *p*	Multivariable *p*
Age, y:mo, mean (SD)	14:11 (1:6)	14:2 (1:4)	0.018	0.202
Sex				
Female	15	13	0.514	
Male	24	15		
Predominant movement disorder				
Spastic	31	22	0.928	
Dyskinetic	8	6		
Ambulation				
GMFCS level III	13	2	0.013	0.027
GMFCS level IV	11	6		
GMFCS level V	15	20		
Hip surgery				
No	14	6	0.202	
Yes	25	22		
ITB				
No	31	21	0.664	
Yes	8	7		
Migration %, most displaced hip				
<50%	33	20	0.004[a]	
50–89%	0	6		

Data are number of participants, unless otherwise stated. [a]Multivariable logistic regression could not be computed because one of the categories contained no hips. GMFCS, Gross Motor Function Classification System; ITB, intrathecal baclofen.

Table 3: Association between Child Health Questionnaire (CHQ) hip pain score and clinical and radiographic variables

Variable	CHQ hip pain score	Univariable *p*	Multivariable *p*
Age		0.044	0.267
Sex			
Female	73 (33.8)	0.721	
Male	76 (32.5)		
Predominant movement disorder			
Spastic	75 (33.5)	0.849	
Dyskinetic	76 (31.3)		
Ambulation			
GMFCS level III	96 (11.2)	0.003	0.001
GMFCS level IV	82 (28.1)		
GMFCS level V	63 (35.9)		
Hip surgery			
No	85 (27.0)	0.120	
Yes	71 (34.4)		
ITB			
No	76 (32.2)	0.572	
Yes	71 (35.8)		
Migration %, most displaced hip (*n*=59)			
<50%	77 (32.1)	0.002	0.005
50–89%	33 (22.5)		

Data are mean (SD). GMFCS, Gross Motor Function Classification System; ITB, intrathecal baclofen therapy.

regression, both GMFCS level V and migration percentage 50% to 89% remained as independent risk factors. The mean hip pain score in patients with normal migration percentage was 77 (SD 32.9) and differed significantly from a score of 33 (SD 22.5) in patients with severely subluxated hips (p=0.003).

The mean value of hip pain interference with daily activities was 3.1 (SD 3.1, range 0–10) and the mean interference with sleep was 1.9 (SD 2.6, range 0–9). Parameters significantly associated with high interference of hip pain with daily activities were GMFCS level V (p=0.030) and migration percentage 50% to 89% (p<0.001). In multivariable linear regression, migration percentage 50% to 89% remained as the only independent risk factor (p<0.001). Parameters associated with high interference of hip pain with sleep were GMFCS level V (p=0.003) and migration percentage 50% to 89% (p<0.001). In multivariable regression both factors were statistically significant (p=0.011 and p<0.001 respectively).

Apart from four patients with one circumstance of hip pain, the other 24 patients had between two and eight circumstances in which they experienced hip pain (Table S1, online supporting information). Pain linked to position included 'long time in the same position' in 21 patients, 'change of position' in 20, and 'during personal care' in 21. Pain was provoked by stretching in 11 patients, by palpation in three, and at weight-bearing in six. Spontaneous pain at night was present in 16 patients and in cold weather in three.

Seven of the 28 patients with hip pain receiving ITB used additional pain medication (paracetamol and/or ibuprofen) daily. Four of these seven patients had severe hip pain. Thirteen patients received medication daily either for spasticity (six patients) or for pain (six patients), or a combination of these (one patient), while the remaining eight patients received pain medication either occasionally (two patients) or not at all (six patients).

The results were compared with the corresponding findings of the same individuals 5 years earlier (Table 4). The mean time between assessments was 5 years 1 month (range 3y 8mo–5y 11mo). The prevalence of hip pain had increased (p=0.041) while the mean migration percentage of the most displaced hip was unchanged (p=0.577). Ten participants had undergone hip surgery between the two data collections. The prevalence of bilateral hip pain had increased from four to 16 patients.

DISCUSSION

The prevalence of hip pain increased with increasing GMFCS levels from level III to V. This shows that hip pain was most frequent in non-ambulatory participants, which is in accordance with previous studies.[2,10,11] The prevalence was 35% in patients in GMFCS level IV and 57% in GMFCS level V. The corresponding rates of proxy-reported hip pain were 28% and 44% in the SPARCLE2 study of adolescents aged 13 to 17 years[2] and 8% and 20% in a registry-based study from Sweden.[11] The reason for our higher hip pain rate in GMFCS level V than that of SPARCLE2 is unclear. One obvious reason for the lower hip pain rates in the Swedish study[11] is that

Table 4: Comparison between the present study and the previous study (5 years earlier) of the same cohort (67 patients)

Variables	Present study	Previous study	*p*
Age, y:mo, mean (range)	14:7 (12:0–17:0)	9:6 (7:0–12:0)	
Hip pain, participants	28 (42)	18 (27)	0.041
Hip pain, all hips[a]	44 (33)	22 (16)	0.001
CHQ hip pain score, mean (SD)	75 (33)	N/A	
Hip surgery	47 (70)	41 (61)	0.031
ITB	15 (24)	10 (15)	0.063
Migration %, most displaced hip, mean (SD)[b]	36 (24)	35 (22)	0.577

Data are *n* (%) unless otherwise stated. [a]Total number of hips *n*=134. [b]Available for 64 participants. CHQ, Child Health Questionnaire; N/A, not available; ITB, intrathecal baclofen.

patients with ITB (almost one-sixth of the population in GMFCS levels IV and V) were excluded from the study. Our data showed that hip pain was present in about half the patients with ITB, which indicates that patients receiving ITB should be included in studies on hip pain.

Pain at any site seems to increase with increasing age in children and adolescents with CP.[2] The prevalence of hip pain was higher in children aged 7 to 16 years than in children aged 4 to 6 years.[11] We found no previous study where hip pain was analyzed longitudinally in the same individuals, as was done in the current study. The prevalence of hip pain increased from 27% to 42% over the 5-year period. The prevalence was stable for GMFCS level III (13%), but increased for GMFCS levels IV and V. Since GMFCS levels were unchanged and no significant increase in mean migration percentage over the 5-year period was seen, we have no clear explanation for the increase of hip pain in non-ambulatory children. One possible reason could be the inclusion of questions giving the CHQ hip pain score in the present study.

Similar to the previous study,[10] independent risk factors for hip pain were GMFCS level V and severe subluxation (migration percentage 50–89%). On both occasions, hip pain was not more frequent in hips with mild or moderate subluxation (migration percentage 33–49%) than in hips with normal migration percentage. This means that a migration percentage of <50% is of little or no clinical significance for hip pain and that other causes should be searched for. Marcström et al. reported a higher rate of pain in patients with a migration percentage of ≥40% compared with children with lower migration percentages, but the side of hip pain was not specified.[11] In our patients, severe subluxation was associated with hip pain in all except one hip. Five of these patients had unilateral subluxation and marked pelvic obliquity, with the high side of the pelvis corresponding to the subluxated hip. All except one had undergone surgery for severe hip subluxation before the present study (one femoral osteotomy and three combined femoral and pelvic osteotomies) but had experienced relapse.

The reason for not including the hips with complete dislocation in the group with severe subluxation in the risk factor analysis for pain was that the prevalence of hip pain differed markedly between these two groups. The rate of hip pain in the group with complete dislocation was very low (one out of eight hips). However, our data must be taken with caution since this group contained only five patients. Three of these patients had painless bilateral complete dislocation. Whether this is a chance finding is difficult to know, because we found no previous study where the prevalence of hip pain in adolescents with severe subluxation and complete dislocation was compared. In non-ambulatory adults, the prevalence of hip pain in dislocated hips in studies that were not population-based has been reported to be 29% to 50%.[8,21,22]

Although the aim of hip screening is to avoid severe subluxation and complete dislocation, this aim is not always achieved. However, if not accompanied by pain or pelvic obliquity, hip dislocation does not need to be a significant problem, and the indications for major bony surgery are open to discussion, especially if the dislocation is bilateral. Two of our three patients with bilateral complete dislocation joined the CPOP at a rather late age (9y) and the parents of the third refused hip surgery. Since they had no hip pain, major hip surgery was not advisable. Two patients had complete dislocation in one hip and severe subluxation in the other. One of these patients had relapse of hip displacement after bilateral femoral osteotomies, but no reoperation was performed since he had no hip pain. The parents of the other had refused hip surgery.

Hip pain was also frequent in hips with normal migration percentages, with a rate of 31%, indicating causes other than subluxation. Two possible causes are deformity of the proximal femoral head and/or neck and a persisting femoral plate (we do not routinely remove plates used for osteosynthesis in children with CP). Both these factors were significantly associated with hip pain. In cases of pronounced femoral deformity, proximal femoral resection should be considered if the patient has significant pain. A plate can cause pain over the trochanter region, especially if the plate protrudes laterally, and removal of the plate would be the logical treatment. Patients who have undergone femoral osteotomy should routinely be asked whether they have such pain. Contractures and severe spasticity could also contribute to hip pain.

Previous studies on hip pain in children and adolescents with CP have not evaluated the characteristics and impact of such pain.[2,10,11] Hip pain was moderate to severe in 23 of 28 participants, occurred in more than half the participants during sleep, and in three of four participants during changes of position and personal care. The interference of hip pain with daily activities and sleep was usually mild or moderate, with a trend towards greater interference with daily activities than with sleep.

Despite daily medication for pain and/or spasms, hip pain was still present in 20 patients, indicating that pain management had been insufficient. Pain assessment in our

surveillance programme (CPOP) includes only the presence and location of pain. We suggest the inclusion of additional information on the laterality of hip pain, the CHQ hip pain score and the interference with daily activities in CP surveillance programmes and to use these parameters to develop guidelines on hip pain management.

Mild hip pain (CHQ hip pain score 70–90) should be addressed by the local care team aiming to avoid situations that provoke pain. Further, we suggest a CHQ hip pain score cut-off at 60 (moderate hip pain) for referral to a multidisciplinary team in specialist healthcare, aiming to assess reasons for hip pain, to develop a pain management plan that includes pharmacological treatment, and to revise it regularly. According to the existing CPOP guidelines, patients with displaced hips (migration percentage ≥40%) should be referred to a multidisciplinary evaluation with an orthopaedic surgeon and a child neurologist. A recent study on non-ambulatory patients with severe hip displacement showed that hip surgery had a good effect on hip pain.[20] In particular, patients with unilateral subluxation combined with pelvic obliquity should be offered surgical treatment, including femoral and/or pelvic osteotomies, if their general condition allows such major surgery. In patients with painless bilateral complete dislocation, surgical treatment to relocate hips is hardly indicated.

There are several limitations to this study. First, the number of patients is relatively small. Second, hip pain was only proxy-reported because a high proportion of participants had intellectual disabilities and/or impaired communication skills. It is difficult to find the 'true' prevalence of hip pain in this population because other conditions can be mistaken for hip pain. Third, the assessment was performed by a new investigator, which might have influenced the reliability of the comparison. There are also several strengths of the study. The participants were recruited from a population-based CP surveillance programme and the same 67 individuals were reassessed for hip pain. Characteristics of hip pain, such as intensity, frequency, circumstances, and the interference of hip pain with daily activities and sleep, were performed for the first time in a population-based study.

In conclusion, our findings confirm that hip pain is a considerable problem for non-ambulatory children and adolescents with CP. The main risk factors were GMFCS level V and severe hip subluxation, but pain was also present in almost one-third of non-displaced hips. The prevalence of hip pain increased, which indicates that an action plan on hip pain management should be included in CP surveillance.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

SUPPORTING INFORMATION

The following additional material may be found online:

Table S1. Data on 28 participants with hip pain

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Supplementary Table 1. Data on 28 participants with hip pain

Age, y:mo	Gender	GMFCS	Surgery	ITB	Intensity	Frequency CHQ	Interference on DA	Interference on Sleep	Side of hip pain	MP MP max	MP MP min	Circumstances	Medication
12:2	F	IV	N	N	4	6	20	0	0	B	30	23	1ac	No
12:6	M	V	Y	N	4	6	20	7	3	B	35	12	2abc 3a	B P° I°
12:7	F	V	Y	Y	2	2	80	0	0	B	NA	NA	2abc	P[d] I°
12:8	M	IV	Y	N	3	3	70	1	0	U	73	23	1c 2a 3a	No
12:8	F	III	N	N	2	2	80	0	0	B	15	13	2a	P° I°
12:9	M	IV	Y	Y	4	4	40	2	2	B	23	19	2a 3ab	P° I°
13:1	F	V	Y	N	4	6	20	0	0	B	15	7	1a	No
13:2	M	V	Y	N	4	4	40	3	6	U	48	40	2abc 3ab	No
13:4	F	V	Y	N	4	3	50	3	2	U	61	27	1b 2abc 3a	B P° N°
13:4	M	V	Y	N	5	6	10	4	4	U	30	25	2b 3a	P[d]
13:5	F	V	Y	N	4	6	20	7	7	U	28	21	2abc 3a	G P°
13:10	M	III	Y	N	3	3	60	5	0	U	34	13*	2a	I°
13:10	F	V	Y	N	4	3	50	3	0	B	31	28	1a 2abc 3a	P[d]
14:0	M	V	Y	Y	5	6	10	6	5	U	52	0	2ac 3a	P[d]
14:0	F	V	Y	N	4	6	20	9	9	B	75	73	1abc 2abc 3ab	P[d] I°

14:0	F	V	Y	N	3	6	30	0	0	U	12	0*	2bc	B G
14:2	F	IV	N	N	3	2	70	1	1	B	25	24	1a 2abc 3a	P^{d}
14:4	F	V	Y	N	3	2	70	0	0	B	26	21	1a 2abc	No
14:6	F	V	Y	N	4	6	20	0	1	U	18	17*	1a 2abc 3a	P^{d}
14:11	M	V	N	Y	3	6	30	5	0	B	15	0	1a 2abc	P^{d} I^{d}
15:1	F	IV	Y	N	4	6	20	10	0	U	75	3	1ac 2abc	B P$^{\circ}$ I$^{\circ}$
15:2	M	V	Y	Y	4	6	20	3	1	B	15	10	1ac 2abc 3a	P^{d}
15:2	M	V	Y	N	4	4	40	4	2	B	38	0	1abc 2abc 3a	B P^{d}
15:2	M	V	N	Y	4	3	50	4	2	B	92	74	2bc	P^{d} I^{d}
15:5	M	V	N	N	4	4	40	0	0	B	26	22	2abc	B G
16:1	M	IV	Y	N	3	3	60	0	0	B	31	26	2c	No
16:6	M	V	Y	Y	6	3	30	8	7	U	70	2	2abc 3a	P^{d}
16:7	M	V	Y	N	4	3	50	2	2	U	33	21*	2bc 3a	P^{d} I^{d}

Abbreviations: Age, y:mo, age in years and months. Gender: F, Female; M, Male. GMFCS, gross motor function classification system. Surgery, hip surgery: Y, Yes; N No. ITB, intrathecal baclofen therapy; Y, Yes; N, No. Characteristics of hip pain: raw score for intensity and frequency (0-6, 0-no pain). CHQ, Child Health Questionnaire hip pain score, scale 0 -100. Interference of hip pain on DA, daily activities, and sleep, numeric rating scale 0-10, 0-no interference. Side of hip pain: B, bilateral; U, unilateral. MP, migration percentage: MP max, the highest MP; MP min, the lowest MP; *, unilateral hip pain in hip with the lowest MP. Circumstances, circumstances of hip pain: provoked pain (1) a) hip mobilization/streching, b) palpation, c) weight bearing; pain linked to position (2) a) long time in same position b) at change of position c) during personal care; spontaneous pain (3) a) at night b) at cold weather. Medication last four weeks: B, Baclofen daily, G, gabapentin daily; pain medication: P, paracetamol, I, ibuprofen, N, naproxen; ^{d}, daily; $^{\circ}$, occasionally; No, no medication for spasticity or pain.

