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CEREBRAL PALSY IN UGANDA: PREVALENCE, MORTALITY, FUNCTIONAL DEVELOPMENT, ACCESS TO SERVICES AND WHEELCHAIR INTERVENTION

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Cerebral palsy in Uganda: Prevalence, mortality, functional development, access to services and wheelchair intervention
THESIS FOR DOCTORAL DEGREE (Ph.D)

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This work is dedicated to the children and young people and their families participating in the studies, without your extended support these studies would not have been possible. Your courage and resilience in the face of adversity is inspiring.

For the children and young people who are no longer with us here on earth, you are often in my thoughts and may you rest in peace.

”A society cannot be equitable unless all children are included, and children with disabilities cannot be included unless sound data collection and analysis render them visible.”

United Nations Children’s Fund (UNICEF), The state of the world’s children 2013, Children with disabilities

PREFACE

We were assessing one of the children in our study, a 17 year old boy who could not use one hand and walked with a limp, I asked the mother if the boy was in school, or did some kind of work at home, she looked at me and replied “Look at him, he is disabled, he cannot do anything”.

For me this exemplifies that childhood disability is not simply a health condition, it is the combination of the child’s health condition, available interventions and contextual factors. Having a background of physiotherapy in Sweden, I know that a child with unilateral cerebral palsy and minor motor impairments such as the boy described above, would receive comprehensive early interventions, inclusive education, and the family would receive training and support. The child would likely have similar future prospects as their peers without health conditions. As compared to the boy in Uganda who lacks education and training, and whose disabilities have been getting more severe over the years due to lack of interventions.

To be born with a health condition in a country where there is a lack of health services and support systems, in combination with stigma, is not equivalent to being born in a country where a child is able to access early interventions and get support throughout their childhood. In other words, the same child would be more disabled in a different context.

I have met many caregivers in Uganda who provide so much love, energy and support to their children with disabilities. They do this even under the extreme pressures of living in poverty, being met with negative attitudes and having many children to take care of. I have also met caregivers who have given up hope and as they have expressed it themselves “I am just waiting for this child to die now”, but I do not blame them for their feelings, I blame the society that fails to support them. I admire the strength and resilience of the mothers, fathers and grandparents who are trying their best to care for their children in an environment that does not respect or support them. This thesis is for them, with hope for a better future.

POPULAR SCIENCE SUMMARY

Children with disabilities living in low and middle-income countries rarely receive the health services that they need, such as medication, therapy and wheelchairs. They are also less likely to attend school. In addition the children and their families are often met with negative attitudes from other people in their communities as well as from health care workers. There is little research done on children with disabilities living in low-income settings. This makes these children invisible and means that they are not included when plans are made for health services. Cerebral palsy is one of the most common physical disabilities among children worldwide. Children with cerebral palsy have difficulties with movement and posture, such as walking, sitting or using their hands. They often also have communication difficulties, intellectual disabilities and epileptic seizures.

The aim of this doctoral thesis is to make children living with cerebral palsy in Uganda visible through population-based studies. We investigated how many children that are living with cerebral palsy in Uganda. We wanted to examine their abilities to move around, to take care of themselves and to communicate. We wanted to explore how many of the children that did not survive, and what the main causes of death were. We wanted to see how their functional abilities such as walking and sitting, progressed over time and compare their development to children in high-income countries. Finally, we wanted to test a strategy for distributing wheelchairs and providing training to make sure that the wheelchairs are used regularly in the child's everyday life.

We found that there were more children living with cerebral palsy in Uganda compared to high-income countries. In the 2-7 year old range we found twice as many children in Uganda as compared to high-income countries. And we think the real number is even higher, as many children had likely died before we could include them in our studies. Children with cerebral palsy in Uganda were 25 times more likely to die during the four-year duration of our study than children that did not have cerebral palsy. The main risk factors for dying were severe malnutrition and severe mobility impairment, such as not being able to walk, crawl or sit. The main causes of death were malnutrition or anaemia and infectious diseases such as malaria.

The children with cerebral palsy in Uganda developed less functional skills over time compared to children with cerebral palsy in high-income countries. This is probably because of their extremely low access to services. For the children that could not walk only 8% had a wheelchair, and none had any kind of walking aid. None of the children had any kind of aids for seeing, hearing or communicating, not even simple aids such as spectacles or

communication boards. One third of the children had epileptic seizures, but only 40% of those were taking antiepileptic medicine. Only 10% of the children had received some sort of rehabilitation services in the 12 months before the study. Many caregivers did not seek care for their child because they lacked money to pay for transport and services, they lacked knowledge of what could help the child and where to seek care, and they had lost hope in their child ever improving.

Through collaboration with the charity Walkabout foundation all the children in our study that could not walk received a donated wheelchair. We included some of the children in a wheelchair study. In the study a therapist team together with the family set goals for the wheelchair use, we then made three home visits to each family over a period of six months to support them in implementing the goals. We found that most families implemented almost all of the set goals for the wheelchair use. The programme increased the children's participation in daily activities. Before the study more than one third of the children did no daily activities they did other than eating and hygiene (such as getting washed and dressed). After the intervention this decreased to only one child (3%).

What we found in our studies highlight the huge inequalities for children with disabilities living in low-income settings. Not alone do they not thrive but they are struggling to just survive. We can expect that this situation is similar for millions of children living with disabilities in low-income settings. Directing interventions towards this group will not only prevent suffering and death, which must be considered essential, but will also allow these children to participate in family and community life.

ABSTRACT

Background and aim: Cerebral palsy (CP) is one of the most common causes of childhood physical disability, but little is known of children and young people with CP living in low and middle-income countries (LMIC). The studies in this thesis are some of the first population-based studies on CP from sub-Saharan Africa. This PhD project aims to describe the prevalence, mortality, functional development and access to care for children and youth with CP in Uganda, and to explore a strategy for wheelchair intervention in a LMIC.

Methods and participants: We did a three stage screening of 31 756 children living in the Iganga/Mayuge Health and Demographic Surveillance Site (IMHDSS), and identified 86 children that were diagnosed with CP, in addition 11 children were found in a triangulation using village key informants. These 97 children were included in a CP cohort, described in study I-IV. Study I and III describe the prevalence, time of injury, functional impairments, care-seeking behaviour and access to services. Study II and IV follow the cohort over a four-year period investigating functional development and mortality. In paper V we conveniently sampled 32 children to be included in an exploratory intervention study testing a goal-directed support program for donated manual wheelchairs

Main findings: The crude prevalence of CP per 1000 children was 2.7 (95% CI 2.2-3.3). The CP prevalence after triangulation was 3.1. The CP prevalence decreased with increasing age, due to a decrease of children with more severe motor impairments. Timing of brain injury was postneonatal (25%) and preterm (2%) and the rest were considered full term. For the children that could not walk 8% had wheelchairs and none had walkers. The children had no assistive devices for communication, vision or hearing. One third of the children had epilepsy, and the treatment gap for epileptic medication was 61%. One third of the children attended school, and school attendance decreased with associated impairment and lower gross motor function. Care seeking for child's motor impairment was low among caregivers, the main barriers to seeking care were lack of money, lack of knowledge and having lost hope. Fifteen children in the CP cohort died over four years. The mortality rate ratio was 25.3 for children with CP compared to the general population. The risk of death for children with CP was higher for children with severe motor impairment and severe malnutrition. The most common causes of death were anemia, malaria and other infections. Children with CP in Uganda had a slower development in mobility and gross motor function compared to children in HIC, because children with mild motor impairments and younger children (2-5 years) did not follow the steep developmental trajectories from high-income countries (HIC). The goal achievement of set goals for wheelchair use in the intervention was high at 82.6% to 100%.

At the start of the wheelchair intervention 12/32 participants had no daily activities other than eating and hygiene, this deceased to 1/31 after the intervention. The main advantages of the wheelchairs according to the caregivers were; not having to carry their child, easier to bring their child, easier feeding, being able to change child's position, increased social interactions with other children and child being happier.

Conclusions: The prevalence of CP in Uganda was higher than in HIC, but this is an underestimate due to high mortality. Children with CP were 25 times more likely to die than children in the general population. Children and young people with CP in Uganda had a slower development in mobility and gross motor function compared to their peers in HIC, this is probably because of their poor access to rehabilitation, assistive devices, health care and education. The wheelchair intervention showed promising results with high attainment of set goals, increased participation in activities, improved positioning, improved mobility and high satisfaction.

The findings from this thesis highlight the urgent need to prioritize research and interventions for children with CP in low-income settings. In the current situation not alone do they not thrive but they are struggling to just survive. Directing efforts towards this group has the potential to reduce mortality, increase participation and help the children achieve their developmental potential.

LIST OF SCIENTIFIC PAPERS

I. Kakooza-Mwesige A, **Andrews C**, Peterson S, Wabwire Mangen F, Eliasson AC, Forssberg H. Prevalence of cerebral palsy in Uganda: a population-based study. The Lancet Global health. 2017;5(12):e1275-e82. doi:10.1016/s2214-109x(17)30374-1

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III. **Andrews C**, Kakooza-Mwesige A, Almeida R, et al. Impairments, functional limitations, and access to services and education for children with cerebral palsy in Uganda: a population-based study. Dev Med Child Neurol. 2019. doi:10.1111/dmcn.14401

IV. **Andrews C**, Namaganda L, Eliasson AC, Kakooza-Mwesige A, Forssberg, H. Functional development in children with cerebral palsy in Uganda: population-based longitudinal cohort study. Dev Med Child Neurol. 2021. doi: 10.1111/dmcn.14996

V. **Andrews C**, Kakooza-Mwesige A, Kamusiime S, Eliasson AC. A family centred goal setting and coaching programme for wheelchairs in Uganda: an explorative intervention study for children and youth with cerebral palsy (Manuscript)

SCIENTIFIC PAPERS NOT INCLUDED IN THE THESIS

Saloojee G, Ekwan F, **Andrews C,** Damiano DL, Kakooza-Mwesige A, Forssberg H. Akwenda intervention programme for children and youth with cerebral palsy in a low-resource setting in sub-Saharan Africa: protocol for a quasi-randomised controlled study. BMJ Open, 11(3), e047634. doi:10.1136/bmjopen-2020-047634

CONTENTS

LIST OF ABBREVIATIONS

CFCS	Communication Function Classification System
CI	Confidence Interval
COD	Cause of death
CP	Cerebral palsy
GMFCS	Gross Motor Function Classification System
GMFM-66	Gross Motor Function Measure 66 items
HINE	Hammersmith Infant Neurological Examination
HRs	Hazard ratios
ICD	International Classification of Diseases
KIM	Key Informant Method
MACS	Manual Ability Classification System
MRI	Magnetic Resonance Imaging
MR	Mortality rate
MRR	Mortality rate ratios
HIC	High-income countries
LMIC	Low and middle-income countries
PEDI	Pediatric Evaluation of Disability Inventory
PEDI-UG	Pediatric Evaluation of Disability Inventory Ugandan version
SCPE	Surveillance of Cerebral Palsy in Europe
SD	Standard deviation
SDG	Sustainable Development goals
VHT	Village Health Team
WHO	World Health Organization

1 INTRODUCTION

Children with disabilities have the right to a full and active life. These rights include effective access to education, health care and rehabilitation services and preparation for employment and recreation opportunities. When these rights are fulfilled they promote self-reliance, help the child achieve their fullest possible individual development and facilitate the child's active participation in the community. These rights are supported by most countries in the world, including Uganda, through the ratification of the "Convention of the rights of the Child" and the "Convention of the rights of People with Disabilities".[1,2]

But the human rights of children with disabilities are far from being realized. Children with disabilities are often stigmatized and discriminated, and compared to children without a disability they are more likely to experience abuse, have lower participation in community activities, attain a lower level of education and lower school attendance.[3-6]

There is a huge paucity of evidence about prevalence, function and interventions for children with disabilities in Uganda and other low and middle-income countries (LMIC). This lack of evidence results in many children not being identified and not receiving much-needed services. The first step towards addressing this injustice is to make these children visible so that they can be included in health policies and health service provision.

Children with disabilities have finally been given an opportunity to be included in the global development agenda with the transition to the Sustainable Development Goals (SDG). The basis of the SDG is "leave no-one behind", with a focus on reaching the groups furthest left behind first, which includes children with disabilities. The SDG emphasizes the need to include people with disabilities in health, education, employment and data collection. To be able to achieve the ambitious SDG targets of ensuring healthy lives and promote well-being for all, at all ages, it is crucial to prioritise children with disabilities.[7]

The aim of this PhD project is to make children with cerebral palsy (CP) in Uganda visible. Our hope is that these studies will draw attention to the life situation for children with disabilities and their families living in a low-income setting.

2 BACKGROUND

2.1 CHILDHOOD DISABILITY

The World Health Organization has estimated that 93 million children are living with a moderate or severe disability, and most of these children live in LMIC. But there is substantial uncertainty about these estimates, due to paucity and limited quality of data from LMIC.[8] A review by Maulik et al found an overall childhood disability prevalence range of 0.4-12.7% in LMIC, this wide range is due to variation in definition, methodology and use of different screening and assessment instruments.[9]

Childhood disability and poverty are interlinked; poverty increases the risk of disability and disability increases the risk of poverty.[8,10] Although it is difficult to establish the causality between poverty and disability, we know that poverty introduces risk factors for disability and disability can put a financial strain on families. Disability can contribute to poverty in families due to extra costs associated with health care and less time for income generating activities due to the increased burden of care.[8] It has been estimated that over 200 million children in LMIC will not fulfill their developmental potential, due to risk factors such as intrauterine growth restriction, malnutrition, infectious diseases including malaria, contaminated drinking water and inadequate cognitive stimulation.[11,12]

2.2 CEREBRAL PALSY

2.2.1 DEFINITION

Rosenbaum et al developed the most commonly used definition of CP in 2007, where they define that; CP is an umbrella term that describes a group of permanent disorders of the development of movement and posture; that cause activity limitations that persist throughout life. The activity limitations are caused by non-progressive disturbances that occurred in the developing fetal or infant brain, during pregnancy, delivery or up to two years of age. The activity limitations can range from severe, where children are unable to walk or sit independently and require support in all activities in daily life, to mild where children can perform most activities independently. Children with CP often have associated impairments in sensation, perception, cognition, communication, behaviour, epilepsy and secondary musculoskeletal problems.[13]

2.2.2 PREVALENCE

Cerebral palsy is one of the most common causes of childhood physical disability.[14] Several HIC have put in place national or regional registers for CP[15], and several large population based studies have been published from these registers. The prevalence rate in HIC is therefore well established at about 1.8-3.1 per 1000 live births.[16-19] But there is a lack of data on CP prevalence from LMIC, a systematic review of studies on CP prevalence published from 1996 to 2013 only included one study from a LMIC, the study was from Turkey and was not population-based.[19] Before this PhD project only four population-based studies had been published from Africa, three from Egypt giving a prevalence of 2.0-3.6 per 1000 children[20-22] and one from South Africa with a prevalence of 10 per 1000 children.[23] This wide range in prevalence probably reflects differences in methodologies, socioeconomic context and presence of risk factors. The wide range of CP prevalence and the few studies available make it difficult to make any general conclusions on the scale of CP amongst children living in LMIC.

2.2.3 RISK FACTORS

The risk factors for CP often overlap and interact with each other and the complexity of aetilogy is yet to be completely understood. The risk factors for CP can be identified either before pregnancy, during pregnancy, perinatally (from birth up to one month of age) or postneonatally (from one month to two years after birth). The risk factors that can be found before pregnancy are history of stillbirths, miscarriages, low socioeconomic status and assisted reproduction. The risk factors identifiable during pregnancy are preterm birth, carrying multiples, male sex of baby, fetal growth restrictions, placental abnormalities, birth defects, genetic factors, substance abuse, maternal infections and maternal thyroid disease or preeclampsia. Perinatal risk factors are acute intrapartum hypoxia ischemia, low birth weight, seizures, jaundice, hypoglycemia and infection. Postneonatal risk factors are stroke, jaundice, infections, surgical complications and accidental brain injury.[14,24,25] Recent studies have demonstrated that CP in children can be caused by genetic factors.[26] Historically birth asphyxia was thought to be the main cause of CP, but in HIC it has been shown that only 10% or less of children with CP clearly experienced major birth asphyxia.[14] The main risk factor for CP in HIC is preterm birth, with over 40% of all children being born preterm.[17,18,27]

Some of the risk factors identified for CP in Africa are the same as in HIC such as premature birth, low birth weight, neonatal jaundice, maternal infections, recurrent miscarriages in mothers and similar conditions in the family. While other major risk factors are found in Africa but rarely in HIC, such as maternal HIV infection, obstructed labor and complications during delivery, neonatal infections, neonatal seizures, and being the first-born baby.[21,22,28,29] Some of the risk factors can be accounted to the poor access to prenatal care and delivery care in sub-Saharan Africa, where almost 40% of births are not attended by skilled personnel.[30] Many of the risk factors are also due to the high prevalence of malaria and other infectious diseases in the region.

