Neonatal brachial plexus palsy : impact throughout the lifespan
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CHAPTER ONE

General introduction

DEFINITION AND CLASSIFICATION

Neonatal brachial plexus palsy (NBPP) is a traction injury to the brachial plexus sustained during birth. Worldwide reported incidences vary per country and per study and range from 0.1 per 1000 live births to 8.1 per 1000 live births.[1] Risk factors for NBPP have been studied widely and it is well known that especially shoulder dystocia (i.e. the baby's shoulder is obstructed by the maternal pelvis) resulting from higher birth weight (>4000 gram) is related to the occurrence of NBPP; and to a lesser degree, multiparous pregnancies, prolonged labour, breech delivery and/or any otherwise difficult delivery.[2,3] Specific manoeuvres and strategies have been developed to address the management of shoulder dystocia, which have been shown to decrease the occurrence of NBPP.[4] Prevalence of NBPP seems to be higher in some western European countries, including the Netherlands (1-2/1000), compared to other regions, such as Finland (1/1000) and the United Kingdom (0.4/1000).[1,5-8]

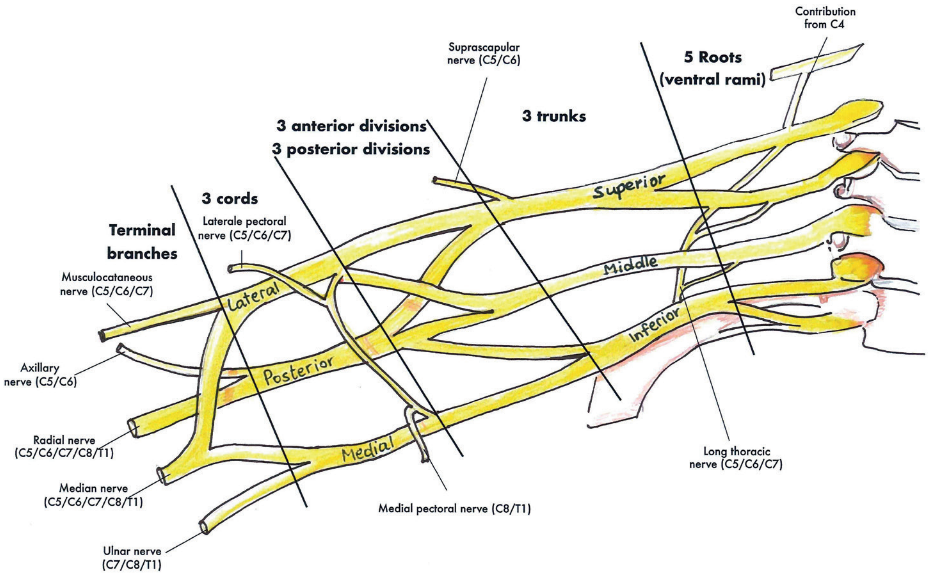

Figure 1 Anatomical representation of the Brachial Plexus

The brachial plexus is formed by the spinal rootlets of the 5th cervical to the 1st thoracic root, which fuse to the superior, the middle and the inferior trunk which in turn branch into 3 anterior divisions and 3 posterior divisions. This results in the formation of the lateral, the posterior and the medial cords which end in the terminal branches: the peripheral nerves of the arm and hand (i.e. Musculocutaneous nerve, Axillary nerve, Radial nerve, Median nerve and Ulnar nerve).