III

TITLE

Health-related quality of life in adolescents with cerebral palsy; a cross-sectional and longitudinal population-based study

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SHORT TITLE

HRQoL domains in adolescents with CP

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CONFLICT OF INTEREST

The authors have no disclosure to make.

DATA AVAILABILITY STATEMENT

Data are available on reasonable request from the corresponding author.

ABSTRACT

Aims

The aims of this population-based cross-sectional and longitudinal study were to investigate different aspects of health-related quality of life (HRQoL) in adolescents with cerebral palsy (CP), to define possible changes from childhood to adolescence, and to identify factors associated with low HRQoL in adolescence.

Methods

Proxy-reports of 64 adolescents, aged 12-17 years, with bilateral CP in GMFCS levels III-V participating in a surveillance program, included five of the six domains from the HRQoL instrument Caregivers Priorities & Child Health Index of Life with Disabilities (CPCHILD): (*1) Activities of Daily Living and Personal Care, (2) Positioning, Transfer and Mobility*, (3) *Comfort and Emotions, (5) General Health* and *(6) Overall Quality of Life,* and the two questions on pain from the Child Health Questionnaire (CHQ). Fifty-eight participants (91%) took part in the longitudinal study.

Results

From childhood to adolescence, the mean CPCHILD domain scores decreased slightly in *General Health* and remained unchanged in the other four domains. In the domain *General Health*, the number of medications increased, which was the reason for the score decrease. Pain severity increased significantly. Severe motor impairment was associated with low scores in domains *1, 2, 3* and *5*, and more severe pain with low scores in domains *2, 3, 5* and *6*. A low domain score in childhood was associated with a low score in each corresponding domain in adolescence.

Interpretation

An assessment of HRQoL should be included in CP surveillance programs because this could identify needs for interventions in individuals with severe CP. This study indicates the importance of improved pain management in both children and adolescents with severe CP.

Key messages:

- During transition from childhood to adolescence, the CPCHILD mean domain scores were mainly unchanged in a population with CP in GMFCS III-V
- Severe motor impairment, severe pain in adolescence, and low HRQoL domain score in childhood, were associated with low HRQoL domain scores in adolescence

INTRODUCTION

Nonambulatory children with cerebral palsy (CP) have an increased risk of developing severe musculoskeletal problems like muscle and joint contractures, hip dislocation and scoliosis. These deformities develop slowly over time and can cause pain and problems with sitting balance and nursing care, necessitating surgical and other interventions. It is imperative to evaluate these interventions using appropriate outcome measures. In addition to using only radiographic outcomes, there is a need to use outcome measures that are more important and meaningful to patients and their caregivers. For this reason, instruments evaluating health-related quality of life (HRQoL) have been developed (1, 2).

Quality of life (QoL) is defined by the World Health Organization as an individual's perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards and concerns (3). One definition of HRQoL is 'an individual's perception of various aspects of their lives that they think is affected by a particular medical condition or treatment' (4). Even though QoL and HRQoL are subjective and should be self-reported, it is often difficult or impossible to obtain such reports in populations with severe CP due to accompanying disturbances in cognition and communication (5). There are two broad types of QoL instruments: generic and condition-specific (2). Generic instruments can be used in different clinical populations, whereas condition-specific instruments are designed to assess the characteristics of a particular condition or disability. The condition-specific questionnaire 'Caregiver Priorities & Child Health Index of Life with Disabilities' (CPCHILD) is one of the recommended measures for HRQoL in paediatric populations with CP (2, 6), because it addresses the caregiver's perspective on aspects of health including severe disability. Short-time positive effects on HRQoL of interventions in severe CP, such as hip and spine surgery (7, 8) and intrathecal baclofen therapy (ITB) (9), have been confirmed using the CPCHILD. Although HRQoL surveillance may also be helpful in defining areas of health concern at the population level, assessment of HRQoL is usually not incorporated in surveillance programs for CP, and we have not been able to retrieve any previous population-based longitudinal studies on HRQoL.

There is no consensus regarding which factors are associated with HRQoL in persons with severe CP. Still, pain has been shown to be a risk factor for poor QoL and HRQoL in several studies (10-13). Further, higher age was associated with lower HRQoL in a cross-sectional study (11), and more severe motor impairment was found to be associated with low HRQoL in adults (13), but differing results have been reported in children and adolescents (10, 11, 14,

15). Thus, more research about associations is needed. Moreover, HRQoL data from population-based surveillance of individuals with CP would be useful for an assessment of changes with age, for further surveillance program development, and for comparison with studies on the effects of various interventions.

The aims of this population-based cross-sectional and longitudinal study were to investigate different aspects of HRQoL in adolescents who followed a CP surveillance program, to define possible changes from childhood to adolescence, and to identify factors associated with low HRQoL in adolescence.

METHODS

Study design and population

This study has both a cross-sectional and a longitudinal design. All 136 eligible young persons, born 2002-2006, living in South-Eastern Norway, enrolled in the Norwegian Quality and Surveillance Registry for Cerebral Palsy (NorCP) (16), with bilateral CP and in Gross Motor Function Classification System (GMFCS) levels III-V (17), were invited to participate in the study in 2013-2014 (15, 18). The study was approved by the Regional Ethics Committee, South-East Norway (2012/2258 REK).

Measures

The data were collected twice, in "childhood" at age 7-12 years in 2013-2014, and in "adolescence" at age 12-17 years in 2019. Data on the CP diagnosis according to Surveillance of Cerebral Palsy in Europe (SCPE) (19), communication function according to the Communication Function Classification System (CFCS) (20), gross motor function according to GMFCS (17), and data on hip and scoliosis surgery and intrathecal baclofen therapy (ITB), were retrieved from NorCP (16).

Data were collected through questionnaires sent by surface mail, and in parallel with a study on pain which included a telephone interview (21). Primary caregivers responded to the CPCHILD questionnaire (1, 22), a condition-specific instrument for the assessment of HRQoL developed for populations with disabilities, such as severe CP, aged 5-18 years (2, 6). Also, the Scandinavian CPCHILD caregiver version has proven to be a sound and valid proxy measure for evaluation and comparison of HRQoL in paediatric populations with CP (23). It consists of six domains: *Activities of Daily Living/Personal Care* (*Personal Care*, 9 items); *Positioning, Transfer and Mobility* (*Positioning*, 8 items); *Comfort and Emotions* (9 items);

Communication and Social Interaction (*Communication*, 7 items); *General Health* (3 items); and *Overall Quality of Life* (*Overall QoL*, 1 item). The domain scores vary from 100 (best) to 0 (worst). The CPCHILD manual provides reference domain scores for CP, GMFCS level V (22). We omitted the domain *Communication* because it was omitted five years earlier (15).

Proxy-reported pain severity according to the two questions on pain in the Child Health Questionnaire (CHQ, Norwegian version) (24) was recorded for the most severe recurrent pain. The questions were: (a) 'During the past four weeks how much bodily pain or discomfort has your child had,' with the response alternatives 'none, very mild, mild, moderate, severe and very severe', and (b) 'During the past four weeks how often has your child had bodily pain or discomfort,' with the response alternatives 'none of the time, once or twice, a few times, fairly often, very often, and every day or almost every day', and were given scores from 1 to 6, respectively. Raw scores were transformed by an algorithm into a single CHQ pain score for pain severity on a 0-100 scale, where 100 indicated no pain (25).

Statistics

SPSS version 27 (IBM, Armonk, New York, USA) was used for the statistical analyses. Data were presented as frequency (%), mean (SD), range or median (range). In longitudinal analyses, mean differences were analyzed with paired samples t-test. For the analyses of factors associated with HRQoL, each of the five CPCHILD domains were analyzed with univariable linear regression for age, sex, predominant movement disorder, GMFCS level, CHQ pain score in adolescence, and for the respective CPCHILD domain score in childhood. Variables with a p-value < 0.1 were analyzed with multivariable linear regression in three models: Model 1 (Basic) included age, sex, predominant movement disorder and GMFCS level. Model 2 (Pain) included variables from Model 1 plus CHQ pain score in adolescence. Model 3 (Longitudinal) included variables from Model 2 plus the corresponding CPCHILD domain score in childhood. Normality of residuals was found to be satisfied. All tests were 2-sided. Differences were considered significant if $p<0.05$. We did not perform imputation of missing domain scores, but excluded participant from the longitudinal analysis in the respective domain.

RESULTS

Seventy-seven of 136 eligible children contributed with childhood data. Six of the 77 participants were lost to follow-up; four died, one emigrated and one left the CP surveillance program. Thus, 71 participants received a postal invitation to participate in adolescence.

Forty-five caregivers responded in written form. Since telephone interview was utilized to collect data on pain, 19 caregivers chose to respond verbally on CPCHILD and CHQ pain questions, giving 64 (90% respondent rate) participants in adolescence. Fifty-eight of the 64 participants (91%) had CPCHILD assessment in childhood, thus comprising a longitudinal sample. All 64 participants had CHQ pain assessment twice. There were no significant differences between 64 participants and 72 non-participants in sex, predominant movement disorder and GMFCS level (Table 1). Characteristics of the participants and their primary caregivers are available in Supplementary Table 1. The mean age of 64 adolescents was 14 years, 6 months (SD 1 year, 5 months). The median time between the two data collections was 5 years, 4 months (range 4 years, 3 months to 5 years, 9 months). The respondent at the two time-points was the same primary caregiver in 54 participants (93%).

The completeness of the response to the CPCHILD items varied from 92 to 100%; the lowest response rate was on the two questions on 'emotions' in domain *Comfort and Emotions* (92% and 94%). There were no significant differences in domain scores between the participants with regard to the response form that was used (written vs. verbal). Three of 58 participants (5%) had missing values in domain scores in childhood.

Cross-sectional study in adolescence

Mean CPCHILD domain scores varied from 43 (*Personal Care*) to 76 (*Comfort and Emotions*) (Table 2). Compared with the data in the CPCHILD manual (22), participants in GMFCS level V in the present data collection had 7-8 points higher mean domain scores in the domain *Personal Care, Positioning* and *Overall QoL* than the scores given in the manual (22) (Table 3). The difference was less than 3 points in the domains *Comfort and Emotions* and *General Health*. There were no significant differences in domain scores whether or not the participants in GMFCS level V had ITB treatment (data not shown).

Longitudinal comparison between childhood and adolescence

There were no significant differences in the mean domain scores between childhood and adolescence, except for *General Health*, which decreased (Table 2). The mean score for item 36 in *General Health* (Medication used last two weeks) decreased significantly from 47 (SD 39) to 37 (SD 41; p=0.001), while there were no significant changes in the other two items' scores. Forty-four participants had an increase in the number of medications, four had a reduction, and ten had no change, while five used no medication at both data collections. The number of participants who had started using medications between the data collections were

(in parenthesis): analgesics such as paracetamol, ibuprofen and/or naproxen (17), laxatives (13), anti-spasticity medication (8), ITB (5), anti-gastro-esophageal reflux medication (6), medication for sleep problems (5), inhalation medication for asthma (5), vitamins (5), medication for urinary tract problems (3), and allergy medication (3).

The mean CHQ pain score decreased from 64 (SD 29) in childhood to 43 (SD 26) in adolescence in 64 participants ($p < 0.001$).

Factors associated with low HRQoL in adolescence

Possible factors associated with low CPCHILD domain scores are shown in Table 4. Sex and predominant movement disorder had $p > 0.1$ in univariable analyses in all five domains and were not included in the three multivariable regression models.

In Model 1 (Basic), severe motor impairment (high GMFCS level) was associated with low scores in all domains except *Overall QoL*. Higher age was associated with low domain scores in *Comfort and Emotions.*

In Model 2 (Pain), more severe pain (lower CHQ pain score) and severe motor impairment were associated with low scores in *Positioning, Comfort and Emotions,* and *General Health.* Severe pain was associated with low scores in domain *Overall QoL.* Severe motor impairment was associated with low scores in *Personal Care.*

In Model 3 (Longitudinal), for all CPCHILD domains a low score in childhood (5 years earlier) was associated with a low score in the corresponding domain in adolescence. More severe pain (lower CHQ pain score) was associated with low scores in all domains except *Personal Care.* Severe motor impairment was associated with low scores in *Personal Care* and *Positioning.* In Model 3, the proportion of explained variances (R^2) varied from 33% in domain *Overall QoL* to 63% in domain *General Health*.

DISCUSSION

The main findings of the present population-based study of adolescents with CP, 12-17 years old, GMFCS III-V were that HRQoL measured by five CPCHILD domains was mainly unchanged over a 5-year period from childhood to adolescence and that the most important factors associated with low HRQoL domain scores were severe motor impairment, pain severity, and corresponding HRQoL domain score in childhood.