2.2.4 IDENTIFICATION AND DIAGNOSIS

Historically the identification of CP in HIC has been made between one to two years of age, but new evidence supports that CP or "high risk of CP" can be accurately identified before five months of corrected age. A combination of assessments with strong predictive validity, together with clinical reasoning is recommended for identification before 6 months corrected age. About half of all infants with CP have high-risk indicators in pregnancy or around the birth period, enabling early screening. For the other half of infants with CP they have no identified risks, and the caregivers or health professionals notice delays in motor milestones, which are usually identified after 5 months of corrected age.[25]

The tools with best predictive validity for identifying CP or high risk of CP before 5 months corrected age are neonatal Magnetic Resonance Imaging (MRI), the Prechtl Qualitative Assessment of General Movements and the Hammersmith Infant Neurological Examination (HINE), for infants with risk indicators, these three tools in combination are more than 95% accurate. The tools with best predictive value after 5 months of corrected age are MRI and the HINE, for infants with risk indicators these two tools are more than 90% accurate. In LMIC where MRI is often not available, it is recommended to use the HINE.[25]

The reasoning behind recommending early detection of CP is so that children can receive early intervention. Early interventions have been suggested to have greater benefit than later intervention, with suggested benefits on brain plasticity, prevention of complications and enhancement of parent and caregiver well being.[25,31] But more high quality research is needed to further investigate the suggested benefits of early intervention.[31] Although it is now possible and recommended to identify children with CP early, this is not being implemented in LMIC. Studies from LMIC have shown that the average age of being referred and diagnosed with CP is 4 years and 6 months, indicating that children with CP in LMIC have no possibility to receive early intervention.[32,33]

With the introduction of surveillance programs for CP all over the world, a general consensus has been reached for how to identify and diagnose children with CP. Many registers have adopted the definition by Rosenbaum et al described above.[13] Surveillance programmes in UK, Europe and Australia has identified the following five key-elements for CP definition: i) its a group of disorders ii) permanent but not unchanging iii) it involves a disorder of movement and/or posture and of motor function iv) it is due to a non-progressive interference/lesion/abnormality v) this interference/lesion/abnormality arises in the developing/immature brain. These five elements reflect the general consensus of the definitions provided to date.[34] To assist with identifying and classifying children with CP the Surveillance of Cerebral Palsy in Europe (SCPE) have developed a decision trees for inclusion and exclusion of children in a CP cohort as well as a decision tree for CP subtypes.[15] It is recommended to review a child identified with CP at 4 or 5 years of age to ascertain the CP diagnosis, using the same criteria and decision trees described above.[34]

2.3 FUNCTIONAL ABILITIES IN CEREBRAL PALSY

2.3.1 FUNCTIONAL CLASSIFICATION SYSTEMS

The functional abilities for children with CP vary considerably, from children being independent in most activities to needing assistance in all activities. Three functional classification systems are widely used and they provide a common language to describe functional abilities for children with CP in gross motor function, fine motor function and communication. The Gross Motor Function Classification System (GMFCS) classifies mobility and postural control. The Manual Ability Classification System (MACS) classifies hand function in relation to children's ability to handle objects in daily life. The Communication Function Classification System (CFCS) classifies ability to communicate, using any method including speech, gestures, sign language and communication devices. All three scales are based on five mutually exclusive functional levels where children at level I have the highest abilities and independence, and children at level V have the least abilities and are dependent in all activities.[35] These three systems compliment each other and should be used together to get a better understanding of the functional profile of CP.[36] See a summary description of the different classification system levels in table 1.

Level	GMFCS	MACS	CFCS
I	Walks without limitations	Handles objects easily and successfully	Effective sender and receiver with unfamiliar and familiar partners
II	Walks with limitations	Handles most objects but with somewhat reduced quality and/or speed of achievement.	Effective but slower paced sender and/or receiver with unfamiliar and/or familiar partners.
III	Walks using a hand-held mobility device	Handles objects with difficulty; needs help to prepare and/or modify activities.	Effective sender and receiver with familiar partners
IV	Self-mobility with limitations; may use powered mobility	Handles a limited selection of easily managed objects in adapted situations.	Inconsistent sender and/or receiver with familiar partners
V	Severely limited self-mobility: transported in a manual wheelchair	Does not handle objects and has severely limited ability to perform even simple actions.	Seldom effective sender and receiver even with familiar partners

Table 1: Summary of the different levels in Gross Motor Function Classification System (GMFCS), Manual Ability Classification System (MACS) and Communication Function Classification System (CFCS).

2.3.2 PREDICTION OF FUNCTIONAL DEVELOPMENT

The development of the classification systems have made it possible to predict future motor function, since they have shown stability over time, with many children remaining in the same classification level. The highest stability has been found for GMFCS, one study showed that 73% of the children remained in the same classification level over a 2-3 year period,[37]

this stability was further supported by another study where 72% of children over 4 years old did not change their classification level over a two year period. [38] The other two classification systems have shown less stability over time, with 49% and 55% of children over 4 years of age remaining in their classification level over a two-year period for MACS and CFCS respectively.[38]

Through utilizing the GMFCS it has been possible to make developmental trajectories for gross motor function, as measured by the Gross Motor Function Measure 66 items.[39-42] Developmental trajectories have also been developed for mobility and self-care abilities, measured by Pediatric Evaluation of Disability inventory (PEDI).[43] These developmental trajectories have been developed from large longitudinal studies of children with CP in Netherlands and Canada.[39,43] Using these developmental trajectories it is now possible to get an idea of the predicted development for a child based on their GMFCS level and age. This is a very important tool for clinicians to use when explaining prediction for the child's gross motor development for caregivers. This tool also makes it easier to plan for which interventions a child may need.[39]

The functional classification scales have shown reliability in two studies from LMIC, one study in Tanzania showed excellent reliability of MACS and GMFCS, and another study from Venezuela showed very good reliability and validity of GMFCS.[44,45] While studies on the stability of the classification systems in LMIC are lacking, making it unclear if GMFCS can be used for predictions of motor function in LMIC.

2.3.3 FUNCTIONAL ABILITIES

It is important to describe the functional abilities for children with CP on a population-based level in order to get an understanding of the needs for service provision. There is a lot of population-based information available on functional abilities for children with CP in HIC; the patterns are similar over continents and countries with a little less than two thirds (56-65%) being independent walkers in most settings (GMFCS I & II), 3-12% being capable of walking using hand-held mobility devices (GMFCS III) and one third (29-33%) being non-independent walkers (GMFCS IV-V).[46-48] Similarly for fine motor function a little less than two-thirds (57-65%) handles objects successfully (MACS I-II), 3-14% handle objects with difficulties (MACS III), and about one third (27-33%) have severe limitations in handling objects (MACS IV-V).[48,49]

The CFCS is the latest of the scales to be developed, and very few population-based studies have been published using this scale. One study from Sweden showed that two fifths of the children were effective communicators (CFCS I-II, 41%), about one fifth were effective communicators with familiar partners (CFCS III, 21%) and two fifths had severe limitations in communication (CFCS IV-V, 38%).[50] Other published studies looking at communication impairment all use different measures and definitions and it is difficult to compare results over countries. But it is clear that many children with CP in HIC have communication

impairments, with impaired speech in half or more (49-61%), and about half of these being non-verbal (24-31%).[47,48]

No population-based studies on functional abilities for children with CP in LMIC had been published before the start of this PhD project. The few available studies were done in clinical settings, and showed a higher proportion of children with more severe motor impairments compared to HIC (GMFCS IV-V, 41-57%).[28,51] But clinical studies are not representative for the general population since children with more severe impairments might be more likely to seek care, especially in LMIC where access to services are scarce.

2.3.4 ASSOCIATED IMPAIRMENTS

The most common associated impairments for children with CP in HIC are intellectual impairment (45-56%), epilepsy (28-44%), severe visual impairment (5-17%), autism spectrum disorder (5-7%) and severe hearing impairment (3-4%).[16,46-48,50,52]

To our knowledge only one population-based study on associated impairments for children with CP in Africa had been published before the start of this PhD project. This publication was from Egypt and showed higher rates of associated impairments with 70% of the children having intellectual impairments, and 52% having active epilepsy.[21] A study done at Mulago hospital in Kampala, Uganda also showed higher rates of associated impairments with 77% of the children having intellectual impairment and 45% having epilepsy.[53] But as mentioned earlier, hospital-based studies are not a true representation of the population.

2.4 MORTALITY IN CEREBRAL PALSY

Several studies from HIC have shown that people with CP have a modestly lower life expectancy than the general population.[54] For children with CP and mild motor impairments the life expectancy may be the same as for the general population, while children with severe motor impairments have an increased risk of premature mortality. The major risk factors for death among people with CP are severe motor impairments, severe cognitive impairments, gastrostomy and need of a feeding tube, and epilepsy. The major causes of death were respiratory, such as pneumonia.[54-56]

Studies from LMIC have also shown a higher risk of premature mortality for children with neurological impairments.[57,58] In a study from rural Kenya the risk of mortality for children with neurological impairments was three to four times higher than for the general population, they found no increased risk by severity in motor impairment, but the risk of death was increased by developmental delay and severe malnutrition.[58] A recent study from rural Bangladesh found that the mortality rate was nearly five times higher for children with CP than the general population. They found that the risk of premature death was higher for

children below five years, for children with more severe motor impairment and associated impairments, and for children with severe malnutrition.[57]

Studies on CP specific mortality in sub-Saharan Africa are missing, but we can suspect that the mortality is high considering the high rates of malnutrition found in studies on children with CP.[59,60]

2.5 MANAGEMENT OF CHILDREN WITH CEREBRAL PALSY

Children with CP are in need of comprehensive health care, rehabilitation and assistive devices to improve function and to prevent secondary impairments such as contractures. Two extensive reviews have identified best practice for management of children with CP in early and later ages. Both reviews highlight the importance of supporting caregivers of children with CP, to optimize the child's development and to protect caregivers' mental health.[25,61]

The first review recommended early diagnosis and referral for children with CP. Children with CP should be referred to CP specific interventions as soon as the child has been identified with CP or high risk of CP, in HIC this can now be done before 6 months of age. Early intervention for children with CP can optimize infant neuroplasticity, prevent complications and enhance caregiver well being. Early interventions should include task-specific motor training, as well as interventions to promote caregiver coping and mental health. It is recommended to manage seizures with medication and monitor the child's weight to avoid malnutrition.[25]

The second review was a systematic review of interventions for children with CP; they recommended several interventions, and disregarded some. Interventions for improved motor function in children with CP should practice real-life tasks and activities using self-generated active movements, at a high intensity, for the achievement of a goal set by the child (or a parent proxy). In contrast passive motor interventions, where the child is not involved in the initiation of the movements, such as neurodevelopmental therapy in the original passive format, are less effective or even ineffective. For tone management it is recommended to use botulinum toxin, intrathecal baclofen, diazepam and selective dorsal rhizotomy. On-going research suggests that contractures can possibly be prevented through high intensity self-generated active movements in the early years. Once a contracture has developed serial casting can be applied to reduce or eliminate early moderate contractures. After the casting has been completed it is recommended to do active strength training and goal directed training to make functional use of the increased range of movement. For severe contractures it might be required to consider orthopedic surgery. Passive stretching in isolation is not recommended for contracture management. Half of all children with CP have swallowing difficulties, and might require non-oral tube feeding. It is very important to manage swallowing difficulties since aspiration leading to respiratory complications is a leading cause of death in HIC.[61]

Providing assistive devices for children with disabilities is an important intervention strategy. Assistive devices can reduce caregiver workload, improve mobility, improve self-care skills and social function and increase children's quality of life.[62-65] Mobility devices are crucial for children with disabilities, they are designed to improve users ability to maintain a body position, and walk or move from one place to another, common examples include wheelchairs, crutches, walking frames and orthoses.[66] Mobility devices can increase participation and activity for children with disabilities.[65]

2.6 ACCESS TO SERVICES IN LOW AND MIDDLE INCOME COUNTRIES

Global data on the need for rehabilitation services, the services provided and the unmet need do not exist.[8] A review article looking at the access to rehabilitation services in LMIC, concluded that access to rehabilitation was poorly measured in studies, but generally shown to be low.[67] There is a huge shortage of rehabilitation professionals in LMIC, where countries with higher needs tends to have lower numbers of skilled workers.[68] In Africa, there is a shortage of both basic and specialist services for children with CP. There is poor availability of diagnostic facilities, shortage of medical personnel with experience and expertise in managing CP as well as medication shortages such as anti-epileptics, and a lack of rehabilitation. This rehabilitation shortage included lack of access to regular therapy, surgical procedures and lack of assistive devices such as wheelchairs.[69]

Global data on the need for and provision of assistive devices for mobility is very limited but the demand is thought to be high, and access is reportedly poor, studies from LMIC found that only 17-37% of people received the assistive devices that they needed.[8,66] The provision of mobility devices is often a low priority for governments, and is therefore not reflected in national legislations, policies and strategies. In many LMIC financial resources are not allocated for development and supply of mobility devices, and the people with disabilities need to pay for the mobility devices out-of-pocket which many have difficulties to afford. There is a lack of properly trained rehabilitation staff for mobility device provision. In addition, service delivery systems in LMIC are often inadequate and only located in major rehabilitation centres, making access difficult for the rural population.

Access to wheelchairs is crucial for people with disabilities. In the absence of national systems for wheelchair deliveries, the main source of wheelchairs in most LMIC is donations from international charities, and they rarely have the capacity or means to develop sustainable service delivery systems.[66] These charities often provide large quantities of wheelchairs at one point in time, and rarely do training or follow up.[70] The impact on the wheelchair users from these large-scale donations are not well established. Studies following up donated manual wheelchairs are inconclusive, some have found low rates of regular usage (7% in India) and high rates of dissatisfaction (60% in Zimbabwe), while a study following up wheelchair donations in India, Chile and Vietnam showed improved health, reduced pain and increased independence.[71-73]

2.7 CHALLENGES AND COPING STRATEGIES FOR CAREGIVERS IN EAST AFRICA

The importance of family centered care for children with CP is now widely recognized within pediatric rehabilitation. A positive caregiving environment nurtures children and improves their health, social competence and functioning.[74] It is important to know what challenges caregivers of children with disabilities in East Africa face, as this should be taken into consideration when planning family centered interventions for children with CP.

Caregivers of children with disabilities in East Africa face a number of challenges, these challenges include factors such as poverty, stress, negative attitudes, cultural beliefs and stigma. Poverty was expressed as a lack of resources to provide both basic necessities such as food and clothes, and also lack of ability to pay for medicines, hospital charges, transport, school fees and assistive devices such as hearing aids and wheelchairs. Stress for caregivers is associated with the extra care needed for their disabled child, leading to having insufficient time for other chores and responsibilities and isolation from community activities. Some community beliefs associate caregivers of children with disabilities with evil spirits, punishment from God or witchcraft, other believe that children with disabilities are shameful for their families and should be kept hidden from other people, these beliefs lead to mental distress among caregivers.[75,76] Caregivers also said that they faced physical difficulties when caring for their child, which often led to muscle pain, especially in relation to carrying their child.[77]

Caregivers of children with disabilities adopt different coping strategies to be able to care for their children. Some of these strategies are: improvising materials in their home for therapy, making their own assistive devices, sharing experiences with other caregivers and spiritual beliefs.[75,76] Caregivers also identified what they needed to care for their child; these needs included having adequate knowledge and skills of the child's condition, access to education for their child and access to assistive devices such as wheelchairs.[76]

2.8 UGANDA COUNTRY PROFILE

The republic of Uganda is a landlocked country located in East Africa. The country enjoys an equatorial climate with plenty of rain and sunshine, it has varying vegetation with tropical rain forest in the South and savannah woodland and semi arid vegetation in the North. In the early years of Uganda's independence the economy was registering high rates of growth and development. Political instability, poor governance and economic mismanagement in the 1970s and early 1980s left Uganda among the worlds poorest and least developed countries. The economy has since then recovered, but Uganda is a low-income country whose economy is mainly dependent on agricultural activities. A majority of the households (69%) are dependent on subsistence farming as their main source of income. Uganda has a population

of more than 34 million people; the population is young with more than half being below 18 years. The annual population growth rate is 3% and the total fertility rate is 5.9 children per women.[78]

The infant and under five mortality rate in Uganda has shown a decrease over the last two decades but it is still high with an infant mortality rate at 43 deaths per 1000 live births, and an under five mortality rate at 64 deaths per 1000 live births. The neonatal mortality has not changed since 2006, and is 27 per 1000 live births.[79] By referring to the trends in figure 1 it can be seen that neonatal mortality now constitutes a large proportion of under five mortality. The main causes of death for children under five were pneumonia (16%), preterm birth (12%), intrapartum related events (11%), diarrhoea (8%) and malaria (8%).[80]

