Health conditions, functioning, and social outcomes in adults with cerebral palsy

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A mind that is stretched by a new experience
can never go back to its old dimensions.

Oliver Wendell Holmes

ABSTRACT

Background: A majority of individuals with cerebral palsy (CP) are adults, and yet healthcare and research are focused on children. In comparison to the consequences in childhood, little is known about the long-term consequences of CP.

Aims: To explore the health, functioning, and social outcomes in a population-based cohort of middle-aged adults with CP in western Sweden.

Methods: The total cohort of individuals with CP born between 1959-1978 in the CP Register of western Sweden formed the basis for this thesis. Childhood data from the CP Register was used to compare survivors from the total cohort with the total cohort. Register data on the survivors' social outcomes and of sex and age matched controls in the general population were gathered from Statistics Sweden and compared. All survivors still residing in the region were invited to a follow-up assessment of impairments and health conditions. The presence of impairments at the follow-up assessment in adulthood were compared to childhood data from the CP Register.

Results: The survivors differed from children with CP in the distribution of CP subtypes and had less severe associated impairments. Among the survivors, there was a decline in walking ability from childhood to adulthood and an increase in individuals with intellectual disability and epilepsy. In adulthood, pain and gastrointestinal, respiratory, and psychiatric disorders were common, and social outcomes, such as education, living arrangements, employment, and income differed greatly from the general population.

Conclusions: CP has serious long-term consequences for health and social outcomes. From childhood to adulthood, the presence and severity of CP-related impairments may change, and other health conditions may develop. In order to improve health and functioning and provide equal opportunities for adults with CP so that they can fully participate in society, it is recommended that specialized services and follow-up be extended into adulthood.

Keywords: cerebral palsy, prevalence, adults, CP subtypes, associated impairments, health conditions, social outcomes

SAMMANFATTNING PÅ SVENSKA

Bakgrund: Cerebral pares (CP) är en rörelsenedsättning som orsakas av en medfödd eller tidigt förvärvad hjärnskada. Förutom nedsatt rörelseförmåga är det vid CP också vanligt med andra funktionsnedsättningar, såsom intellektuell funktionsnedsättning, nedsatt kommunikationsförmåga, samt epilepsi. De allra flesta barn med CP överlever till vuxen ålder. Därför finns det idag omkring 3 gånger så många vuxna med CP som barn med CP. Trots detta är både sjukvård, habilitering och forskning fokuserad på barn med CP, och man vet ganska lite om situationen för de vuxna. Vilken uppföljning och specialistvård som erbjuds vuxna med CP varierar stort över landet.

Syfte: Att undersöka hälsa, funktionsförmåga och livssituation för medelålders vuxna med CP i Västsverige idag.

Metod: Västsvenska CP registret har registrerat alla barn i regionen som fått diagnosen CP sedan 1950-talet. Detta register användes för att identifiera alla vuxna med CP i Västsverige, födda 1959 - 1978. Förekomsten av funktionsnedsättningar hos de som fortfarande var i livet jämfördes med förekomsten i den ursprungliga gruppen. Uppgifter om levnadsförhållanden från Statistikmyndigheten (SCB) användes för jämförelser mellan de nu levande vuxna med CP och jämnåriga i befolkningen. Alla vuxna med CP födda 1959 - 1978 som fortfarande var bosatta i Västra Götaland bjöds också in till en uppföljande undersökning av funktionsförmåga, hälsa och livssituation.

Resultat: De överlevande vuxna hade i mindre omfattning nedsatt gångförmåga, intellektuell funktionsnedsättning och epilepsi som barn, jämfört med den ursprungliga gruppen. Vid uppföljningen i vuxen ålder hade dock flera av dem försämrats i gångförmåga eller fått epilepsi, och ytterligare några hade bedömts ha intellektuell funktionsnedsättning. Vanliga hälsoproblem i vuxen ålder var tex smärta, sjukdomar i mag-tarmkanal och luftvägar, samt psykiatrisk problematik. Jämfört med övriga befolkningen var det färre bland de vuxna med CP som var sammanboende, hade högskoleutbildning eller anställning. Medelinkomsten bland de vuxna med CP var lägre, och många hade anställning med lönebidrag.

Slutsats: CP har långtgående konsekvenser för funktionsförmåga, hälsa och livssituation i vuxenlivet. Behovet av regelbunden uppföljning och specialistvård kvarstår i vuxen ålder.

LIST OF PAPERS

This thesis is based on the following studies, which are referred to in the text by their Roman numerals.

I. Jonsson, U., Eek, M. N., Sunnerhagen, K. S., & Himmelmann, K. (2019). Cerebral palsy prevalence, subtypes, and associated impairments: A population-based comparison study of adults and children. *Developmental Medicine & Child Neurology*, 61(10), 1162-1167.

II. Jonsson, U., Eek, M. N., Sunnerhagen, K. S., & Himmelmann, K. (2021). Changes in walking ability, intellectual disability, and epilepsy in adults with cerebral palsy over 50 years: a population-based follow-up study. *Developmental Medicine & Child Neurology*, 63(7), 839-845.

III. Jonsson, U., Eek, M. N., Sunnerhagen, K. S., & Himmelmann, K. (2021). Health conditions in adults with cerebral palsy: the association with CP subtype and severity of impairments. *Frontiers in Neurology*, 12, 732939.

IV. Jonsson, U., Himmelmann, K. Social outcomes in middle-aged adults with cerebral palsy compared to the general population - a register study. *In Manuscript.*

CONTENTS

ABBREVIATIONS

ADHD	Attention Deficit Hyperactivity Disorder
BMI	Body Mass Index
CFCS	Communication Function Classification System
CP	Cerebral Palsy
CPUP	Cerebral Pares Uppföljnings Program (Follow-up programme for people with Cerebral Palsy)
DSM-V	Diagnostic and Statistical Manual of Mental Disorders, Fifth edition
EDACS	Eating and Drinking Ability Classification System
EEG	Electroencephalogram
FSS	Fatigue Severity Scale
GMFCS	Gross Motor Function Classification System
ICD-10	International Classification of Diseases, Tenth edition
ICF	The International Classification of Functioning, Disability and Health
ID	Intellectual Disability
IQ	Intelligence Quotient
LISA	the longitudinal integrated database for health insurance and labour market studies
MACS	Manual Ability Classification System
MS	Multiple Sclerosis
NICE	National Institute for Health and Care Excellence
SCPE	Surveillance of Cerebral Palsy in Europe
VGR	Region Västra Götaland
WHO	World Health Organization

THESIS AT A GLANCE

Study	Aim	Methods	Results	Conclusions
I Survivors	To compare the prevalence of CP subtypes and impairments in adult survivors, with the prevalence in children.	Cross-sectional study using CP Register data from childhood. A comparison of the adult survivors born 1959-1978, with the total cohort born 1959-1978, and with the most recent cohort born 2007-2010.	The adult survivors differed from the total cohort born 1978-1959 and from the cohort born 2007-2010, in the distribution of CP subtypes and the prevalence of impairments.	Prevalence of impairments in adults with CP should not be estimated based on the prevalence in children. Population-based studies of adults are needed.
II Changes over time	To examine changes in walking ability, intellectual disability, and epilepsy in individuals with CP over 50 years.	Longitudinal study of adult survivors with CP (born 1959-1978) using CP Register data and follow-up assessment data.	Over time, there was a decline in walking ability and an increase in individuals with intellectual disability and epilepsy.	The impairments of an individual with CP may change throughout the lifespan, creating a need for follow-up in adulthood.
III Health conditions	To explore the health conditions of adults with CP.	Cross-sectional study of health conditions in adults with CP using follow-up assessment data and medical records.	The most common health conditions were pain, gastrointestinal, respiratory, and psychiatric disorders.	Health conditions that are common in CP need to be included in the follow-up of adults with CP.
IV Social outcomes	To compare social outcomes in adults with CP with the general population.	Cross-sectional comparison of social outcomes in adults with CP to matched controls in the general population using register data from Statistics Sweden.	Living with a partner or child, having completed tertiary education or being employed was less common among adults with CP.	Improvements of services and support are needed to enable adults with CP to participate to their fullest potential, in all aspects of life.

INTRODUCTION

Cerebral palsy (CP) is a childhood-onset motor disorder, that currently affects around 1.6 per 1,000 liveborn children in high-income countries[1]. Historically, both research and health care has focused on children with CP, but for many decades, the majority of children with CP have survived into adulthood[2-6]. Today, about 75% of individuals with CP in high-income countries are adults[7], and consequently, CP can no longer be considered a childhood condition. Instead, it is a condition that should be viewed in a lifetime perspective. In order to identify the needs for care and support in adulthood and to develop evidence-based treatments suited for adults with CP, more research is needed with a focus on adults. The aim of this thesis was to explore the health conditions, functioning, and social outcomes of adults with CP in western Sweden.

DEFINITION

Several definitions of CP have been proposed over the years, all describing CP as a group of conditions with motor impairments caused by an early childhood brain injury[8-11]. In 1964, CP was defined by Bax as "A disorder of movement and posture due to a defect or lesion of the immature brain."[8]. Today, the definition by Rosenbaum from 2007 is the most prevailing, stating that:

> "Cerebral palsy (CP) describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to nonprogressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behavior, by epilepsy, and by secondary musculoskeletal problems."[9].

The etiologies of brain injury in CP are heterogeneous and often result from a combination of events or risk factors. Possible events or risk factors are: genetic causes, cerebral malformations, preterm birth, birth asphyxia, pre- or perinatal infections, perinatal stroke, and socioeconomic factors[11]. In addition to the differences in etiology, the type and severity of impairments also vary considerably between individuals with CP. Therefore, in order to describe each individual´s functional profile, specific classification systems for each function

are applied[9,12]. The classifications of neurological symptoms, CP subtypes, motor impairments, and associated impairments in CP will be described in the following sections.

NEUROLOGICAL SYMPTOMS

The predominant neurological symptoms in CP are paresis, spasticity, dyskinesia (dystonia and choreoathetosis), and ataxia[13]. Paresis, or muscle weakness, can range in severity from very slight weakness to complete paralysis. Spasticity can be described as a velocity-dependent increase in muscle tone, resulting from a hyperactive stretch reflex[14,15]. Dyskinesia on the other hand, is primarily characterized by involuntary movements and postures. In CP, these involuntary movements are often subdivided into dystonia and choreoathetosis[16]. Dystonia can be described as intermittent or sustained muscle contractions that cause recurring abnormal postures[17,16]. In choreoathetosis, the involuntary movements are more random and unpredictable and can be either sudden and jerky, or constant and writhing[17,16]. Ataxia is a movement disorder that primarily affects coordination and balance[18]. The neurological symptoms of CP can be mild or severe and occur separately or in combination[13]. Based on clinical experience, people with CP often use the term “spasticity” to describe all forms of increased muscle tone, stiffness, and involuntary movements. In this sense of the word, “spasticity” is maybe the most well-known feature of CP.

CP SUBTYPES

CP subtype classifications are based on the type and localization of neurological symptoms. Since the first subtype classifications in the late 19th century, several comparable classifications have been developed[19-21]. The Swedish classification by Hagberg, includes five subtypes: spastic hemiplegia, spastic diplegia, spastic tetraplegia, dyskinetic, and ataxic CP. Hemiplegia referred to symptoms localized to one side of the body, diplegia to symptoms from the lower extremities, and tetraplegia to symptoms from both the lower and upper extremities. According to Hagberg´s definition, all cases where the upper extremities were less affected than the lower extremities should be classified as diplegic[22]. However, the application of classification systems has differed between countries. Differing delineations between diplegia and tetraplegia, differing classifications of individuals with mixed motor types (for example, both spasticity and dyskinesia), and the use of other terms such as

quadriplegia, triplegia, and double hemiplegia have made international comparisons challenging[20,23]. In 2000, a harmonized classification was created by the Surveillance of Cerebral Palsy in Europe (sCPe)[21]. This classification has four subtypes: spastic unilateral, spastic bilateral, dyskinetic and ataxic CP. Translated from the Swedish classification by Hagberg, spastic hemiplegia becomes spastic unilateral, while spastic diplegia and tetraplegia are combined to form spastic bilateral CP.