With respect to the extent of the nerve injury in NBPP, Algimantas Narakas proposed a classification based on the level(s) of nerve injury at early presentation, i.e. when infants are 2-3 weeks old.[9,10] This classification distinguishes 4 levels (I-IV): I Upper Erb's palsy (rootlets C5-C6), II Extended Erb's palsy (rootlets C5-C6 and C7), III Total plexus palsy (rootlets C5-T1) and IV Total plexus palsy (rootlets C5-T1) with Horner's syndrome (ipsilateral miosis and ptosis).[9] Erb's palsies (C5-C6) are the most common form of NBPP injuries, total lesions (C5-T1) comprise around 15%, and isolated lower plexus palsies (Klumpke's palsy C8-T1) are very rare.[11-13]

A severity classification of peripheral nerve injuries in general (including NBPP) has been described by Seddon in 1943, which was refined later by Sunderland.[14,15] *Neurapraxia* is the least severe injury: temporary function loss without structural nerve damage. In case of *Axonotmesis* the nerve fibers (axons) are ruptured but the surrounding structures (endoneurial tubes, perineurium) remain intact. Outgrow of axons (estimated at 1 millimetre per day) will lead to spontaneous recovery in the course of months. In *Neurotmesis* the integrity of both the axon and surrounding structures are lost, and spontaneous recovery will not occur. Another type of injury is *Avulsion* of the nerve rootlets from the spinal cord (pre-ganglionic tear); spontaneous recovery will not occur.[16,17]

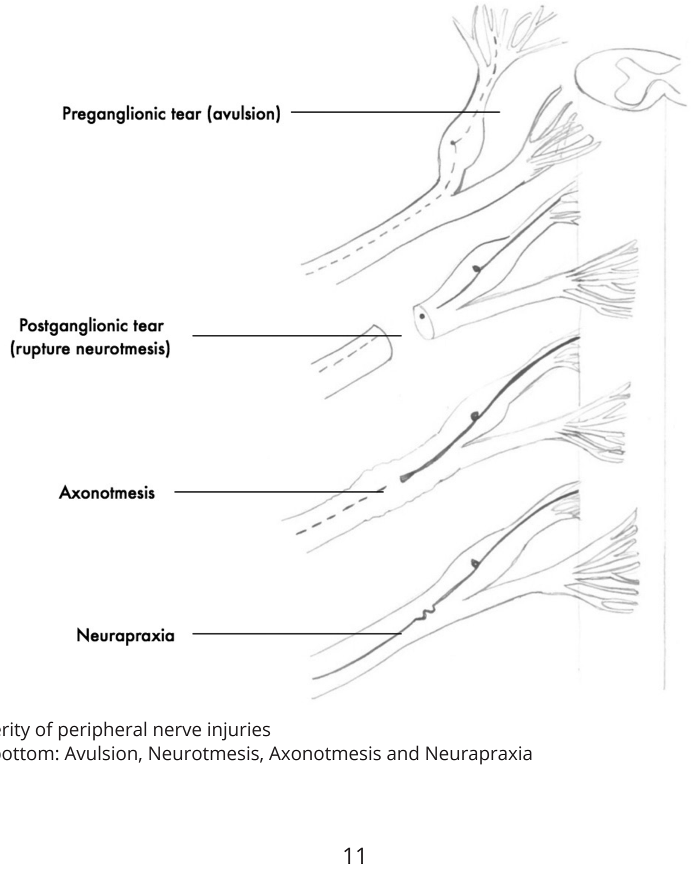

Figure 2 Severity of peripheral nerve injuries
From top to bottom: Avulsion, Neurotmesis, Axonotmesis and Neurapraxia

The natural history of NBPP has been studied by different authors but recovery rates vary greatly due to methodological differences among these papers.[1,2,13,18,19] A systematic review concluded that rates for incomplete spontaneous recovery probably range between 20% and 30%.[13] In infants who do not show spontaneous recovery, the underlying nerve lesion constitutes of neurotmesis or root avulsion, which necessitates early nerve surgery.[13] Usually different forms of injuries within the brachial plexus elements are present in a single patient, which makes comparisons between patients difficult due to heterogeneity.[2,13]