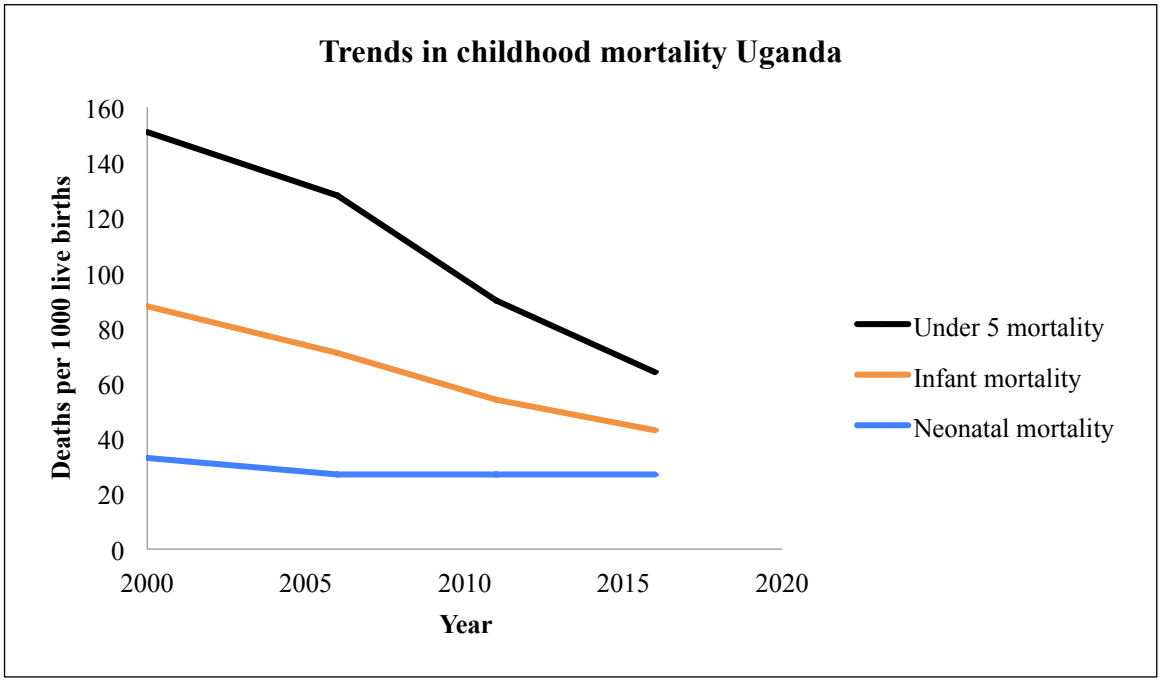

Figure 1. Trends in childhood mortality in Uganda, extracted from the Uganda demographic and health survey 2016[79]

Looking at antenatal and postnatal care, more than half (60%) of the mothers attended more than four antenatal care visits, and a majority of mothers delivered their babies with skilled assistance (74%), but almost half (43%) received no postnatal care for them or their baby in the first two days after their delivery.[79]

2.9 HEALTH PROVISION SYSTEM IN UGANDA

Health care services in Uganda are provided from the public sector, the private non-for profit sector, private health practitioners and traditional and complimentary medicine practitioners. The public health provision system in Uganda comprise of health centers at level I-IV and hospitals (general, regional and national). Health centers level I consists of trained community volunteers that form village health teams (VHT) and provide health promotion and education and serve as a link between the communities and the health professionals.

Health centers II-III provide basic out-patient and outreach health services. Health center IV provides in-patient care and more complicated procedures. The health system in Uganda faces a number of challenges, including a critical shortage of health care personnel, regular shortage of medicines, underfinancing and heavy dependence on development aid and out-of-pocket expenditure. User fees in public health facilities were abolished in 2001, even so 28% of households spend more than 10% of total household consumption on health goods and services such as medical care fees, drugs and "gratuities" in the public sector.[81]

There is a huge shortage of therapist staff, especially in rural areas. In Iganga and Mayuge districts there are 2 physiotherapists in a population of close to 1 million people.[78,82] The first health contact a person with a neurology condition will have is the VHT; patients will then be referred up the chain of health centres (II-IV) without accessing any specialist services, and will eventually be referred to Mulago national referral hospital where they can access a specialist neurology clinic that is run once a week by 2 pediatricians with neurology training. But long distances, delays at health facilities, poor quality of services and poverty make it difficult for caregivers to go to the hospital for specialized care.[83]

There are also a number of Non Governmental Organisations that provide services in different regions in Uganda, with most services provided in the urban areas, including specialist rehabilitation, provision of assistive devices and specialist surgical procedures. But their services are not nationally or regionally coordinated and it is difficult to assess their impact.

3 RATIONALE FOR THE STUDIES

Even though it is estimated that millions of children suffer from disabilities around the world, they are being neglected both in research and service provision. There is a huge paucity of evidence about prevalence, function and interventions for children and young people with CP in Uganda and other LMIC. This lack of evidence results in many children and young people not being identified and not receiving much-needed services.

The first step towards addressing this injustice is to make these children and young people visible so that they can be included in health policies and health service provision. Opportunities for children and young people with CP are limited in Uganda, they are often not diagnosed, and they seldom receive the appropriate services or assistive devices. There is a need for studies on the prevalence, function and impairments of children and young people with CP in Uganda, to be able to provide basic data for health policy and planning. There is also a need for more research on the impact of wheelchair charity, and alternative ways of distributing wheelchairs in LMIC should be developed and evaluated.

4 AIMS AND OBJECTIVES

OVERARCHING AIM

The aim of the thesis is to assess the current situation and identify needs of children and young people with cerebral palsy in a population based cohort in rural Uganda. The hope is to generate information that will illuminate these children's and young people's situation and explore the feasibility of a goal-directed coaching programme for wheelchair users.

OBJECTIVES

- To describe the prevalence, functional level and time of injury of children with CP. (Paper I)
- To estimate the mortality rate of children with CP over a four-year period, and identify risk factors and causes of death, and compare this to the general population of children living in the same area. (Paper II)
- To describe functional limitations and associated impairments of children with CP. And to describe the care seeking behaviour of caregivers, and also access to assistive devices, rehabilitation and education. (Paper III)
- To follow the functional development of a population based cohort of children and young people with CP in Uganda over a four year period, and compare their development with developmental trajectories from high-income countries. (Paper IV)
- To evaluate a goal-directed coaching programme for children and young people with CP and their families in a low-income setting, which aims to facilitate daily use of wheelchairs and increase participation in home and family activities and improve positioning. (Paper V)

5 STUDY DESIGN AND METHODS

The five papers in this thesis all include children and young people from a population-based CP cohort living in a mainly rural area in Eastern Uganda. This cohort was identified through a large-scale population-based screening in 2015 utilizing a population-based research platform. An overview of the papers, research questions and methods used can be seen in Table 2.

Table 2. Overview of study designs and research methods

Paper	Research questions	Study design and participants	Primary outcomes	Data analysis
I	What is the prevalence of childhood CP in Uganda?	Three-stage cross sectional method to screen for CP in children aged 2-17 years living in IMHDSS (n=31 756).	CP diagnosis and clinical subtype, Time of injury, Functional level	Descriptive statistics, Multiple imputation, chi-square test, regression analysis
II	What is the mortality and causes of death for children with CP in Uganda?	Longitudinal study: 1) Population based cohort of children with CP (n=97). 2) General population cohort in IMHDSS (n=41 319)	All case mortality, Immediate Cause of Death, Weight and height, Associated impairments, Functional level	Descriptive statistics, mortality calculations, cox proportional hazard regression models, Kaplan Meier method, log-rank test
III	What kind of functional limitations and associated impairments do children with CP in Uganda have? –And what is their access to services?	Population-based cross sectional study of a cohort of children with CP and their caregivers (n=93)	Functional level, Activities in daily life, Associated impairments, Access to education, assistive devices and care seeking	Descriptive statistics, qualitative content analysis, chi square test, Monte Carlo simulation, linear regression model
IV	Do children and young people with CP in Uganda have slower development than in high-income countries?	Longitudinal study of a population based cohort of children and young people with CP (n=81).	Functional level, Activities in daily life, Gross Motor function	Descriptive statistics, developmental trajectory comparisons, Wilcoxon signed rank test
V	Can a goal-directed coaching programme for wheelchairs be effective in Uganda?	An exploratory intervention study (n=32)	Participation in day-to-day life, Goal-achievement, frequency of wheelchair use, Caregiver satisfaction with wheelchairs	Descriptive statistics, calculations of goal attainment, qualitative content analysis

5.1 STUDY SETTING AND POPULATION

The studies for all five papers were conducted in the Iganga-Mayuge Health and Demographic Surveillance Site (IMHDSS). The IMHDSS was set up in 2004 as a Makerere University and Karolinska Institutet bilateral research collaboration, to serve as a research platform for community based epidemiological research and research training. The IMHDSS covers a population of over 90,000 people in 65 villages in an area of 155km^2 in the districts of Iganga and Mayuge in Eastern Uganda, 120 km east of the capital city Kampala along the Uganda-Kenya Highway. Trained data collectors using data collection forms and hand-held computers follow the basic demographics such as births, deaths and migration of the population bi-annually through door-to-door visits to over 18,000 households. The IMHDSS organization consists of a management team, a data collection team and a data management team, as well as community volunteers who report deaths and births within the population. The site provides a platform for researchers wishing to carry out large population based studies, and has hosted several large studies since its inception.[84]

The IMHDSS population is mainly rural, with a minority residing in either urban or peri-urban areas. The main source of income is agricultural activities in the rural population, and running small-scale shops/business for the peri-urban population. The population is very young, with about half being below 15 years. The childhood mortality rates are very high, with an under 5 year mortality rate of 58.6 per 1000 live births, and most of these deaths occur before the child reached one year with an infant mortality rate of 37 per 1000 live births and a neonatal mortality rate of 29 per 1000 live births. In the neonatal period the main causes of death were stillbirth, birth injury or asphyxia and prematurity, beyond the neonatal period the main causes of death were malaria (59%) and malnutrition (15%).[84]

The infrastructure in the area is poorly developed, with poor sanitation and hygiene and low levels of protected water sources. The IMHDSS community is served by two hospitals and 16 community-based lower-level health centers. In addition to this each village has a Village Health Team, comprising of two trained community volunteers from the village, to facilitate health promotion e.g., for immunization coverage and health service utilization.[84] At the time of the studies there were no regular services aimed at children and young people with disabilities provided within the study area, neither through public nor private providers.

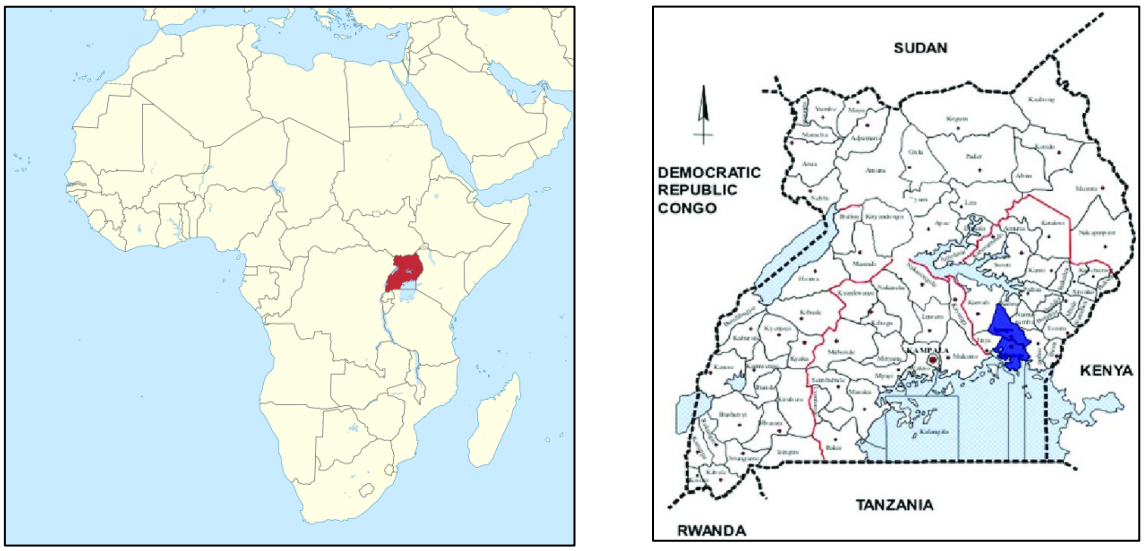

Figure 2. Showing from left to right: map of Africa with Uganda in the shaded area, map of Uganda with the IMHDSS in shaded area

5.2 STUDY DESIGN AND DATA COLLECTION

All the studies in this thesis include the same population-based cohort of children and young people with CP living in the IMHDSS. This CP cohort was identified through a large-scale population based screening in 2015. The screening was done in three stages, and a triangulation was done to identify potentially missed cases. The children were assessed with standard neurological assessments and a therapist assessment focused on functional abilities. The children were diagnosed with CP and classified into clinical subtypes according to Surveillance of Cerebral Palsy in Europe (SCPE).[15] Caregivers of the children were interviewed about pregnancy, birth history, medical problems, development, sociodemographic factors, access to education and assistive devices and care-seeking practices. In 2016, all children and young people with a need were given a donated manual wheelchair, and we conveniently sampled 32 of these children for an exploratory intervention study. In 2019, the entire CP cohort was followed-up and the therapist team assessed the surviving children and young people, repeating the functional measures from 2015 and interviewing caregivers that had received wheelchairs to evaluate the intervention. Caregivers of the 15 children that had passed away were interviewed using verbal autopsy interviews.

5.2.1 THREE STAGE POPULATION BASED SCREENING WITH TRIANGULATION

Stage I: Field assistants asked two screening questions to the head of the households when performing the regular census door-to-door visit of all households in the IMHDSS. The field assistants were fluent in the local language Lusoga and English and had received a two-day training on the study aim and the two questions.

Stage II: Specially trained field assistants visited all households where a child had a positive response to either question, following a protocol that included questions for the head of the household and a basic assessment of the child's mobility and hand function with the aid of an observer flow-chart, adapted from the SCPE decision tree.[15]

Stage III: The children that screened positive in stage II were invited to go to the Iganga Referral hospital, where they were assessed by a team of one clinical officer, one nurse, one nursing assistant and one neurological expert (either a neurologist or a trained therapist (the PhD student or a Ugandan therapist). The team did a standard neurological assessment of each child using a reporting form, measured weight and height and interviewed the caregiver using a questionnaire on pregnancy, birth history, medical problems, development and sociodemographic factors. The CP diagnosis and subtype were set using the SCPE criteria and flow scheme.[15]

Triangulation: To account for possible missed children with CP in the population we used key informants in all the study villages, they were members of the communities with good knowledge of the village population i.e. members of village health teams or community workers. They were asked by the field assistants to identify children with symptoms similar to the children identified in the screening. These children then went through the clinical assessment in stage III.

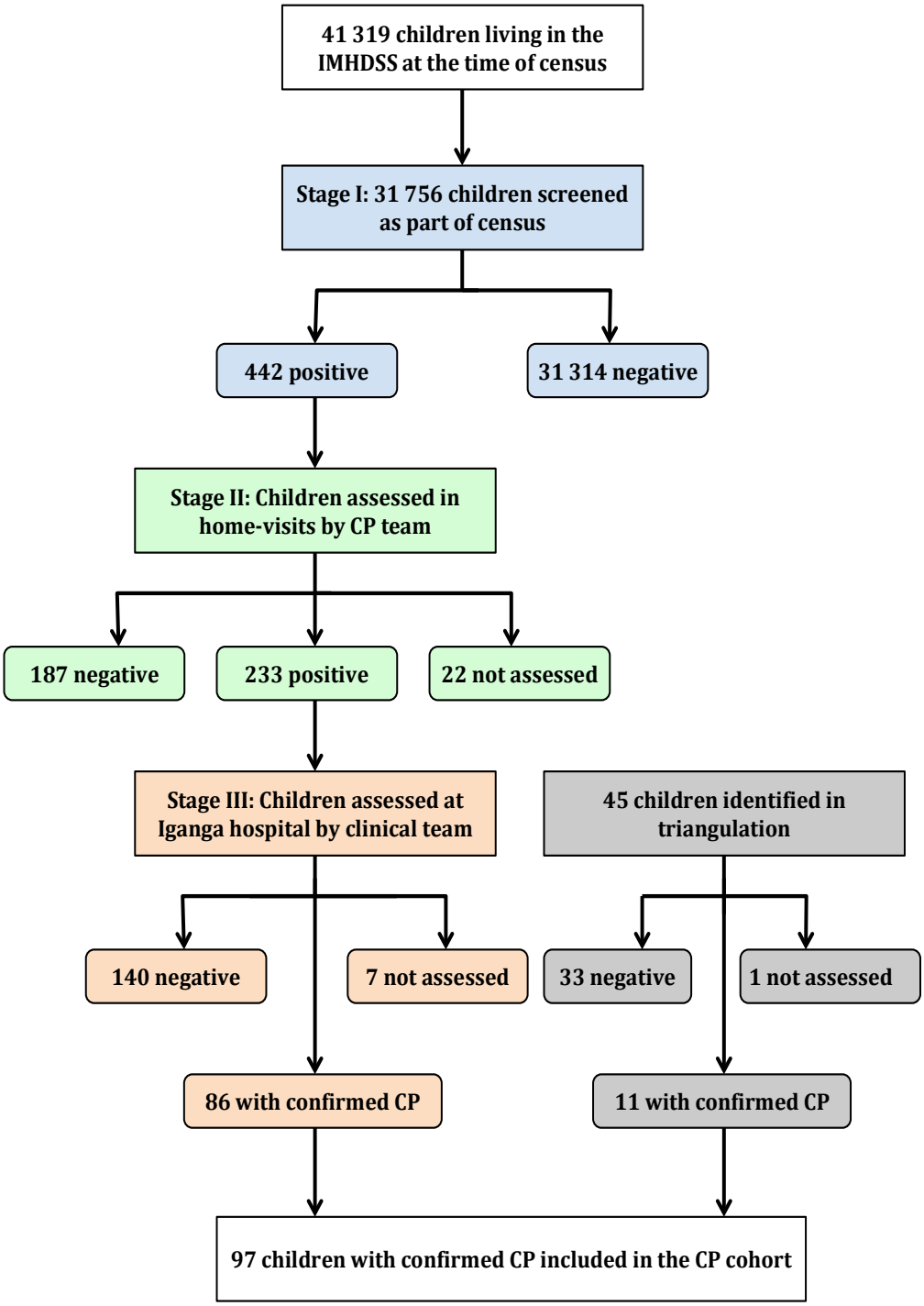

Figure 3. Flow chart of the screening to identify the population-based cohort of children with CP

5.2.2 THERAPIST ASSESSMENT

All children identified as having CP from the screening and triangulation were invited to participate in a comprehensive assessment by a specially trained therapist team. The therapist team consisted of one Ugandan occupational or physiotherapist, one Swedish physiotherapist (the PhD student) and a community mobilizer. The assessments were done either at the participants home or at a health facility close to their home. A Ugandan physiotherapist or occupational therapist interviewed the caregiver using the Pediatric evaluation of disability inventory Ugandan version (PEDI-UG) in the caregivers preferred language of English or Luganda, the interview would take between 15-60 minutes, depending on the child's ability level. After the PEDI-UG interview the caregiver was interviewed by the same therapist using a pretested, semi-structured questionnaire with closed and open-ended questions on school attendance, care-seeking and assistive devices. The child was assessed by another therapist using the Gross Motor Function Measure 66 items (GMFM-66) in a relatively standardized environment. Children that had independent mobility were tested at their closest health facility, using the same equipment at both assessments, while children with no mobility were often tested at their home. The GMFM-66 assessment would take between 20-60 minutes.