The distribution of subtypes in children with CP has also varied between countries and has fluctuated over time in response to developments in healthcare[24,25,23]. Many different events or risk factors can cause CP, and if one is prevented or treated, this can affect the prevalence and severity of CP, as well as the distribution of CP subtypes[26,24]. For example, in countries where kernicterus is prevented or treated, there has been a decrease in dyskinetic CP[27]. Another example is therapeutic hypothermia. When this treatment was introduced, the number of term babies with CP due to asphyxia decreased[27].

Population-based studies have reported the distribution of CP subtypes in children as 29-36% spastic unilateral, 42-55% spastic bilateral, 4-19% dyskinetic, and 4-5% ataxic CP[28,29,25,23]. In adults, only two population-based studies report subtype distribution. These studies have reported 31-44% spastic unilateral, 49-60 spastic bilateral, and 6-9% other types[30,31]. The distribution of CP subtypes may differ between adults and children due to differences in the healthcare provided at the time of birth, but also due to the association between CP subtype and survival[2,4].

MOTOR IMPAIRMENT

Today, the severity of motor impairment in CP is most often described with the Gross Motor Function Classification System (GMFCS). This classification is based on the mobility method most often used by the individual in their daily life. It is independent of the neurological symptoms and the subtype classification. The GMFCS has five levels, and the gross motor function required for each GMFCS level differs depending on the age of the individual. The descriptors for each GMFCS level in the age range 12-18 years, which is the age range used for adults, are presented in Figure 1[32].

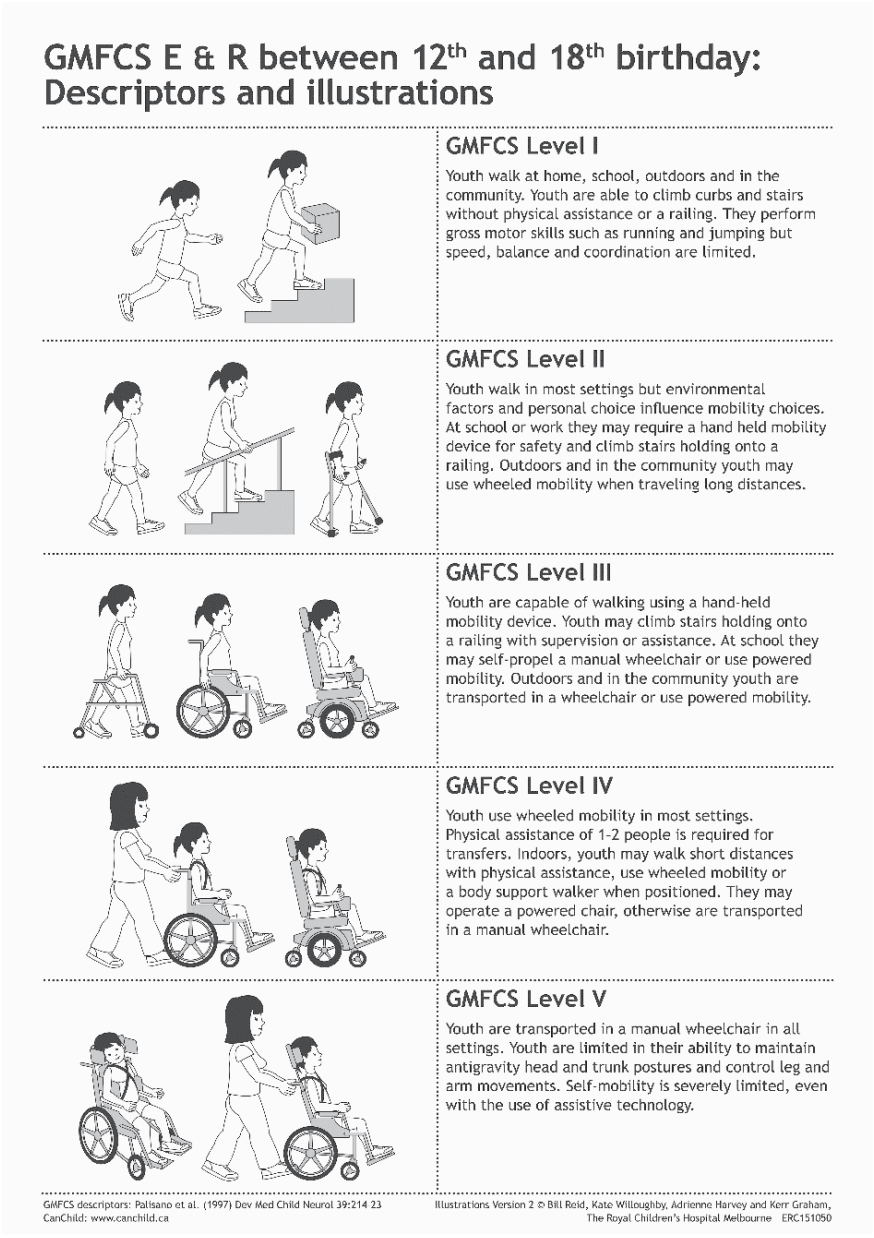

Figure 1. *Schematic overview of the Gross Motor Function Classification System (GMFCS) levels for ages 12-18. Accessed at www.CanChild.ca. Descriptors by Palisano et al. Illustrations by Reid, Willoughby, Harvey, and Graham. Printed with permission.*

The GMFCS distribution in children has been reported as 58-61% at level I-II, 9-11% at level III and 31% at level IV-V[28,33]. The GMFCS levels have been shown to be stable from early childhood until young adulthood[34]. Less is known about the longitudinal trajectories of GMFCS levels later in adulthood. According to a systematic review, many adults with CP experience a decline in walking ability[7]. However, population-based studies assessing GMFCS levels in adulthood seem to be lacking[7].

ASSOCIATED IMPAIRMENTS

For a comprehensive overview of the functional profile of an individual with CP, a classification of CP subtype and motor impairment is not sufficient. In addition, the presence and severity of associated impairments need to be described. For this reason, several classification systems similar to the GMFCS have been developed[35]. One such system is the Communication Function Classification System (CFCS), which classifies the ability to communicate into five levels[36,37]. In this classification, effective communication is described as sending and receiving messages correctly and at a comfortable pace. Individuals classified as level I communicate effectively with unfamiliar partners, while individuals at level V seldom communicate effectively even with familiar partners. Among Swedish adolescents with CP 49% have been classified at level I and 14% at level V[38]. Other analogous examples of classification systems are the Manual Ability Classification System (MACS)[39], and the Eating and Drinking Ability Classification System (EDACS)[40]. Nevertheless, several of the associated impairments are still described without classification scales, such as epilepsy and disturbances of cognition, vision, hearing, and behavior. The term "behavior" in the definition of CP from 2007 included autism spectrum disorder, Attention Deficit Hyperactivity Disorder (ADHD), and mood and anxiety disorders[9]. In a recent Swedish study, where all children with CP were assessed for these disorders, the prevalence of autism spectrum disorder was 30%, and ADHD 30%[41]. Both autism spectrum disorder and ADHD are associated with intellectual disability[42], and all three diagnoses are associated with an increased risk of mortality[43,44]. There is therefore reason to suspect that the prevalence of autism spectrum disorder and ADHD would be lower in adults than in children. However, the prevalence of these disorders in adults with CP is unknown. Based on clinical experience, adults with CP have not routinely been assessed for autism spectrum disorder or ADHD. Many times, their problems with behavior or attention have not been given a separate diagnosis but has been considered part of their CP. As a result, studies

based on diagnostic codes would likely underestimate the prevalence of these disorders.

COGNITION

Disturbance of cognition is one of the associated impairments of CP[9]. It can range from a mild impairment of a specific cognitive function to profound intellectual disability[45]. However, it is important to note that there are also individuals with CP without any cognitive impairments or with above average intelligence[45].

Intellectual disability (formerly "mental retardation") is currently defined in the Diagnostic and Statistical Manual of Mental Disorders, Fifth edition (DSM-5) as a condition with deficits in both intellectual and adaptive functioning, originating in childhood[46]. However, in Swedish clinical practice, the definition most often used is the definition in the International Classification of Diseases (ICD-10)[47], where an intelligence quotient (IQ) of below 70 is required for a diagnosis of intellectual disability. In CP, assessments of intellectual function can be challenging, due to associated impairments of communication or hand function. As a result, IQ is sometimes based on estimates rather than an assessment[48].

The prevalence of intellectual disability in children with CP varies widely between studies[49]. A systematic review has reported the prevalence of intellectual disability in children with CP to be 49%, with results from individual studies varying from 23% to 62%[33]. Studies from the Nordic countries have found intellectual disability in 31-53% of children with CP[50,51,41]. The prevalence of cognitive impairments in adults with CP is uncertain. Intellectual disability in CP is associated with shorter survival[6,2]. The prevalence of intellectual disability among adults may therefore be lower than in children. On the other hand, milder or more specific cognitive impairments may not become apparent until adulthood, with the increasing challenges of independent living and employment[52]. Based on clinical experience, such milder or more specific cognitive impairments are commonly seen in adults with CP who have difficulties achieving the participation in society that they wish for. To elucidate the burden of cognitive impairments in adults with CP, population-based studies of cognitive function in adults with CP are needed, where assessments are carried out in adulthood[52].

EPILEPSY

Epilepsy is another common associated impairment in CP[9]. Epilepsy has been defined as a disorder with "…an enduring predisposition to generate epileptic seizures"[53]. An epileptic seizure is a form of transient and excessive neuronal activity in the brain, and two unprovoked seizures are generally required for a diagnosis of epilepsy[53]. Epileptic seizures can be partial or generalized and can be brief and subside without medication or be prolonged and require medication or emergency care[54,55]. Seizure freedom can be successfully achieved with antiepileptic drugs in about two thirds of cases[56]. When an individual has been seizure-free for ten years and off antiseizure medication for the last five of these ten years, their epilepsy can be considered resolved[53]. Moreover, some forms of childhood epilepsy are self-limited and will resolve with age[53,57].Once resolved, a certain risk for recurrence will always remain [53].

Specific challenges apply to diagnosing and treating epilepsy in CP. Seizure freedom is less commonly achieved in CP[58]. However, in CP, non-epileptic paroxysmal events (e.g. staring episodes or dystonic postures) may be mistaken for epileptic seizures. Additionally, because there is an underlying brain injury, an electroencephalogram (EEG) may show focal epileptiform activity, even if the paroxysmal events are non-epileptic[59]. As a result, epilepsy and drug-resistant epilepsy may be over diagnosed in CP[59,60]. Another challenge in epilepsy and CP is the risk for recurrence after discontinuation of treatment. Several of the known risk factors for recurrence are common in CP, for example, early age of onset, abnormal neurological exam, and intellectual disability[61].

The population-based prevalence of epilepsy in children with CP has been reported as 32-43%[62-64]. Prevalence is associated with CP subtype and is increased in children with more severe motor impairment or intellectual disability[64,63,62,65]. Drug-resistant epilepsy has been reported in 35-55% of children with epilepsy and CP[64,66,58].

Longitudinal studies of epilepsy in children with CP show both that new cases can develop, and existing cases can become seizure-free or resolve[57,58,66], but these studies do not continue into adulthood. The only study that followed up on epilepsy in adults with CP reported an unchanged proportion with epilepsy after 14 years but did not examine changes on an individual level[67]. Few studies report population-based the prevalence of epilepsy in adults with CP, but systematic reviews have found the prevalence of epilepsy in adults with CP to be around 28%[68,69].

THE INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH (ICF)

The International Classification of Functioning, Disability and Health (ICF) was developed by the World Health Organization (WHO) as a way to describe and classify functioning, disability and health[70]. It is built on a biopsychosocial model of disability, describing disability as a result of the interaction between a health condition, the individual, and the environment. The disability can then be classified and graded as a dysfunction in any of the three levels of functioning: body function, activity, or participation. The ICF model highlights the network of factors involved in a disability, and in doing so it also provides a map of approachable avenues for alleviating the disability (Figure 2). For example, if the goal is improved participation, interventions can be aimed at any of the other factors involved in the disability: activities or body functions, environmental factors or personal factors, or health conditions.