TREATMENT OF NBPP

Early nerve surgery, or 'primary surgery', is indicated in those children with NBPP who show no, or limited, recovery of arm function over time. There is no generally accepted consensus on how to select infants for nerve surgery.[20] Many treating physicians agree that a total brachial plexus lesion is indicative for nerve surgery at an early age.[18,21,22] The oldest 'rule' was provided by Alain Gilbert, who employs absence of biceps recovery at the age of three months as indication for nerve reconstruction.[23] Howard Clarke employs a more stepwise approach with different indicators at different ages.[24]
At the Leiden University Medical Center (LUMC) in The Netherlands, we endeavour early surgery, i.e. complete lesions at three months of age, and incomplete lesions between 3 and 6 months, mainly based on absence of elbow flexion recovery.[25] Ancillary investigations, specifically needle electromyography at the age of 1 month, aid in early identification of severe nerve lesions.[26] Depending on the nature of the nerve lesion, different surgical modalities may be indicated. These include nerve grafting after excision of the neuroma, nerve transfers (e.g. intercostal nerves to musculocutaneous nerves) or a combination of techniques.[22,27-29]
A prospective randomized trial does not exist to answer the question for the indication for early nerve surgery.[30] Meta-analysis of the available literature has been performed with varying outcome.[18,22] These attempts were seriously hampered by different outcome measures used and bias by indication, which makes pooling of data from different studies virtually impossible.[31]

The LUMC is one of the three NBPP expert centers in the Netherlands. Early referral to one of these centers is very important to be able to decide whether nerve surgery treatment as described above is needed.[32] At the LUMC, 1142 patients with NBPP have been evaluated and/or treated until January 2015. Of these 1142 patients, 534 underwent primary (nerve) surgery.

When conservative treatment or primary nerve surgery does not lead to satisfactory function recovery, and limitations in using the affected upper extremity persist, a secondary surgical procedure may be indicated.[2] Persisting functional limitations can be related to the shoulder, the elbow and/or the hand/wrist with close interaction between these joints and whole body

function thus determining functionality for a specific patient as such. In the LUMC, 257 secondary surgical procedures were performed (up to January 2015) consisting of 166 procedures around the shoulder, 29 around the elbow and 62 around the hand/wrist.
Most secondary surgical procedures are performed about the shoulder since decreased active shoulder external rotation range of motion (ROM) (i.e. enabling hand to mouth and hand to head movements) is the most common remaining functional deficit in NBPP. These functional deficits originate from muscle imbalance with subsequent soft tissue and joint contractures resulting in glenohumeral joint deformity.[2,33-35]
To address limited external rotation, various treatments can be performed: botulinum toxin injections in contracted muscles, surgical contracture releases, muscle lengthening, muscle tendon transfers or osteotomies.[34,36-40] Muscle tendon transfers and internal contracture releases around the shoulder are widely used and widely studied.[41] Most studies, however, were mainly focused on ROM and Mallet scores (Mallet scale: instrument measuring general shoulder movements[42]) and did not measure patient or parent satisfaction, functional outcome or quality of life (QoL). Furthermore, most studies were not controlled and could easily be biased by the co-interventions like prior surgical treatment, nerve surgery, and conservative interventions. Also, most studies did not report the clinical course over time.
Regarding the elbow, possible procedures could be pronation osteotomies, possibly in combination with m. biceps tendon rerouting or a release of the membrana interossea to obtain a more functional position of the arm.[43,44] To create some active elbow flexion in case of a complete paralysis of the flexors, a so-called Steindler procedure (flexor pronator group transfer) can be performed, due to which the elbow can be flexed by the normally innervated wrist flexors.[45,46] Surgical options for correction of elbow flexion contractures exist, but give residual flexion contractures of up to 30 degrees. An open release is preferred by our group due to the complications (i.e. additional nerve injuries) seen with arthroscopic releases of the elbow.
To obtain a more functional hand, a variety of muscle tendon transfers remain, usually to improve active wrist extension, thumb extension and /or finger extension.[44,47,48]