After the PEDI-UG interview the therapist would classify the child's function using the Gross Motor Function Classification System (GMFCS), the Manual Ability Classification System (MACS) and the Communication Function Classification System (CFCS). The therapist who did the PEDI-UG interview would then discuss and explain the classifications for the therapist that assessed the child, and they would together agree on the functional classifications.

The picture shows the therapist team during a home visit

5.2.3 WHEELCHAIR INTERVENTION

Through collaboration with the charity Walkabout Foundation, the participants in the studies identified to be in need, received a donation of a manual wheelchair in 2016. We conveniently sampled 32 of these children and young people to participate in an exploratory intervention study testing a goal-directed support program for donated manual wheelchairs. A Ugandan occupational therapist fluent in English and the local language Lusoga, a Swedish physiotherapist (the PhD student) and a community mobilizer implemented the intervention.

The intervention included a first home-visit where the therapists fit the wheelchair and discussed the child's and young person's normal day and what they would like to use the wheelchair for. Based on this the caregiver, and if possible the child or young person, set practical goals for the use of the wheelchair in their day-to-day life, with the therapist coaching them to set goals that were specific, measurable, attainable, time-specific and realistic. The therapists did three home visits after the goals were set, after one month, after two months and after six to ten months. The aim of the home visits was to facilitate use of the wheelchair and goal attainment, and to help problem solve any difficulties encountered. At the six to ten-month home-visit, information was collected in report forms on the child's or young person's daily activities and attainment of set goals; the caregiver was interviewed using a questionnaire with closed and open-ended questions on wheelchair use in different activities and advantages and difficulties encountered.

The picture on the left shows the therapist and the family discussing the goals for wheelchair use, while the picture on the right shows one of the donated wheelchairs and the occupational therapist Sauba Kamusiime.

5.2.4 FOUR-YEAR LONGITUDINAL FOLLOW-UP

Families of children and young people in the CP cohort were contacted in 2019 either by phone or through a home visit, to inquire if their child was still alive and to invite them to participate in the studies. If the child or young person had passed away, an experienced field assistant with counseling skills from the IMHDSS made a home visit to perform a verbal autopsy interview with the caregiver, following standard health and demographic surveillance site procedures.[85] Each surviving child and young person was invited to participate in a second therapist assessment by the trained therapist team. The assessment was done in the families' home, or at a close-by health facility. The outcome measures were the same as in the 2015 assessment: PEDI-UG, GMFM-66, GMFCS, MACS and CFCS. The caregivers of the children and young people that had received wheelchairs were also interviewed using a structured questionnaire with closed and open-ended questions on wheelchair use.

5.3 STUDY PARTICIPANTS

This thesis contains four papers of a population-based CP cohort (Paper I-IV), and one intervention study with children and young people sampled from the same cohort (Paper V). An overview of the study participants for Paper I-V are presented in Figure 4.

Paper I: This study included a screening of 31 756 children aged 2-17 years living in the IMHDSS at the time of the surveillance round from March 1, 2015 to June 30, 2015. The screening identified 86 children with CP; a triangulation exercise identified an additional 11 children with CP, giving a total number of 97 children included in the CP cohort. The inclusion criteria were living in the IMHDSS at the time of the surveillance round and receiving a CP diagnosis from our research team.

Paper II: This study included the 97 children in the CP cohort identified in 2015 and followed until 2019, and a general population cohort which included 41 319 children aged 2-17 years living in the IMHDSS on 1st January 2015 and followed until 31st December 2017.

Paper III: This study included 93 children in the CP cohort assessed at the therapist assessment in 2015; between the screening and the therapist assessment two children passed away and two were lost to follow up.

Paper IV: This study included the children and young people in the CP cohort assessed at the therapist assessment in 2015 that were still alive and available for the therapist assessment in 2019, for final analysis 81 children and young people with assessments at both points in time were included.

Paper V: This study included 32 children and young people that were conveniently sampled in 2016 from the children identified in the screening in 2015. The inclusion criteria for the study were non-independent walkers and having a CP diagnosis.

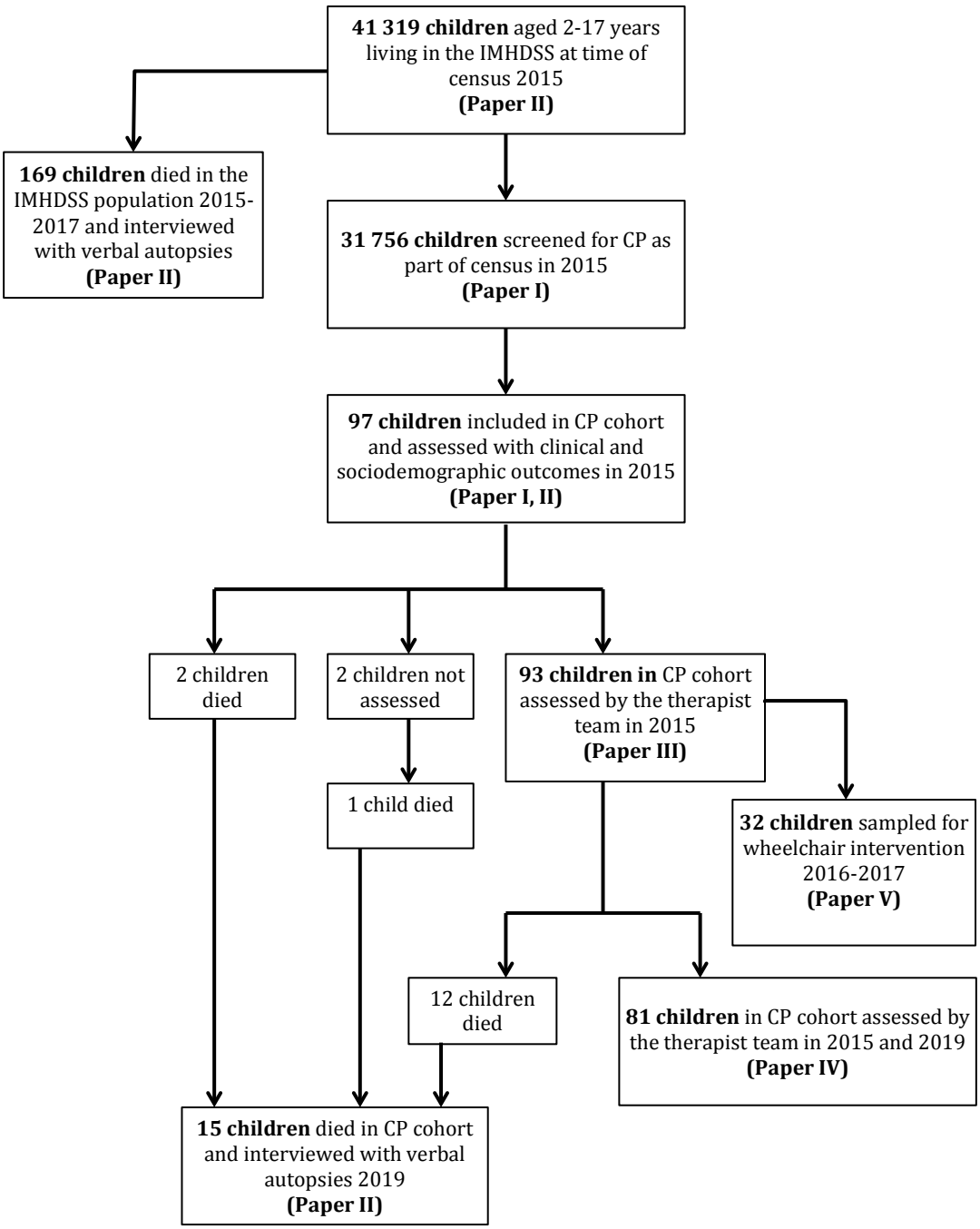

Figure 4. Flow chart of participants in Paper I-V
IMHDSS=Iganga Mayuge Health and Demographic Surveillance Site

5.4 OUTCOMES AND MEASURES

An overview of the main outcomes and measures used in Paper I-V are shown in table 3, and the outcome measures are described in more detail in this section.

Table 3. Overview of main outcomes and measures used in Paper I-V

OVERVIEW OF MAIN OUTCOMES AND MEASURES		
Outcome	**Measure**	**Paper**
CP diagnosis and clinical subtype	Two screening questions	I
	SCPE decision tree	
	SCPE Hierarchical classification tree of cerebral palsy sub-types	
Time of injury	Questionnaire on pregnancy, birth history, medical problems, development and sociodemographic factors	I
All cause mortality	Follow-up of the CP cohort, Surveillance of the general population cohort	II
Mortality rates and mortality rate ratios		
Immediate Cause of Death	Verbal autopsy interview	II
Weight and height	Weighing scale and tape measure	II
Associated impairments	Questionnaire on pregnancy, birth history, medical problems, development and sociodemographic factors	II,III
	Clinical examination form	
	Therapist assessment form	
Access to education, assistive devices and care seeking	Questionnaire on school attendance, care-seeking and assistive devices	III
Activities in daily life	PEDI-UG	III,IV
Functional ability level	GMFCS	I-V
	MACS	III-V
	CFCS	III-V
Gross Motor function	GMFM-66	IV
Participation in day-to-day life	Interview about daily/weekly/monthly/rare activities	V
Goal-attainment	Goal-setting form	V
Caregiver satisfaction with wheelchairs	Caregiver questionnaire: with closed and open-ended questions on frequency of use of wheelchairs in different activities and advantages and difficulties encountered while using the wheelchairs	V

PEDI-UG=Pediatric Evaluation of Disability Inventory Ugandan version
CFCS=Communication Function Classification System
GMFCS=Gross Motor Function Classification System
MACS= Manual Ability Classification System
GMGCS-66=Gross Motor Function Measure 66 items

Cerebral palsy diagnosis and clinical subtypes

The two screening questions asked by the field assistants in each household in the IMHDSS to screen for children with CP were derived from the Ten Question screen for childhood disability[86], and were adapted to the cultural context and terminology and translated to the local language Lusoga. The two questions were:

1. Is there anyone in this household aged between 2-18 years who has got brain damage or has difficulty in moving his/her arms or legs?
2. Is there anyone in this household aged between 2-18 years who has difficulty in understanding and may be referred to as mentally dull or slow and drips saliva or does not speak normally?

We used the international definition and classification system for CP and the SCPE decision tree to guide the screening procedure in stage II and to set the CP diagnosis in stage III.[13,15] In stage III of the screening we used the SCPE hierarchical classification tree to classify the children to clinical subtypes; spastic bilateral, spastic unilateral, dyskinetic, ataxic or not classified.[15] Each child's diagnosis and subtype were discussed by the Ugandan and Swedish team members via the internet using video clips of each child.

Time of injury

At stage III of the screening process, a nurse interviewed the caregiver using a questionnaire on pregnancy, birth history, medical problems, development and sociodemographic factors. Information was collected on gestational age at birth, and harmful events during pregnancy, birth or after birth. We categorized the event that possibly resulted in CP as preterm birth (if child was born before 37 weeks of gestational age), post-neonatal incident (event occurring more than one month after birth); the remaining children were considered to be neonatal full-term.

All cause mortality

After the four year longitudinal follow-up of the 97 children and young people in the CP cohort as well as the three year surveillance of the general population cohort, we determined the all cause mortality during the 54-month follow-up period (1 March 2015-30th August 2019) for the CP cohort, and the 36 month follow-up period for the children and young people in the general population cohort (1st January 2015-31st December 2017. Person observation months were calculated for each child from time of start of observation period until death or end of observation period.

Mortality rate and mortality rate ratios

Using the all cause mortality calculation of person observation months we determined the frequency of death occurrence in the CP cohort and the general population cohort through calculating mortality rates (MR). The MR were calculated as number of deaths in each cohort per 100 000 person observation years, with 95% corresponding confidence intervals. To compare the mortality between the CP cohort and the general population cohort we calculated Mortality Rate Ratios (MRR), where the number of deaths per 100 000 person observation years in the CP cohort were divided by the number of deaths per 100 000 person observation years in the general population cohort, with 95% corresponding confidence intervals. Standardized MR and standardized MRR were calculated using the general population as the reference, accounting for different age distributions between the two cohorts.

Immediate cause of death

An experienced field assistant with counselling skills from the IMHDSS made a home visit to perform a verbal autopsy interview with the caregiver, following standard Health and Demographic Surveillance Site procedures.[85] The immediate Cause of Death (COD) was assigned by two physicians assigned by the IMHDSS, they independently reviewed the information and assigned codes using the international classification of death algorithm (ICD-10 codes). If the COD assigned by the two physicians was not in agreement a third physician was consulted.

Associated impairments

Information on associated impairments in intellect, behaviour, vision, hearing and seizures was collected from three different sources;

1. Nurse interview of caregiver at stage II, using a questionnaire on pregnancy, birth history, medical problems, development and sociodemographic factors.
2. Information from the reporting form at the standard neurological assessment done by a clinician.
3. Information reported from the therapist assessment forms.

Associated impairments were considered unconfirmed when reported from one source, and confirmed when reported by two sources or more.

Activities in daily life: Pediatric Evaluation of Disability Inventory Luganda version (PEDI-UG)

The caregivers of the children and young people were interviewed by the Ugandan occupational or physiotherapist using the PEDI-UG. The Pediatric Evaluation of Disability Inventory (PEDI) is a recommended clinical assessment tool for children with CP; it measures activities in daily life in the dimensions of self-care, mobility and social function.[87,88] The original PEDI was developed in USA, but it has been translated to Luganda and adapted to the Ugandan cultural and social context (PEDI-UG).[89] The PEDI-UG has shown good-to-excellent psychometric properties to measure the functional performance of typically developing children aged 6 months to 7 years 6 months in Uganda.[90] Our research group recently performed a study with children and young people with CP in Uganda aged 2 to 22 years and found a high validity for the use of PEDI-UG in this population. (Amer et al., submitted manuscript)

Functional classification levels

The therapist team classified the children in the CP cohort functional abilities using three different classification systems developed for children with CP. The Gross Motor Function Classification System Expanded and Revised (GMFCS-E&R) was used to classify gross motor function such as sitting, standing, crawling and walking and the need for assistive devices and assistance.[91] We used the Manual Ability Classification System (MACS) to classify how children use their hands to handle objects in daily activities, and the Communication Function Classification System (CFCS) to classify the child's everyday communication performance.[92,93] These three systems have shown validity and reliability for measuring function in children with CP, and when used together they give a holistic understanding of the child's functional level.[35,36] In addition, the GMFCS and MACS have predictive properties since they have shown stability over time. The classification systems all have 5 mutually exclusive functional levels, where children at level I have the most abilities and independence and children at level V have the least abilities and are dependent on assistance.[35]

Gross motor function 66 items (GMFM-66)

The physiotherapist or occupational therapist assessed the children in the CP cohort using the GMFM-66. This tests the child's maximum capacity in the five dimensions of lying and rolling, sitting, crawling and kneeling, standing and walking, running and jumping.[94] The GMFM-66 has good psychometric properties for the assessment of children with CP, and is a useful outcome measure to detect changes in gross motor function over time.[94,95]

5.5 STATISTICAL ANALYSIS

Simple descriptive statistics to describe the frequency and distribution of the study outcomes were used in all the studies. The other statistical methods used in each study are described below.