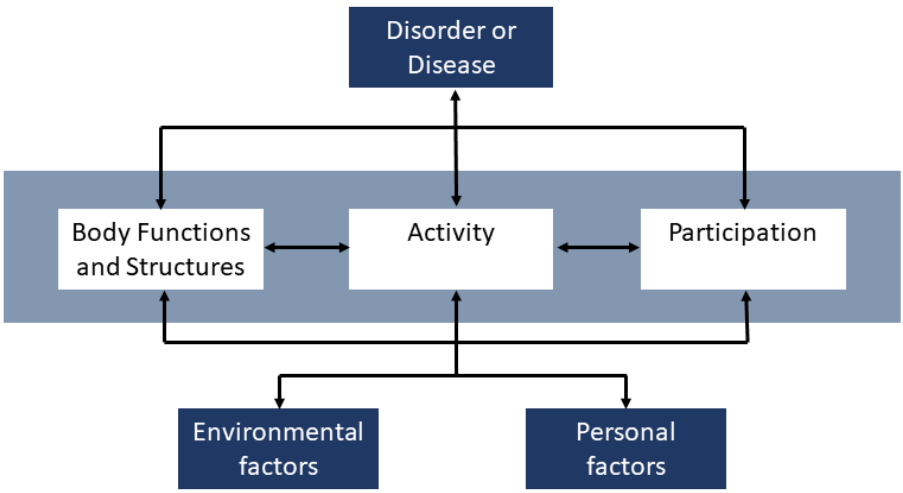

***Figure 2**. Schematic overview of the International Classification of Functioning Disability and Health (ICF) by the World Health Organization. Adapted.*

In CP, the prevalences of various impairments are related to each other. For example, individuals with more severe walking impairments have a higher prevalence of intellectual disability, epilepsy, and severe visual impairment[65]. As many as 15% of adults with CP have four or more associated impairments[31]. Based on clinical experience, when an individual has several associated

impairments, one impairment often interferes with coping strategies, treatments, or assistive devices for another impairment, making the situation for that individual all the more challenging. However, the ICF model is still a productive way of thinking about disability and possible interventions.

HABILITATION

In Sweden, habilitation is a part of the public healthcare system. Habilitation resembles rehabilitation but instead of acquired disabilities, habilitation units are specialized in developmental disabilities, such as intellectual disability, autism spectrum disorder and developmental motor disorders. Interventions aim to improve functioning and facilitate independence in daily life and participation in society[71]. Child habilitation units are available nationwide, and their multiprofessional teams include pediatric neurologists, psychiatrists, nurses, physiotherapists, occupational therapists, psychologists, speech and language pathologists, dieticians, and social workers[72]. In Sweden, children with cerebral palsy are followed-up by the child habilitation units until they turn 18. Adult habilitation on the other hand, has not been defined or organized in a corresponding way[73,74]. In many places the adult habilitation teams do not include physicians. Some teams offer only temporary interventions and no ongoing follow-up. Furthermore, a CP diagnosis in itself may not be considered sufficient cause for being admitted to the adult habilitation unit.

CP IN ADULTHOOD

HEALTH CONDITIONS

In recent years there has been growing awareness that adults with CP experience not only the impairments and musculoskeletal problems associated with CP, but other health conditions as well. Some of the most commonly reported other health conditions in CP are hypertension (26%), asthma (24%), anxiety (21%) depression (21%)[69], and pain (70%)[75]. A recent review reported a higher prevalence of many health conditions in adults with CP compared to the general population, including type 2 diabetes, asthma, epilepsy, depression, anxiety, schizophrenia, bipolar disorder, liver disease, stroke, ischemic heart disease, hypertension, osteoporosis, and chronic kidney disease[69]. Some of these conditions may be directly related to the brain injury that caused the CP, and others may be complications of the associated impairments[76]. However, for many health conditions, such as heart failure, liver disease and renal disease, the mechanisms linking them to CP have not yet been elucidated.

Multimorbidity, defined as having at least two chronic health conditions (other than CP), is more common than in the general population[77,78]. Multimorbidity has been found in 24% of young adults with CP and 58% of middle-aged adults with CP[78,77]. A more severe motor impairment is related to a higher prevalence of multimorbidity[77,78]. Multimorbidity is also related to survival, as the mortality rate in adults with CP has been shown to increase with the number of health conditions[79]. In the United States, the mean age of death for individuals with CP is 50 years, compared to 74 years in the general population[80]. The leading cause of death in adults with CP is respiratory diseases[81,82], with a 14-fold increased risk compared to the general population[82].

FATIGUE

Fatigue affects about 50% of adults with CP[83], compared to about 10-20% of the general population[84,85]. Fatigue has been defined as "a reduced capacity to sustain force or power output (physiological), reduced capacity to perform multiple tasks over time (psychological), and simply a subjective experience of feeling exhausted, tired, weak, or having lack of energy"[84]. Instruments used to assess fatigue in CP often focus on either physical fatigue, or combinations of physical and mental fatigue[86]. One of the more commonly used instruments is the Fatigue Severity Scale (FSS) which focuses on physical fatigue[86,83]. Adults with CP perceive physical activities, general demands of life, and sleep problems to be the most common factors contributing to their fatigue[87]. There has been conflicting evidence as to whether overweight, low fitness levels and sedentary behavior are related to fatigue in CP[88,89]. It has been hypothesized that it may not be the fitness level or activities in themselves, but rather an imbalance between fitness levels and everyday activities that causes fatigue[89]. Fatigue affects activity and independence, and has been shown to be related to pain, depression, a decrease in walking ability, low life satisfaction and fewer work hours among those with employment[90-93,85].

DECLINE IN WALKING ABILITY

Prior studies have indicated a decline in walking ability in 25-56% of adults with CP, often with a debut before the age of 30[7,92,94,68]. The nature of this decline varies between studies. It can be described for example as a shorter walking distance, a greater need for assistance, more pain or fatigue when walking, or walking with greater effort[7]. There are numerous possible reasons for this decline. With time, the impairments of CP may lead to secondary musculoskeletal conditions such as contractures, hip dislocation, scoliosis,

osteoarthritis, disc degeneration, spinal stenosis, and osteoporosis[95,69,96-100]. These secondary musculoskeletal conditions may then cause pain, fractures, spinal cord injury, or impaired lung function[95,101,75,102]. Simultaneously they may aggravate existing problems with weakness, spasticity, balance and range of motion, all of which can contribute to a decline in walking ability[92,103,104]. In addition to secondary musculoskeletal conditions, other contributing factors to walking decline have been proposed, such as fatigue, obesity, sedentary behavior, and fear of falling[7,94,105,92,106].

SOCIAL OUTCOMES

Social outcomes can include for example completing an education, being able to live independently, finding a partner, having children, and obtaining gainful employment. According to the United Nations Convention on the Rights of Persons with Disabilities, persons with disabilities should have equal rights to live independently, be included in the community, marry, study and gain a living[107]. Nonetheless, studies have shown that young adults with CP struggle to establish themselves as independent adults participating in society[108-111]. Compared with young adults in the general population, more young adults with CP live with their parents and fewer are married, have completed tertiary education, or gained employment[112,113]. The proportion of adults with CP who have completed tertiary education ranges from 4% to 33%, and the employment rate ranges from 18% to 53%, depending on the population studied[114-119,112,120]. A Swedish study found that in the age group 20-24 years, 63% lived with their parents and only 12% were competitively employed, while in the age group 40-49 years, 4% lived with their parents and 26% were competitively employed[120]. However, even though the employment rate is higher in older individuals, there has been no indication of employment rates in adults with CP improving in recent decades[121,30]. Based on the available evidence, the social outcomes of adults with CP seem to vary considerably between countries, with age, and with the severity of impairments, but nevertheless differ from the general population. Possible explanations for the social outcomes in adults with CP include not only the presence of impairments and other health conditions, but also societal attitudes, accessibility in the community, and the availability of specialized healthcare, support services, personal assistance, and economic support[114,73,108,122,123,120].

LACK OF FOLLOW-UP

CP is a condition with complex interactions between neurological symptoms, impairments, and other health conditions. In addition to motor impairments, 25% of adults with CP have two or more chronic health conditions[78] and 45%

have two or more associated impairments, all of which may require care coordination[31]. The need for coordinated specialized care in adulthood has been well described, for example, in the British NICE guidelines[124]. CP is as common in adults as Parkinson's disease or Multiple Sclerosis (MS), two other neurological conditions associated with extensive disability[31]. Access to specialized care for these conditions is generally undisputed in adult healthcare. However, even though specialist care for children with CP is well established in most high-income countries, it is often lacking in adult healthcare[73,124-127,31,111]. In Sweden there are vast regional differences in access to organized follow-up, multi-professional habilitation teams and specialized healthcare for adults with CP[73,74].

Adults with CP experience numerous challenges in accessing appropriate healthcare[127,128]. A recent review found a lack of knowledge, experience, and understanding of CP in adult healthcare, as well as poor care coordination and lack of physical accessibility[128]. About half of adults with CP received regular check-ups. However, adults with CP visited the emergency department 81 times per 100 person-years (equaling 81 visits per 100 adults observed for one year) and a general practitioner 404 times per 100 person-years[128]. Another study found that adults with CP were admitted to hospital 10 times more often than the general population[129]. Not surprisingly, individuals with CP also have an increased risk of early mortality compared to the general population[2,6].

POPULATION-BASED REGISTERS

Population-based CP registers are crucial for accurate prevalence estimates[130]. Many such CP registers have been initiated worldwide in the last decades and are planned to extend into adulthood over time[131]. One of these registers is the Swedish cerebral palsy follow-up program (CPUP), a combined follow-up program and healthcare quality register with national coverage[132]. The CPUP welcomes individuals of all ages and has expanded quickly to include all children with CP and a substantial proportion of adults with CP in Sweden. However, only adults admitted to the habilitation units are included in the CPUP, making it not quite representative of all adults with CP in Sweden.

In the absence of population-based CP registers, studies of adults with CP have often been based on convenience samples, American insurance claims databases, or general healthcare registers, making the interpretation of results problematic[7,68,133]. In studies based on convenience samples, individuals with impairments of cognition or communication have often been excluded for practical or legal reasons. Studies of insurance claims databases provide data

on large samples, but only include individuals covered by that specific insurance plan[133]. Both insurance claims databases and healthcare registers rarely contain disease-specific information, such as CP subtype, associated impairments, and level of functioning[133,134]. Furthermore, there are numerous reports of adults with CP who do not access specialist healthcare, as well as a lack of knowledge among healthcare providers about CP[73,125,128,31]. Consequently, CP related health problems that are misinterpreted, misdiagnosed, or treated with non-prescription medications may go undetected in studies based on these types of registers. Taking all of this into account, the prevalence estimates pertaining to adults with CP are uncertain[68].

THE CP REGISTER OF WESTERN SWEDEN

The CP Register of western Sweden is one of the oldest, still active population-based CP registers in the world[130]. It is considered to have near complete coverage of children with CP in western Sweden since 1959 [22]. Data is entered into the register at one timepoint when the individual is between four to eight years of age. No follow-up data is entered thereafter. The catchment area of the register is the counties of Västra Götaland, Halland, and Jönköping. With a total population of 2.4 million, it is an area that can be considered fairly representative of Sweden as a whole. For over six decades now, studies based on this register have described the changes in CP prevalence, etiologies and impairments[22,27,25]. Since the oldest participants in this CP Register are now middle-aged adults, it provides a rare opportunity for population-based studies of CP in this age-group.

SWEDISH REGISTERS

Sweden has a centuries-old history of population registers. Furthermore, since 1947, all Swedish citizens are assigned a unique personal identification number, facilitating the linking of data from different registers[135]. In addition to the CP Register of western Sweden, this thesis also accessed the Swedish Population Register (Folkbokföringsregistret) and the longitudinal integrated database for health insurance and labour market studies (LISA database). The Swedish Population Register includes information on for example: name, address, date of birth, and date of death[136]. The LISA database is managed by Statistics Sweden and compiles data from several government agencies. It includes data on civil status, education, employment, income, and social benefits[137].