There was a good accordance between the CPCHILD domain scores of our participants in GMFCS level V and previous studies. The corresponding mean domain values at GMFCS

level V in the CPCHILD manual (22) differed from our results in three domains *Personal Care*, *Positioning* and *Overall QoL*, but not in the remaining two domains. The Scandinavian validation study of CPCHILD (23) with populations recruited from surveillance programs also showed good agreement with the present results, as the mean differences in domain scores were 2-5 points in *Comfort and Emotions* and *General Health* and 6-11 points in the other three domains. In a study using the CPCHILD in patients scheduled for scoliosis surgery, Miyanji et al. (8) reported mean preoperative domain scores, which were similar to our results in adolescence. We found no significant differences in mean domain scores when participants in GMFCS level V receiving ITB were excluded from the analyses, confirming that the inclusion of participants receiving ITB did not violate the generalizability of the study. There was no information on the use of ITB in the CPCHILD manual (22) or in the Scandinavian validation study (23).

The domain *General Health* score deteriorated over the five-year period whereas the other four domain scores did not change significantly. Despite pain increase from childhood to adolescence over five years in the study population (21), mean score in domain *Comfort and Emotions* was unchanged. Considering that seven of nine items within the domain ask for pain or discomfort, this might indicate that the *Comfort and Emotions* construct is less sensitive to pain changes than the two CHQ pain questions. This is a reminder to always consider the properties of available questionnaires when designing a study. The domains *Personal Care* and *Positioning* ask for a grading of performance and assistance in the activities of daily living (22). The two domain scores were unchanged from childhood to adolescence, indicating that availability of devices and help from caregivers remained stable. The domain score in *Overall QoL* was also unchanged from childhood to adolescence. This domain is a complex and existential concept, which in CPCHILD is based on a single item; thus, the score seems to be of questionable reliability in contrast to QoL questionnaires that include several items and domains. The mean score of 66 indicates a quite high degree of well-being. This could be caused by the 'disability paradox', which means that people with significant health problems can be highly satisfied with some aspects of their lives. In accordance with this, a study of adults with moderate or severe disabilities found that more than half of the individuals reported excellent or good QoL (26).

The CPCHILD domain *General Health* is defined by three items: the frequency of visits to hospital, grading of general health during the last two weeks, and the number of medications taken. Only the item score on medication decreased from childhood to adolescence. One could argue that increased number of medications does not necessarily reflect a decrease in

general health. If the increased medication had a positive effect for the patient, it would imply an improved health. *General Health* in CPCHILD is not possible to compare directly to other instruments because of differences in the construct.

Due to the lack of longitudinal observational studies on HRQoL using CPCHILD, we searched also for studies on QoL. In contrast to our findings, Rapp et al. (12) reported a change in several QoL domains in children over five years as measured by KIDSCREEN (27). QoL decreased in six domains and was stable in three (*Physical wellbeing, Autonomy,* and *Social acceptance*). Still, Vargus-Adams (28) reported a decline in the domain *Health* as measured by CHQ, but the observation time was only one year.

In the analyses of factors associated with HRQoL, we used three multiple regression models. With regard to the association between high motor impairment and low HRQoL, our findings confirmed the findings regarding the domains *Personal Care, Positioning, Comfort and Emotions* and *General Health* in childhood (15), but GMFCS level V was no longer associated with low domain scores in *Overall QoL*. An association between high motor impairment and low HRQoL was also reported in a Swedish study in adults (13) and a Dutch study in children (14). However, these findings were not consistent with those of Findlay et al. (11) who reported no association between GMFCS levels and HRQoL. A direct comparison is difficult because of differences in outcome measures, age groups, and GMFCS levels. In contrast, the association between high pain severity and low HRQoL domain scores was in line with the results of previous studies on QoL and HRQoL in both paediatric (11, 12, 29) and adult populations (13) despite different pain measures. Rapp et al. (12) used pain severity during the previous week and Findlay et al. (11) used pain that interfered with daily activities. Elema et al. (29) used transformed scores from the CPCHILD items on pain in the domain *Comfort and Emotions*. We used a pain severity score based on pain intensity and frequency during the previous four weeks to capture the severity of recurrent pain. Since our sample consisted of individuals with substantial activity limitations, we wanted pain to be considered independent of activities. We also wanted to include all pain and therefore applied a continuous pain severity measure. In our study, more severe pain in adolescence was associated with low scores in all CPCHILD domains except *Personal Care* which is in line with the findings of Elema et al. (29). Low domain scores in childhood were associated with low domain scores in each corresponding HRQoL domain in adolescence, which is in line with the European multicenter studies on both self-reported (10) and parent-reported QoL (12). These findings are a reminder that an early focus on pain and HRQoL is important in CP surveillance. On explained variance, the proportion increased with the introduction of CHQ

pain score and the domain scores from childhood. However, low values in *Personal Care* and *Overall QoL* indicate that additional factors should be considered in future studies.

There were some limitations to this study. First, our population sample was small. Second, the research was based only on proxy-reports. This was necessary because we wanted to investigate a whole paediatric cohort with severe CP without excluding those who were not able to self-report. Responses to questions on emotions were missing more often than those on other questions despite the fact that all the informants were primary caregivers. One reason could be that even primary caregivers had difficulties to interpret the emotions in adolescents with impaired cognition and communication. Third, we omitted the domain *Communication* from the data collection in adolescence because this domain had been omitted at the data collection in childhood. The reason was that our previous study (15) focused on the association between hip displacement and HRQoL domain scores, and we considered this domain was less relevant for that issue. However, the domain *Communication* was rated as highly important in the initial development of CPCHILD (1) and upon reflection we should have included it.

There were also several strengths of this study. The participants were recruited from a population-based CP registry with high data correctness (100%) and completeness (76%) (30). There were no significant differences between responders and non-responders in childhood (18), nor in adolescence, which ensured the generalizability of our findings. Further, the response rate of 90% in adolescence was high. The reason for this was probably that we did not have to rely on postal responses, because a parallel study included a telephone interview (21). We also secured that the same proxy-reporter responded at both time-points. This minimizes variability due to proxy-reporters' personal factors.

The clinical implication of the present findings is that lower HRQoL is a considerable challenge in children and adolescents with severe CP. We propose to include HRQoL assessment in CP surveillance programs because this could identify needs for interventions, such as mobility and communication assistive devices and timely medical and surgical treatment. This study also adds to the evidence base indicating the importance of improved pain management in both children and adolescents with severe CP.

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Table 1. Comparison of participants and non-participants				
		Participants	Non-participants	P-value
Number, n		64	72	
Sex				
	Female	26 (40.6)	45 (62.5)	0.709
	Male	38 (59.4)	27 (37.5)	
Predominant movement disorder				
	Spastic	50 (78.1)	51 (70.8)	0.318*
	Dyskinetic	14 (21.9)	18 (25.0)	
	Ataxic	0 (0)	3 (4.2)	
Motor impairment according to GMFCS				
	GMFCS level III	13 (20.3)	19 (26.4)	0.679
	GMFCS level IV	16 (25.0)	18 (25.0)	
	GMFCS level V	35 (54.7)	35 (48.6)	
Statistics: Pearson chi2 test. *Fisher's exact test.				

Table 2 CPCHILD domain scores in adolescence in cross-sectional sample and in childhood and adolescence in longitudinal sample of young people with CP

	Cross-sectional sample Adolescence N=64	Longitudinal sample*			
		Adolescence	Childhood	Mean.diff (95%CI)	p-value
Domain 1: Activities of Daily living and Personal care*					
All participants	43 (14.7)	43 (14.8)	42 (14.6)	1.9 (-2.3 to 6.2)	0.368
GMFCS III	56 (17.7)	58 (16.7)	49 (16.8)	8.7 (-1.7 to 19.1)	0.091
GMFCS IV	42 (17.8)	44 (18.9)	44 (12.3)	0.7 (-8.7 to 10.0)	0.878
GMFCS V	39 (8.0)	38 (7.5)	38 (13.9)	0.1 (-5.7 to 5.9)	0.974
Domain 2: Positioning, Transfer and Mobility*					
All participants	44 (17.0)	44 (17.0)	40 (17.3)	3.5 (-0.5 to 7.5)	0.082
GMFCS III	67 (11.9)	66 (12.6)	61 (12.3)	4.5 (-4.7 to 13.6)	0.302
GMFCS IV	45 (15.6)	45 (16.1)	40 (12.6)	5.1 (-1.3 to 11.5)	0.107
GMFCS V	35 (10.2)	35 (10.3)	33 (14.3)	2.5 (-3.8 to 8.7)	0.424
Domain 3: Comfort and Emotions					
All participants	76 (18.2)	75 (18.5)	72 (18.3)	3.4 (-2.2 to 8.9)	0.233
GMFCS III	87 (12.1)	85 (12.6)	86 (8.8)	-0.6 (-6.6 to 5.5)	0.837
GMFCS IV	81 (14.9)	82 (14.3)	75 (11.9)	7.8 (-0.3 to 15.8)	0.058
GMFCS V	69 (19.1)	69 (19.6)	66 (20.2)	2.8 (-6.5 to 12.1)	0.543
Domain 5: General Health					
All participants	65 (22.9)	65 (23.5)	70 (23.2)	-5.4 (-10.0 to -0.8)	0.021
GMFCS III	90 (7.5)	91 (7.5)	95 (4.0)	-3.6 (-9.8 to 2.6)	0.221
GMFCS IV	68 (22.8)	68 (23.6)	80 (15.8)	-11.7 (-19.5 to -3.8)	0.007
GMFCS V	55 (19.7)	54 (19.8)	58 (21.3)	-3.4 (-10.7 to 3.9)	0.345
Domain 6: Overall Quality of life					
All participants	66 (20.7)	66 (21.3)	66 (26.3)	0.0 (-6.5 to 6.5)	1.000
GMFCS III	75 (18.5)	76 (19.6)	82 (18.9)	-5.5 (-22.5 to 11.6)	0.493
GMFCS IV	66 (15.9)	66 (16.5)	73 (18.6)	-7.1 (-14.5 to 0.2)	0.055
GMFCS V	62 (22.6)	63 (23.0)	58 (28.4)	4.8 (-4.9 to 14.6)	0.317

Data are mean (SD). Mean difference is mean score in adolescence (age 12-17 years) minus mean score in childhood (age 7-12 years). *Number of paired sample tests varied from 56 to 58 due to missing values in childhood. In domain 1: N=11 in GMFCS III, N= 13 in GMFCS IV and N=32 in GMFCS V. In domain 2: N=11 in GMFCS III, N= 14 in GMFCS IV and N=31 in GMFCS V. In domain 3: N=11 in GMFCS III, N=14 in GMFCS IV and N=33 in GMFCS V. In domain 5: N=11 in GMFCS III, N=14 in GMFCS IV and N=33 in GMFCS V. In domain 6: N=11 in GMFCS III, N=14 in GMFCS IV and N=33 in GMFCS V.

GMFCS, Gross Motor Function Classification System.

Table 3. CPCHILD domain scores for participants in GMFCS level V and corresponding scores given in the CPCHILD manual.

CPCHILD Domain	Data collection*		CPCHILD manual n=35
	Adolescence	Childhood	
1: Activities of Daily Living and Personal Care	39 (8)	38 (14)	31 (15)
2: Positioning, Transfer and Mobility	35 (10)	33 (14)	28 (14)
3: Comfort and Emotions	69 (19)	66 (20)	68 (23)
4: Communication and Social interaction	Not examined	Not examined	43 (24)
5: General Health	55 (20)	58 (21)	57 (17)
6: Overall Quality of Life	62 (23)	58 (28)	55 (25)

Data are mean (SD). *In adolescence N=35 in five examined CPCHILD domains. In childhood N varied from 31 to 33; domain 1: N=32, domain 2: N=31, domain 3: N=33, domain 5: N=33, domain 6: N=33.

CPCHILD, Caregiver Priorities & Child Health Index of Life with Disabilities

Table 4. Analyses on possible factors associated with HRQoL domain scores using three stepwise regression models

	Univariable analyses B non-adjusted (95% CI) p-value	Model 1 Multivariable B adjusted (95% CI) p-value	Model 2 Multivariable B adjusted (95% CI) p-value	Model 3 Multivariable B adjusted (95% CI) p-value
Domain 1: Activities of Daily Living and Personal Care				
Age	2.61 (0.11 to 5.12) 0.041	2.00 (-0.32 to 4.32) 0.089	1.41 (-1.12 to 3.95) 0.270	1.34 (-1.19 to 3.88) 0.292
GMFCS	-8.00 (-12.18 to -3.81) <0.001	**-7.47 (-11.64 to -3.31) 0.001**	**-7.14 (-11.33 to -2.94) 0.001**	**-7.12 (-11.52 to -2.71) 0.002**
CHQ pain score in adolescence	0.16 (0.02 to 0.29) 0.028	-	0.08 (-0.06 to 0.22) 0.262	0.05 (-0.09 to 0.19) 0.478
Respective domain score in childhood	0.42 (0.17 to 0.67) 0.002	-	-	**0.27 (0.03 to 0.51) 0.028**
R^2	-	0.23	0.25	0.36
Domain 2: Positioning, Transfer and Mobility				
Age	1.72 (-1.25 to 4.69) 0.252	-	-	-
GMFCS	-14.79 (-18.65 to -10.93) <0.001	**-14.79 (-18.65 to -10.93) <0.001**	**-13.90 (-17.68 to -10.12) <0.001**	**-9.65 (-14.50 to -4.79) <0.001**
CHQ pain score in adolescence	0.23 (0.07 to 0.38) 0.005	-	**0.15 (0.03 to 0.26) 0.016**	**0.16 (0.04 to 0.27) 0.007**
Respective domain score in childhood	0.61 (0.40 to 0.82) <0.001	-	-	**0.31 (0.08 to 0.53) 0.008**
R^2	-	0.49	0.53	0.59
Domain 3: Comfort and Emotions				
Age	4.04 (0.99 to 7.09) 0.010	**3.38 (0.49 to 6.27) 0.022**	0.84 (-1.92 to 3.60) 0.546	0.38 (-2.60 to 3.36) 0.800
GMFCS	-9.00 (-14.30 to -3.69) 0.001	**-8.11 (-13.29 to -2.93) 0.003**	**-6.65 (-11.21 to -2.09) 0.005**	-4.07 (-9.27 to 1.12) 0.122
CHQ pain score in adolescence	0.41 (0.26 to 0.55) <0.001	-	**0.35 (0.19 to 0.50) <0.001**	**0.38 (0.22 to 0.53) <0.001**
Respective domain score in childhood	0.34 (0.08 to 0.60) 0.010	-	-	**0.24 (0.004 to 0.47) 0.046**
R^2	-	0.23	0.42	0.49
Domain 5: General Health				
Age	0.69 (-3.35 to 4.74) 0.733	-	-	-
GMFCS	-16.57 (-22.49 to -10.66) <0.001	**-16.57 (-22.49 to -10.66) <0.001**	**-15.15 (-20.92 to -9.39) <0.001**	-4.60 (-11.14 to 1.94) 0.164
CHQ pain score in adolescence	0.32 (0.11 to 0.53)	-	**0.23 (0.05 to 0.41)**	**0.26 (0.11 to 0.41)**