Irrespective of treatment choices (e.g. conservative, primary and/or secondary surgery), pediatric physical therapy is important in the management of NBPP.[49] The physical therapist monitors motor performance, joint mobility and muscle strength over time, but more importantly instructs the parents on how to handle (e.g. carry, pick up and clothe) their baby and how to perform exercises to maintain passive ROM. In The Netherlands, physical therapy may start hospital based, always followed by home-based therapy, or starts home based within 7-10 days after birth.[49,50] This home-based therapy is usually guided and monitored by a pediatric physical therapist working in primary care. From the start, passive ROM exercises should be performed for shoulder abduction, forward flexion, internal and external rotation; elbow flexion and extension; wrist extension, pronation and supination; as well as finger flexion, extension and thumb opposition and reposition. These exercises are important in order to maintain passive mobility for future active movement to be unrestrained.[49,51]

Depending on neurological recovery these passive ROM exercises are continued at least until a better prognosis can be predicted. In growing infants glenohumeral joint movement exercises have been described in order to prevent joint and muscle contractures and to normalise shoulder movements.[50,52,53] Contracture prevention can also be supported by applying serial casting, orthoses, dynamic splints or botulinum toxin.[40,54,55] Further treatment should consist of monitoring and improving motor development and motor function. Physical therapy is continued over time depending on treatment history and recovery and a functional, tailored to the individual, therapy program should be applied in combination with home exercises to maintain and/or improve functional abilities. Constraint induced movement therapy, and possibly bimanual intensive training, have also been suggested and described to improve function.[52,56] However, these interventions are not systematically studied and their added value to rehabilitation programs remains to be proven.

CONSEQUENCES OF NBPP IN RELATION TO THE INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH

NBPP may have functional consequences throughout life.[19,57-71] Depending on initial neurological damage and damage extent, functional recovery and treatment, these consequences may vary from minor to very severe. At different stages of the child's life (from infant to toddler, to preschool age, to grade school age, to adolescence) and even in adulthood NBPP may have its consequences and might influence choices in life (school, education, profession, work etc.). The interaction between the health problem (NBPP) and its consequences in various health related components (body functions and body structures, activities, participation and environmental and personal factors) is represented in the International Classification of Functioning, Disability and Health model (ICF).[72] The ICF was originally accepted in 2001 and a children and youth version, emphasizing the influence of personal factors and environmental factors on the health problem (e.g. the role of parents, family, school, individual background etc.) was derived from the original ICF Model (ICF-CY).[72] As of 2012 the additional components of the ICF-CY (i.e. personal factors and environmental factors) were merged into the ICF creating one model to classify functioning, disability and health throughout the lifespan.[72]
Figure 3 shows an example of the ICF model in relation to a possible problem due to NBPP.

In Table I the most common consequences of NBPP are presented in relation to the ICF model.[66] As can be seen in Table I, NBPP has impact on various components of the ICF. Although the relation between the ICF components and quality of life (QoL) is complex and depends for example on life expectations, it is likely that the condition also affects QoL. In children with NBPP, a decreased QoL and limited upper extremity functioning (UEF) compared to their healthy peers has been reported for children older than 2 years.[73-75]
In addition, NBPP may also have impact on family and parental QoL. Throughout the child's life parents may be worried what the future for their child will bring and what consequences