KNOWLEDGE GAP

On account of the scarcity of data on adults with CP, data on children with CP are commonly used as a proxy. This is problematic for several reasons. As described earlier, the prevalence of CP, the subtype distribution, and the severity of impairments is likely to differ between children and adults. Impairments may have worsened with age or caused secondary health problems. There are also differences between children and adults in living arrangements, family support, and expectations for personal responsibility and achievements in society. But even more importantly, there are numerous differences between children and adults in body composition, body functions, psychological maturity, and common health disorders. There is good reason why pediatric and adult healthcare are separate medical specialties.

When this thesis was initiated, there were very few population-based studies on impairments, health conditions or social outcomes of adults with CP. The research on adults with CP has expanded considerably in the subsequent eight years, but the difficulties in conducting population-based studies remain. Furthermore, there is still a serious lack of evidence-based guidelines on the prevention and treatment of health problems in adults with CP[124]. In conclusion, research specifically aimed at adults with CP is needed to guide treatment, organize healthcare and provide social support in adulthood.

This thesis aimed to provide population-based data on health conditions, functioning, and social outcomes in adults with CP. It is hoped that the results can be used as a basis for future advancements, giving adults with CP better chances for independence, participation, health, and survival.

AIM

The overall aim of this thesis was to explore the impairments, health conditions, and social outcomes in a population-based cohort of adults with cerebral palsy (CP) in western Sweden.

The specific aims of the four studies included in the thesis were:

Study I SURVIVORS

To compare the prevalence of CP subtypes, walking ability, intellectual disability and epilepsy in individuals with CP who survived into adulthood, with the prevalence in children with CP.

Study II CHANGES OVER TIME

To examine longitudinal changes in walking ability, intellectual disability, and epilepsy in individuals with CP over 50 years.

Study III HEALTH CONDITIONS

To explore the health conditions of adults with CP and analyze the associations with CP subtype and severity of impairments.

Study IV SOCIAL OUTCOMES

To compare living arrangements, education, employment, income, and social benefits in adults with CP with the general population.

METHODS

This thesis comprised four quantitative observational studies originating from the population-based CP Register of western Sweden. All four studies were population-based retrospective cohort studies focused on the first complete cohorts entered into the CP Register (individuals with CP born 1959-1978). All four studies include participants with all CP subtypes and all levels of physical, intellectual, and communicative function. A schematic overview of the research designs and study populations of the four studies is presented in Table 1.

Table 1. *Research designs, study populations, and reference populations in this thesis.*

	Study I	Study II	Study III	Study IV
Study design	Cross-sectional	Longitudinal + cross-sectional	Cross-sectional	Cross-sectional
Inclusion criteria	CP Register adult survivors born 1959-1978	CP Register adult survivors born 1959-1978	CP Register adult survivors born 1959-1978 + Adults with CP moved into VGR born 1959-1978	CP Register adult survivors born 1959-1978
Exclusion criteria	Deceased Emigrated Unidentifiable	Deceased Emigrated Unidentifiable Residing outside of VGR No reply/declined	Deceased Emigrated Unidentifiable Residing outside of VGR No reply/declined	Deceased Emigrated Unidentifiable
Study population	n=581	n=142	n=153	n=565
Reference population 1	CP Register total cohort born 1959-1978 n= 723			General population age + sex matched n=1130
Reference population 2	CP Register total cohort born 2007-2010 n=205			

CP, cerebral palsy; unidentifiable, person in the CP Register with incomplete personal identification number; VGR, Region Västra Götaland.

PARTICIPANTS

SURVIVORS (STUDY I)

A flow-chart of the inclusion process for all of the studies in the thesis is shown in Figure 3. In 2017, a search was performed in the Swedish Population Register for all individuals in the total cohort born between 1959-1978 who were included in the CP Register (n=723). All individuals who could be identified as alive were included in the study (n=581). Individuals who had emigrated could no longer be confirmed to be alive. In the 1960s and 1970s, participants were entered into the CP Register with name, address, and date of birth, not with the unique personal identity numbers used in Sweden today. Therefore, some individuals who had moved and changed their name were not traceable and could not be confirmed to be alive. The total cohort born 1959-1978 was used as a reference population, and a second reference population of contemporary children with CP, comprised of the most recent cohort in the CP Register (individuals born 2007-2010) was also identified (n=205).

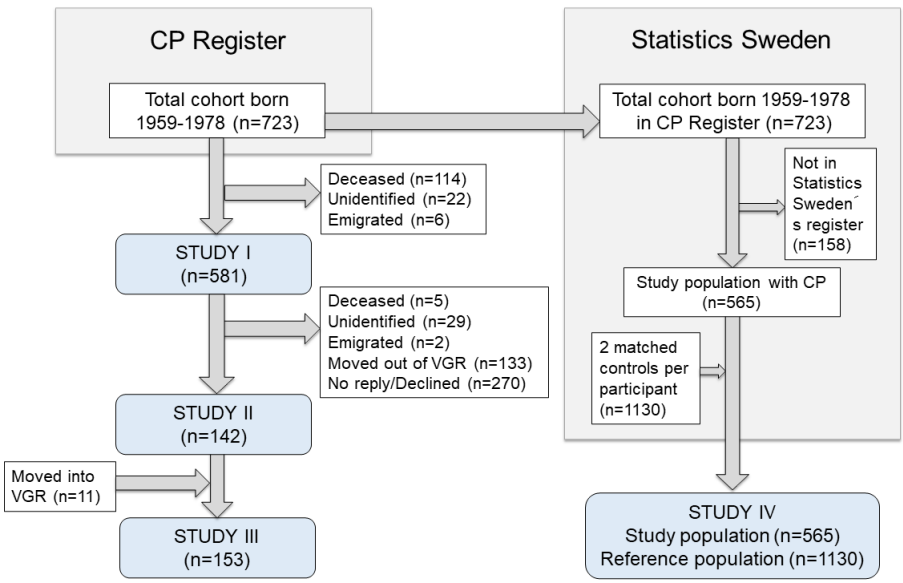

Figure 3. *Flow-chart of the inclusion process for studies I-IV in this thesis. VGR, Region Västra Götaland of western Sweden.*

CHANGES OVER TIME (STUDY II)

All survivors from the CP Register cohort born between 1959-1978 who were still residing in the Region of Västra Götaland in 2016 (n=417) were invited to a follow-up assessment. All survivors who participated in the follow-up assessment were included in the study (n=142).

HEALTH CONDITIONS (STUDY III)

The study population in Study III included all participants in Study II (n=142). Additionally, information about the study was spread through patient organizations and habilitation units. All individuals with CP (born between 1959-1978) who had moved into the Region Västra Götaland and who replied to the invitation, were included (n=11).

SOCIAL OUTCOMES (STUDY IV)

All individuals in the CP Register born between 1959-1978, who were still alive in 2013 and could be identified in Statistics Sweden´s registers, were included in the study population (n=565). A reference population from the general population, comprised of two controls per participant and matched for age, sex, and area of residence, was selected by Statistics Sweden (n=1130).

DATA COLLECTION

SURVIVORS (I)

Childhood data on CP subtypes and impairments were gathered from the CP Register for both the study population and the reference populations. The data sources for each study are shown in Table 2.

CHANGES OVER TIME (STUDY II)

Childhood data on CP subtypes and impairments were gathered from the CP Register. Data on impairments in adulthood were collected at a follow-up assessment. These follow-up assessments were conducted by the research team between 2016-2019, either at the Regional Rehabilitation Centre, at a local habilitation unit or as a home visit. All researchers involved in the follow-up assessments were healthcare professionals with extensive clinical experience with patients with CP.

Table 2. *The data sources used for each study in this thesis.*

Data source	Study I	Study II	Study III	Study IV
CP Register (childhood)	CP subtype walking ability ID epilepsy	CP subtype walking ability ID epilepsy	CP subtype	walking ability
Follow-up assessment (adulthood)		walking ability ID epilepsy BMI pain fatigue	walking ability ID communication BMI blood pressure health conditions	
Medical records (childhood + adulthood)			health conditions	
Statistics Sweden (adulthood)				social outcomes

CP; cerebral palsy, ID; intellectual disability, BMI; body mass index

The follow-up assessment consisted of an interview, a physical examination, and questionnaires. The interview was conducted by either the author of this thesis (rehabilitation physician) or the main supervisor (pediatric neurologist) and included both a medical history and social outcomes. The medical history was gathered through a semi-structured interview covering all types of medical health problems, symptoms, treatments, and operations. More specific information on the experience of pain was gathered using a questionnaire, that covered localization, intensity, frequency and duration. Data on social outcomes, such as living arrangements, education, employment, assistance in daily activities, and contacts with healthcare professionals were also gathered through a semi-structured interview. The physical examinations were conducted jointly by the physician who conducted the interview, and a physiotherapist. Blood pressure (mmHg), weight (m), and height (kg) were measured, and body mass index (BMI) (kg/m^2) was calculated[138]. Functioning was assessed according to the GMFCS[139] and the CFCS [36]. The Fatigue Severity Scale questionnaire was administered by an occupational therapist or a speech and language therapist.

The location, pace, assistance, and method of communication with which the follow-up assessment was conducted were adapted to suit the functioning and preferences of each participant. In cases where a participant with an intellectual disability was unable to answer a question, a proxy answer from their accompanying assistant was recorded.

HEALTH CONDITIONS (STUDY III)

All participants were assessed as described in STUDY II. Additionally, medical records for the participants were collected from the hospitals and adult habilitation units in Västra Götaland. The medical records were then scrutinized for additional information on health conditions by the author of this thesis.

SOCIAL OUTCOMES (STUDY IV)

The personal identification numbers of the total cohort born between 1959-1978 in the CP Register were sent to Statistics Sweden, along with CP Register data on walking ability. Statistics Sweden selected a control group from the general population, matched for age, sex, and area of residence. A pseudonymized dataset with the requested social outcomes for the participants and for the control group was created by Statistics Sweden and sent back to the research team for analysis. The social outcome data were obtained from Statistics Sweden´s longitudinal integrated database for health insurance and labour market studies (LISA)[137] and included: living arrangements, education level, employment, subsidized employment, disposable income, and social benefits, such as social welfare (support for basic living expenses), housing allowance (rent support), student aid (support for students in higher education), sickness benefits (temporary compensation when on sick leave), unemployment benefits (temporary compensation for loss of employment), disability pension (long-term compensation when unable to work due to disability or illness), and disability allowance (support for disability-related expenses).

DEFINITIONS AND CLASSIFICATIONS

DEFINITION OF CP

Individuals in the study population of this thesis were entered into the CP Register of western Sweden in the 1970s. At that time, the CP Register applied the definition by Bax, describing CP as "a disorder of movement and posture due to a defect or lesion of the immature brain."[8].

CP SUBTYPES

The Swedish classification of CP subtypes was applied when the participants were entered into the CP Register[22]. This classification was used in Study I and the sCPe classification in studies II and III[21]. The differences between the Swedish classification and the sCPe classification are shown in Table 3.

Table 3. *The differences between the Swedish and the sCPe classification of CP subtype.*

	Swedish classification	sCPe classification
CP Subtype	Spastic hemiplegia	Spastic unilateral
	Spastic diplegia Spastic tetraplegia	Spastic bilateral
	Dyskinetic	Dyskinetic
	Ataxic	Ataxic

CP, Cerebral palsy; sCPe, Surveillance of Cerebral Palsy in Europe

MOTOR IMPAIRMENT

The Swedish classification of motor impairment with three levels: mild (walking without aids), moderate (walking with aids), or severe (using wheeled ambulation) was applied at the time of entry into the CP Register. This classification was used in studies I, II and III. In Study III, the Gross Motor Function Classification Scale (GMFCS) from the follow-up assessment in adulthood was used[32]. The GMFCS is described in detail in Figure 1, page 4. The differences between the two classifications are shown in Table 4.

Table 4. *The differences between the previously used CP Register classification of motor impairment, and the current GMFCS classification.*

	CP Register classification	GMFCS classification
Motor impairment	Mild	GMFCS I GMFCS II
	Moderate	GMFCS III
	Severe	GMFCS IV GMFCS V

CP, Cerebral palsy; sCPe, Surveillance of Cerebral Palsy in Europe; GMFCS, Gross Motor Function Classification System

INTELLECTUAL DISABILITY

Intellectual disability was defined in the CP Register as an assessed or estimated IQ < 70 at the time of entry into the register in childhood. No new IQ test was administered at the follow-up assessment in adulthood. Instead, participants were classified as having an intellectual disability in adulthood if they self-reported an intellectual disability or if they had received social support designed for individuals with intellectual disability, (group homes, sheltered employment or special schools). The CP Register classification of intellectual disability in childhood was used for studies I and II. The follow-up assessment classification of intellectual disability in adulthood was used for Study II and III.