	0.003		**0.012**	**0.001**
Respective domain score in childhood	0.73 (0.54 to 0.92) <0.001	-	-	**0.60** **(0.38 to 0.82)** **<0.001**
R^2	-	0.34	0.40	0.63
Domain 6: Overall Quality of Life				
Age	3.15 (-0.42 to 6.71) 0.083	2.70 (-0.85 to 6.25) 0.133	0.73 (-2.99 to 4.45) 0.695	0.98 (-2.74 to 4.70) 0.599
GMFCS	-6.20 (-12.56 to 0.16) 0.056	-5.49 (-11.86 to 0.87) 0.090	-4.36 (-10.51 to 1.79) 0.162	-0.05 (-6.68 to 6.58) 0.988
CHQ pain score in adolescence	0.31 (0.12 to 0.50) 0.001	-	**0.27** **(0.06 to 0.48)** **0.012**	**0.22** **(0.02 to 0.42)** **0.030**
Respective domain score in childhood	0.39 (0.20 to 0.58) <0.001	-	-	**0.35** **(0.15 to 0.55)** **0.001**
R^2	-	0.09	0.18	0.33
Univariable analyses for variables age, sex (p>0.1), predominant movement disorder (p>0.1), GMFCS and CHQ pain score in adolescence were performed with 64 participants. Univariable analyses for domain scores in childhood and multivariable regression analyses in Model 3 were performed with 56-58 participants due to three missing values in domain scores in childhood				
GMFCS, Gross Motor Function Classification System. CHQ, Child Health Questionnaire.				

Supplementary Table 1. Characteristics of participants in adolescence (in cross-sectional and longitudinal sample) and characteristics of their primary caregivers			
		Cross-sectional sample	Longitudinal sample
Participants, n		64	58
Age, y:mo			
	Mean (SD)	14:6 (1:5)	14:6 (1:5)
	Range	12:2-17:0	12:5 - 17:0
Sex			
	Female	26 (41)	24 (41)
	Male	38 (59)	34 (59)
Predominant movement disorder			
	Spastic	50 (78)	46 (79)
	Dyskinetic	14 (22)	12 (21)
Communication according to CFCS			
	CFCS level I	5 (8)	5 (9)
	CFCS level II	9 (14)	8 (14)
	CFCS level III	2 (3)	2 (3)
	CFCS level IV	13 (20)	11(19)
	CFCS level V	21 (33)	20 (35)
	Nor known	14 (22)	12 (21)
Motor impairment according to GMFCS			
	GMFCS level III	13 (20)	11 (19)
	GMFCS level IV	16 (25)	14 (24)
	GMFCS level V	35 (55)	33 (57)
Intrathecal baclofen therapy		15 (23)	14 (24)
	Before first data collection	10	9
	Between data collections	5	5
Anti-epileptic drug therapy		32 (50)	28 (48)
Hip surgery		45 (70)	43 (74)
	Before first data collection	40	38
	GMFCS level III	8	8
	GMFCS level IV	7	6
	GMFCS level V	25	24
	Between data collections	9	9
	GMFCS level IV	1	1
	GMFCS level V	8	8
Scoliosis surgery		8 (13)	6 (10)
	Before first data collection	1	0
	Between data collections	7	6
Primary caregivers			
Age, y:mo			
	Mean (SD)	46:6 (5:10)	46:6 (6:0)
	Range	28:3 – 59:7	28:3 – 59:7

Sex			
	Female	55 (86)	50 (86)
	Male	9 (14)	8 (14)
Parental relationship to the participant			
	Biological parent	55 (86)	50 (86)
	Foster/adoptive parent	4 (6)	4 (7)
	Professional worker	5 (8)	4 (7)
Data are n (%), unless stated otherwise.			
CFCS, Communication Function Classification System. GMFCS, Gross Motor Function Classification System.			

IV

Title: Frequency of general practitioner consultations and pain as a reason for encounter in children with cerebral palsy; a Norwegian national registry linkage study

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Short title: GP consultations and pain in children with cerebral palsy

Key points:

- Children with CP do not meet their GP more often than children in the general population do
- GPs perform more administrative work for children with CP than for their other paediatric patients
- GPs code pain as a RFE less frequently in consultations with children with CP than in consultations with children in the general population

Abbreviations

GP General Practitioner

ICPC-2 The International Classification for Primary Care, 2nd Revision

KUHR The Norwegian Directorate of Health's database for the control and reimbursement of health expenses

NorCP The Norwegian Quality and Surveillance Registry for Cerebral Palsy

RFE Reason for encounter

Abstract

Objective

The aim was to compare the frequency of daytime contacts, and pain as a reason for encounter (RFE) with a general practitioner (GP), in children with cerebral palsy (CP) to that of the general paediatric population.

Design

Linkage study of two national registries

Setting

The study investigates daytime contacts in the period 2006 to 2018 using the Norwegian Directorate of Health's database for the control and reimbursement of health expenses. Children with CP were identified using linkage to the Norwegian Quality and Surveillance Registry for Cerebral Palsy (NorCP).

Subjects

All children born 1996 to 2012 who contacted a GP were included. Children with CP registered in NorCP were cases and children not registered in NorCP were controls.

Main outcome measures

Frequencies of all daytime contacts, including consultations and administrative contacts were analyzed. International Classification for Primary Care was applied for RFE. Frequencies of consultations with pain as a RFE were analyzed.

Results

Cases accounted for 0.46% of all daytime contacts and 0.27% of all daytime consultations, the latter corresponding with the estimated national prevalence of CP. GPs registered more

administrative contact and coded pain as a RFE less frequently in consultations with cases (6%) than with controls (12%).

Conclusion

Children with CP did not consult a GP more often than the general paediatric population did. In consultations, GPs should ask for pain even if the child with CP or parent does not address pain. The local multidisciplinary team should encourage the family to consider consulting a GP if the child is in pain.

Key words: child health, cerebral palsy, disability, primary health care, pain, reason for encounter, health registry

Introduction

An increasing number of children live with chronic health conditions (1) requiring measures from a variety of health care providers (2). In Norway, the health authorities affiliate every citizen with a general practitioner (GP) whom one can consult for current medical needs and who interacts both with other locally based professionals and with specialist care when necessary. The GPs' position is unique and makes the GP a cornerstone in the network of care recommended for management of chronic medical conditions. This continuity of primary care is associated with both lower morbidity and mortality in the general population (3). Children under the age of 16 years do not pay a consultation fee, while for patients above 16 years an upper limit for personal annual health care costs is set (4). This ensures affordable medical services for all inhabitants. Still, knowledge on GPs' involvement in the management of chronic health conditions is scarce. Pain, both acute and chronic, is a health complaint managed often by Norwegian GPs (5).

Cerebral palsy (CP) is the most common chronic motor disorder in children (6), often accompanied by disturbances in sensation, perception, cognition, communication and behavior, epilepsy and secondary musculoskeletal problems (7). The great variety of impairments and medical needs in CP, together with the emerging insights in disease trajectories from CP surveillance programs, makes CP a relevant model health condition in exploring GPs' involvement in the care for children with chronic health conditions.

Pain is more common in children with CP than in the general paediatric population as about three of four children with CP are in pain (8, 9), in contrast to about one in five to one in six in the general paediatric population (10, 11). While headache and abdominal pain top the pain sites list in the general paediatric population (11), musculoskeletal pain is dominating in the population with CP (12-14). Causes of musculoskeletal pain in CP are

muscle overuse, immobilization, strain caused by involuntary movements, atypical compression from the imbalance of muscle activation across joints and their combinations (15). Further, abdominal pain has a high prevalence in children with severe CP (13). The current opinion is that the high prevalence of pain in CP reflects health care deficiencies (16, 17), and that studies on pain management are needed (18) to inform initiatives which aim to decrease pain.

In the present study, we compared the frequency of daytime GP contacts, and pain as a reason for encounter (RFE) in children with CP to that of the general paediatric population. The null hypotheses were:

1. The frequency of daytime paediatric consultations for all reasons is not affected by CP diagnosis
2. The frequency of daytime paediatric consultations because of pain is not affected by CP diagnosis
3. The frequencies of daytime paediatric consultations because of headache, abdominal, and musculoskeletal pain, are not affected by CP diagnosis.

Materials and Methods

Study design

The study compares a registry-based cohort of children with CP (cases) to the general population of the same age (controls), linking two national databases: KUHR, the Norwegian Directorate of Health`s database for the control and reimbursement of health expenses (19), and the Norwegian Quality and Surveillance Registry for Cerebral Palsy (NorCP) (20).

Data sources

World Health Organization (WHO) accepts International Classification for Primary Care (ICPC-2) as a RFE classification in primary care or general practice wherever applicable (21). The World Organization of Family Doctors (Wonca) owns ICPC-2, and its use is license-based. ICPC-2 has been in use since 1998 in Norway, and in electronic format since 2002 (22). The last revision of ICPC-2 was in 2003, and the KUHR registry holder assumes correct use of the electronic version as of 2006. ICPC-2 consists of 17 chapters on organ systems. Each chapter includes codes for symptoms and complaints (numbers 01 to 29), process codes (numbers 30 to 69) and disease codes (numbers 70 to 99).

In Norway, GPs have an agreement on reimbursement of health expenses from the government through the KUHR database (19). Reimbursement requires registration of the type of contact and at least one ICPC-2 code. The age at each contact is registered automatically due to the use of the national personal identification number.

Since 2004, all children with CP in Norway, born 1996 and later, are invited to register in NorCP and follow a CP surveillance program. CP diagnosis is confirmed by a paediatrician at the age of five years according to the algorithm given by the Surveillance of Cerebral Palsy in Europe (23). Children with CP were identified in KUHR using the national personal identification number applied in both databases. To ensure a confirmed CP diagnosis, children born later than 2012 were not included in the study.

Study population

All children born 1996-2012 registered in KUHR in the period 2006-2018 were included. Children registered in NorCP were cases, and children not registered in NorCP were controls.

Variables

All contacts during afternoon and night, holidays and weekends were excluded in order to focus on GPs' daytime work only. Outcome variables were number and type of GP daytime contacts, and number of ICPC-2 codes considered to reflect pain as a RFE.

Contacts during daytime were grouped using mutually exclusive reimbursement codes. Physical or electronic encounters with a GP (the latter in use from 2013), were labelled consultations, while activities not requiring direct contact between the GP and the patient were labelled administrative contacts. The latter include simple contacts (patient's attendance at the medical center not meeting the GP), GPs' interdisciplinary interactions with other professionals in primary care such as a meeting or a telephone call, referrals without consultation, and prescription renewals (in use from 2011 as a separate reimbursement code).

Analysis on pain as a RFE was performed in the consultations only. ICPC-2 codes regarded relevant for pain are listed in Table 1, and are in further text labelled "pain codes". Codes from the ICPC-2 chapter "L Musculoskeletal" are labelled "musculoskeletal pain", and codes from other chapters are collapsed and labelled "other pain". We also grouped the pain codes according to three most frequent anatomical pain sites: headache, abdominal and musculoskeletal pain. In cases, the ICPC-2 disease codes for CP (Neurological disorder N99) was included.

Statistics

STATA version 16 (Stata Corp LLC, Texas, USA) was used for the statistical analysis. Data are presented as number and percentage of contacts. STATA calculator for cohort studies was used to calculate a risk ratio with 95 % confidence interval (CI) for three age groups (0-5, 6-11 and 12-17 years), thus adjusting for age. Risk ratio below one means that cases had lower risk than controls, and above one that cases had higher risk than controls.

Ethics

This study was approved by the Regional Committee for Medical and Health Research Ethics, South-East Norway (reference 2018/1250). National standards for storage and handling of data were applied to ensure privacy and protection.

Registration

The study had been registered in Open Science Framework on Dec 18th 2019.

Results

During the period 2006-2018, there were 23,616,791 daytime contacts, 108,413 (0.46%) in cases, and 23,508,378 (99.54%) in controls. The cases accounted for 0.27% of all 16,057,216 consultations. Cases accounted for 0.28, 0.30 and 0.21 % of consultations in age groups 0-5, 6-11 and 12-17 years respectively. Among the administrative contacts, cases accounted for 0.49% of all 4,785,643 simple contacts, 2.87% of all 469,953 interdisciplinary interactions, 1.37% of all 969,913 referrals, and 1.12% of all 1,334,066 prescriptions. The risks for a daytime contact being a simple contact, a GP's interaction with other professionals, a referral, or a prescription, were higher in cases than in controls in all three age groups, except for simple contacts in the age group 12-17 years in which the risk was lower in cases than in controls, Table 2.

GPs used ICPC-2 pain codes in 2,630 (6.1%) of the 43,302 consultations with cases, and in 1,902,399 (11.9%) of the 16,013,914 consultations with controls. The frequencies of consultations with pain codes were higher in older age groups both in cases (3.3 vs. 6.8 vs. 10.7%) and controls (5.1 vs. 15.3 vs. 18.6%), Table 3. Similar findings were present in the frequencies of consultations with musculoskeletal pain codes (cases 1.7 vs. 3.5 vs. 6.3% and controls 1.8 vs. 7.4 vs. 11.7%). The risk that a consultation included a pain code was lower in cases than in controls at all ages, Table 4. The risk that a consultation included a pain code grouped as "musculoskeletal pain" was lower in cases than in controls in the age groups 6-11 years and 12-17 years, while there was no difference between cases and controls in the age group 0-5 years. The risk for codes indicating headache and abdominal

pain was lower in cases than in controls in all age groups. In cases, *Neurological disease, other* (N99), was the only RFE coded in 7,199 (16.6%) of 43,302 consultations.