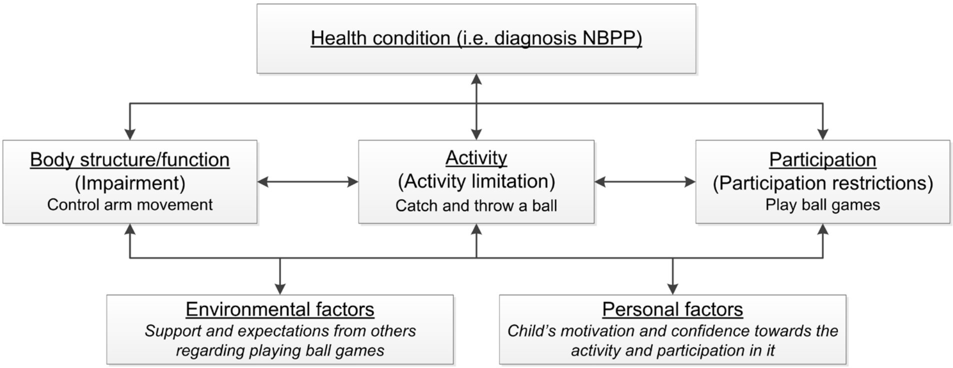

Figure 3 ICF model in relation to possible NBPP problems (impaired control of arm movement)
Model based on the ICF model of the World Health Organisation (WHO).[72]

NBPP will have on the QoL of their child. Age does not seem to have an effect on the family impact but having a younger child with NBPP (age 0-2 years) has greater impact on maternal QoL.[76,77] Parents of children with NBPP, aged 0-18 years, feel that the condition of their child has impact on the family in terms of finances, personal strain, social and mastery problems. Furthermore, parents have an increased risk of psychological problems, distress and a lower QoL. Condition severity is significantly associated with these problems.[58,75-79] How upper extremity functioning (i.e. performing daily activities) and perceived QoL in children under 2.5 years of age are associated to family impact as a whole was not yet known.

THE LONGER-TERM CONSEQUENCES OF NBPP IN ADOLESCENTS AND ADULTS

Only a few studies investigated NBPP in adolescents and (young) adults. Daily functioning (e.g. dressing, washing) in young adults with NBPP has been described as limited, in the majority of patients due to pain.[69,80] Physical problems related to NBPP during normal activities such as cycling and swimming also have been reported. However, only a small proportion of the patients reporting these problems seem to be unable to participate in these activities.[81]

Little was known about the impact of NBPP on patient-perceived participation in society in adult life. There were no studies available focusing on this domain of the ICF and therefore it was unclear to what extent patients experience restrictions in education, work, leisure, sports and/or social activities. Moreover, prior to the current thesis it was unknown whether NBPP has any influence on choice of education and/or work.

Table I Possible consequences of NBPP summarized in relation to the ICF model as derived from focus group research.[66]

Body structures	Body functions	Activities	Participation
• Nerve damage • Muscle atrophy • Muscle stiffness • Joint capsule shortening / stiffening • Connective tissue shortening/ stiffening • Bony deformities • Skin scar tissue	• Decreased muscle force • Decreased muscle endurance • Joint instability • Impaired joint mobility • Gross motor function impairment • Fine motor function impairment • Sensory loss • Pain • Altered body image	Impaired ability to: • Reach • Grasp • Throw • Catch • Push • Pull • Manipulate in hand • Write • Lift objects • Carry objects • Climb • Swim • Perform gross motor activities • Perform fine motor activities • Care for oneself (hair, skin, teeth, nails etc. put on/take off clothes etc, eating/drinking etc.) • Clean • Store daily necessities	Problems in: • Child-parent relationships • Physical activity • Sports • Playing (with Peers) • Hobbies • School • Seeking employment • Work
Environmental factors		**Personal factors**	
• Parents • Siblings • Family • School • External expectations • Assistive devices • Health professionals • Strangers • Domestic animals • Support and relationships • Attitude of 3rd persons • Health services • Education and training services		• Age • Gender • Race • Personal/social experiences • Preferences • Internal expectations	