COMMUNICATION

The ability to communicate was classified at the follow-up assessment according to the Communication Function Classification Scale (CFCS)[36]. This classification was used in Study III.

EPILEPSY

Epilepsy was defined as either having recurring epileptic seizures or taking anti-epileptic medications. Studies I and II included only current epilepsy, while Study III included both current and resolved epilepsy.

PAIN

In studies II and III, pain was classified as present if the participant reported having recurring or current pain at the follow-up assessment. Pain of any origin was included. The participants then classified their pain intensity as mild, moderate or severe, the frequency as daily, weekly, or monthly, and the duration as more, or less, than three months.

FATIGUE

Fatigue was assessed with the Fatigue Severity Scale (FSS). The FSS is a questionnaire with nine items, scored on a seven point Likert scale, where the score ranges from nine to 63 and higher scores indicate more severe fatigue[140]. These fatigue scores were used in Study II.

OTHER HEALTH CONDITIONS

In Study III, all health conditions (except pain, see above) were classified as present if symptoms, treatments, or diagnoses were reported by the participant, or mentioned in the medical records in free text or as diagnose codes. Both current and previous health conditions were included. All psychiatric disorders treated with either counselling or medication were included. All respiratory disorders were included. Problems with phlegm in airways was included as a health condition, even if not diagnosed or treated. All gastrointestinal tract disorders were included. Upper gastrointestinal disorder was defined as either taking proton-pump inhibitors or having any of the following: heartburn, gastroesophageal reflux disease, gastritis, or peptic ulcers. Pressure ulcers were classified as present if self-reported or mentioned in medical records as a pressure ulcer that could be considered grade II-IV, according to international guidelines[141]. Underweight was defined as BMI < 18.5 kg/m^2 and obesity as BMI ≥ 30 kg/m^2 [138]. At the follow-up visit, hypertensive blood pressure was defined according to the NICE guidelines as ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic blood pressure[142]. A diagnosis of hypertension was classified as present if the participant was treated with antihypertensive medication.

SOCIAL OUTCOMES

In Study IV, the individual´s educational level was classified into five levels according to their highest completed education: less than nine years, primary school (9 years), secondary school (2-4 years), tertiary education (2-4 years) or post-graduate (4 years). Living arrangements were classified as “living with a partner or a child”, “living with parents”, or “living alone”. Group-home residents were classified as “living alone”. Individuals who were employed in November of 2013, full-time or part-time, competitively or with wage subsidies, were classified as employed. Individuals with sheltered employment without wages were classified as not employed. Disposable income included all forms of income after taxes had been deducted. Social benefits received at any time during 2013 were classified as received.

STATISTICAL ANALYSES

The statistical methods used in the thesis are presented in Table 5. Descriptive statistics were used to present participant characteristics and the prevalence of impairments and other health conditions. Differences in the distribution of categorical variables between groups were assessed using either the Pearson chi-square test or the Fisher´s exact test when observations were few. The association between variables on an ordinal scale, such as the GMFCS or CFCS, and the presence of health conditions were analyzed with the Mantel-Haenzsel (Linear-by-Linear Association) test. For analyses of associations between walking ability and fatigue or BMI, the participants were divided into three groups according to their level of walking impairment. The median Fatigue Severity Scale (FSS) score and median BMI for each group was calculated, and the association with walking ability was analyzed with the Kruskal-Wallis test. Changes in impairments between two time points were analyzed with McNemar´s test for nominal data and Sign test for ordinal data. Differences in employment rate, adjusted for education, were analyzed with binary logistic regression. A two-tailed p-value of < 0.05 was considered significant. Statistical analyses were conducted using IBM SPSS statistics version 25 and 28 and R version 4.3.1 (R Foundation for Statistical Computing).

Table 5. *Overview of the statistical methods used in this thesis.*

Statistical method	Study I	Study II	Study III	Study IV
Descriptive statistics				
Mean, Median		X	X	X
n, percent	X	X	X	X
Comparisons between groups				
Chi-square, Fisher´s exact	X	X	X	X
Mantel-Haenzel			X	
Kruskal-Wallis		X		
Independent sample T-test				X
Analyses of changes over time				
McNemar's		X		
Sign test		X		
Regression analysis				
Binary logistic regression				X

ETHICAL CONSIDERATIONS

The studies in this thesis were approved by the Regional Ethics review board in Gothenburg and the Swedish Ethical Review Authority (2014-01-16 Reg.no. 777-13; 2015-07-07 Reg.no. T313-15/777-13; 2015-12-17 Reg.no. T1037-15/777-13; 2018-07-16 Reg.no. 572-18 and 2019-11-05 Reg.no. 2019-05518) and adhered to the ethical principles of the World Medical Association Declaration of Helsinki[143].

Studies I and IV were based solely on register data that were pseudonymized before analysis; informed consent was not required. The participants were not contacted and the potential risks of inclusion in the studies were considered very low. Potential benefits of inclusion were improved healthcare and social support for adults with CP in the future.

All participants of studies II and III, or their legal guardians, gave informed consent. The participants had been included in the CP Register in early childhood. Some were not aware they were in a CP Register, and a few were not aware that they had CP. It is therefore natural that being invited to participate in a study of CP could stir up various feelings and raise certain questions. Some participants had questions about the CP Register, their diagnosis, or about hospital stays or treatments in childhood, which we did our best to answer. Others had not been followed-up since leaving pediatric care and were grateful for a CP check-up. Many participants expressed a wish to contribute to research and to help remedy the lack of knowledge about adults with CP.

Individuals with intellectual disability or communication impairments are often excluded from studies, and less is known about their healthcare needs. Therefore, we made it a priority to include them in our studies. Individuals with intellectual disability may not always have the capacity to understand certain questions or to answer for themselves. Some of them are dependent on a caregiver to interpret their wishes in everyday life, and the same is true for their participation in research. In order to give participants with intellectual or communication impairments the best possible chance of expressing themselves, the interviews were adapted to the needs of each participant. Augmentative and alternative communication was used as needed, and questionnaires were administered in writing, orally, with pictorial scales, or Talking Mats[144,145]. If a participant with an intellectual disability was not able to understand a question, a proxy answer was recorded.

RESULTS

LOST TO FOLLOW-UP

All individuals in the total cohort born between 1959-1978 in the CP Register of western Sweden were included in the thesis (n=723). A flow-chart of the inclusion process is shown in Figure 3, page 18.

In Study I, 114 individuals from the total cohort were deceased. Six had emigrated and 22 lacked a complete personal identification number in the CP Register and could not be identified in the Swedish Population Register. In the comparisons between the total cohort and the survivors, 28 participants were excluded due to missing data on walking ability (n=24) or intellectual disability (n=4).

In Study II, 275 of the 417 invited individuals did not participate. Five passed away after the census but before participating, while 86 declined to participate and 184 did not reply. Nine non-participants had missing data on walking ability and were therefore excluded from the analysis of walking ability. Analyses of CP Register data showed no differences between participants and non-participants in age (p=0.1), sex (p=0.9), or walking ability (p=0.13). However, intellectual disability and epilepsy were more common among non-participants (p<0.01 and p<0.01) (Figure 4).

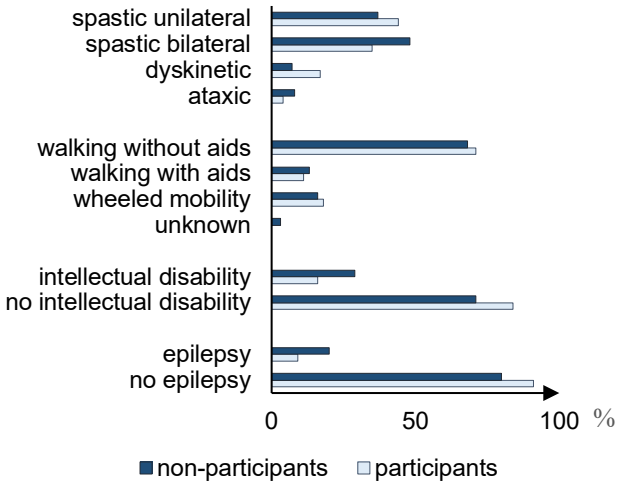

Figure 4. *Study II. The distribution of CP subtypes and impairments, in participants and non-participants.*

Study III included the same participants as in Study II, with the addition of 11 participants who had moved into the Region Västra Götaland after the age of 4-8 years.

In Study IV, 158 individuals from the total cohort (n=723) were excluded as they were deceased or could not be identified in Statistics Sweden´s registers. The majority of these individuals are likely the same individuals who were excluded in studies II and III due to being deceased, emigrated or lacking a complete personal identification number in the CP Register.

SURVIVORS (STUDY I)

Characteristics of the participants in the four studies of the thesis are detailed in Table 6. In 2017, only 581 of the 723 individuals in the total cohort (born 1959-1978) were still alive, and the prevalence of CP in adults born between 1959-1978 in western Sweden was 1.1 per 1,000 inhabitants.

***Table 6**. Characteristics of the study populations in studies I-IV in this thesis. n (%).*

	Study I	Study II	Study III	Study IV
Study population	581 (100)	142 (100)	153 (100)	565 (100)
Sex, Female	244 (42)	60 (42)	66 (43)	236 (42)
Age, median	N/A	48	48	44
Range, years	39-58	37-58	37-58	35-54
CP subtype				
Spastic unilateral	227 (39)	62 (44)	63 (41)	
Spastic bilateral	257 (44)	50 (35)	55 (36)	
Dyskinetic	52 (9)	24 (17)	29 (19)	
Ataxic	45 (8)	6 (4)	6 (4)	
Walking impairment				
Mild (GMFCS I-II)	409 (70)	88 (62)	92 (60)	390 (69)
Moderate (GMFCS III)	72 (12)	18 (13)	18 (12)	71 (13)
Severe (GMFCS IV-V)	87 (15)	36 (25)	43 (28)	90 (16)
Unknown	13 (2)	0	0	14 (2)
Epilepsy	79 (14)[a]	26 (18)[a]	44 (29)[b]	
Intellectual disability	145 (25)	31 (22)	34 (22)	

CP, cerebral palsy; GMFCS, Gross Motor Function Classification System; [a] = current epilepsy; [b]= current and resolved epilepsy; N/A, not available.

Compared to the total cohort of children with CP born between 1959-1978, the children who survived to 2017 had a lower prevalence of severe motor impairment (p=0.004), intellectual disability (p=0.002), and epilepsy (p=0.037). The distribution of CP subtypes among survivors also differed from the distribution in the total cohort (p=0.002). The CP subtypes spastic tetraplegia and dyskinesia were less common among survivors. A similar pattern was seen when the survivors were compared to the most recent cohort in the CP Register (children born between 2007-2010). All three impairments and the CP subtypes spastic tetraplegia and dyskinesia were less common among survivors than among children with CP born between 2007-2010.

CHANGES OVER TIME (STUDY II)

The distribution of walking impairment among survivors had changed from childhood to adulthood (p=0.001). In adulthood, the proportion of survivors walking without aids had decreased and the proportion using wheeled ambulation had increased. There was also an increase in the proportion of participants with intellectual disability (p=0.039) or epilepsy(p=0.015) (Figure 5).