Paper I: Cerebral palsy prevalence was estimated with 95% Confidence Intervals (CI) by dividing the number of children with CP identified in the screening by the total number of children that were screened at stage I. Multiple imputation was used to adjust for between stage attrition of the screening. Chi square test was used to investigate differences between the group screened at stage I, and the entire population living in the IMHDSS at the time of the screening. Generalized linear models were used to study associations, a p-value of less than 0.05 was considered statistically significant. Poisson regression was used to study the association between number of children with CP and age. Negative binominal regression with the log link function was used to study the association between number of children with CP and GMFCS level, clinical CP subtype and time of injury.

Paper II: We calculated MR per 100 000 person observation years and MRR using the general population cohort as the reference. To assess nutritional status of the children we calculated Z-scores for weight-for-age, height-for-age and weight-for-height. Children were considered severely malnourished if they had a Z-score below -3 standard deviations (SD) for at least one of the three measures. Cox proportional hazard regression models were fitted to compute hazard ratios to investigate the contributions of age, sex, GMFCS level, associated seizures and malnutrition on mortality for children with CP. We estimated survival probabilities using the Kaplan-Meier method. We compared survival curves between groups and subgroups using the log-rank test.

Paper III: Chi square test was used to compare GMFCS levels and MACS levels between a younger and older age group (2-5 years and 6-17 years). A Monte Carlo simulation was done for categories with few individuals. To compare the development of functional ability over time in Uganda with a HIC, we used PEDI data from a Swedish cohort of 116 children with CP aged 3 to 15 years.[96] We used linear regression models with PEDI scores as the dependent variable and combinations of GMFCS or MACS level, age, group (Sweden or Uganda) and interactions as independent variables. The open-ended questions from the questionnaire on seeking care and assistive devices were analyzed using qualitative content analysis in six steps inspired by Graneheim and Lundman.[97]

Paper IV: We calculated the difference in scores for GMFM-66 and PEDI-UG between the two assessments ("score change"). We compared our data to developmental trajectories from high-income countries in GMFM-66[40-42] and PEDI[43], and determined each individual's amount of deviation (either negative or positive) from the median in GMFM-66 and the modelled developmental trajectories for PEDI, we called this the "reference score". We calculated the reference score for first and second assessment, and then calculated the difference between the two scores ("reference score change"). We used the Wilcoxon signed rank test to see if there was any significant change between the first and second assessment in scores and reference scores. To establish the effect of age and functional level on development we analyzed the data in different subgroups in GMFCS levels and age groups. A Bonferroni correction was applied to correct for multiple comparisons.

Paper V: The goal achievement was calculated through dividing the number of set goals with the number of achieved goals. The open-ended questions from the questionnaire on advantages and challenges of using the wheelchair were analyzed using qualitative content analysis in six steps inspired by Graneheim and Lundman.[97]

5.6 ETHICAL CONSIDERATIONS

In the design of this PhD project we have followed Karolinska Institutet's Ethical Guidelines for international collaborations. The Higher Degrees Research and Ethics Committee of the School of Public Health, College of Health Sciences, Makerere University, and the Uganda National Council for Science and Technology have approved all of the studies in this PhD project. The participants in all of our studies were children and young people aged 2-23 years and their caregivers. Before data collection, the children and young people and their

caregivers were informed of the aim of the studies and the study procedure, that participation was voluntary and that they could at any time choose to no longer take part in the research. The data collectors read a consent form for the caregivers and asked if they were willing to participate, and the consent form was either signed in writing or with a thumbprint. For children and young people over the age of seven years an assent form was read out and signed, if the child or young person were able to communicate and understand adequately. All the data was collected in paper form or on handheld tablets, and stored securely to assure confidentiality. When the data is being presented or published we make sure to anonymize it so it cannot be tracked back to the participants. We have gotten a special ethical approval for presenting photos from our studies, as long as the participants consent.

We have faced a number of ethical considerations when performing these studies. In Uganda it is often a stigma to have a child with a disability, this can lead to social exclusion in the communities. By looking for these children and asking them to participate in this research we are exposing them in their home environment. Another major ethical consideration is that to identify and diagnose children with CP can create a demand for specialized services, that at the moment are not readily accessible in this area of Uganda.

To address these ethical considerations we have included different strategies in our studies that will increase the benefits for the participants.

We are using occupational and physiotherapists in all of the studies, with experiences from working in the communities in Eastern Uganda. Each caregiver and child got some one-on-one time with the therapists, where they could get some information on their child's condition, advice on referral services and how to best care for their child. Many of the caregivers had not previously gotten the chance to talk with a specialist about their child's condition, and this gave them an opportunity to learn more, and get answers to any questions they might have had. The research group that the PhD student is a part of are planning to implement a multicomponent intervention, the Akwenda CP programme that is set to start at the end of 2021. The programmes main component is peer-to-peer training of caregivers of children and young people with CP. This programme aims to equip caregivers with knowledge and techniques that will help them to best care for their child, and decrease their caregiving load and stress.[98]

All non-walking children identified in study I had the possibility of receiving a donation of a wheelchair through our collaboration with Softpower Health and the Walkabaout foundation. Wheelchairs are highly valued in Uganda, but are not accessible for most people. A wheelchair reduces the caregiving workload, increases independence for the children, and in our experience they lead to more community acceptance for disabled children.

Children and young people with CP are vulnerable to medical conditions and malnourishment, during the hospital and health facility assessments medical conditions observed such as infectious diseases, epilepsy or malnourishment were referred to existing health services at the Iganga hospital. During the home visits we sometimes observed medical conditions, malnourishment and neglect, when needed we provided transport and help with referral to health care.

The larger project that this PhD project was a part of was designed in two parts, one epidemiological part followed by an intervention. We thought it would be unethical to identify children with CP without trying to help improve their situation. Study 5 (Wheelchair intervention) provided participants with wheelchairs and strategies to use them. When implementing the planned Akwenda CP programme, we will offer the participants in study 1-5 to be part of a multidimensional intervention.[98] This intervention will aim to increase caregiver knowledge and reduce stress, to improve motor function, daily activities and participation for the children and young people and to increase community awareness of CP. Hopefully this intervention will be of great benefit for the participants, and if the program proves successful it can serve as a model for implementation in other low-income settings.

In addition, our hope is that these studies will make the needs of the children and young people and their caregivers visible, this has the potential to influence health planners and policy makers, which would be beneficial for children and young people with CP and their caregivers.

6 MAIN FINDINGS

From a screening of 31 756 children, aged 2-17 we identified 86 children that were diagnosed with CP by our team. In addition 11 children were found in the triangulation, giving a total number of 97 children with CP included in our CP cohort. Paper I-IV includes descriptions of this CP cohort, looking at prevalence, time of brain injury, subtype, functional level, associated impairment, access to assistive devices, care seeking practices, mortality and functional development. Paper V includes a convenient sample from the CP cohort and describes the implementation and evaluation of a wheelchair intervention programme. This chapter summarizes the main findings of the PhD project, for more detailed information see the re-prints of Paper I-V, appended to this thesis.

6.1 BACKGROUND DEMOGRAPHICS

The gender distribution for the children in the CP cohort showed a slightly larger proportion of males (57% vs 43%). Most of the children lived in rural areas (72%), and most households (83%) lived below the international poverty line of 1.9USD per person per day. Most of the main caregivers of the children were mothers (72%) followed by grandmothers (18%), about half of the main caregivers had a primary education (51%), while one fifth (19%) had no education. The caregivers mainly worked as subsistence farmers (70%) or were involved in petty trade such as selling food items or running small scale business (14%). (Paper II)

6.2 CEREBRAL PALSY PREVALENCE

To estimate the CP prevalence we included the 86 children identified with CP in our screening, giving a crude prevalence rate of 2.7 (95% CI 2.2-3.3) per 1000 children. The prevalence increased to 2.9 (95% CI 2.4-3.6) per 1000 children after we adjusted for attrition (accounted for cases lost between stages in the screening). And the crude prevalence including the children from the triangulation was 3.1 per 1000 children. We found fewer older children (8-17 years) with CP compared to younger children (>8 years); consequently the older children had a lower crude prevalence compared to younger children. (Paper I)

The association between number of children with CP and age was significant (estimated coefficient -0.07366, p=0.0025); the expected number of children with CP decreased with age with a multiplicative factor of 0.93. We investigated the association between the decrease in children with CP over age and gross motor function level using a negative binominal

regression model, we found this association to be significant (estimated coefficient -0.05778, p=0.023), the effect of age was only significant for children with low gross motor function (GMFCS level IV-V, -0.2136, p=0.008). This shows that the lower number of older children with CP was driven by a decrease in the number of children with higher GMFCS levels, as illustrated in figure 5. (Paper I)

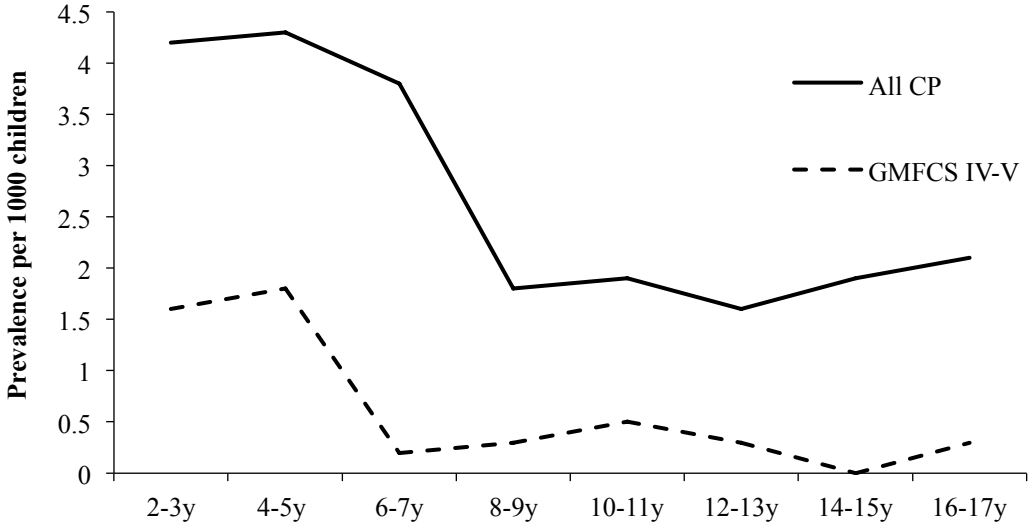

Figure 5. Estimated crude prevalence of CP by age goup
GMFCS=Gross Motor Function Classification System

6.3 TIME OF BRAIN INJURY

We analyzed the information provided by the caregiver interview in stage III on gestational age at birth, and harmful events during pregnancy, birth or after birth. Out of the 97 children in the CP cohort we found that two (2%) were born preterm (before 37 weeks of gestational age), and that a post-neonatal event possibly caused CP in 24 (25%) of the children, the remaining children were considered full term. The children with post-neonatal acquired CP typically had a normal perinatal history, but the children suddenly became ill with fever and convulsions, followed by a chronic motor impairment. (Paper I)

6.4 FUNCTIONAL CLASSIFICATION LEVELS

When looking at the functional classifications in younger compared to older children in our CP cohort we observed differences in distribution, see Figure 6. The younger children had a larger proportion of severe functional limitations compared to the older, in gross motor function (GMFCS IV-V: 2-5 years, 36% vs 6-17 years 10%) and fine motor function (MACS IV-V: 2-5 years 48% vs 6-17 years 10%). These differences in proportion between the two age groups (2-5 years vs 6-17 years) were significant in both gross motor function (GMFCS $p=0.002$) and fine motor function (MACS $p=0.01$). We compared our results with a population-based cohort in Sweden[48], and we found that for the older age group (6-17 years) there were significant differences between the Uganda cohort and the Swedish cohorts in both GMFCS levels ($p<0.001$) and MACS levels ($p=0.006$), with less severe impairments in the Ugandan cohort. For the younger age group (2-5 years) there were significant differences in GMFCS levels ($p<0.01$), with proportionally more severe impairments in the Ugandan sample. (Paper III)

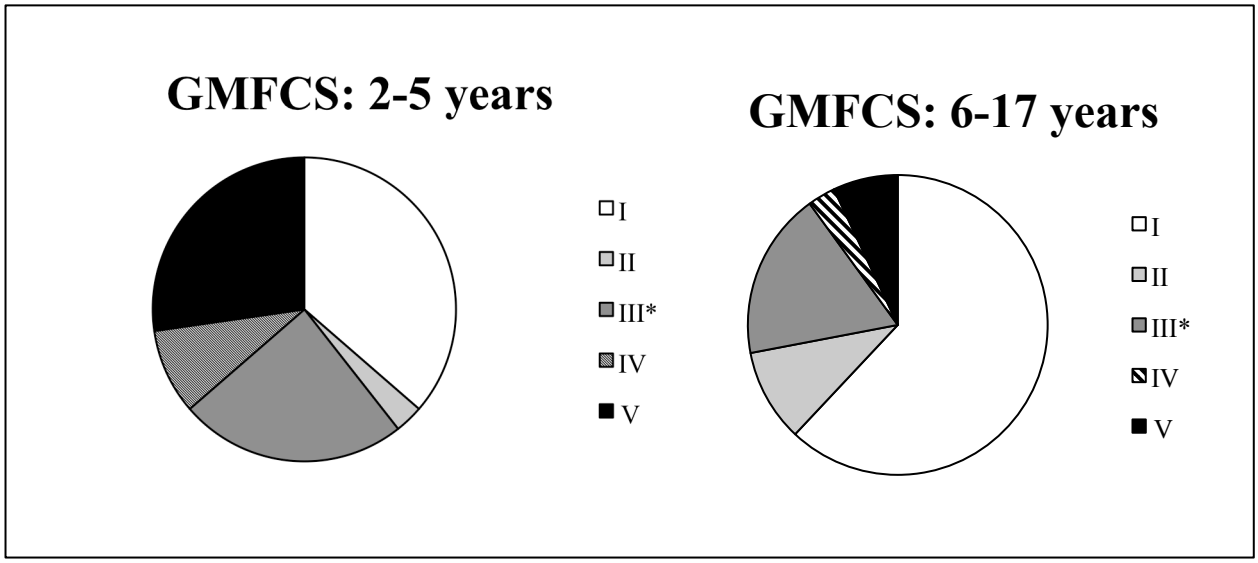

Figure 6: Distribution of Gross Motor Function Classification System (GMFCS) levels for the 93 children assessed by the therapist's team in 2015, in the younger and older age groups.

Note that the GMFCS level III were slightly adapted to the Ugandan environment, none of the children in the Ugandan cohort had assistive devices for functional walking; therefore children that can sit independently and move shorter distances (crawling etc.) but not walk (without assistive devices) were included in GMFCS level III. (Paper III)

For the two assessments done four years apart 57% of the children and young people did not change their GMFCS level, 60% did not change their MACS level and 55% did not change their CFCS level (Paper IV).