Discussion

We found that children with CP accounted for 0.27 % of the GPs' paediatric daytime consultations, that GPs performed more administrative work for their paediatric patients with CP than for their other paediatric patients, and that in daytime consultations, pain was a less frequent RFE in children with CP than in the general paediatric population.

The prevalence of CP in Norway has been calculated to 2.5 (95% CI 2.4 - 2.7) per 1,000 (24), which corresponds with our finding that cases accounted for 0.27% (or 2.7 per 1000) of all daytime consultations. In other words, as a group, the paediatric population with CP had a similar frequency of GP consultations to that of the general paediatric population. In contrast, cases were overrepresented in reimbursement codes for GPs' administrative work. This was as expected, since GPs have the authority to confirm their patients' right to the majority of health and welfare benefits; in other words, they have a "door-keeper" role in the Norwegian health care system. Still, in the age group 12-17 years controls had a higher risk for simple contacts than cases. An explanation may be that in 2016, new legislation required all high school students to provide a note from a GP if school absence was longer than two days. Populations with chronic health conditions, such as CP, were to some degree exempt from this rule.

We analyzed only daytime contacts because we were interested in continuous care provided by the regular GP, as opposed to out-of-hour services. Our findings confirm that GPs are involved in the network of care for children with CP. Pain related codes were analyzed in consultations only, because we were interested in contacts with the possibility

of physical assessment in order to search for a cause of pain. The latter choice was supported by a Norwegian study that reported good correspondence between the patient record and diagnosis (ICPC-2 code) in consultations, but recommended caution if including simple contacts in the analysis of RFE in contacts with GPs (22).

The frequency of pain codes was lower in cases (6% of consultations) than in controls (12% of consultations). The ICPC-2 provides a choice to code a RFE as a symptom, a process, or a disease. In cases, the disease code *Neurological disorder (N99)* including CP was the only code in almost 17% of all daytime consultations. This finding might be a sign of inequity in coding between the population with CP and the general population. We hypothesize that in a busy clinical practice, an already established disease code could compete with a new ICPC-2 code for a current symptom or a process. Also, the reimbursement is not dependent on type or number of ICPC-2 codes. These factors might have caused an information bias. On the other hand, the complexity of chronic conditions may influence the caregivers' expectations to a GP (25), and result in a preference to discuss recurrent pain during consultations in the specialist health care instead of during GP consultations. An indication for this is the finding in a previous study that Norwegian youth with CP contacted a GP only when their pain became severe (26).

The frequency of pain codes was higher in older age groups in both cases and controls. The latter finding is in accordance with studies on pain as a RFE in the general paediatric population (11), and on pain prevalence in the paediatric population with CP (9, 13, 27, 28). An explanation can also be that adolescents with chronic conditions such as CP go through a period of transition of health care, gradually ending regular follow-up in the specialist paediatric health care at the age of 18 years.

The risk for musculoskeletal pain as the RFE did not differ between cases and controls in the youngest age group, while older children with CP had a lower risk than controls. An

explanation could be that the CP surveillance program in specialist health care includes assessment and treatment for musculoskeletal issues and movement disorders. Treatments such as botulinum toxin injections, intrathecal baclofen therapy, and corrective surgery in the limbs, are often offered in school age, and include follow-up in the specialist care. This could have reduced the need for a GP consultation for musculoskeletal pain in the older age groups.

The risk for a consultation for headache and abdominal pain was lower in cases than in controls in all three age groups. We do not have any reason to believe that such pain is less frequent in the population with CP. Thus, we hypothesize that in young people with CP, headache and abdominal pain were either not reported to a GP, or not coded by the GP.

This study has some limitations. First, ICPC-2 uses the wording "symptom/complaint" and seldom "pain" in chapter L Musculoskeletal. We assumed that pain is the most common complaint/symptom in this organ system and therefore the most relevant reason for encounter with a GP. Further, information on frequent consulters among cases might have influenced our findings. This is a topic for future studies. Another topic for future research is GPs´ attitudes and knowledge regarding follow-up of children with chronic conditions such as CP.

There are also several strengths of the study. NorCP has high completeness (76%) and high correctness (100%) of CP diagnosis (24). Since Norwegian primary health care and specialist health care are state-funded, the market for private health services for children is limited. These factors ensure the generalizability of the study.

In conclusion, the study findings indicate that the potential of GPs' involvement in pain management in pediatric CP is not fully exploited despite high availability and low costs. In order to improve pain management in CP, we advocate that all involved in the process of care take a proactive approach. In consultations, GPs should ask for pain even if the

child with CP or parent does not address pain. Health care professionals in the local multidisciplinary team should encourage the family to consider consulting a GP if the child is in pain. Health care specialists should encourage the family to connect with a GP and a relevant patient organization. Simple measures such as introducing a pain diary whenever pain is recognized and offering feasible educational material might contribute to enhanced family empowerment, common language on pain and shared decisions on pain management.

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Disclosure

The authors report there are no conflicting interests to declare.

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Table 1 Selected ICPC-2 codes from the chapters A, D, L, N, S and U grouped into "Musculoskeletal pain" and "Other pain"

"Musculoskeletal pain"	"Other pain"
L Musculoskeletal	A General
L01 Symptom/complaint in neck	A01 General pain
L02 Symptom/complaint in back	
L03 Symptom/complaint in low back	D Digestive
L04 Symptom/complaint in chest	D01 Abdominal pain
L05 Symptom/complaint in flank/axilla	D02 Abdominal pain epigastric
L07 Symptom/complaint in jaw	D04 Rectal/anal pain
L08 Symptom/complaint in shoulder	D06 Abdominal pain location other
L09 Symptom/complaint in arm	
L10 Symptom/complaint in elbow	N Neurological
L11 Symptom/complaint in wrist	N01 Headache
L12 Symptom/complaint in hand/finger	N95 Tension headache
L13 Symptom/complaint in hip	
L14 Symptom/complaint in leg/thigh	S Skin
L15 Symptom/complaint in knee	S01 Pain/tenderness skin
L16 Symptom/complaint in ankle	S29 Skin symptom/complaint
L17 Symptom/complaint in foot/toe	S97 Chronic ulcer skin
L18 Muscle pain	
L19 Symptom/complaint in muscle	U Urological
L20 Symptom/complaint in joint	U01 Painful urination
L29 Symptom/complaint in musculoskeletal other	U13 Bladder symptom/complaint
	U29 Urinary symptom/complaint

Table 2 Distribution of 23 616 791 daytime contacts in children with CP (cases) and children in general population (controls) according to the type of contact

	Cases	Controls	Risk Ratio (95% CI)
Age 0-5 years	**35 855**	**8 855 216**	
Consultations	19 054 (53.1)	6 733 815 (76.0)	0.36 (0.35-0.37)
Simple contacts	7 099 (19.8)	1 458 201 (16.5)	1.25 (1.22-1.28)
Interactions	3 622 (10.1)	102 776 (1.2)	9.28 (8.97-9.60)
Referrals without consultation	4 185 (11.7)	368 380 (4.2)	3.02 (2.93-3.12)
Prescriptions	1 895 (5.3)	192 044 (2.2)	2.50 (2.39-2.62)
Age 6-11 years	**43 082**	**7 498 501**	
Consultations	15 335 (35.6)	5 019 346 (66.9)	0.28 (0.27-0.28)
Simple contacts	9 574 (22.2)	1 508 783 (20.1)	1.13 (1.11-1.16)
Interactions	5 246 (12.2)	159 237 (2.1)	6.22 (6.04-6.40)
Referrals without consultation	6 546 (15.2)	364 849 (4.9)	3.46 (3.37-3.55)
Prescriptions	6 381 (14.8)	446 286 (6.0)	2.72 (2.65-2.80)
Age 12-17 years	**29 476**	**7 154 661**	
Consultations	8 913 (30.2)	4 260 753 (59.6)	0.30 (0.29-0.30)
Simple contacts	6 753 (22.9)	1 795 233 (25.1)	0.89 (0.86-0.91)
Interactions	4 600 (15.6)	194 472 (2.7)	6.48 (6.29-6.69)
Referrals without consultation	2 562 (8.7)	223 391 (3.1)	2.93 (2.82-3.05)
Prescriptions	6 648 (22.6)	680 812 (9.5)	2.75 (2.68-2.83)

Note: Data are number (%) of daytime contacts for the three age groups.

Table 3 Daytime consultations given a pain related ICPC-2 code in children with CP (cases) and children in the general population (controls)

	Cases	Controls
Consultations, age 0-5 y	**19 054**	**6 733 815**
All pain	631 (3.3)	341 855 (5.1)
Musculoskeletal pain	318 (1.7)	119 719 (1.8)
Other pain	313 (1.6)	222 136 (3.3)
Consultations, age 6-11 y	**15 335**	**5 019 346**
All pain	1045 (6.8)	768 234 (15.3)
Musculoskeletal pain	542 (3.5)	369 463 (7.4)
Other pain	503 (3.3)	398 771 (7.9)
Consultations, age 12-17 y	**8 913**	**4 260 753**
All pain	954 (10.7)	792 310 (18.6)
Musculoskeletal pain	563 (6.3)	499 452 (11.7)
Other pain	391 (4.4)	292 858 (6.9)

Data are number (%) of all daytime consultations for all pain (musculoskeletal and other pain). Pain codes, as listed in Table 1, are included in “All pain”, “Musculoskeletal pain” and “Other pain”.

Table 4 Risk ratio analyses for All pain, Headache, Abdominal and Musculoskeletal pain in children with CP (cases) compared to that in children in the general population (controls)

	Cases	Controls	Risk ratio (95%CI)
Age 0-5 years, all consultations	**19 054**	**6 733 815**	
All pain	631	341 855	0.64 (0.59-0.69)
Headache	16	12 192	0.46 (0.28-0.76)
Abdominal pain	145	128 711	0.39 (0.33-0.46)
Musculoskeletal pain	318	119 719	0.94 (0.84-1.05)
Age 6-11 years, all consultations	**15 335**	**5 019 346**	
All pain	1045	768 234	0.41 (0.38-0.43)
Headache	79	75 916	0.34 (0.27-0.42)
Abdominal pain	248	254 521	0.31 (0.27-0.35)
Musculoskeletal pain	542	369 463	0.46 (0.42-0.50)
Age 12-17 years, all consultations	**8 913**	**4 260 753**	
All pain	954	792 310	0.53 (0.49-0.56)
Headache	83	101 472	0.39 (0.31-0.48)
Abdominal pain	185	140 335	0.62 (0.54-0.72)
Musculoskeletal pain	563	499 452	0.51 (0.47-0.55)

All pain includes all codes listed in Table 2. The following ICPC-2 codes were included in the three anatomical localizations: “Headache” (N01 and N95), “Abdominal pain” (D01, D02, D04 and D06) and “Musculoskeletal pain” (as listed in Table 2).

10 APPENDICES

10 APPENDICES

Appendix A Content of an envelope sent to participants (Papers I-III)

Invitation

Februar 2019

Kjære foreldre,

Det gjelder prosjektet ***"Hoftesmerter og hofteoperasjoner hos barn med cerebral parese".***

Tusen takk for at dere deltar i studien! Det har nå gått fem år siden foreldre ble intervjuet og fylte ut spørreskjema og tiden er kommet for å gjøre det på nytt. Dette er nødvendig for å få kunnskap om forløpet av hoftesmerter hos barn med cerebral parese. **Hvert eneste svar er viktig og vil være nyttig i vårt videre arbeid med behandling av barn med cerebral parese. Jo flere som svarer, jo mer kan vi stole på resultatene.**

Denne gangen er det nok at en av foreldrene fyller ut spørreskjema og at samme forelder intervjues. Vi ber om svar på de samme spørsmålene som sist ved å fylle ut vedlagte skjema, helst innen 7 dager. Intervjuene vil bli gjennomført i ukene 9, 10 og 11. Vi ber om to tidspunkt som passer på vedlagte svarslipp og at svaret om ønsket tidspunkt sendes på e-post til uxsemu@ous-hf.no snarest. Alternativt ber vi at det merkes av to tidspunkt på svarslippen og denne sendes til oss i vedlagte frankerte returkonvolutt sammen med utfylt spørreskjema. Hvis ingen av tidene passer ber vi deg gi beskjed på e-post eller skrive en kommentar på svarslippen. Intervjuet tar ca. 15 min.

Resultater fra første del av studien er publisert i form av to vitenskapelige artikler som du kan finne på www.pubmed.org:

Journal of Pediatric Orthopaedics B 2016, 25:217-221: ***Hip pain is more frequent in severe hip displacement: a population-based study of 77 children with cerebral palsy.*** Kjersti Ramstad, Terje Terjesen

Acta Orthopaedica 2017 Apr; 88(2):205-210: ***Severe hip displacement reduces health-related quality of life in children with cerebral palsy. A population-based study of 67 children.*** Kjersti Ramstad, Reidun B Jahnsen, Terje Terjesen.

Når studien er ferdig, kommer vi til å sende en artikkel til CP-bladet.

Ta gjerne kontakt hvis du lurer på noe! Takk for at du tar deg tid til å delta!

Vennlig hilsen

Selma Mujezinovic Larsen	Kjersti Ramstad	Terje Terjesen
Overlege i barnesykdommer	Overlege i barnesykdommer	Overlege i ortopedi
PhD kandidat	Prosjektleder,PhD	Professor emeritus
Seksjon for nevrohabilitering		Ortopedisk avdeling

Barneavdeling for nevrofag Rikshospitalet Oslo Universitetssykehus

E-post: uxsemu@ous-hf.no kjeram@ous-hf.no

Schedule for an interview

Svarslipp vedrørende telefonintervju i studien

Hoftesmerter og hofteoperasjon hos barn med cerebral parese:

Vennligst noter dette deltagernummeret _____ i studien når du svarer på

e-post (uxsemu@ous-hf.no). Samme nummer skal være notert på spørreskjema!