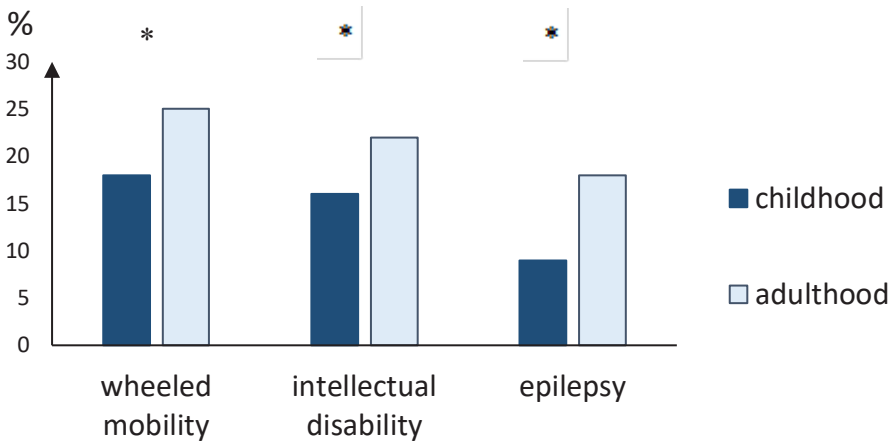

***Figure 5**. Study II. The prevalence of wheeled mobility, intellectual disability and epilepsy in childhood and adulthood in survivors with CP (n=142). *= significant difference, p<0.05.*

While there was an increased prevalence of impairments on group level, there were also a few participants with improved walking ability (n=4), participants with resolved epilepsy (n=6) and participants who no longer met the criteria for intellectual disability (n=2). The changes in walking ability for each individual are shown in Figure 6.

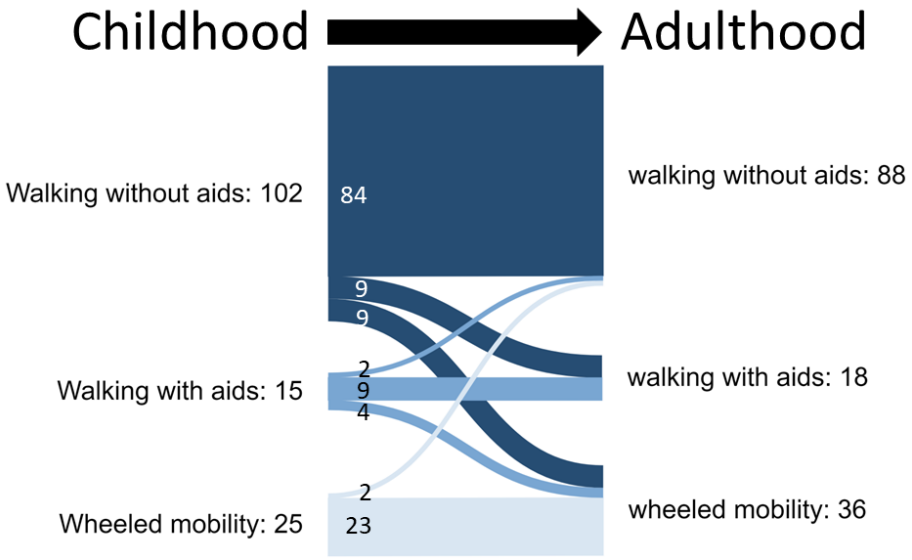

***Figure 6**. Study II. Changes in walking ability from childhood to adulthood, in 142 participants with CP.*

At the follow-up assessment in adulthood, there was a difference between the CP subtypes in the proportion of participants with a decline in walking ability (p=0.013), a new diagnosis of intellectual disability (p=0.042), or epilepsy (p=0.039). A decline in walking ability, or a new diagnosis of intellectual disability were most common among participants with dyskinetic CP, while new cases of epilepsy were most common in spastic unilateral CP. Neither walking ability nor the presence of intellectual disability or epilepsy in adulthood was associated with age or sex. Furthermore, there was no association between walking ability in adulthood and fatigue, pain, or body mass index (BMI).

HEALTH CONDITIONS (STUDY III)

The most frequently reported health conditions were pain, epilepsy, gastrointestinal, psychiatric, and respiratory disorders (Table 7). Among the gastrointestinal health conditions, dysphagia, constipation, and upper gastrointestinal disorders were the most frequent. Depression was the most common psychiatric disorder, and pneumonia and problems with phlegm were the most common respiratory disorders.

***Table** 7. Study III. Health conditions in 153 participants with CP by subtype of CP, GMFCS level, and ID. n (%).*

	Pain	GI disorders	Psychiatric disorders	Respiratory disorders	Epilepsy	Pressure ulcers
Total	100 (65)	94 (61)	60 (39)	46 (30)	44 (29)	14 (9)
CP subtype	*p=0.029**	*p <0.001**	*p=0.378*	*p=0.006**	*p=0.122*	*p=0.048*
Unilateral	36 (57)	19 (30)	20 (32)	10 (16)	23 (37)	2 (3)
Bilateral	43 (78)	43 (78)	24 (44)	20 (36)	11 (20)	6 (11)
Dyskinetic	19 (66)	26 (90)	14 (48)	14 (48)	7 (24)	6 (21)
Ataxic	2 (33)	6 (100)	2 (33)	2 (33)	3 (50)	0 (0)
GMFCS level	*p=0.397*	*p <0.001**	*p=0.481*	*p <0.001**	*p=0.856*	*p <0.001**
I	37 (62)	20 (33)	21 (35)	8 (13)	17 (28)	1 (2)
II	21 (66)	21 (66)	12 (38)	9 (28)	10 (31)	0 (0)
III	12 (67)	12 (67)	9 (50)	6 (33)	6 (33)	1 (6)
IV	18 (69)	24 (92)	12 (46)	13 (50)	3 (12)	5 (19)
V	12 (71)	17 (100)	6 (17)	10 (59)	8 (47)	7 (41)
ID	*p=0.003**	*p <0.001**	*p=0.373*	*p=0.056*	*p <0.001**	*p <0.001**
IQ<70	15 (44)	32 (94)	12 (35)	15 (44)	18 (53)	12 (35)
IQ>70	85 (71)	62 (52)	48 (40)	31 (26)	26 (22)	2 (2)

CP, Cerebral palsy; GMFCS, Gross Motor Function Classification System; ID, Intellectual disability; Unilateral, spastic unilateral CP; Bilateral, spastic bilateral CP; IQ, Intelligence Quotient; GI, gastrointestinal tract; p-values refer to Fisher´s exact test, for variation across subtypes or presence of ID and to Linear-by-Linear Association for trends across GMFCS-levels. * = significant, p<0.05. Percentages are the proportion of participants of the given subtype of CP, or GMFCS level, or ID, reporting a certain health condition.

The proportion of participants reporting a health condition varied depending on CP subtype, GMFCS level and intellectual disability (Table 7). The prevalence of pain, pressure ulcers, respiratory disorders, and gastrointestinal disorders, differed significantly depending on the subtype of CP. A more severe motor impairment was significantly associated with a higher prevalence of pressure ulcers, respiratory disorders, and gastrointestinal disorders. Intellectual disability was significantly related to a higher prevalence of gastrointestinal disorders, epilepsy, and pressure ulcers. It was also significantly related to a higher prevalence of pneumonia and problems with phlegm, although not with the combined category of all respiratory disorders. Analyses of associations between health conditions showed that participants with dysphagia had a higher prevalence of pneumonia and problems with phlegm than participants without dysphagia.

Table 8. *Study III. Self-reported pain characteristics in 100 participants with CP.*

Pain	n	(%)
Intensity		
Mild	17	(17)
Moderate	58	(58)
Severe	25	(25)
Frequency		
Monthly	13	(13)
Weekly	23	(23)
Daily	47	(47)
Unknown	17	(17)
Duration		
< 3 months	8	(8)
> 3 months	75	(75)
Unknown	17	(17)
Pain medication		
yes	30	(30)

Two thirds of the participants reported pain (n=100). Among them, almost half experienced daily pain. Furthermore, a majority of the participants with pain reported moderate to severe pain intensity, or a pain duration of > 3 months (Table 8). Among participants without intellectual disability, the proportion reporting pain was related to the severity of walking impairment (p=0.022). However, when analyzing those with intellectual disability, there were fewer who reported pain, and no association with walking impairment was found (p=0.134).

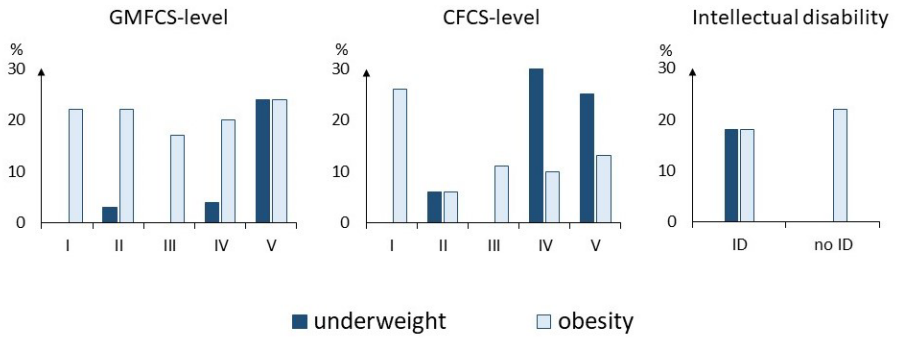

***Figure** 7. Study III. The proportion of participants with underweight or obesity by GMFCS level, CFCS level and presence of intellectual disability. GMFCS, Gross Motor Function Classification System; CFCS, Communication Function Classification System; ID, intellectual disability. Underweight, body mass index < 18,5 kg/m2; obesity, body mass index ≥= 30 kg/m2.*

Obesity was present in 21% and was not significantly related to CP subtype, intellectual disability or severity of motor impairment or communication impairment. However, underweight, which was present in 4%, was related to intellectual disability ($p<0.001$), a more severe motor impairment ($p<0.001$), and a more severe communication impairment ($p<0.001$) (Figure 7). Furthermore, all participants with gastrostomy (n=5) had an intellectual disability, as well as a severe motor and communication impairment (GMFCS and CFCS levels IV and V).

A more severe communication impairment (CFCS) was associated with intellectual disability ($p<0.001$); Figure 8.

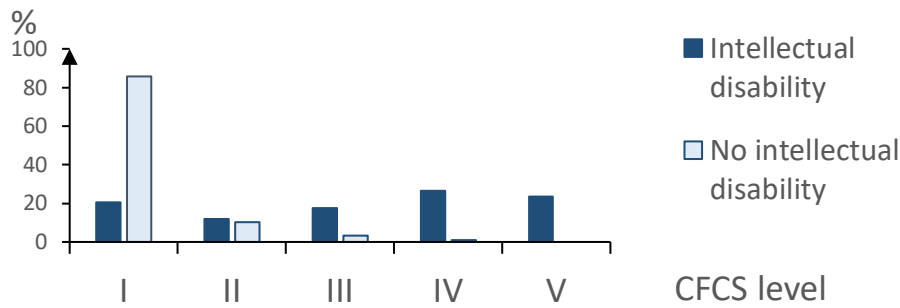

***Figure 8.** Study III. Proportion of participants with intellectual disability by level of communication impairment (CFCS level), in 153 participants with CP.*

SOCIAL OUTCOMES (STUDY IV)

Descriptive data of social outcomes are presented in more detail in the manuscript for Study IV. A summary of the social outcomes in adults with CP and in the general population is presented in Table 9. There were significant differences between adults with CP and the general population in living arrangements, education level, and employment rate. Compared with the general population, a larger proportion of adults with CP lived alone or with their parents, and a smaller proportion lived with a partner or a child. A smaller proportion of adults with CP had completed tertiary education or were employed. The differences between adults with CP and the general population in living arrangements, education, and employment were significant for both men and women and for all age groups. Disability pension, disability allowance, and wage subsidies were more common in adults with CP. Having received social benefits, such as housing allowance, social assistance, student aid, sickness benefits and unemployment benefits was equally common in adults with CP and the general population.

Table 9. *Study IV. Social outcomes in adults with CP(n=565) compared to the general population(n=1130).*

	Cerebral palsy	General population
	%	%
Living arrangements *		
Living with a partner or child	28	70
Education level *		
Tertiary education or more	20	39
Employment *		
Employed	50	86
Social benefits		
Subsidized employment *	17	2
Disability pension *	56	6
Disability allowance *	31	1

CP, Cerebral Palsy; Employment, registered in November of 2013; Social benefits, received at some point during 2013; *= significant difference between adults with CP and the general population ($p<0.05$), Pearson chi-square-test. Missing data for living arrangements and all social benefits: CP (n=9), general population (n=23).