6.5 IMPAIRMENTS AND ACCESS TO SERVICES

An overview of impairments and access to assistive devices and antiepileptic medicine are shown in table 4. Out of the 93 children seen at the therapist assessment 37 were not independent walkers, only 3 of these had wheelchairs in working condition, and none had assistive devices for walking (walkers, canes, crutches). Two of the children that were living in the same compound shared a locally made wooden walker for knee walking. Out of the 34 children that could not walk independently and had no assistive devices for mobility, 21 could move independently shorter distances by rolling, creeping, crawling, bottom shuffling or walking while holding on to stable objects (such as walls or furniture), while 13 children had no form of independent mobility, and were dependent on being carried by caregivers. Eighteen children were dependent of support while sitting, but only one child had a special chair for sitting, made locally. The children with hearing or vision impairment had no assistive devices, such as spectacles or hearing aids. The children that had communication difficulties had no kind of assistive devices for communication. Out of the 33 children with confirmed seizures only 13 were currently taking antiepileptic medication, giving a treatment gap of 61%. (Paper III)

Table 4: access to assistive devices and antiepileptic medicine

Impairments	**N=93**	**Assistive devices and antiepileptic medicine**
Non-independent walkers (GMFCS III-V)	37	3 children had wheelchairs 2 children shared a knee-walker
Non-independent sitters (GMFCS IV-V)	18	1 special made chair for sitting support
Non-verbal (6-17 years)	22	No assistive devices for communication
Confirmed seizures	33	13 taking antiepileptic medication
Confirmed vision impairment	11	No assistive devices for seeing
Confirmed hearing impairment	7	No assistive devices for hearing

Legend: Presence of impairments and access to assistive devices and antiepileptic medication in the CP cohort seen at the therapist assessment. Confirmed impairments means that two or more of the sources observed impairment

6.6 IMPAIRMENTS AND ACCESS TO EDUCATION

About one third of the children in the CP cohort had no associated impairments (32%), one-third had one associated impairment (37%) and one third had two or more associated impairments (31%). Intellectual impairment was the most common confirmed associated impairment (54%) followed by seizures (35%). School attendance was lower for children with associated impairments, and decreased with GMFCS and CFCS levels as illustrated in figure 7. One third of the children aged 6-17 years attended school (n=18/60). (Paper III)

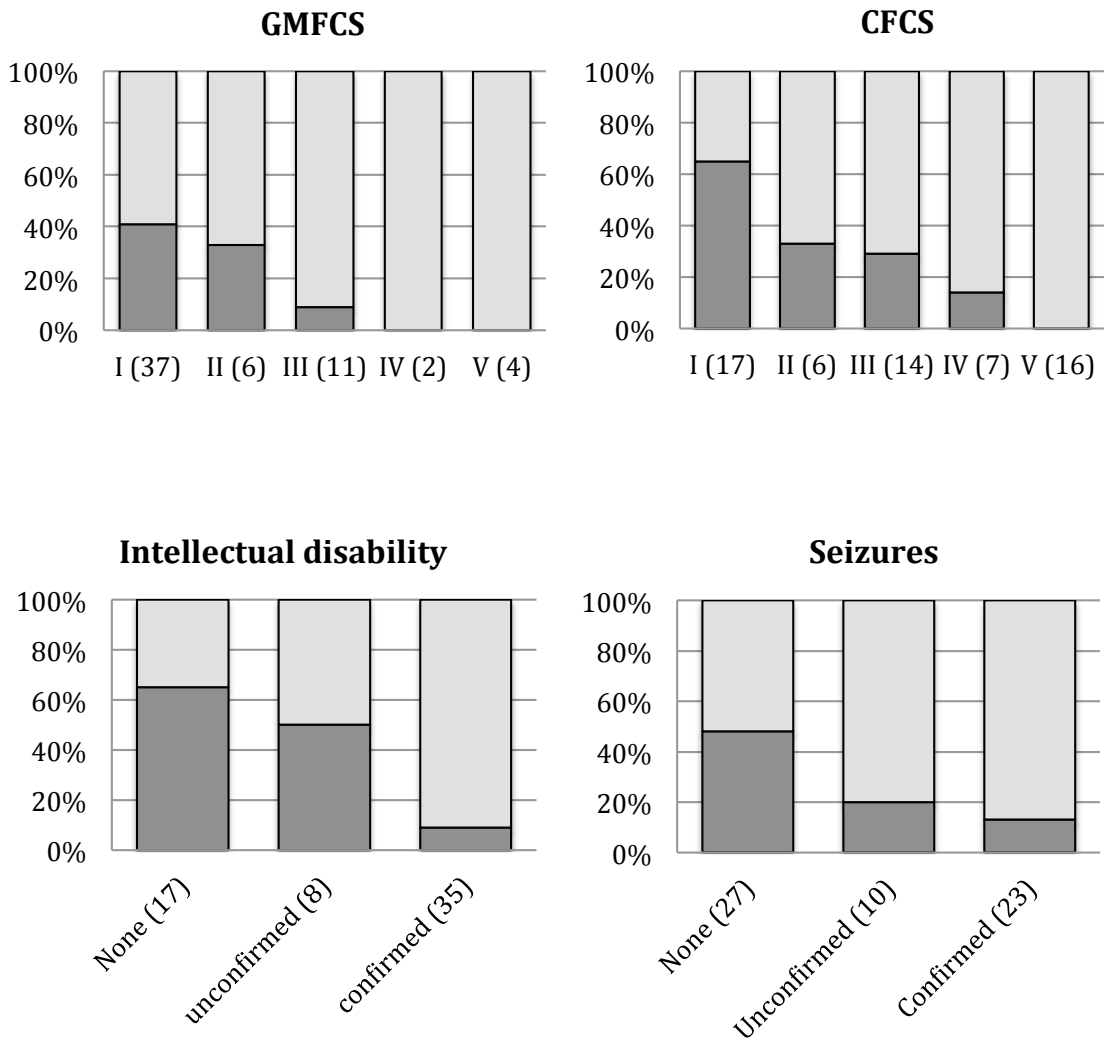

Figure 7: School attendance in children with cerebral palsy aged 6-17 years according to impairments: attending (dark grey; n=18); not attending (light grey; n=42)

6.7 CARE SEEKING BEHAVIOR

Out of the 93 caregivers seen at the therapist assessment, 74 wanted their child to improve in activities such as rolling, sitting, crawling, standing, walking or using their hands. But only one third (23/74) had sought help the previous year for the child's motor impairments. The most common visited care providers were government hospitals or health centers, traditional medicine practitioners and non-governmental organization led health programmes. Only 10% of the caregivers that wanted help for their child's motor function had received some sort of rehabilitation (7/74), and none of the children attended regular therapy services. We did a qualitative content analysis of reasons for not seeking care among the 51 caregivers that had not sought any care the previous year; the main themes are presented in table 5. (Paper III)

Table 5: Main caregiver themes for not seeking care for their child's motor improvement

Main theme	Description
Lack of money	Lack of money to seek help, to pay for transport, services and assistive devices
Lack of knowledge	Lack of knowledge of what is wrong with the child, what could be done, what kind of help that could be received and where to search for help or assistive devices.
Lost hope	Having lost hope that the child will ever improve, this could often be related to having sought help previously and not having received the help that they wanted.

6.8 MORTALITY PATTERNS AND CAUSES OF DEATH

From the 97 children included in the CP cohort in 2015, 15 had died during the four years of the study period (2015-2019), their mean age of death was 10.2±5.9 years, nine had GMFCS III-V and 10 had severe malnutrition. In the general population of children living in the IMHDSS during the time of the 2015 screening (41 319), 169 had died during the three years of the observation period, with a mean age of death at 7.2±4.8 years. The MR was 3952 per 100 000 person years in the CP cohort, and 137 per 100 000 person years in the general population cohort. The standardized mortality rate for the CP cohort was 3455 per 100 000 person years, with a standardized MRR of 25, using the general population as the reference. (Paper II)

In the general population the MR was highest in the youngest age group (2-6 years), and the effect of age was significant (log-rank, $p<0.0001$). For the CP cohort the survival probability was not significantly different between the age groups (log rank, $p=0.28$). Although the MR decreased with increasing age in the CP cohort, we found a higher MRR in the oldest age group (10-17 years, 39.6) compared to the youngest age group (2-6 years, 21.0), this is because of the steeper decrease in MR with increasing age in the general population. (Paper II)

Children in the CP cohort with severe motor impairment had a higher MR (GMFCS IV-V; 8718 per 100 000 person years) than children with mild motor impairment (GMFCS I-II; 1305 per 100 000 person years), and the risk of death was almost seven times higher for children with severe motor impairments than those with mild impairments (cox model, hazard ratio 6.8: $p=0.007$). The children with severe malnutrition had a higher MR (5880 per 100 000 person years) than children that did not have severe malnutrition (1626 per 100 000 person years), and the risk of death was almost four times higher in children with severe malnutrition than in those without (cox model, hazard ratio 3.7; $p=0.052$) (Paper II)

For the fifteen children in the CP cohort the immediate causes of death were anaemia/malnutrition (n=6), malaria (n=4), pneumonia (n=3) and meningitis (n=2). While Anaemia/malnutrition (22%) and malaria (19%) were also the main causes of death for the general population, they also had other major contributors such as gastro-intestinal disorders or diarrhoea (13%), other non-communicable disease (18%) and external causes including injuries (10%). (Paper II)

6.9 FUNCTIONAL DEVELOPMENT IN UGANDA

The findings from paper III indicated that children with milder gross motor impairments (GMFCS I-II) had an increase in mobility skills with age in Uganda ($p<0.001$), while no significant difference in skills was found for children with moderate impairment (GMFCS III, $p=0.2$) or severe motor impairment (GMFCS IV-V, $p=0.72$). While paper IV showed that there was no development in gross motor function and mobility over the four years for the children and young people in the Ugandan cohort, with no significant difference between assessments for GMFM-66 ($p=0.792$) or PEDI mobility ($p=0.171$). (Paper IV)

In summary, the cross sectional study indicated an increase in mobility skills for children at GMFCS I-II, but the longitudinal study did not support this increase in mobility skills and showed that the children and young people in Uganda had no development over age in mobility or gross motor function.

The findings from paper III indicated that children with the mildest fine motor impairments (MACS I) had an increase in self-care skills with age in Uganda ($p=0.02$), while no significant difference in skills was found for children at MACS level II ($p=0.38$) or MACS level III-V ($p=0.09$). (Paper III) While paper IV showed that the children and young people in Uganda had an increase in self-care scores over the four years (score change +4.5, $p=<0.001$). This was driven by an increase in scores for the children and young people with milder and moderate motor impairments (GMFCS I-II & GMFCS III), and the children below 12 years, while no difference were seen for the children and young people over 12 years, or the children and young people with severe motor impairments (GMFCS IV and V).

In summary, in both Paper III and Paper IV we found that the children and young people with mild motor impairments had a positive development in self-care skills.

6.10 FUNCTIONAL DEVELOPMENT COMPARED TO HIGH INCOME COUNTRIES

In paper III we compared our data from the 93 children in the CP cohort assessed by the therapist team with a convenient cohort of 116 children aged 3 to 15 years from Sweden.[96] In paper IV we assessed the children and young people in our CP cohort (n=81) at two different times and compared them with developmental trajectories from HIC for GMFM-66[40-42] and PEDI.[43]

In paper III we found that there was a difference in mobility skills between Uganda and Sweden for children at GMFCS level I-II and III, with a stronger positive correlation with age in Sweden than in Uganda ($p<0.001$). In paper IV we found that the children and young people in the Ugandan cohort scored below the developmental trajectory at both assessments in GMFM-66 and PEDI mobility. Negativity was greater at the second assessment for both GMFM-66 ($p=0.002$) and PEDI mobility ($p=0.036$), indicating that children and young people in Uganda negatively deviated from the developmental trajectories from HIC. The

negative deviation in GMFM-66 was driven by the youngest children (2-5 years), the oldest children and young people (12-18 years) and the children and young people with mild motor impairments (GMFCS I-II). While the negative deviation in PEDI mobility was driven by the youngest children (2-5 years).

In summary, in both Paper III and Paper IV we found that children and young people in Uganda had a slower development than their peers in HIC in both mobility and gross motor function. Children and young people with mild motor impairments (GMFCS I-II and younger children (2-5 years) mainly drove this slow development, since they had lower skills than expected for their age compared to their peers in HIC.

In paper III our results indicated that there was a significant difference between the development in Sweden and Uganda, with a lower increase in self-care scores over age in Uganda for MACS I ($p=0.02$), and MACS II ($p=<0.001$), while no significant difference was found for MACS IV-V ($p=0.38$). In paper IV we found that the children and young people in Uganda scored below the developmental trajectory at both assessments, but there was no significant difference in reference scores between the two assessments, indicating that the developmental trajectory for self-care in Uganda was similar to HIC.

In summary, Paper III indicated that the children in Uganda had a slower development in self-care skills, but this was not supported in paper IV, which found that the development trajectory for self-care in Uganda was similar to HIC.

6.11 WHEELCHAIR INTERVENTION

Through collaboration with the charity Walkabout Foundation all children and young people in need in the CP cohort received a donated wheelchair, out of these we conveniently sampled 32 children and young people to be included in the wheelchair intervention study. The children and young people were all non-independent walkers (GMFCS III, IV & V), and were aged 3-18 years at the time of wheelchair distribution with a mean age of 8.0 years. (Paper V)

The therapist and the caregiver agreed on goals for how and when the wheelchair should be used to increase the child's or young person's mobility, positioning and participation in everyday life. The mean number of goals set for each child or young person was 5.2 (range 3-8). Goal achievement for daily and weekly goals during the intervention period ranged from 83% to 100%. (Paper V)

At the start of the wheelchair intervention none of the children and young people had a wheelchair. The children and young people at GMFCS level IV-V were completely dependent on being carried by caregivers, only four children and young people had somewhere to sit, the rest were lying on the ground. After the intervention all children and

young people used their wheelchair daily for mobility, and all children and young people at GMFCS level IV-V used their wheelchair daily for positioning in sitting. (Paper V)

At the start of the intervention two thirds of the children and young people (41%) had no daily activities other than eating and hygiene, while after the intervention only one child (3%) had no daily activities other than eating and hygiene. The mean number of daily activities increased from 0.8 at the start of the intervention to 1.8 at the end of the intervention. The number of weekly/monthly/rarer activities also increased after the intervention, with over one third having no activities at the start (38%) down to only one child after the intervention (3%). Daily wheelchair use after three years was 44%, the main reason for not using the wheelchair was that the wheelchair was broken or the wheelchair did not fit anymore. (Paper V)

More than half of the caregivers (61%) found no difficulties with the wheelchair. The main themes from the caregivers that had difficulties with the wheelchairs were: problems to feed child in wheelchair, construction problems (such as not enough support for head) and parts of the wheelchair being worn out, and swollen feet. The themes on the advantages with the wheelchair according to caregivers are presented in table 6. (Paper V)

Table 6: Main advantages of wheelchairs according to caregivers

Main advantages	**Example**
Not having to carry the child and easier to bring child	"The child had become so heavy for us to carry on our backs, but ever since I got this wheelchair it has become so easy for us to go with him whenever possible. Mobility in all ways has become so easy for us" (Mother of 7 year old boy, GMFCS level III)
Child being able to change position	"He no longer has to stay in lying position all the time." (Mother of 6 year old boy, GMFCS level V)
Easier to feed child	"Feeding has also become easy for me, I don't have to be around for the child to feed, anyone can help me." Mother of 6 year old boy, GMFCS level IV
Child being happier	"My child has achieved peace and joy through the wheelchair because he has got a means to move himself from place to place, he has learned how to push himself." (Mother of 17 year old male, GMFCS level III)
Increased social interactions with other children	"She got a chance of moving around with fellow children because it is now easy for anyone to take her with them" (Grandmother of 9 year old girl, GMFCS level III)

7 DISCUSSION

The studies in this thesis were the first to provide population-based information about children and young people with CP in sub-Saharan Africa. Through utilizing the infrastructure of a demographic surveillance site we could screen over 30 000 children and identify a CP cohort in a rural area of Eastern Uganda. We used international validated classifications and assessment tools which made it possible for us to compare our cohort with HIC, showing novel results on functional abilities and development. Our findings will hopefully have an impact on future research and interventions for children and young people with disabilities in low-income settings. In this chapter I will discuss our main findings in detail in relation to other research in the field.

7.1 HIGH PREVALENCE OF CEREBRAL PALSY

Prevalence data is crucial for developing policies and guidelines for health services, education and other support services. The lack of rigorous studies in LMIC has seriously hampered the inclusion of children with CP in both national and international programmes; contributing to their low access to services and exclusion from education and participation in society. Population based studies on CP in LMIC have been scarce, with most studies being done in clinical settings. In fact, our research is among the first population-based studies on children with CP in LMIC, and the first studies in Sub-Saharan Africa.

We found a high prevalence rate of children with CP when we screened all children aged 2-17 years in a mainly rural area in Eastern Uganda. The estimated crude prevalence of children with CP per 1000 children was 2.7; this increased to 2.9 after adjusting for attrition, and 3.1 when we included the children identified in the triangulation (Paper I). This prevalence is higher than what has been reported from HIC, where the prevalence is 1.8-2.3 per 1000 live births.[17-19,27]

The last decade has seen an increase of population-based studies in LMIC, two studies recently published have in accordance with our findings found a higher CP prevalence rate per 1000 children in LMIC than in HIC, at 3.4 in Bangladesh[99], and 3.6 in Egypt[22], two studies found a similar rate to HIC at 2.04 in Egypt[21] and 2.3 in Nigeria[100], while one study from China showed a lower prevalence rate of 1.25[101]. These differences in prevalence rate could be due to different methods of screening and diagnosis but might also reflect regional differences in population demographics, risk factors, mortality and access to health services.

In Uganda, we found an even higher crude CP prevalence rate for children aged 2-7 years at 4.0 per 1000 children as compared to older children aged 8-17 years at 1.9 per 1000 children

(Paper I). These results indicate that for the younger children with CP in Uganda the prevalence rate is about double to HIC, and the lower prevalence in older children is probably due to a high mortality, with many children dying before they reach older ages. This indicates that the measured prevalence rate in Uganda is affected by survival bias and should be considered an underestimate.

We theorized that many of the children with CP in our studied population probably died before two years of age, and could not be included in the screening, and therefore the prevalence rate in Uganda is probably further affected by survival bias. This theory is supported by the low proportion of preterm born children (2%) in our CP cohort in Uganda (Paper I), compared to HIC were more than 40% of all children with CP are born preterm.[17,18,27] This lower proportion of children with CP born preterm in LMIC was also observed in other population-based studies, ranging from 8-17%.[21,99,100] The proportion of children with CP being born preterm was lowest in the studies from Sub-Saharan Africa with 2% in Uganda (Paper I) and 8% in Nigeria[100], probably because of high neonatal mortality in the region, with preterm birth complications being one of the leading causes of neonatal deaths in Africa, accounting for 10% of all deaths in this region.[102]

7.2 DISTRIBUTION OF GROSS MOTOR FUNCTION LEVELS

Previous studies in LMIC have concluded that the proportion of children with CP with more severe motor impairment is higher in LMIC than in HIC, but these studies have been done in clinical settings.[28,51] Clinical studies are heavily affected by selection bias in LMIC, where access to care is limited, and the more severely affected children might be overrepresented, since children with milder CP might not be brought in for care. We published the first population based description of motor function in a LMIC using international classification levels, and we found that the distribution of gross motor function in children in Uganda was in fact similar to that in HIC[16,17,48], with most children having mild impairments in motor function, and 60% being classified at GMFCS level I-II. (Paper I)

But this comparison is misleading. When looking at our CP cohort in different age groups, we found that the proportions of motor impairment in Uganda was heavily affected by survival bias, with a decline in children with severe motor impairment (GMFCS IV-V) with increasing age, due to a higher risk of death (Paper I & II). The proportion of younger children with severe motor impairments was three times higher for children aged 2-5 years, as compared to older children aged 6-17 years. And the Ugandan cohort has proportionally more severe motor impairments for the younger children and a larger proportion of mild motor impairments for the older children, when compared to a Swedish cohort[48] of children with CP. (Paper III)

It is also worth considering that our cohort did not include the children that might have died before two years of age. Population based studies from LMIC that include children below 2 years of age have found higher proportions of children with more severe motor impairments

than what we have found in our Ugandan CP cohort.[32] Considering the high mortality found in our CP cohort over the four years (Paper II), it is very likely that our Ugandan cohort is missing a large proportion of children with CP and more severe motor impairment that died before two years of age.