Vi ber at samme forelder som tar telefonintervju også fyller ut vedlagt spørreskjema. Mor__/Far__

Vennligst noter telefon- eller mobilnummer du ønsker å bli ringt opp på i e-posten_____.

Tusen takk at du tar deg tid til å delta i fortsettelsen av studien!

Selma Mujezinovic Larsen

Oslo universitetssykehus Februar 2019

Uke 9 - 25.02.-03.03.2019

Mandag	Tirsdag	Onsdag	Torsdag	Fredag	Lørdag
9-12	9-12	9-12	9-12	9-12	X
12-14	12-15	12-15	12-15	X	X
17-19	X	17-19	17-19	X	16-18

Uke 10 - 04.03.-10.03.2019

Mandag	Tirsdag	Onsdag	Torsdag	Fredag	Lørdag
9-12	9-12	9-12	9-12	9-12	X
12-14	12-15	12-15	12-15	12-15	X
17-19	X	17-19	17-19	X	16-18

Uke 11 - 11.03.-17.03.2019

Mandag	Tirsdag	Onsdag	Torsdag	Fredag
9-12	9-12	9-12	9-12	X
12-14	12-15	12-15	12-15	X
17-19	X	17-19	17-19	X

Vennligst noter flere alternativer hvis mulig. X i skjema over betyr at Selma ikke er tilgjengelig.

Annet tidspunkt hvis tidspunkter over ikke passer:_____

Dette skjema legger du i returkonvolutten dersom du ikke benytter e-post.

Attachments:

Questionnaires CHQ-pain questions, BPI-pain interference and body map, CPCHILD

SMERTE – spørsmål til foreldre

1. I løpet av de siste 4 ukene, hvor sterke smerter eller ubehag har barnet ditt hatt?

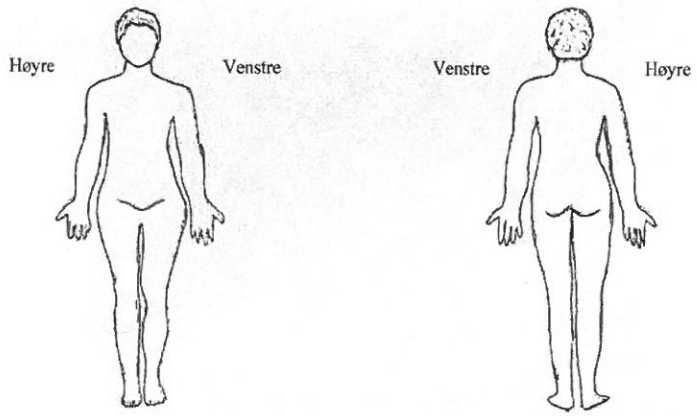
☐ Ingen ☐ Meget svake ☐ Svake ☐ Moderate ☐ Sterke ☐ Svært sterke

2. I løpet av de siste 4 ukene, hvor ofte har barnet ditt hatt kroppslig smerte eller vondt?

☐ Aldri ☐ En eller to ganger ☐ Noen få ganger ☐ Ganske ofte ☐ Meget ofte ☐ Hver/nesten hver dag

Hvis barnet ikke har hatt smerter, behøver du ikke å svare på flere spørsmål på denne siden.

Hvis barnet har hatt smerter:
Vil du skravere de områdene på kroppen hvor du tror barnet ditt har hatt smerter de siste 4 ukene. Marker også med et kryss der du tror smertene har vært sterkest:



3. Sett en ring rundt det tallet som for de siste 4 ukene best beskriver hvor mye smertene har virket inn på

Daglig aktivitet

0 **1** **2** **3** **4** **5** **6** **7** **8** **9** **10**
Ikke påvirket Fullstendig påvirket

Søvn

0 **1** **2** **3** **4** **5** **6** **7** **8** **9** **10**
Ikke påvirket Fullstendig påvirket

Tror du at det er årsakssammenheng mellom CP og smertene ?

Ja☐ Nei☐

Hvor tror du smertene kommer fra? Muskel/skjelett☐ Annet ☐ beskriv:.....

Spørsmålene 1og 2 er hentet fra CHQ – Child Health Questionnaire (norsk versjon 1997 Flatø B, Førre og medarbeidere). Figuren og spørsmål 3 er hentet fra BPI – Brief Pain Inventory (norsk versjon Klepstad P og medarbeidere 2002). Spørsmålene er lett modifisert.

CPCHILD©

Caregiver Priorities & Child Health Index of Life with Disabilities

(Omsorgsgivers prioriteringer & helseregister for barn med funksjonshemninger)

Instruksjon

1. Dette spørreskjemaet handler om ditt barns helse, komfort og velbefinnende, og om å gi omsorg for hans/hennes behov.

2. Vennligst les instruksjonene nøye.

3. Vennligst svar på alle spørsmålene ved å sette ring rundt tallet som passer best. Du kan skrive kommentarer/klargjøringer i mellomrommet under hvert spørsmål.

For eksempel

	BEHOV FOR ASSISTANSE									
Tenk over hvordan hver enkelt av følgende aktiviteter **vanligvis** utføres av/for ditt barn. Vurder hvor **vanskelig** hver av disse aktivitetene var i løpet av de 2 siste ukene, **og** velg **hvilken grad av assistanse** som var nødvendig for å hjelpe ditt barn til å utføre disse aktivitetene.								TOTAL	MODERAT	MINIMAL	SELVSTENDIG
I løpet av de 2 siste ukene, Hvor vanskelig var følgende:	Ikke Mulig	Svært vanskelig	Vanskelig	Litt vanskelig	Lett	Svært lett	Ikke vanskelig i det hele tatt				
1. Ta på/bruke noe på føttene? (sokker, sko, skinner, etc	0	1	2	3	4	⑤	6	0	1	②	3

I eksemplet over ble aktiviteten å ta på/bruke noe på føttene rangert som *svært lett*, og barnet hadde behov for *minimal* grad av assistanse til å ta på noe på føttene.

4. På slutten av hver seksjon er det plass til å føre opp elementer du savner i spørreskjemaet, og som du mener er viktige for ditt barns helse, komfort og velbefinnende.

Barnets navn:_____

Navn på forelder eller omsorgsgiver som fyller ut spørreskjemaet:

_____

Dato:_____

DEL 1: PERSONLIG STELL

Tenk over hvordan hver enkelt av følgende aktiviteter **vanligvis** utføres av/for ditt barn. Vurder hvor **vanskelig** hver av disse aktivitetene var i løpet av de 2 siste ukene, **og** velg **hvilken grad av assistanse** som var nødvendig for å hjelpe ditt barn til å utføre disse aktivitetene.								BEHOV FOR ASSISTANSE			
I løpet av de 2 siste ukene, hvor vanskelig var følgende:	Ikke mulig	Svært vanskelig	Vanskelig	Litt vanskelig	Lett	Svært lett	Ikke vanskelig i det hele tatt	TOTALT	MODERAT	MINIMAL	SELVSTENDIG
1 . å spise/drikke eller bli matet?	0	1	2	3	4	5	6	0	1	2	3
2. opprettholde munnhygiene? (holde munn og tenner rene)	0	1	2	3	4	5	6	0	1	2	3
3. bading/vasking?	0	1	2	3	4	5	6	0	1	2	3
4. toalettsituasjonen? (blære- og tarmfunksjon, hygiene, osv.)	0	1	2	3	4	5	6	0	1	2	3
5. å skifte bleier/undertøy?	0	1	2	3	4	5	6	0	1	2	3
6. ta på/av klær på overkroppen? (skjorte, jakke, osv.)	0	1	2	3	4	5	6	0	1	2	3
7. ta på/av klær på underkroppen? (bukser, stillongs, osv.)	0	1	2	3	4	5	6	0	1	2	3
8. ta på/bruke noe på føttene? (sokker, sko, skinner, osv.)	0	1	2	3	4	5	6	0	1	2	3
9. hårpleie (vaske, tørke, børste/gre, flette, osv.)	0	1	2	3	4	5	6	0	1	2	3
1A. annen aktivitet innen personlig pleie? Beskriv:_____	0	1	2	3	4	5	6	0	1	2	3
1B. annen aktivitet innen personlig pleie? Beskriv:_____	0	1	2	3	4	5	6	0	1	2	3

DEL 2: STILLING, FORFLYTTING & MOBILITET

Tenk over hvordan hver enkelt av følgende aktiviteter **vanligvis** utføres av/for ditt barn. Vurder hvor **vanskelig** hver av disse aktivitetene var i løpet av de 2 siste ukene, **og** velg **hvilken grad av assistanse** som var nødvendig for å hjelpe ditt barn til å utføre disse aktivitetene.								BEHOV FOR ASSISTANSE			
I løpet av de 2 siste ukene, hvor vanskelig var følgende:	Ikke mulig	Svært vanskelig	Vanskelig	Litt vanskelig	Lett	Svært lett	Ikke vanskelig i det hele tatt	TOTALT	MODERAT	MINIMAL	SELVSTENDIG
10. å komme seg inn og ut av sengen?	0	1	2	3	4	5	6	0	1	2	3
11. å komme seg inn og ut av rullestol/stol?	0	1	2	3	4	5	6	0	1	2	3
12. å sitte i rullestol/stol?	0	1	2	3	4	5	6	0	1	2	3
13. å stå for trening/forflytting?	0	1	2	3	4	5	6	0	1	2	3
14. å forflytte seg i hjemmet? (på hvilken som helst måte)	0	1	2	3	4	5	6	0	1	2	3
15. å forflytte seg utendørs (på hvilken som helst måte)	0	1	2	3	4	5	6	0	1	2	3
16. å komme seg inn og ut av transportmidler (bil, varebil, buss)	0	1	2	3	4	5	6	0	1	2	3
17. å besøke offentlige steder (park, teater, severdigheter, osv)	0	1	2	3	4	5	6	0	1	2	3
2A. andre aktiviteter? Beskriv:_____	0	1	2	3	4	5	6	0	1	2	3
2B. andre aktiviteter? Beskriv:_____	0	1	2	3	4	5	6	0	1	2	3

DEL 3: VELVÆRE & FØLELSER

I løpet av de 2 siste ukene, hvor ofte opplevde barnet ditt smerte eller ubehag...	HVER DAG	VELDIG OFTE	GANSKE OFTE	NOEN FÅ GANGER	EN ELLER TO GANGER	INGEN GANGER	INTENSITET STERK	MODERAT	MILD	INGEN
18. ved spising /drikking eller mating?	0	1	2	3	4	5	0	1	2	3
19. i løpet av toalettsituasjon? (blære- og tarmfunksjon, hygiene, bleieskift, osv.)	0	1	2	3	4	5	0	1	2	3
20. under på-/avkledning?	0	1	2	3	4	5	0	1	2	3
21. under forflytting eller stillingsendringer?	0	1	2	3	4	5	0	1	2	3
22. I sittende posisjon?	0	1	2	3	4	5	0	1	2	3
23. mens hun/han lå i sengen?	0	1	2	3	4	5	0	1	2	3
24. som forstyrret ditt barns søvn?	0	1	2	3	4	5	0	1	2	3
3A. under andre aktiviteter? Beskriv:_____	0	1	2	3	4	5	0	1	2	3
3B. under andre aktiviteter? Beskriv: _____	0	1	2	3	4	5	0	1	2	3

I løpet av de siste 2 ukene, hvor ofte var barnet ditt:										
25. urolig, oppbrakt eller sint?	0	1	2	3	4	5	0	1	2	3
26. lei seg eller trist?	0	1	2	3	4	5	0	1	2	3

DEL 5: HELSE

I løpet av de 2 siste ukene...	*Vennligst sett ring rundt svaret som passer best*					
34. Hvor mange ganger har ditt barn hatt behov for å oppsøke lege eller sykehus?	Innlagt mer enn 7 dager	Innlagt mindre enn 7 dager	3 eller flere ganger	2 ganger	1 gang	Ingen ganger

I løpet av de 2 siste ukene...	*Veldig dårlig*	*Dårlig*	*Noenlunde bra*	*Bra*	*Veldig bra*	*Utmerket*
35. Hvordan vil du beskrive ditt barns generelle helse?	**0**	**1**	**2**	**3**	**4**	**5**

36. Skriv opp medikamentene ditt barn har brukt i løpet av de siste 2 ukene

0. **Ingen medikamenter**
1. _____
2. _____
3. _____
4. _____
5. _____
6. _____
7. _____
8. _____
9. _____

DEL 6: DITT BARNS GENERELL LIVSKVALITET

I løpet av de 2 siste ukene...	*Veldig dårlig*	*Dårlig*	*Noenlunde bra*	*Bra*	*Veldig bra*	*Utmerket*
37. Hvordan vil du vurdere ditt barns generell livskvalitet?	**0**	**1**	**2**	**3**	**4**	**5**

DEL 8: OPPLYSNINGER OM DITT BARN

1. Mitt barn er en:	☐ **Gutt** ☐ **Jente**
2. Hva er ditt barns fødselsdato:	_____/_____/_____ dag måned år
3. Hvilket trinn er det høyeste ditt barn har fullført? (ett kryss)	**Barnehage** _____ **1. klasse** _____ **2. klasse** _____ **3. klasse** _____ **4. klasse** _____ **5. klasse** _____ **6. klasse** _____ **7. klasse** _____ **8. klasse** _____ **9. klasse** _____ **10.klasse** _____ **1. år videregående** _____ **2. år videregående** _____ **3. år videregående** _____ **4. år videregående** _____ **5. år videregående** _____

DEL 9: OPPLYSNINGER OM DEG

1. Er du:	☐ **Mann** ☐ **Kvinne**
2. Hva er din fødselsdato:	_____/_____/_____ dag måned år
3. Hvilke av følgende beskrivelser passer best til din nåværende yrkesstatus? (sett kryss ved alle som passer)	**Er ikke i arbeid pga mitt barns helse** _____ **Er ikke i arbeid av andre grunner** _____ **Ser etter arbeid utenfor hjemmet** _____ **Arbeider fulltid eller deltid (enten utenfor hjemmet eller i hjemmefirma)** _____ **Er hjemmeværende** _____
4. Hvilket av følgende utsagn beskriver best ditt forhold til barnet:	**Biologisk forelder** _____ **Steforeldre** _____ **Fosterforeldre** _____ **Adoptivforeldre** _____ **Verge** _____ **Profesjonell omsorgsarbeider** _____ **Andre (forklar)** _____
5. I gjennomsnitt, hvor mange dager per uke er du ansvarlig for omsorgsaktiviteter overfor ditt barn?	_____ **dager per uke**
6. Hva er din høyeste fullførte utdanning?	**Ungdomsskole** _____ **Videregående** _____ **Fagbrev** _____ **Høyskole eller universitets-utdanning** _____ **Annen utdanning (beskriv)** _____

Hvor lang tid har det tatt deg <u>kun å fylle ut</u> dette spørreskjema (timer / minutter):_____

TAKK FOR DELTAGELSEN!