The employment rate and the mean disposable income for adults with CP were significantly lower than for the general population. When analyzed according to educational level, adults with CP had a significantly lower employment rate at primary, secondary and tertiary school level, and a significantly lower disposable income at primary, secondary, and tertiary school level (Figure 9).

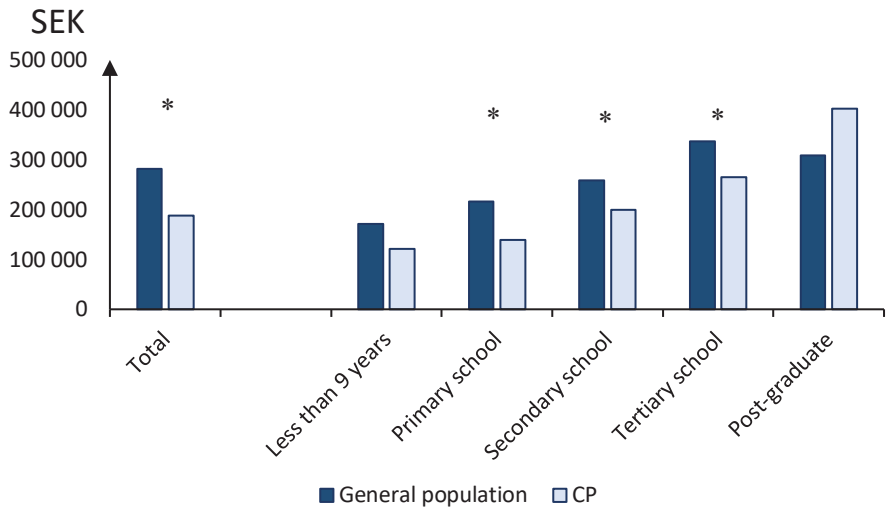

***Figure 9**. Study IV. Mean yearly disposable income by education level in adults with CP and in the general population. CP, cerebral palsy; SEK, Swedish crowns. *= significant difference, p<0.05, independent samples T-test. Missing data on income: CP (n=9), general population (n=23).*

In adults with CP, walking ability in childhood was related to social outcomes in adulthood (Table 10). Those who were able to walk in childhood (with or without aids) had better outcomes regarding living arrangements, education, and employment compared to those who used wheeled mobility. Even so, there were still significant differences in living arrangements, tertiary education and employment between those who could walk without aids and the general population.

Table 10. *Study IV. The proportion of individuals living with a partner or child, had completed tertiary education or were currently employed, in adults with CP and in the general population. Adults with CP subdivided into three groups according to level of walking ability.*

	cerebral palsy			general population
	wheeled mobility	walking with aids	walking without aids	
Living with partner/ child %	4	27	33	72
Tertiary education %	6	23	22	39
Employed %	11	37	63	86

CP, cerebral palsy; percentages refer to the proportion of participants within each level of walking ability who have had the specified social outcome. Missing data on all three social outcomes: CP (n=9), general population (n=23).

The participants in studies I and IV originated from the same cohorts in the CP Register and the inclusion and exclusion criteria were very similar, making these two groups of participants close to identical. Study I showed that intellectual disability was related to walking ability, and Study IV showed that social outcomes were related to walking ability. The results from studies I and IV are presented side by side below (Figure 10).

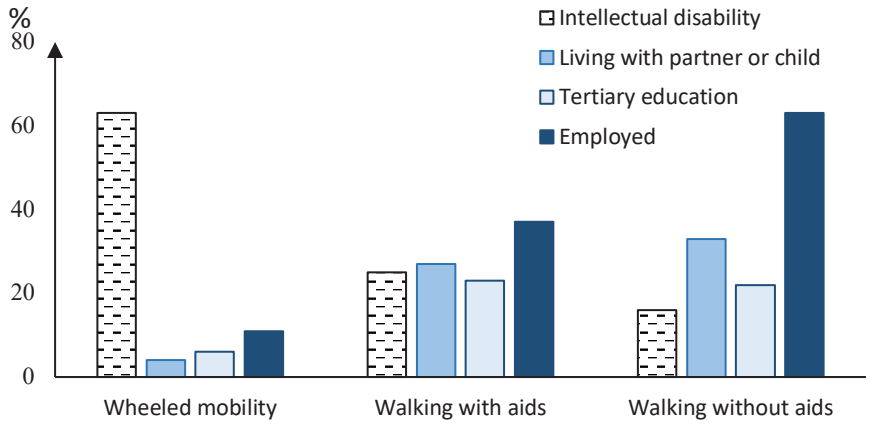

Figure 10*. Studies I and IV. The presence of intellectual disability in childhood (n=581) and the social outcomes in adulthood (n=565) in participants with CP grouped according to walking ability.*

DISCUSSION

KEY FINDINGS

All studies in this thesis were population-based and included individuals with all subtypes of CP and all levels of impairments. According to our results, individuals with CP who survived to middle age differed significantly from children with CP in the distribution of CP subtypes and in the prevalence of impairments. These differences were seen both in relation to children with CP born 50 years ago and to children with CP born today. Follow-up from childhood to adulthood showed individual changes in walking ability, epilepsy, and intellectual disability among survivors. In adulthood, other health conditions such as pain, gastrointestinal, psychiatric, and respiratory disorders were common. Several of these health conditions were related to CP subtype or associated impairments. Social outcomes such as living arrangements, education level, employment and income differed significantly between adults with CP and the general population.

PREVALENCE OF CP

The prevalence of CP in the population born between 1959-1978 in western Sweden decreased from 1.7 per 1,000 live births in childhood[22], to 1.1 per 1,000 inhabitants in adulthood. Given that CP is known to affect survival[2,6,80], a decrease was to be expected. However, this was one of the first population-based studies to examine the prevalence of CP in adults. In the absence of population-based registers, the prevalence of CP in adults is largely unknown. Instead, the number of adults with CP is often estimated based on birth prevalence and anticipated life expectancy, and estimates have varied greatly, from 17 to 50 million people worldwide[104,146].

CP SUBTYPE DISTRIBUTION

The present study is also one of very few studies showing the population-based distribution of CP subtypes in adults. Our results show a lower proportion of spastic tetraplegia and dyskinetic CP in adults compared to children from the same region. Again, this is not surprising, as previous studies have shown worse survival in these subtypes[2]. Knowledge of the CP subtype distribution in the whole population can be helpful in determining whether a study population is representative of the whole population of adults with CP. For example, according to our results, 1% of adults with CP had tetraplegia, while some hospital-based studies in other countries have reported a prevalence of quadriplegia as high as 55-76%[77,126,78]. To some extent, this difference may be

explained by differences in classification[23] or differences in healthcare that affect impairment load and survival[24]. But to a large extent, the difference is likely explained by the hospital-based sample and the association between CP subtype and impairment severity. Individuals with tetraplegia generally have more impairments[65], making them more likely to visit hospital clinics and be included in hospital-based studies. Of course, as long as the results are not assumed to apply to all adults with CP, it is not necessarily a problem if studies are not population-based. In fact, the impairment profile and health conditions of adults with CP vary to such a large extent between individuals that it could often be more meaningful to study subgroups of the population.

PREVALENCE OF IMPAIRMENTS

A comparison of the survivors with the total cohort of children with CP showed that during childhood, a lower proportion of survivors had severe motor impairments, intellectual disability, and epilepsy. Based on these results it would be natural to assume that the prevalence of impairments would be lower in adults than in children. However, we also found that among the survivors, the presence of impairments increased from childhood to adulthood. These two trends, reduced survival in the more impaired children, and the development of impairments in survivors over time, partly counteracted each other. Consequently, when comparing the prevalence of impairments in the total cohort in childhood, with the prevalence among survivors in adulthood, the net result was a higher prevalence of severe motor impairment in adulthood (25%) and a lower prevalence of intellectual disability (22%). The prevalence of epilepsy was unchanged (18%).

DECLINE IN WALKING ABILITY

This study was a population-based follow-up of walking performance, as assessed by a medical professional in childhood and then again in adulthood. In adulthood, walking ability had declined in 19% of the participants who were able to walk in childhood. This is low compared to previous studies which have reported walking decline in the range of 25-56% [7,68]. There are several possible explanations for this. First, previous studies have mostly been cross-sectional and often based on self-reports[7]. Second, many studies on walking decline have been hospital-based, and highly functional individuals may be underrepresented[7].

Third, a decline in walking ability can manifest in many different ways, for example in walking distance, the need for aids, fall frequency, effort, or the associated level of pain. Results may vary depending on which aspect of walking ability is studied[7]. And finally, walking capacity (what an individual can do under optimal conditions) and walking performance (what an individual chooses to do in their daily lives) are two separate concepts, and a change in one does not equal a change in the other[147]. In our study we were limited to a three-level classification of walking performance (walking without aids/walking with aids/wheeled mobility). This allowed for wide variations within each level, where a moderate decline in strength, balance, speed or endurance may not affect the classification level of walking ability. In addition, there are also environmental and social factors that may influence the chosen method of mobility[148] In our study, there were participants who had experienced an obvious decline in various aspects of walking ability, but as they chose to refrain from using walking aids or wheeled mobility, they were still classified as "walking without aids".

We found no association between walking ability in adulthood and pain, fatigue, or body mass index (BMI) in adulthood. Nevertheless, if the association between these factors could have been studied longitudinally, the results may have been different. In conclusion, our results support earlier findings of a decline in walking ability in adulthood. However, the level of walking ability classified according to the chosen method of mobility, appear to be comparatively stable in adulthood.

INTELLECTUAL DISABILITY

At the follow-up in adulthood, an additional ten individuals were classified as having an intellectual disability, making the prevalence 22%. By definition, intellectual disability has to originate in childhood. Nevertheless, in some individuals, it is not formally diagnosed until later in life when increasing demands make challenges more obvious. Among adults with CP there are many who have never had their cognitive function formally assessed. For individuals with intellectual disability, receiving a formal diagnosis is crucial since it ensures the right to certain forms of social support, such as special schools, group homes, and sheltered employment. For individuals with more specific cognitive impairments, an assessment of cognitive function in adulthood can be of equal importance. Such an assessment can provide knowledge about personal strengths and weaknesses, enabling appropriate support at home as well as in the workplace[52]. In Sweden, the opportunities for

adults who wish to be assessed are limited, a problem that the CPUP follow-up program is now working to ameliorate[52].

EPILEPSY

The proportion of survivors who had epilepsy at some point in time was 29%, which was in line with recent systematic reviews[68,69]. To our knowledge, this was the first population-based study of epilepsy in CP that followed up on individual cases from childhood to adulthood. Our results indicated that epilepsy treatment in CP did not always have to be lifelong, as has often been assumed. Even if the risk of recurrence is greater in CP, there are also individuals with CP who stay seizure free after discontinuation of treatment. This knowledge may be of importance when weighing the risks and benefits of discontinuing epilepsy treatment in adults with CP who are seizure free. However, further research is needed to clarify the risk factors for recurrence of epilepsy in adults with CP.

HEALTH CONDITIONS

The most common other health condition was pain (65%), which is in accordance with previous studies[75,68]. We found that a more severe walking impairment was associated with more pain, but only in participants without intellectual disability. Among participants with intellectual disability, no such association was seen. This may indicate that adults with intellectual disability may not always manage to articulate their pain even with the help of alternative and augmentative communication. For these individuals, a pain assessment scale such as the Abbey Pain scale may be helpful, as it enables carers to assess non-verbal signs of pain[149].

A majority of adults with CP had some form of gastrointestinal disorder (61%), such as dysphagia, upper gastrointestinal disorders, or constipation. In CP, the brain injury can affect the enteric nervous system controlling the gastrointestinal tract, thereby causing gastrointestinal dysfunction[150]. However, in adults in the general population, gastrointestinal conditions often have other causes, such as lifestyle or medications[151,152]. The standard treatments may thus be directed towards causes in the general population may not always be applicable to adults with CP. Adults with CP often report that healthcare professionals are not knowledgeable about the repercussions of CP[128]. This may be one example of such a situation.

More than one third of participants had been treated for a psychiatric disorder (39%), most often depression or anxiety. Previous studies have found a

prevalence of these conditions of around 20% of adults with CP[82]. This could be due to the fact that our study covered a longer time span than most other studies and included all episodes of depression or anxiety that had been treated with either medication or psychotherapy.