Table 7 summarizes the distribution of motor function level found in population-based studies in LMIC. The distribution of motor severity in population based studies from LMIC in Asia indicate that severe impairments in motor function (GMFCS IV-V) are more common (40-60%) than in HIC (29-33%)[46-48]. While population based studies from Africa have a similar or even lower proportion than in HIC, with 20% in Uganda (Paper III) and 28% in Nigeria[100]. These differences could be related to difference in methods, all studies except for our studies on the Uganda cohort used the key informant method (KIM), whereby community based key informants identify children with suspected CP and refer them for further assessments, this method does not involve door-to-door screening as we did in Paper I. It has been suggested that the KIM method has a lower rate of case-ascertainment as compared to door-to-door screening.[99] But considering the similarities in motor function proportions between the Ugandan study and the Nigerian study using the KIM, it is more likely that these results reflects differences in Africa compared to Asia. This could suggest that there is an excessive mortality for children with CP and severe motor impairment in Africa. This theory of a higher mortality in Africa compared to other LMIC is further supported by our finding of a 25 times higher mortality rate for children with CP in Uganda compared to the general population (Paper II), while a similar study from Bangladesh found a five times higher mortality for children with CP compared to the general population.[57]

Table 7. Distribution of gross motor function in population based studies in LMIC

Country	Year	Method	I-II	III	IV-V
Uganda 2-5 (paper III)	2019	Door-to-door	39	24	36
Uganda 6-17 (paper III)	2019		72	18	10
Uganda all (Paper I)	2017		60	20	20
Nigeria[100]	2020	KIM	58	14	28
Nepal[32]	2021	KIM	45.1	14.8	40.1
Bangladesh[99]	2018	KIM	31.8	21.6	46.6
Bangladesh[32]	2021	KIM	26.1	22.1	51.8
Indonesia[32]	2021	KIM	16.2	23.8	60

KIM=Key Informant Method

7.3 HIGH MORTALITY RATES

Several of the findings in our cross-sectional studies of the CP cohort indicated a high mortality for children with CP in Uganda. We found a significant decrease in the number of children with CP with increasing age; this was driven by a decrease of children with severe motor impairments (GMFCS IV-V) (Paper I) and the younger children (2-5) years had a significantly larger proportion of severe impairments compared to the older (6-17 years), in both gross and fine motor function. (Paper III) Based on these findings of age differences in our CP cohort we hypothesized that there is a high mortality for children with severe motor impairment in Uganda.

To confirm this hypothesis we did a longitudinal study of our CP cohort in Uganda, and our results are quiet shocking. We found an excessive premature mortality, were children with CP in our cohort was 25 times more likely to die than the general population (Paper II). This is in stark contrast with studies from HIC, where children with CP only show modestly reduced life expectancy compared to the general population.[54] A large population based study in Sweden that followed children with CP found that 4% had died over a period of 19 year[56], this can be compared to 15.5% of the children dying in our cohort over the much shorter time period of four years. (Paper II)

There is a paucity of population-based information on mortality for children with CP in LMIC, although two studies were recently published, one on children with CP in Bangladesh[57] and one on children with neurological impairments in Kenya.[58] In accordance with our findings these studies found a higher mortality rate for children with neurological impairments compared to the general population; with a five times higher mortality rate for children with CP in Bangladesh, and a three to four times higher mortality rate for children aged 6-10 years with neurological impairments in Kenya.[57,58] The study in Kenya had a lower mortality rate than we found in Uganda, but this could be due to the inclusion of all children with neurological impairments, and not only CP. The study did in fact find that children with cognitive and motor impairments (who likely had CP) were largely responsible for the high mortality.[58] We found that the mortality rate for children with CP in Uganda was 25 times higher than the general population, compared to five times higher in Bangladesh. This could be partly due to the higher mortality in the general population found in Bangladesh compared to Uganda (403 versus 137 deaths per 1000 000 person years). But this is not the sole explanation, since the crude mortality rate for children with CP in Bangladesh was about half of what we found in Uganda (1950 deaths versus 3953 deaths per 100 000 person years), indicating a higher mortality for children with CP in Uganda. One explanation for this higher mortality in Uganda could be that we included all children found from two years of age, while the mean age of diagnosis in Bangladesh was five years, and therefore many children might have died before being included in the Bangladesh study. Another explanation is that our study might be representative to rural areas in sub-Saharan Africa, where the rates of malnutrition are high, where malaria is endemic, where the population is poor and health-care provision is scarce, as is the case in Iganga/Mayuge. (Paper II & III)

7.3.1 RISK OF DEATH

The risk of death in the Ugandan CP cohort was seven times higher for children and young people that had severe motor impairments (GMFCS IV-V) as compared to mild motor impairments (GMFCS I-II). (Paper II) This is in accordance with findings from both HIC[55,56] and LMIC[57], where children with CP with more severe motor impairments have the highest risk of death. Many of the children with severe motor impairment in Uganda also had severe malnutrition, and the children with severe malnutrition had an almost four times higher risk of dying. In fact most of the children with CP in Uganda were malnourished, with a high proportion being severely malnourished (Paper II). High rates of malnutrition have been found in other studies on children with CP from LMIC, in both clinical studies[59] as well as community studies.[60] Malnutrition could be a major explanation to the high mortality rates in LMIC, making children with CP weaker and more vulnerable to infectious diseases.

Children with CP and severe motor impairment often have feeding and swallowing problems that lead to prolonged stressful meal times, reduced nutrition status, and a high risk for aspiration that can lead to respiratory difficulties and infections.[103] In HIC several methods are used for safe and sufficient nutrition in children with CP such as tube feeding and gastrostomy.[56] These interventions could be difficult to implement in a low-income setting without the risk of infections and severe complications.

7.3.2 MAIN CAUSES OF DEATH

All of the deaths for the children with CP in Uganda were caused by either anemia related to malnutrition, malaria or other infectious diseases. While these factors caused about half of the deaths in the general population, other causes were also common such as diarrhea, non-communicable diseases and external injuries. (Paper II) The children with CP in Uganda that cannot walk spend less time outside of their home environment and are less mobile than their peers, and this can account for them having fewer deaths related to injuries or ingestion of unhealthy items. In HIC the most common cause of death for children with CP was respiratory failures, often due to asphyxiation or pneumonia.[55,56]

This indicates different causes of death for children with CP in Sub-Saharan Africa where malaria is endemic, and children with CP are often malnourished and more vulnerable to infectious diseases. There is a need to target children with CP in Sub-Saharan Africa with both nutritional interventions and preventive measures for malaria infections, such as insecticide treated mosquito nets.

7.3.3 MORTALITY FOR OLDER CHILDREN

Even though the mortality rate was higher in the younger age groups in our CP cohort, the mortality rate ratio was higher in the older age groups, because of a steeper decrease in mortality with increasing age in the general population. The mean age of death was higher for children with CP (10 years) compared to the general population (7 years). (Paper II). This finding of children with CP dying at a later age was supported by the sharp decline of children with CP at about eight years of age seen in our cross sectional description of the CP cohort (Paper I).

We presented these results at a workshop for Ugandan therapists that have years of experience of working with children with disabilities and their families in rural Uganda, and they had some very interesting explanations. They described a situation in which caregivers tried many things for the child's improvement when they were younger, but eventually as the child grew older without much improvement they lost hope in their child. In addition the caregivers might as the child grows older have younger children to mind and might not have the same time to care for their child. This combination of having lost hope in the child and less time to care for the child might result in poorer care practices, such as reduced time for feeding. This hypothesis is supported by our findings that caregivers had reported having lost hope in their child (Paper III).

Caregivers in LMIC get little support in caring for their child, and they face a multitude of challenges such as stigma, negative attitudes and negative cultural beliefs.[75,76] We also found that caregivers feel that they lack the knowledge of their child's condition, where to seek care and what to expect in the future (Paper III). This lack of awareness among caregivers has also been found in another study from Uganda.[76] The lack of awareness can lead to unrealistic expectations for their child's development and this in combination with the low access to rehabilitation services, are probably all contributing factors to the caregivers having lost hope

These findings highlight the importance of training caregivers on their child's condition and what they can expect their child to be able to achieve in the future. This should be done with caution and cultural awareness, so as not to discourage the caregivers from caring for their child. It is also important to focus on interventions with realistic goals for the child's improvement based on their functional motor abilities. Seeing improvements in their child's function is a strong motivator for caregivers of children with disabilities in LMIC.[104]

7.4 POOR ACCESS TO REHABILITATION SERVICES

A majority of the caregivers wanted their child to improve in motor function, but only one third had sought help in the 12 months before the study, and only 10% had received some sort of rehabilitation services. (Paper III) Poor service coverage for children with CP is a global problem, and has been reported from other LMIC, where 31-66% have never received any kind of rehabilitation services.[32,105,106]

In Africa, child neurology services are scarce, there are no procedures on how to manage different neurological conditions, and referral systems are often unpredictable and dysfunctional. As an example of the scarcity of services, the national referral hospital in Kampala is the only public facility that offers specialist services for children with neurological impairments in Uganda.[83]

There are numerous other barriers to accessing care for children with disabilities in Africa other than poor service provision. Some barriers are related to lack of community awareness of disabilities resulting in stigma, negative attitudes and cultural beliefs such as the child being cursed or possessed. Another set of barriers are related to quality and availability of rehabilitation services; with lack of knowledge among health care professionals, lack of rehabilitation workers, unclear referral pathways, rehabilitation services being far away and physical inaccessibility of health facilities. Another major barrier is lack of awareness of the child's diagnosis and treatment options among caregivers. According to Adugna et al, the major barrier was poverty among families resulting in inability to pay for transport costs, assistive devices or treatment costs.[104]

Similar results were found in our study with barriers to care seeking for caregivers of children with CP in Uganda being; lack of money, lack of knowledge of the child's condition, lack of knowledge on what could be done to help the child, not knowing where to seek care, and having lost hope of their child ever improving. (Paper III) Most families in our studies were subsistence farmers living well below international poverty levels, and travel costs were a barrier to accessing scarce services. Previous studies in Uganda have also shown that lack of money is a barrier to accessing care, and that caregivers move around between service providers, both traditional and modern, resulting in a lot of time and money being spent on fruitlessly seeking a cure.[76] The quest for a cure for their child is probably a reflection of the family's lack of understanding of the child's condition and what to expect for their child in

the future. These unrealistic expectations coupled with erratic services could be a reason why many caregivers expressed that they had lost hope for their child.

To be able to overcome barriers to health care it is important to identify facilitators. The facilitators that have been identified are positive attitudes among family and community members, visible health improvements seen for the child as a result of treatment, having group sessions as compared to individual sessions, awareness raising activities in the communities, caregiver training on child's condition, financial support from government or organizations and getting incentives such as toys, transportation money, food and assistive devices.[104]

7.5 EXTREMELY LOW ACCESS TO ASSISTIVE DEVICES

Lack of access to assistive devices prevents dignified participation in daily life. Assistive devices should be provided as an integrated part of rehabilitation services. They can enable mobility, positioning and participation in activities. Access to assistive devices is a must if children with disabilities are to participate in the community, enjoy their human rights and live in dignity.[66] The children in the studies had inadequate access to the assistive devices that they needed to be able to actively participate in their daily environment. None of the children had assistive devices for vision, hearing or communication, not even simple devices that could be made with limited resources, such as communication boards or pictures. Only 8% of the children that could not walk had wheelchairs in working condition, and none had walkers for functional walking, only one child had a specially made chair for supported sitting. (Paper III)

For the children and young people in Uganda that could not walk this lack of assistive devices meant that their only form of mobility would be crawling on the ground or being carried by their caregivers. And for the children and young people that could not sit independently, lack of supported sitting devices meant that they would spend all day lying down, with no possibility to change position. This lack of assistive devices led to low participation for children with disabilities in daily activities. (Paper V)

Unfortunately this inhumane situation for children in Uganda is not unique, but often the reality in LMIC. We cannot estimate how big the unmet need for assistive devices is, since we do not even know how many people that are living with disabilities in LMIC, or what their needs are.[66] Other studies on children with CP in LMIC have in accordance with our studies found extremely low access to assistive devices for mobility for children that cannot walk at 2.6-5.5%.[99,105,107] This low access to assistive devices for mobility is a reflection of

the low priority given by many LMIC countries to children with disabilities, where provision of assistive devices often is not included in national legislation, policies or strategies.[66]

The Sustainable Development goals (SDGs) build on the Millennium Development goals (MDGs), with a special focus on key gaps and states that "no one should be left behind". And that strategies should start addressing the groups left the furthest behind first; which includes children with disabilities. To be able to achieve the SDGs and make sure that no one is left behind, there is a need for both national and international agencies to prioritize universal access to high-quality affordable assistive devices for children with disabilities.[108]

7.6 DEVELOPMENT OF A WHEELCHAIR STRATEGY

While access is the crucial first step, the second step is to make sure that assistive devices can be efficiently used to improve functioning in the users daily environment. Wheelchairs are a crucial assistive device for mobility, positioning and participation for children with disabilities. In the absence of national systems for wheelchair deliveries, the main source of wheelchairs in most LMIC is donations from international charities. These charities often provide large quantities of wheelchairs at one point in time, and rarely do training or follow up.[70] These practices are not in accordance with the guidelines developed for LMIC by the World Health Organization (WHO), promoting comprehensive service delivery for wheelchair provisions, including user training, follow up and maintenance.[109] The charity model for wheelchair provision has been heavily criticized[70,72,73] and shown inconclusive results of effectiveness.[71-73]

To address this problem, we decided to try to develop a strategy for wheelchair service provision in low-income settings based on the WHO guidelines, with a special focus on user training and support services, through a goal-setting and coaching programme implemented over a 6-10 month period, described in detail in Paper V. This relatively simple to implement and low-cost strategy showed extremely promising results. With high daily usage of the wheelchairs, high attainment of set goals, increased participation in activities, improved positioning, improved mobility and very high satisfaction (Paper V). Other studies from LMIC have shown positive results in user satisfaction and quality of life when implementing more comprehensive wheelchair services based on the WHO guidelines.[110,111] We believe that Paper V can be used to inform future research in the field, and to serve as a model to guide service planning for wheelchair service providers in LMIC.

7.7 LOW ACCESS TO EDUCATION

Access to education for children with CP in rural Uganda was very low, with only one third (30%) of the children aged 6-17 years attending school. (Paper III) This is far below school attendance in the general population in Uganda, were a majority of children attend school (74-87%).[78] These finding are not unique for children with CP in Uganda; children with CP have been found to have low school attendance in other population-based studies from LMIC, with the lowest proportion in Indonesia (5.6%), followed by Bangladesh (24.9%) and Nepal (39%).[32] In fact, children with disabilities in LMIC are almost always substantially less likely to attend school than their peers without disabilities.[6,112] In almost all countries the gap in access to education is substantially larger for children with disabilities than other strong predictors of school attendance such as poverty, gender and rural residence[112]; children with disabilities are one of the most marginalized and excluded groups when it comes to education.[4]

The sustainable development goal number 4 calls for "inclusive and quality education for all"; to be able to attain this it is important to target inclusion in education for children with disabilities to make sure that no one gets left behind.[6] All children have the same right to education, but in reality children with disabilities are often being denied this right. This has lifelong implications that undermine possibilities for future gainful employment for children with disabilities and their families. The children themselves have less possibilities for future income generating activities, caregivers might have a hampered opportunity for earning a living if they cannot send their children to school and sometimes girls become caregivers of their disabled sibling instead of attending school.[4]

To improve school attendance for children with CP it is important to identify factors associated with not attending school. For the children with CP in Uganda, the school attendance was lowest for children with moderate to severe gross motor impairment, communication impairments, intellectual disabilities and seizures. (Paper III) We found that school attendance decreased with an increase in GMFCS levels, with no attendance for GMFCS level IV-V and only one child attending school at GMFCS level III. (Paper III)

The school attendance for the children at GMFCS level III-V did not increase after they were included in the wheelchair intervention and given a donated wheelchair. (Paper V) This finding indicates that a wheelchair on its own is not enough of a facilitator for school attendance for children that cannot walk. This could be related to other barriers in access such

as lack of adapted school environment, lack of someone helping the child in school, and because most children in our study had additional associated impairments that might have served as barriers to attending school such as un-medicated seizures and communication impairments. Similar results were found in a study in Indonesia, where donated wheelchairs did not increase school enrolment or employment status, they recommended further investigation of barriers such as accessibility, public transport and attitudinal barriers.[111]

It is also worth noting that even for children with mild motor impairments school attendance was very low (40%). (Paper III) This is probably due to associated impairments in communication, intellectual disability and convulsions serving as barriers. About one third of the caregivers of the children at GMFCS level I-II that did not attend school stated that the reason for this was that the child had convulsions.