Appendix B Interview Guides (Papers I-III)

Appendix B1 Interview Guide for data collection in adolescence (Norwegian)

Telefonintervju ID _____ Dato for intervju:_____ Intervjuer_____

Forsikre deg om at du snakker med rett person___. Mor_____ Far_____

Presenter deg

Er spørreskjemaene mottatt? Ja___ Nei___ Besvart Ja___ Nei____

Har respondenten noen spørsmål om prosjektet?_____

Sjekk at opplysninger om behandling fra CPOP stemmer GMFCS

GMFCS____ Operasjoner_____

Siste røntgenbilde av hoftene tatt omtrent når? _____

Hvor ble røntgen bilde tatt?_____

Hvis bilde er tatt før 2017 er det, i følge ortoped, aktuelt å ta nytt så fort som mulig, senest mai-juni 2019

Godtar foreldre at nytt rtg. bilde rekvireres lokalt? Ja____ Nei____

Har barnet fått botulinumtoksin - injeksjoner i hoftemuskler/på innsiden eller baksiden av lårene det siste året ? Ja___ Nei___

Gjennomgått hofteoperasjon? Ja____ Nei___

Hvis ja – hvor mange ganger? ____

Omtrent når?_____

På hvilke(t) sykehus?

Har barnet gjentatte smerter? Hvis nei – gå videre til spørsmål 10.

Hvis ja; Hva er det som gjør at respondenten mener at barnet har smerter?

Hvor sitter smertene (bruk Body map)?

Hvis det er smerter fra flere lokalisasjoner, spør eventuelt for hver for hver lokalisasjon – og i alle fall for smerter fra hofteområdet:

Når/ i hvilke situasjoner opptrer smertene?

Hva lindrer smertene?

Hva gjør smertene verre?

Gitt håndkjøpspreparat siste 4 uker?

Hva tror respondenten at smertene skyldes?

For smerter fra hofteområdet:

Still spørsmålene fra spørreskjema 1 (elementer fra CHQ og BPI) og fyll ut skjemaet

I løpet av de siste 4 ukene, hvor sterke smerter eller ubehag har barnet ditt hatt?

_____	_____	_____	_____	_____	_____
Ingen	Meget svake	Svake	Moderate	Sterke	Svært sterke

I løpet av de siste 4 ukene, hvor ofte har barnet ditt hatt kroppslig smerte eller vondt?

_____	_____	_____	_____	_____	_____
Aldri	En eller to Ganger	Noen få ganger	Ganske ofte	Meget ofte	Hver/nesten hver dag

Sett en ring rundt det tallet som for de siste 4 ukene best beskriver hvor mye smertene har virket inn på

Daglig aktivitet

0	1	2	3	4	5	6	7	8	9	10
Ikke påvirket										Fullstendig påvirket

Søvn

0	1	2	3	4	5	6	7	8	9	10
Ikke påvirket										Fullstendig påvirket

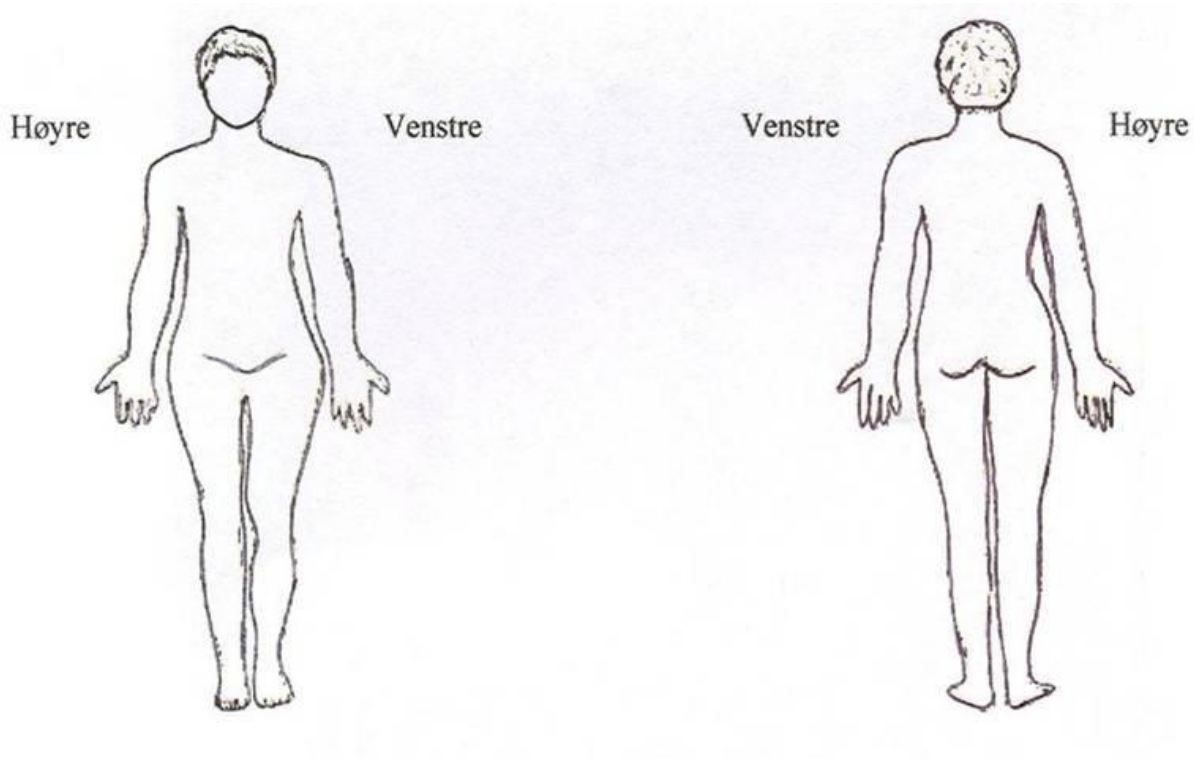
10. Forsikre deg om at spørreskjemaene vil bli fylt ut og sendt inn.

Presiser at spørsmålene på spørreskjemaet CPCHILD gjelder alle typer smerter (gjelder livskvalitet generelt).

Den valgte versjonen av CPCHILD er forkortet og består av 16 delspørsmål, hele CPCHLD har 36 spørsmål.

11. Takk for deltakelsen i prosjektet ☺

12. Body Map side 3



Body Map

Appendix B2 Interview Guide for data collection in childhood (Norwegian)

1. Forsikre deg om at du snakker med rett person

2. Presenter deg

3. Er spørreskjemaene mottatt? Ja Nei

4. Har respondenten noen spørsmål om prosjektet?

5. Sjekk at opplysninger om behandling fra CPOP stemmer

Noen gang brukt SWASH ortose? Ja Nei

Noen gang fått botulinumtoksin-injeksjoner i hoftemuskler? Ja Nei

Gjennomgått hofteoperasjon? Ja Nei

Hvis ja – hvor mange ganger? Omtrent når ? På hvilket sykehus?

6. Har barnet gjentatte smerter?

Hvis nei – gå videre til pt.7.

Hvis ja -

Hva er det som gjør at respondenten mener at barnet har smerter? (de fleste av barna kan ikke snakke)

Hvor sitter smertene?

Hvis det er smerter fra flere lokalisasjoner, spør for hver lokalisasjon:

Når/ i hvilke situasjoner opptrer smertene?

Hva lindrer smertene?

Hva gjør smertene verre?

Hva tror respondenten at smertene skyldes?

For smerter fra hofteområdet:

Spør spørsmålene fra spørreskjema 1 (elementer fra CHQ og BPI) og fyll ut skjemaet

7. Forsikre deg om at spørreskjemaene vil bli fylt ut og sendt inn.

Presiser at spørsmålene på spørreskjemaet CPCHILD gjelder alle typer smerter (gjelder livskvalitet generelt).

8. Takk for deltakelsen i prosjektet

Appendix C Excerpt from the code liste of «Normaltariffen» (Paper IV)

1ad Enkel pasientkontakt ved personlig frammøte eller ved bud. Taksten forutsetter at det gis råd/veiledning. Gjelder ikke når kontakten/forespørselen resulterer i skriving av resept, sykmelding, rekvisisjon eller henvisning, jf. takst 1h og 1i.
Ugyldig takstkombinasjon: 1ak, b, d, f, g h og i, 2, 3, 4, 11, 12, 13, 14, 15, 21, 217c, 612, 621, 622, 623, 624

1bd Enkel pasientkontakt ved papirbrev eller telefonsamtale. Taksten forutsetter at det gis råd/veiledning. Gjelder ikke når kontakten/forespørselen resulterer i skriving av sykmelding, rekvisisjon eller henvisning, jf. takst 1h.
Ugyldig takstkombinasjon: alle

1be Enkel pasientkontakt, forespørsel, rådgivning ved elektronisk kommunikasjon i tråd med Norm for informasjonssikkerhet i helse-, omsorgs- og sosialsektoren. Taksten forutsetter at det gis råd/veiledning. Gjelder ikke når kontakten/forespørselen resulterer i skriving av sykmelding, rekvisisjon eller henvisning.
Ugyldig takstkombinasjon: alle

1f Telefonsamtale eller skriftlig kommunikasjon om enkeltpasienter med fysioterapeut, kiropraktor, kommunal helse- og omsorgstjeneste (pleie- og omsorgstjeneste, helsestasjon og skolehelsetjeneste), NAV Sosiale tjenester og bedriftshelsetjeneste, samt med farmasøyt på apotek og pedagogisk personell i psykiatritjenester, skole og barnehage. Legen må på anmodning oppgi hvem/ hvilken instans man har vært i kontakt med. Taksten forutsetter at det gis råd/veiledning eller ordinasjoner. Taksten kan også kreves av avtalespesialist ved kontakt med pasientens fastlege eller dennes stedfortreder.
Ugyldig takstkombinasjon: alle

1h Utfylling av sykmeldingsblankett (Blankett NAV 08.07.04) når pasienten er forhindret fra å søke lege, rekvisisjon til røntgen og fysioterapi og henvisning til spesialist ved enkel pasientkontakt. Taksten inkluderer forespørsel, rådgivning
Ugyldig takstkombinasjon: alle unntatt 8, 1e og 701-743

1i Skriving av e-resept
Ugyldig takstkombinasjon: alle unntatt 1e og 701-743

2ad Konsultasjon hos allmennpraktiserende lege
Ugyldig takstkombinasjon: 1, 2ak, 3, 4, 11med unntak av 11e, 12, 13, 14, 15, 21, 22, 217c, 621, 622, 623, 624

2ae E-konsultasjon hos fastlege.
Ugyldig takstkombinasjon: Alle unntatt 2cd, 2cdd, 2dd, 2ld, 2p, 612 a og b, 615, 616 og 617.

11ad Sykebesøk ved allmennpraktiserende lege.

Ugyldig takstkombinasjon: 1, 2, 3, 4, 11ak, 12, 14, 15, 217c

14 Møtegodtgjørelse med reisetid når legen deltar i tverrfaglige samarbeidsmøter (herunder telefonmøter med mer enn 2 deltagere og videokonferanse) med helse- og/eller sosialfaglig personell som et ledd i behandlingsopplegg for enkeltpasienter, herunder i basisteam, ved møte i ansvarsgruppe i forbindelse med legemiddelassistert rehabilitering og i møte om individuell plan. Taksten kan ikke benyttes i forbindelse med samarbeid internt i tverrfaglige medisinske sentra og lignende. Taksten kan ikke benyttes som godtgjørelse for fast oppsatte samarbeidsmøter, med mindre det gjelder samarbeid om konkrete pasienter.
Beregnes for arbeid i inntil en halv time og repeteres deretter per påbegynt halvtime. Taksten dekker også praksisutgifter. Taksten beregnes for den samlede møte-/reisetid, ikke per pasient. Legen må på anmodning opplyse hvem det har vært holdt møte med. Taksten kan ikke kreves dersom møtet avlyses eller dekkes av NAVs L-takster. Taksten kan ikke benyttes av legevakt.
Ugyldig takstkombinasjon: alle unntatt 1

Appendix D Approvals attached to the thesis (TILLATELSER)

1. Approval from the Regional Committee for Research Ethics (Papers I-III)
2. Approval from the Regional Committee for Research Ethics (Paper IV)
3. Consent for CPRN and CPOP in Norwegian (General Papers I-IV)
4. Guidelines on use of data from CPRN and CPOP (General Papers I-IV)
5. Approval CPOP First Data Collection Ramstad 2012
6. Invitation Letter (First Data Collection) and Consent for both data collections (Papers I-III)
7. Approval CPOP Second Data Collection Ramstad Larsen 2018 (Papers I-III)
8. Application PVO (Data for Papers I-III)
9. Approval PVO (Data for Papers I-III)
10. Application Health Directorate on Linkage study April 2019 (Paper IV)
11. Approval Health Directorate June 2019 (Paper IV)
12. Approval CPRN Linkage study (Paper IV)
13. Approval PVO on linkage study (Data for Paper IV)

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Gjøril Bergva	22845529	31.01.2013	2012/2258/REK sør-øst D
			Deres dato:	**Deres referanse:**
			11.12.2012	

Vår referanse må oppgis ved alle henvendelser

Til Kjersti Ramstad

2012/2258 Hoftesmerter hos barn med cerebral parese

Forskningsansvarlig: Oslo Universitetssykehus
Prosjektleder: Kjersti Ramstad

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK sør-øst) i møtet 10.01.2013. Vurderingen er gjort med hjemmel i helseforskningsloven (hfl.) § 10, jf. forskningsetikklovens § 4.