COMPREHENSIVE ASSESSMENT OF THE CONSEQUENCES OF NBPP

Assessing and monitoring consequences of NBPP on all ICF components is important to understand the progress of NBPP throughout life, to prove efficacy of (new) treatment and to evaluate outcome of (surgical) interventions. In NBPP research, multiple outcome instruments were used, but no consensus exists on which instruments to use.[82] Moreover, only few outcome measures were validated for use in NBPP and a large proportion of the chosen instruments were only used in one or two studies. Often self-developed questionnaires were used without reporting on these instruments' psychometric properties.[82-85] The most common used outcome measures were mainly based on measuring bodily functions (e.g. active ROM, muscle strength) and bodily structures (e.g. passive ROM, muscle length) but seldom on activity and participation levels, which determines functionality as such. Rarely environmental and personal factors were taken into account.[82] Although improving participation throughout life is in the end the main goal of most interventions, it was almost never measured in clinical studies. Furthermore, not many studies assessed patient (or parent) expectations and satisfaction and/or cosmetic consequences of NBPP treatment.[82-85] Table II gives an overview of outcome measures used in NBPP research. It includes the Pediatric Outcome Data Collecting Instrument (PODCI), a well-known instrument regarding QoL measuring aspects across the ICF domains. It assesses different aspects of daily living, overall health and pain in children and adolescents with musculoskeletal disorders.[86] The PODCI is reliable, validated, suitable and tested for children and adolescents (2-18 years old) with Musculoskeletal disorders, including NBPP.[87-90] A Dutch version of this instrument was prior to this thesis not available. As can also be seen in Table II not many instruments were available for arm and hand function, especially not measuring parent reported spontaneous use in daily life.[85] Although the impact of NBPP on family has been described using multiple outcome instruments[75,76,79], these instruments were not mentioned in the systematic reviews regarding outcome measures in NBPP.[82-85]

Despite the comprehensive amount of literature on NBPP and the available outcome measures, not all aspects of NBPP have been researched and there is a lack of well validated outcome measures for NBPP.
For example, healthcare use in children with NBPP and factors which influence this, both in the short and long term, and in regard to whether they are currently in follow-up or not had not been researched. It is important to understand to what extent children with NBPP use care and which patient characteristics, QoL and physical functioning parameters influence this healthcare use. Furthermore, it remains unclear whether patients (or their parents/caregivers) have unmet information needs. This is important to investigate given that clinical, shared, decision making in NBPP is influenced by given or sought information.[91]
To fully understand outcome of NBPP, it is important to take into account all aspects of NBPP including family impact, perceived and/or reported QoL, participation, healthcare use, information need as well as upper extremity functioning (including hand use at home) to be able to understand the consequences of NBPP on life. When the consequences of NBPP on life are better understood, healthcare professionals are more able to support parents and/or patients throughout the NBPP treatment phase and possibly beyond.

Table II Overview of (more) often used outcome measures in NBPP research subdivided in ICF domains. Outcome measures extracted from 4 systematic reviews containing instruments used in NBPP research until 2015.[82-85]

Body structures	**Instrument**	**Type of instrument**	**Region**
ROM (passive/active)	• Goniometer (Degrees)	Device	• Shoulder/Elbow/Wrist/Hand
ROM indexes	• Mallet scale • Gilbert scale • Active movement scale • Toronto test score	Physical examination index	• Shoulder/Elbow • Shoulder/Elbow • Shoulder/Elbow/Wrist/Hand • Elbow/Wrist/hand
Imaging	• MRI • CT • X-ray • Ultrasound	Medical device	• Shoulder/Elbow/Wrist/Hand
Body Functions	**Instrument**	**Type of instrument**	**Region**
Muscle strength indexes	• Medical Research Council • Narakas • Raimondi scale • Gilbert Raimondi scale • Al-Qattan classification • Hand strength (grip)	Physical examination index	• Shoulder/Elbow/Wrist/Hand • Shoulder/Elbow/Wrist/Hand • Wrist/Hand • Elbow • Shoulder/Elbow/Wrist/Hand • Hand
Muscle strength	• Hand Held Dynamometry	Device	• Shoulder/Elbow/Wrist/hand
Functional test	• Towel test • Cookie-test • Nine hole peg test • Pick up test	Physical examination	• Shoulder/Elbow/Wrist/Hand • Elbow • Hand • Shoulder/Elbow/Wrist/Hand
Nerve function	• EMG	Medical device	• Shoulder/Elbow/Wrist/Hand
Nerve function (sensation)	• Semmes Weinstein test • 2 Point Discrimination test • Stereognosis	Physical examination index	• Hand • Shoulder/Elbow/Wrist/Hand • Hand
Activities and Participation	**Instrument**	**Type of instrument**	**Measuring goal/Region**
	• CAPE • ABILHAND (KIDS) • CHEQ • DASH • SF-36	PROM	• Participation/Whole body • Activity/ Shoulder/Elbow/Wrist/Hand • Activity/Hand • Activity/ Shoulder/Elbow/Wrist/Hand • Activity/Participation/Whole body
	• BPOM • AHA	Functional activity assessment	• Activity/ Shoulder/Elbow/Wrist/Hand • Activity/ Shoulder/Elbow/Wrist/Hand