One third reported respiratory disorders (30%), such as problems with phlegm, asthma or a history of pneumonia. The problems with phlegm in airways that are frequently seen in CP do not have a suitable ICD-10 diagnostic code and are therefore not detected in healthcare registers. Instead, there is a high prevalence of asthma (24%)[69] in adults with CP in such studies. In CP, many different factors may interact and cause respiratory disorders[101]. For example, motor impairment and scoliosis can reduce airway clearance[153]. Gastroesophageal reflux disease and dysphagia can cause aspiration and chronic airway inflammation[153]. Both of these pathways can then lead to impaired lung function, respiratory failure, and result in premature death[101,153]. This is another example where a health condition such as asthma can have other causes in adults with CP compared to the general population, and therefore needs to be treated differently.

Respiratory disorders are the leading cause of death in adults with CP[81,82,6,2], making these conditions important targets for preventive care. Dysphagia is a known risk factor for respiratory disorders[153]. In our study, dysphagia was associated with problems with phlegm or pneumonia. Problems with phlegm and pneumonia were also associated with the following impairments: intellectual disability, dyskinetic subtype of CP, and a less functional GMFCS level, all of which have been associated with poorer survival[2,6]. Consequently, in the follow-up of individuals with these impairments, extra attention should be given to respiratory disorders. However, as the evidence for most interventions is weak[154,155], treatments must be based on clinical experience and the effects closely monitored.

Individuals with intellectual disability had a higher prevalence of pneumonia, problems with phlegm, epilepsy, pressure ulcers, gastrointestinal disorders, and underweight. Intellectual disability was also associated with severe communication impairment. As individuals with intellectual disability are known to have poorer survival and are often dependent on others to access healthcare, these findings underscore their need for regular follow-up in adulthood[156,157].

Obesity and sedentary behavior have been suggested to play a role in the development of walking decline in CP[106]. Among our participants, 21% were obese compared to 13% in the general population in Sweden[158]. However, we found no association between obesity and walking ability. Underweight may be a more immediate health problem than obesity. In our study, all participants who were underweight had an intellectual disability. Moreover, there was a close relationship between underweight and severe impairments of communication and mobility, indicating that the responsibility for interventions must lie with carers and healthcare professionals.

SOCIAL OUTCOMES

A majority of adults with CP lived alone. In the general population, the majority lived with a partner or child. Living with one´s parents was more common among adults with CP than in the general population. The proportion of adults with CP living with their parents was similar to what was reported for adults with CP in this age group in a Swedish study from 2021[120]. However, among young adults aged 25-29 years, as many as 28% lived with their parents[120].

In our study, it was twice as common for adults in the general population to have completed a tertiary education compared to adults with CP. This difference is consistent with a Danish study of individuals born between 1965-1978 with data from 1999[119]. In contrast, an Australian study from 2020 found similar proportions of young adults with CP who had completed tertiary compared to young adults in the general population. However, this did not seem to affect employment rates. The employment rate among young adults with CP was only 33% compared to 76% in the general population in Australia[112].

Among adults with CP, 50% were competitively employed. This is substantially more than the 19-33% found in population-based studies from Denmark, Canada, and Australia[112,119,114]. One explanation for this could be that one third of the adults in our study who were employed had wage subsidies, a form of support that may not be available in other countries.

We found a lower employment rate and lower disposable income in adults with CP compared to the general population. Similar findings were recently reported in another Swedish study[121]. When adjusting for education level these differences remained. This can be explained in part by the higher prevalence of intellectual disability among adults with CP. The register data from

Statistics Sweden does not differentiate between special schools and mainstream schools. Therefore, among those who have completed primary and secondary education, there is a bigger proportion of adults with CP who have gone to special schools and who would not be expected to be competitively employed. However, as there are no special schools offering tertiary education, the difference in employment rate and income between adults with CP and the general population at that level must have other explanations. There are many plausible explanations, from individual factors such as pain, fatigue, and other health conditions that lower work capacity[93,159], to societal barriers such as prejudice, discrimination, and a lack of workplace accommodations and community transportation[114,112,160].

The social outcomes in adults with CP were related to the level of walking ability. As shown in Study I, the prevalence of intellectual disability in the cohort of adults with CP was also related to walking ability. Consequently, it can be either walking impairment or intellectual disability, or a combination of the two, that influence social outcomes. A certain difference in social outcomes between adults with CP and the general population is to be expected, considering that severe physical, intellectual and communication impairments are more common in adults with CP. However, the difference between less severely affected adults with CP and the general population may to some extent be a result of inadequate support and therefore be amenable to interventions.

When studying social outcomes, it is important to keep in mind that social outcomes are not goals in themselves. Not everyone wants a partner or an employment, and some partners or employments can be more harmful than beneficial. However, this applies to adults with CP as well as to the general population and should not cause a difference between the groups. The goal should be for everyone to have equal opportunities for independence and participation in society, as stated in the United Nations Convention on the Rights of persons with disabilities[107].

METHODOLOGICAL CONSIDERATIONS

STUDY POPULATION

The study populations in this thesis all originated from the population-based CP register of western Sweden. All individuals in the CP Register born between 1959-1978 who could be identified as alive were included in studies I and IV. For studies II and III, all individuals still residing in the Västra Götaland Region were invited to participate. Thus, individuals with all CP subtypes and all levels of impairments were included. The participants came from all parts of the region, city and countryside, and resided in group homes or in their own homes. Of course, since they all came from Västra Götaland and received healthcare in the region's pediatric clinics and habilitation units as children, there is a possibility that they may not be fully representative of adults with CP in the entire Swedish population. On the same note, Sweden is a high-income country with well-developed public healthcare and social support, and the results of these studies should be seen in light of these circumstances.

ASSESSMENTS

The follow-up assessments in studies II and III were conducted during the years 2016-2019. The location and timing of the follow-up assessments were adapted to suit the participants. However, participating in a follow-up assessment can still be demanding, as the procedure took about three hours and involved answering many questions and undergoing a physical exam. It is possible that individuals with deteriorating health refrained from participating because this seemed too demanding. On the other hand, it was clear that some participants chose to participate because they were experiencing problems related to their CP and wanted a check-up and advice on how to proceed.

Interviewing participants where functional levels vary to a large extent requires individual adaptations. For this reason, a semi-structured form was used for interviews. All areas were explored in detail with each participant, but some participants were able to talk freely and give all the relevant information, while others needed to be asked very specific questions. Some participants started to give a general answer and then turned to their parent or assistant for specifics. Some were not able to understand or answer the interview questions at all, and in those cases, all questions were asked to the parent or assistant. If the participant used alternative and augmentative communication, their method of communication was used. Additionally, picture-based scales and Talking Mats were used when needed. It is possible that the different methods of gathering

data could have influenced the data. However, in order to be able to do a population-based study that includes individuals with intellectual disability and communication impairments these adaptations were necessary. The alternative would have been to also interview individuals without these impairments with the same alternative and augmentative communication, which was not considered feasible.

In Study II walking ability was classified the same way as in the CP Register, to permit comparisons between childhood and adulthood. This classification had three levels, based on method of mobility in everyday life. However, in order to detect and measure the subjective decline in walking ability reported by adults with CP, other measurement tools or rating scales might be better suited, such as for example the Timed Up and Go[161], the six-minute walk test[162], or the Functional Mobility Scale[163-165]. In the future, longitudinal studies measuring the many different aspects of walking ability are needed, to help identify preventable mechanisms leading to decline in walking ability.

In Study II and III, a semi-structured interview was used to gather medical history. The interview was conducted by one of two physicians with extensive experience of patients with cerebral palsy. This clinical experience was necessary to be able to pose suitable follow-up questions, to ensure that all areas of health were properly explored, and that all health conditions were correctly understood, affirmed or denied. With a structured interview or a questionnaire, the risk of missing or misinterpreting symptoms would have been substantial. With an unstructured or qualitative interview, this risk would have been even bigger. However, the interview situation involves a risk for bias as the follow-up questions may be perceived as leading or the participants may give answers that they believe are desirable. Awareness of these risks and measures taken to counteract them cannot guarantee that there is no bias. The health conditions were classified as present or not present. However, in reality, the severity of symptoms is on a continuous scale. We strived to be as consistent as possible, but in classifying the presence of a health condition, there will always be a certain degree of subjectivity, both on the part of the participant and the interviewer.

STRENGTHS AND LIMITATIONS

A strength of this thesis is the population-based study population, which is rare in research on adults with CP. The fact that the participants were identified through a register means that there is background data available on non-participants, which aids in the evaluation of representativeness. The study population is also older than in many other studies, providing new information on the lives of middle-aged adults with CP.

Another strength is that for studies II and III, even though the participants were identified through a register, the data was gathered specifically for this study. Therefore, the study was not limited to predetermined variables in registers. The combination of an interview, a physical exam, and questionnaires in the follow-up assessment allowed for a thorough understanding of each participant, increasing the accuracy of the data.

Studies I and IV on the other hand, were limited to the variables available from the CP Register and Statistics Sweden. For example, Statistics Sweden did not specify whether an exam was from a special school or a mainstream school, information that would have been valuable in our study.

Another limitation was the underrepresentation of individuals with intellectual disabilities in studies II and III. Since the participants with intellectual disability had a higher prevalence of several health conditions in our study, the prevalences we present for the whole population may be slightly underrated.

CONCLUSIONS

This thesis aimed to explore the health, functioning and social outcomes of a population-based cohort of middle-aged adults with CP in western Sweden. The results of the four studies show that adults with CP differ from children with CP in the distribution of CP subtypes, and the prevalence of associated impairments. The reason for these differences is that individuals with less severe impairment in childhood have better survival. However, in some of the survivors the impairments change over time. In addition to the impairments, other health conditions, such as pain, gastrointestinal disorders, and respiratory disorders are common in adults with CP. The prevalence of a number of these health conditions is associated with CP subtype and associated impairments. In adulthood, the social outcomes of individuals with CP differ greatly from the general population, in terms of education, employment, income, and living arrangements.

Taking all of this into account, it is clear that adults with CP need more support than what is provided today in order to achieve good health and functioning and have equal opportunities to participate in society.

FUTURE PERSPECTIVES

Two essential measures that can be recommended to improve the situation for individuals with CP in a lifetime perspective, would be to extend the regular follow-ups at the habilitation units and the access to specialized services, into adulthood. This would provide the necessary basis for adult healthcare professionals to acquire knowledge and experience of the specific challenges involved in CP and enable them to offer individuals with CP appropriate care. It would also create a starting point for the interventional studies that are needed to form evidence-based guidelines, guidelines that are currently lacking in almost all areas of medical care for adults with CP.

Today, health professionals at the habilitation units are often aware of the medical conditions affecting adults with CP but cannot provide the appropriate treatments within their organization. At the same time, the specialized services that provide treatment for the general population are not knowledgeable of how CP affects the individual. Therefore, designing and implementing interventional studies that include adults with CP and, for example, respiratory disorders or gastrointestinal disorders would likely require cooperation across professions and organizations.

Another way to enhance research on adults with CP is through the CPUP. The CPUP is a national quality register and follow-up program for individuals with CP and a valuable resource for research[132]. However, the inclusion of adults in CPUP is managed by the habilitation units and is limited by the fact that a large part of the adults with CP are not known by the habilitation units. Hopefully in the future, all adults with CP who so wishes can be welcomed at the habilitation units and included in the CPUP.

ACKNOWLEDGEMENTS

If this section were to include a thorough description of all the support I have been given and the gratitude I feel towards each person, it would have to be longer than the whole rest of the thesis. The PhD studies have been a journey, but it has not been a lonesome journey through uncharted territory. Other researchers have travelled this route before me, fellow PhD students have travelled alongside, and other people have stepped in and helped in so many ways.

First of all, I would like to express my deepest gratitude to all the participants with cerebral palsy who so generously shared their time and experiences with us. My deepest thanks also go to my fellow researchers who were engaged in the gathering of data, and to my supervisors Kate Himmelmann, Meta Nyström Eek and Katharina Stibrant Sunnerhagen, without whom this research would not have been possible.

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