Other factors that might have resulted in exclusion from education in our cohort could be the low knowledge found among caregivers of their child's condition, and the fact that many caregivers said that they had given up hope for their child. (Study III) Further factors for low school attendance have been identified in other studies, such as educators unwillingness to include children with disabilities in their classes, and lack of training for teachers.[4]

7.8 SLOWER FUNCTIONAL DEVELOPMENT IN UGANDA

Children and young people with CP in Uganda had a slower functional development compared to HIC. (Paper III & IV) In addition, most children and young people had less functional abilities in gross motor, mobility and self-care compared to their peers in HIC. (Paper IV) Over the four years we followed the children and young people they had no development in gross motor function or mobility abilities, not even the children and young people with mild motor impairments (GMFCS I-II) or the youngest children aged 2-5 years. (Paper IV) This unexpected finding stands in contrast to HIC where children with mild motor impairments show a steep developmental trajectory for gross motor function and mobility during their first 6 years of life.[39,43]

The slow development of functional skills in Uganda led to a negative deviation from the steep developmental trajectories from HIC. The youngest children and the children and young people with mild impairment drove this negative deviation, since they had no development in mobility or gross motor function. These findings indicate that young children and children with milder forms of CP do not reach their full developmental potential.

Although previous clinical studies in Africa have found low proportions of children with mild motor impairments (23-30%).[53,113] our population based study (Paper II) and another population based study from Africa[100] suggest that about two thirds (60-65%) of the children have mild motor impairments (GMFCS level I-II). This might be because of the high mortality rates observed for children with more severe motor impairments in the communities in Uganda (Paper II), but it likely also reflects a recruitment bias where children with milder motor impairments might not be seeking health care to the same extent. This indicates that the children who have the most potential development are not being reached by rehabilitation services. This could seriously curtail the children's development and might lead to less levels of independence, which will hamper the possibilities for their future.

The slow development for the younger children in Uganda also indicates how important it is with early diagnosis and intervention. The crucial importance of early diagnosis and early intervention in motor learning has gained more recognition, and in HIC it is now possible to accurately detect and diagnose CP before six months.[25] While population based studies from LMIC indicate that many children with CP have a delayed diagnosis, often after 4 years of age.[32] The Prechtl general movement assessment can be used for assessing children that are just a few months old, it is low-cost, time efficient and has high sensitivity and specificity in predicting future gross motor performance, it has been used successfully in a few LMIC, but more research is needed.[114]

When hypothesizing about the causes underlying the lower abilities and slower development in Uganda, the worse socioeconomic circumstances and access to services were considered to be a plausible explanation. The developmental trajectories from HIC were developed from cohorts of children in Canada and Netherlands that received a range of medical, orthopedic and developmental services and all children received rehabilitation services such as physical and occupational therapy.[39,43] In contrast, the children in our study had extremely low access to rehabilitation services, assistive devices and education (Paper III). Which is the reality for most children living with CP and other disabilities in LMIC.[4,6,32,83,99,105,106,112]

Our studies provide evidence of the effectiveness of comprehensive rehabilitation and medical services for children with CP, by showing that the development is significantly slower when there is very limited access to these services. There is a chance that other differences in biology or pathology between children living in Sub-Saharan Africa and HIC might influence the children's development, as supported by the lower proportion of children with preterm cases found in our cohort (Paper I), but because we compared children classified

at the same functional impairment level and the same age, these differences are unlikely to be major factors.

These findings highlight the huge inequalities for children with disabilities living in LMIC; they do not reach the same potential as children living at the same functional impairment level in HIC, because they cannot access rehabilitation services. There is an urgent need to develop comprehensive rehabilitation services for children living in LMIC in order to give these children a chance to reach their full functional development potential.

8 METHODOLOGICAL CONSIDERATIONS

Strengths of the population based screening

A methodological strength of our studies is the utilization of the IMHDSS, which bi-annually collects information from all households living in the catchment area of the site, making it possible to reach all children by interviewing the household head. This method made it possible for us to do the first large scale population based studies on children with CP in sub-Saharan Africa, including more than 30 000 children. Without the utilization of the infrastructure of the IMHDSS we would never have managed to organize or finance studies of this magnitude or reach.

The utilization of the IMHDSS also made it possible for us to do comparisons between the children in the CP cohort and the larger general population living in the same area. This added a lot of value to our studies, since we could show distinct differences between children with CP and children without CP living in the same area.

We could also utilize the verbal autopsy data from the IMHDSS, which is collected continuously for all reported deaths within the sites monitored population. This made it possible for us to compare mortality between our CP cohort and the general population, living in the same area with the same risk factors and socioeconomic context.

Limitations of the population based screening

There is a possibility that we missed some children with CP in the population-based screening, there is a lot of stigma attached to having a child with disabilities in sub-Saharan Africa, and this might lead to caregivers hiding their disabled children. The design of the screening relied on the household heads to willingly share information with us about the children living in their household. But from our experience from collecting the data for the study, there was a high interest in participating in the studies, since caregivers were hoping to avail some help for their children's impairments.

To try to make sure that we did not miss any children in the screening we used two screening questions validated for use in low-income settings[86], they were adjusted in a previous qualitative study (unpublished) to suit the local terminology and culture.

To further make sure we did not miss any children with CP in the screening we did a triangulation with village informants identifying children with suspected CP in their villages, and we did identify 11 additional children with CP that we included in our cohort. It is worth nothing that almost all of the children in the triangulation (10/11) had been missed because the head of households gave negative responses to both screening questions, and that none of these children had severe motor impairment (none at GMFCS 4-5). This indicates that the

screening questions might miss children with CP that have milder impairments in function, since household heads answered negatively to the screening questions. It is worth considering that future screening exercises might need to re-formulate the screening questions, or consider including a triangulation to account for possibly missing children with mild motor impairments.

Although we took a lot of measures to try and identify all the children with CP in the population, there is still a risk that some children with CP were missed in the 2015 screening, which would affect the results from the studies of our CP cohort.

Using proxy interviews

Since the studies included young children as well as a majority of the children having impairments in communication and intellect we were heavily dependent on proxy interviews of caregivers for much of the data collection. Caregivers might have a different view of what is important to their children, then what their children would deem important. We have throughout our studies been clear on whom we collected the information from, and not interpreted the caregivers answers as coming from their children.

Low number of participants in cohort

Another limitation of our studies is the relatively small number of children with CP included in our cohort. This reduced the statistical power and made more detailed analysis difficult. But considering the number of households that we needed to screen to identify our cohort, it would have been difficult to get a larger population-based sample in the study area.

Measuring timing of brain injury

We were relying on caregiver history for the timing of the event that possibly caused the brain injury that resulted in CP. This presents with a lot of uncertainty, caregivers were asked to recall events that happened years before the study, and this poses a large risk of re-call bias. Caregivers might not remember events that they did not deem important at the time, or they might have developed their own explanation of the cause of the child's disability that might affect their answers to the questions. But, considering the design of the study it would have been difficult to collect this information in another manner, since the local health facilities do not keep easy accessible records of their patients, and many caregivers delivered their child at home and had poor access to health services before, during and after birth.

Verbal autopsies for determining cause of death

Verbal autopsy is a standardized procedure to determine the cause of death in demographic surveillance sites, whereby specially trained data collectors interviews the caregiver taking care of the person during the event that led to their death. The verbal autopsies in our studies followed the standard procedure according to the IMHDSS, whereby the interviews are done within a few months after the death, but there is still a risk of recall bias from the caregiver. The cause of deaths were not diagnosed at the time by a health professional through diagnostic testing, but determined after the child's death by two physicians going through the information from the caregiver interview; this is done to account for irregularly kept hospital records and deaths that occurred at home without health care contact.

The use of international classification and assessment tools

Another strength of this project is that we have used internationally acclaimed and validated classification and assessment tools, this makes it possible to compare the results from our studies with other countries. We have also used the internationally recognized definition of CP as described by SCPE[15], making our data comparable to population-based studies in HIC.

We did come across some challenges when applying HIC tools in a low-income setting, especially in regard to GMFCS which is focused on children's use of assistive devices, which were rarely available in our studies in Uganda. Below I have described how we adapted the GMFCS to better suit the Ugandan setting, maybe this adaption can be useful for other studies in LMIC.

Level	**GMFCS-HIC**	**GMFCS-Uganda**
I	Walks without limitations	Walks without limitations
II	Walks with limitations	Walks with limitations
III	Walks using a hand-held mobility device	Walks using hand-held mobility device. If child does not have mobility devices, child can sit independently and are independent in mobility in their home-environment using different crawling techniques.
IV	Self-mobility with limitations; may use powered mobility	Self-mobility with limitations; child cannot sit independently, child might be able to roll or move in belly-crawling short distances. Child may use powered mobility (if available).
V	Severely limited self-mobility: transported in a manual wheelchair	Severely limited self-mobility: child need assistance for all transfers and mobility, transported in manual wheelchair (if available)

Measuring associated impairments

A limitation is that we did not use standardized methods to assess associated impairments, due to lack of available expertise in the rural area where we were working. What we did instead was to use a questionnaire based on the Washington group extended question set of functioning, which is recommended for screening in low-income countries where appropriate specialists and equipment are lacking.[115]

Utilizing a trained local therapist team

A strength of this study was that we used a local team of trained therapist for most of our assessments. This meant that we could provide professional and well-informed answers to all questions and concerns that the caregivers might have had about their children. In addition we used some of the same therapists in both the 2015 and 2019 data collection, this would ensure that the assessment were done in a similar way at both assessments.

Generalizability

Our studies were done in a rural area, where a majority of the caregivers were subsistence farmers living below the poverty level. Our results might therefore not be transferrable to more urban areas in Uganda or other LMIC.

Limitations for Paper V: the wheelchair intervention

Because of the low number of children that were possible to include in the wheelchair intervention from the CP cohort, we could not have a control group. This makes it difficult to say which effects are attributed to the donated wheelchair, and what are attributed to the intervention programme. In addition our results might be effected by the caregivers wanting to give positive replies, since they might not want to seem ungrateful for the wheelchair, or they might fear that if they are negative they will not be included in future interventions.

9 CONCLUSIONS

The papers presented in this PhD project bridge an important knowledge gap; they are among the first population-based studies on cerebral palsy in a LMIC, and the first in Sub-Saharan Africa.

Our findings demonstrate that the prevalence rate for CP is higher in rural Uganda than in HIC, and it is about double for younger children. We found fewer children with CP in the older age groups, indicating a high mortality for children with severe motor impairments. The CP prevalence rate in Uganda is probably heavily affected by survival bias and should be considered an underestimate. We found a shockingly 25 times higher mortality rate for children with CP in Uganda compared to the general population. Children with severe motor impairments and severe malnutrition had the highest risk of death. This illustrates that there is a need to develop strategies specially adapted to low-income settings to improve feeding practices for children with CP, especially for children with severe motor impairment.

The children and young people with CP in Uganda had a slower development in functional skills than their peers in HIC; this slow development is probably due to their poor access to rehabilitation, assistive devices, health care and education. The access to these services was extremely low in Uganda. Caregivers rarely sought care for their child and we identified many barriers to care seeking such as lack of money, lack of knowledge and having lost hope for their child. This developmental shortfall and lack of services led to many children with CP being excluded from community activities, and not even being able to participate in basic daily life activities.

To try and improve this inhumane situation we developed and implemented a goal-directed coaching programme for wheelchair use. This relatively simple to implement and low-cost strategy showed extremely promising results, with high daily usage of the wheelchairs, high attainment of set goals, increased participation in activities, improved positioning, improved mobility and very high satisfaction with wheelchairs. We hope that our results can be used to inform future research in the field, and to serve as a model to guide service planning for wheelchair service providers in LMIC.

The findings from our studies highlight the huge inequalities for children with disabilities living in LMIC; not alone do they not thrive but they are struggling to just survive. We found a shockingly high mortality rate, which is a hidden humanitarian crisis that needs to be urgently addressed. We also found that children with CP in Uganda do not reach the same potential as children living at the same functional impairment level in HIC, because they cannot access rehabilitation services. We can expect that this situation is similar for millions of children living with disabilities in low-income settings. Directing interventions towards this group will not only prevent suffering and death, which must be considered essential, but will also allow these children to participate in family and community life in a dignified manner while fulfilling their basic human rights.

10 RECOMMENDATIONS

There is an urgent need to include people with CP in existing services, and to develop new comprehensive rehabilitation services. This can improve children's chances of survival, their general health and give these children a chance to reach their full functional development potential. Our studies provide insights on needs, barriers and facilitators for children and young people with CP living in Uganda. My recommendations for ways forward and future research are the following:

Recommendations for policy makers and health planners

- The needs and rights of children nd young people with disabilities should be included in policy documents and health plans.
- Assistive devices for positioning, mobility, communication, seeing and hearing should be prioritized as a key component of health care services since they are crucial for participation for children and young people with disabilities.
- Relevant guidelines need to be developed for the screening and management of different neurological conditions in Uganda.
- There is a need to develop financial support systems for care access, so that caregivers can afford to take their children to the service providers.
- It is important to work with communication and advocacy on childhood disability and child rights at policy, health provision and community level to try to work against stigma, negative attitudes and harmful cultural beliefs.

Recommendations for education planners

- Training on disability inclusion and seizures should be included and regulary enforced in teacher training curriculum.
- School environments should be made accessible, for example with ramps and adapted toilet facilities.

Recommendations for health care providers

- Timely treatment of infectious diseases such as malaria should be prioritized, since it has the potential to prevent brain injuries in young children.
- There is a need to target children with CP in Sub-Saharan Africa with preventive measures for malaria infections, such as insecticide treated mosquito nets.
- There is a need for medical management of seizures to be available and provided free of charge, this has the potential to prevent further brain damages.

- All health professionals need to receive training on different disability diagnoses and referral pathways.
- Children with CP need special support for their nutritional management. Community management of acute malnutrition strategies should include special provisions for children with disabilities.

Recommendations for rehabilitation service providers

- The GMFCS, MACS and CFCS are easy to understand and use for therapist in Uganda, but should not be used for developmental predictions in low-income settings.
- PEDI-UG is recommended to be used as an outcome measure in clinical practice.
- Goal directed training should be implemented.
- Wheelchair donations should be accompanied with a support and follow up program.
- Children with CP and mild motor impairment (GMFCS I-II) have a missed developmental potential, they need to get prioritized in rehabilitation services aimed at increased functional abilities.
- Children with CP and moderate motor impairment (GMFCS III) needs assistive devices for walking and goal-directed walking practice.
- Children with CP and more severe motor impairment need nutritional management, interventions should be aimed at improving feeding practices and nutritional intake.
- Caregivers need to get training on their child's condition and how to best care for and support their child as well as training on nutrition and best feeding practices.
- Group sessions are a facilitator for care access, as it can develop a sense of peer-to-peer support.
- Incentives such as provision of food, toys, transportation refunds and assistive devices can motivate caregivers to seek care.

Recommendations for research

- Additional population-based studies on the prevalence, functional impairments and needs of children with CP in LMIC are urgently needed, so they can be made visible and included in national and international programmes for service planning.
- More information is needed on early screening and diagnosis tools suitable for low-income settings, such as the Prechtl general movement assessment and HINE.
- There is a need to develop and implement studies on comprehensive rehabilitation interventions especially designed for low-income settings.

11 FUTURE PERSPECTIVES

There is a need to explore strategies for delivering comprehensive rehabilitation services at a community level in a low-income setting. To address this need our international research group has developed a multicomponent intervention; the Akwenda CP programme that will be implemented in the area of the IMHDSS, where all of our studies have taken place.

The Akwenda programme has five dimensions: i) caregiver-led training workshops ii) therapist-led practical groups sessions iii) provision of assistive devices iv) goal-directed training and v) community communication and advocacy. The aim of the programme is to improve participation, motor function and activity for children with CP, to improve quality of life and knowledge and reduce stress for caregivers, and to improve knowledge and attitudes towards children with CP in the communities.

At the core of the Akwenda programme are the caregiver led training workshops that are run by trained parent facilitators that themselves are parents to children with CP. The aim of the caregiver-led training workshops is for caregivers to support each other. And to train caregivers on what CP is and how to best care for and support their child, this will include nutrition, positioning and communication training. The intervention will include therapists that together with the families will set practical goals for goal-directed training, and are responsible for determining which assistive devices the child needs, and together with the caregivers decide how they should be used. The therapists will also be running workshops on assistive devices, goal-directed training, nutrition and epilepsy. The assistive devices will as far as possible be made locally using locally available materials. The communication and advocacy will be run by a social worker that will identify stakeholders in the communities and invite them to workshops, other communication avenues will also be used such as local radio talk shows.

The intervention will be implemented over a one-year period, and results of the intervention will be compared with a control group. This planned intervention will contribute to the knowledge base on strategies for LMIC, and can hopefully be used as a model to guide future interventions for children with disabilities in low-income settings.

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