Prosjektomtale
Formålet er å undersøke sammenhenger mellom gjentatte muskel-skjelettsmerter, hofteluksasjon (hoftene helt eller delvis ut av ledd) og livskvalitet hos barn med cerebral parese (CP). Hofteluksasjon skjer vanligvis i småbarnsalderen, derfor er forebygging og behandling mest aktuelt i denne aldersgruppen. Studien vil øke kunnskapen om sammenhenger mellom hoftenes stilling, muskel-skjelettsmerter og livskvalitet. Utvalget består av 143 barn født i 2002-2006 som deltar i et nasjonalt oppfølgingsprogram for barn med CP (CPOP), og som ikke kan gå uten hjelpemidler. Disse er fulgt opp hvert halvår med klinisk undersøkelse etter protokoll, samt røntgenbilder av hoftene. Da denne pasientgruppen svært ofte har kognitive utfordringer i tillegg til de motoriske, vil foreldrene til barna bli bedt om å fylle ut spørreskjema om barnets livskvalitet og bli intervjuet på telefon om barnet har smerter. Svarene vil bli relatert til det siste røntgenbildet og behandling rettet mot hofteluksasjon. Prosedyren vil bli gjentatt etter fem år. Samtykke innhentes fra foreldrene.

Vurdering
Komiteen har vurdert søknaden og har ingen innvendinger til at prosjektet gjennomføres.
Komiteen har imidlertid en kommentar til informasjonsskrivet:

Det skal innhentes samtykke fra foreldrene. Første side i informasjonsskrivet gir imidlertid inntrykk av at man henvender seg til barna. Det bes om at skrivet blir revidert slik at det er klart hvem som er adressaten.

Vedtak
Med hjemmel i helseforskningsloven § 9 jf. 33 godkjenner komiteen at prosjektet gjennomføres under forutsetning av at ovennevnte vilkår oppfylles.

I tillegg til vilkår som fremgår av dette vedtaket, er godkjenningen gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad og protokoll, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 31.12.2019. Av dokumentasjonshensyn skal opplysningene likevel bevares inntil

31.12.2024. Opplysningene skal lagres avidentifisert, dvs. atskilt i en nøkkel- og en opplysningsfil. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for «Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse og omsorgssektoren».

Dersom det skal gjøres vesentlige endringer i prosjektet i forhold til de opplysninger som er gitt i søknaden, må prosjektleder sende endringsmelding til REK.

Prosjektet skal sende sluttmelding på eget skjema, senest et halvt år etter prosjektslutt.

Klageadgang
Du kan klage på komiteens vedtak, jf. forvaltningslovens § 28 flg. Klagen sendes til REK sør-øst D. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK sør-øst D, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Vi ber om at alle henvendelser sendes inn på korrekt skjema via vår saksportal: http://helseforskning.etikkom.no. Dersom det ikke finnes passende skjema kan henvendelsen rettes på e-post til: post@helseforskning.etikkom.no.

Vennligst oppgi vårt referansenummer i korrespondansen.

Med vennlig hilsen

Stein A. Evensen
Professor dr. med.
Leder

Gjøril Bergva
Rådgiver

Kopi til: k.c.l.carlsen@medisin.uio.no; godkjenning@ous-hf.no

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Tor Even Marthinsen	22845521	19.09.2018	2018/1250/REK sør-øst C
			Deres dato:	**Deres referanse:**
			12.06.2018	

Vår referanse må oppgis ved alle henvendelser

Kjersti Ramstad
Oslo Universitetssykehus

2018/1250 Hvorfor oppsøker barn og unge med cerebral parese fastlegen?

Forskningsansvarlig: Oslo universitetssykehus HF
Prosjektleder: Kjersti Ramstad

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK sør-øst) i møtet 23.08.2018. Vurderingen er gjort med hjemmel i helseforskningsloven (hforsknl) § 10.

Prosjektomtale
Prosjektet tilhører gruppen av prosjekter om cerebral parese (CP) ved OUS. Formålet er å studere om behandlingen utenfor sykehus kan bli bedre ved å undersøke om og hvorfor barn med CP oppsøker fastleger og spesielt om fastleger er involvert i behandling av smerter. Bakgrunnen er at helsetjenester til funksjonshemmede barn er dårlig koordinert og tre av fire barn med CP har smerter. Gjeldende oppfatning er at den høye smerteforekomsten ved CP kan minskes ved bedre helsetjenester. Prosjektet er en populasjonsbasert kohortestudie med utgangspunktet i barn som er registrert i CPRN/CPOP (Cerebral Parese Registeret i Norge/Cerebral Parese Oppfølgingsprogram). Vi vil hente data om årsak til kontakt med fastleger fra KUHR–databasen (Kontroll og utbetaling av helserefusjoner) for barn med og uten CP og sammenlikne disse. Sammenlikning med barn uten CP er nødvendig fordi alle barn går til lege og smerter er et vanlig symptom. Funnene vil veilede tiltak for behandling og samhandling.

Vurdering
Komiteen har ingen forskningsetiske innvendinger til prosjektet.

Prosjektet er delvis basert på samtykke, og delvis basert på dispensasjon fra taushetsplikt. Selve studiegruppen, barn med cerebral parese (CP), har samtykket til at opplysninger samles inn og oppbevares i Cerebral pareseregisteret i Norge og Cerebral pareseoppfølgingsprogrammet (CPRN/CPOP). Komiteen mener dette samtykket også er dekkende for den koblingen som skal gjøres mot KUHR. Selv om samtykket ikke eksplisitt nevner KUHR blant de registrene det kan tenkes koblet mot, er såpass mange tilsvarende registre beskrevet at det må antas at pasientene aksepterer slike koblinger.

Kontrollgruppen skal trekkes fra Folkeregisteret, og kan komme til å bestå av opptil 11 000 aldersmatchede barn. Søker angir dette som et estimat; endelig antall bestemmes i samråd med statistiker og KUHR. Opplysningene som skal samles inn fra kontrollgruppen er informasjon om alder, kjønn, bosted og kontakt med fastlege.

Dispensasjon fra taushetsplikt
Som et ledd i dette prosjektet søkes det om fritak fra kravet om å innhente samtykke. Søker grunngir dette

ønsket blant annet på følgende måte:

Kontrollgruppa omfatter så mange personer at det vil være umulig å innhente samtykke, i tillegg til at skjevhet mhp sosioøkonomiske forhold mest sannsynlig også ville gjøre seg gjeldende her. Det er god grunn til å tro at sosiøkonomiske forhold påvirker utfallsmålet i studien (ICPC2-koder fra fastleger) og at evnt. skjevheter i utvalgene vil føre til at resultatene ikke blir representative for gruppene. Vi regner ikke med at forekomsten av CP påvirkes vesentlig av sosioøkonomiske forhold i høyinntektsland, og forutsetter derfor at sosioøkonomiske forhold er omtrent like i pasientgruppa og i kontrollgruppa. Vår samlede vurdering er at vi ikke ville kunne få svar på forskningsspørsmålene hvis det skulle innhentes samtykke samt at det er umulig å innhente samtykke p.g.a. det store antallet deltakere.

Det angis videre: *Resultatene fra studien er av vesentlig interesse for samfunnet fordi CP er en av de vanligste funksjonshemmingene hos barn i høyinntekstland som gir livslange utfordringer. Det er gjentatte ganger vist at helsetilbudet til barn og unge med funksjonshemminger er fragmentert og dårlig koordinert samtidig som fastleger forutsettes å ha en sentral og koordinerende rolle. Barn med CP har i mindre grad kontakt med fastleger enn forutsatt av helsenyndighetene, og barn med CP og smerter ser ikke ut til å kontakte fastlege før smertene blir sterke. Kunnskap om barn med CP sine kontakter med fastleger sammenliknet med normalbefolkningen vil grunnlag for målretting av tiltak som kan føre til et bedre og mer helhetlig helsetilbud til pasientgruppen.*

Komiteens vurdering
I henhold til helseforskningslovens § 35 kan REK bestemme at helseopplysninger kan eller skal gis fra helsepersonell til bruk i forskning, og at det kan skje uten hinder av taushetsplikt. Det samme gjelder opplysninger innsamlet i helse- og omsorgstjenesten. Dette kan bare skje dersom slik forskning er av vesentlig interesse for samfunnet og hensynet til deltakernes velferd og integritet er ivaretatt. Den regionale komiteen for medisinsk og helsefaglig forskningsetikk kan sette vilkår for bruken, blant annet for å verne de registrertes grunnleggende rettigheter og interesser.

Komiteen mener søker har argumentert godt for behovet for denne studien. Det oppleves som viktig at man får større kunnskap om pasientgruppen. All den tid formålet med prosjektet fremstår som viktig, er det dermed heller ikke uvesentlig å fremholde faren for skjevhet i utvalget som en rimelig grunn for å søke om unntak fra samtykkekravet.

Det er marginalt med opplysninger som skal samles inn fra kontrollgruppen. Noen av opplysningene er rent generiske – alder, kjønn, bosted – mens data om fastlegebesøk er avgjørende for prosjektets hypotese. Ingen av opplysningene oppleves som spesielt sensitive for komiteen, og det kan vanskelig sies at uthenting av variablene vil være i strid med deltakernes velferd eller integritet.

Komiteen godkjenner derfor at prosjektet gjennomføres uten at det innhentes samtykke.

Komiteen vurderer videre at det heller ikke er nødvendig at de deltakerne det her gjelder, informeres om bruken av helseopplysningene til forskning, jf. personvernforordningens artikkel 14, punkt 5.

Vedtak
Komiteen har gjort en helhetlig forskningsetisk vurdering av alle prosjektets sider. Prosjektet godkjennes med hjemmel i helseforskningsloven § 10.

Komiteen gjør samtidig oppmerksom på at etter ny personopplysningslov må det også foreligge et behandlingsgrunnlag etter personvernforordningen. Det må forankres i egen institusjon.

Godkjenningen omfatter at helseopplysninger innsamlet i helsetjenesten kan gis fra helsepersonell til bruk i prosjektet uten hinder av taushetsplikt, i tråd med det som er angitt i søknad og protokoll, med hjemmel i helseforskningslovens § 35.

Tillatelsen er gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknaden og protokollen, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 31.12.2028. Av dokumentasjonshensyn skal prosjektopplysningene likevel bevares inntil 31.12.2033. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Komiteens avgjørelse var enstemmig.

Komiteens vedtak kan påklages til Den nasjonale forskningsetiske komité for medisin og helsefag, jf. Forvaltningslovens § 28 flg. Eventuell klage sendes til REK Sør-Øst. Klagefristen er tre uker fra mottak av dette brevet.

Sluttmelding og søknad om prosjektendring
Prosjektleder skal sende sluttmelding til REK sør-øst på eget skjema senest 30.09.2028, jf. hfl. § 12. Prosjektleder skal sende søknad om prosjektendring til REK sør-øst dersom det skal gjøres vesentlige endringer i forhold til de opplysninger som er gitt i søknaden, jf. hfl. § 11.

Med vennlig hilsen

Britt Ingjerd Nesheim
professor dr. med.
leder REK sør-øst C

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11 ERRATA

Name of the candidate: Selma Mujezinovic Larsen					
Title: Pain and health-related quality of life in children and adolescents with cerebral palsy					
Coding in "Type of correction":					
cor	correction				
colotf	change of layout or text format – description of change				
Chapter in the thesis	**Page**	**Line**	**Original text**	**Type of correction**	**Corrected text**
Preface	4 of 74	1	… cerebral palsy	cor	… cerebral palsy (CP).
Preface	5 of 74	4	… in Trondheim (NTNU)	cor	… in Trondheim (Norwegian University of Science and Technology)
Summary	8 of 74	27	… six CPCHILD domains. Paper IV…	colotf - space between the paragraphs to be deleted	… six CPCHILD domains. Paper IV…
Summary	9 of 74	1	… daytime contacts (type, RFE) in period…	cor	…daytime contacts with regard to type of contact and reason for encounter (RFE), in period…
Summary	9 of 74	19	… in adolescence. Paper IV…	colotf - space between the paragraphs to be deleted	… in adolescence. Paper IV…
Sammendrag	11 of 74	4	…og hoftesmerter (Papers I-II)…	cor	… og hoftesmerter (Artiklene I-II)
Sammendrag	11 of 74	11	…Paper III hadde vi…	cor	… Artikkel III hadde vi…
Sammendrag	11 of 74	18	…i ungdomstiden. Paper …	colotf -space between the paragraphs to be deleted/corr	… i ungdomstiden. Artikkel …
2	23 of 74	19	…of Pain (15, 16)	Colotf – missing (IASP)	… of Pain (IASP), (15, 16).
2	25 of 74	10-11	The following classifications are relevant in Papers I-III included in the thesis:	Cor	The following three classifications are relevant in the thesis:
2	25 of 74	14	…CP subtypes (27):	Colotf – erase (27)	… CP subtypes:
2	29 of 74	7	… and last up …	cor	… and lasts up…
4	35 of 74	1	Caregivers Priorities	cor	Caregiver Priorities

4	35 of 74	27	… (5) (papers I-IV).	cor – erase (papers I-IV)	… (5).
5	42 of 74	Table	HRQoL domains in CPCHILD Domain 1 … Domain 2 … Domain 3 … Domain 5 … Domain 6 …	cor -erase word "Domain" 5 times	HRQoL domains in CPCHILD 1 … 2 … 3 … 5 … 6 …
6	44 of 74	26	Both studies …	cor	The studies …
6	45 of 74	19	…focused on a…	cor	… focused also on a…
6	46 of 74	3	… appropriate. Paper IV	colotf – space between the paragraphs to be erased	… appropriate. Paper IV
6	52 of 74	28	Paper II	cor	Paper I
6	52 of 74	29	Paper III	cor	Paper II
6	53 of 74	1	Paper II	cor	Paper I
6	63 of 74	19	… both children with CP	cor	…both children and adolescents with CP
10	75 of 158*		10 APPENDICES "placement"	colotf - comes twice due to merging of files	10 APPENDICES should appear after Papers I-IV as page 138 of 158
*The thesis has page numeration from 1-74, while Chapter 9 PAPERS follows on Pages 75-137 of the merged pdf file. Chapter 10 APPENDICES follows on Pages 138-158. Since merging of several pdf-files had been done, the page numeration for pages 75-158 is not visible in the submitted version.					