Activities and Participation (incl. Environmental factors)	Instrument	Type of instrument	Measuring goal/Region
	• PODCI	PROM	• Activity/Participation/ Whole body with specific Upper extremity part
	• PEDI	PROM via interview	• Actvity/Participation/ Whole body

ROM: Range of Motion, MRI: Magnetic Resonance Imaging, CT: Computer Tomography, EMG: Electromyography, PROM: Patient Reported Outcome Measure, CAPE: Children's Assessment of Participation and Enjoyment, CHEQ: Children's Hand use Experience Questionnaire, DASH: Disability of the Arm, Shoulder and Hand, SF-36: Short Form 36, BPOM: Brachial Plexus Outcome Measure, AHA: Assisting Hand Assessment, PODCI: Pediatric Outcome Data Collecting Instrument.

OUTLINE OF THIS THESIS

Given the lack of knowledge and available outcome measures the aims of this thesis are:

I. Evaluation of functional outcome of secondary surgery around the shoulder (internal rotation contracture release and external rotation tendon transfers) in the short term and the long term with emphasis on pre-operative nerve surgery.

II. Translation, cross cultural adaptation and evaluation of an outcome measure to evaluate physical functioning and QoL and evaluation of an instrument measuring spontaneous hand use at home.

III. Comprehensive description of the impact of NBPP on the family, on QoL, on Healthcare use and Information need and on participation in adolescents/adults and/or children with NBPP (all part of the ZAP Plexus study: Zorg (Care), Activities and Participation in patients with NBPP).

Chapter 2 describes the short term functional outcomes, including QoL and parental satisfaction, of an internal rotation contracture release and muscle tendon transfers of the mm. Latissimus Dorsi and Teres Major for external shoulder rotation.
Chapter 3 describes the long-term outcomes of internal contracture releases and/or muscle tendon transfers around the shoulder for children with and without a history of nerve surgery.
Chapter 4 exemplifies the cross-cultural translation and adaptation of a well-known musculoskeletal QoL questionnaire, the PODCI, into Dutch. This translated version of the PODCI was used in the ZAP Plexus study as QoL instrument but also as reference instrument for validation of the Hand Use at Home questionnaire (HUH) in children with NBPP.
Chapter 5 illustrates the construct validity and test-retest reliability of the newly developed HUH in children with NBPP or unilateral cerebral palsy (UCP) aged 3-10 years old.

Chapters **6, 7 and 8** are part of the ZAP Plexus study in which age specific outcome measures were used to investigate the impact of NBPP on the family, on QoL, on Healthcare use and Information need and on participation in adolescents/adults and/or children with NBPP. An overview of the used outcome measures is provided in Appendix I.

Chapter 6 reports the parent-perceived family impact, QoL and upper extremity functioning in children with NBPP aged 0-2.5 years old.
Chapter 7 specifies healthcare use and information needs in (parents of) 0-18-year-old children with NBPP.
Chapter 8 describes restrictions in participation, and QoL, but also influence of NBPP on (choice of) education and work in adolescents and adults with NBPP.
Chapter 9 Summary and general discussion
Chapter 10 Summary of this Thesis in the Dutch language.

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