On the road to optimize rehabilitation for young individuals with acquired brain injury

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CHAPTER 1

General introduction

Definitions, incidence, classification of severity, and stages of recovery of Acquired Brain Injury among young individuals between 4 and 25 years old

Definitions

Acquired Brain Injury (ABI) is a collective term for brain injury that occurs after birth and leads to a disruption in the developmental (life) line.[1] ABI encompasses both traumatic brain injury (TBI) and non-traumatic brain injury (nTBI). TBI is caused by external trauma, such as traffic and sports accidents, or violence, while nTBI refers to brain injuries caused by internal factors like brain tumors, stroke, or meningitis.[1]

Incidence

ABI has a substantial global incidence, with an estimated 54-60 million cases of TBI and 15 million cases of nTBI occurring annually.[2] The global incidence rate of TBI in children and adolescents aged 0 to 18 years is estimated to range from 47 to 280 per 100,000 individuals per year, but the rates vary across countries.[3] No global annual incidence rates for nTBI are available, likely due to the diverse range of causes and different registration systems. For stroke specifically a systematic review and meta-analysis on pediatric stroke in hospitals found an estimated global pooled incidence rate for all ischemic strokes in children up to 18 years old of 5.6 per 100,000.[4] Regarding ABI in general, studies conducted in the United States and Finland have shown an increasing incidence and prevalence of ABI among young individuals over the past years.[3,5,6]

In the Netherlands in 2013 the estimated yearly incidence of ABI among young individuals under the age of 25 was 586 per 100,000 citizens for TBI and 191 for nTBI.[7] Consistent with international literature,[3,5,6] a Dutch monitor on national child safety indicated a rise in the incidence of TBI cases due to increasing traffic incidents.[8]

Classification of severity and stages of recovery

The severity of TBI is typically determined by means of the Glasgow Coma Scale[9] and the duration of Post Traumatic Amnesia,[10] which are both generally determined at hospital admission. In case of nTBI, the modified Rankin Scale is often used in pediatric stroke.[11] However, there is currently no severity classification available for other specific nTBI subtypes, such as brain tumors. It is important to note that these severity classifications are only applicable to young individuals with TBI or nTBI who were admitted to or were assessed in the hospital so that they are not available for the whole ABI population.

With respect to recovery after TBI and some forms of nTBI such as stroke, three general stages can be identified.[7,12,13] The acute phase, the first hours to weeks after onset, during

which young individuals with ABI may be either hospitalized or not, depending on the cause, origin, and timing of the injury. The second stage is the subacute or recovery period, during which patients may be treated either at home, with or without primary care treatment like physical therapy, or in a hospital or rehabilitation center. Finally, for TBI and some forms of nTBI, the participation or chronic phase is when most individuals are returning to participation in society and in the community, such as in school, work, and sports. Treatment may still be necessary during this stage. The duration of these stages can vary widely among individuals due to potential relapses and differences regarding specific consequences.[12-17] Approximately 70% of young individuals with ABI recover within the first six months to one year following the injury, while the remaining 30% experiences persistent daily-life consequences.[7,12-20] Notably, the severity of the brain injury was found to only have a weak relation with the persistence of these consequences.[7,18-21]

Consequences of ABI in young individuals with ABI (4-25 years old).

The consequences of ABI can be classified according to the World Health Organization (WHO) International Classification of Functioning, Disability, and Health (ICF). This classification system describes the consequences of a health condition across various domains: body functions and structures, activities and participation, and environmental and personal factors (Figure 1).[22] In research cohorts, the ICF offers the potential to be used as a framework to systematically select assessments and interventions for children, adolescents and young adults covering the age range of 4-25 years with a specific health condition.[25,26]

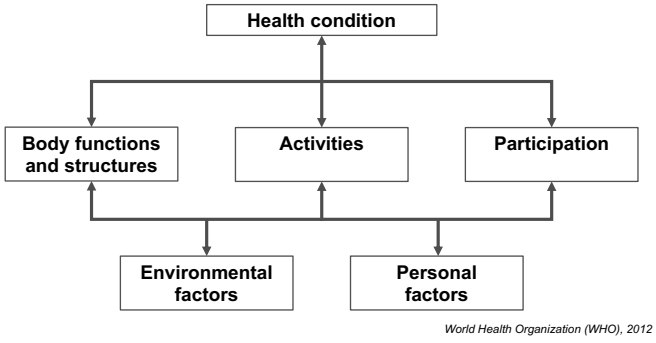

Figure 1. The International Classification of Functioning, Disability, and Health (ICF) framework.

Apart from a description of the consequences of a health condition per domain, the overall health status of an individual including his/her/x physical, emotional, cognitive and social

functioning is commonly defined as Health-Related Quality of Life (HRQoL).[22,27] In children, adolescents, and young adults with ABI the consequences may persist and negatively affect the totality of physical, mental, cognitive, and social-emotional skills and competencies.[7,19,21,28-30] The negative effects of ABI on HRQoL have been demonstrated in pediatric TBI,[28] pediatric stroke, and brain tumor populations.[29,30] Diminished HRQoL may persist for years after the brain injury onset and may influence various transition moments from childhood to adulthood.[25,26,31]

Body functions and structures: Fatigue

In terms of the ICF domain body functions and structures, the potential consequences of ABI involve physical problems such as motor impairments, and pain.[32,33] Moreover, one of the most frequently reported consequences of ABI is fatigue.[7,18,19,34] Fatigue is defined as 'the experience of exhaustion and a decreased capacity for physical or mental activity because of an imbalance in the availability, use or restoration of resources needed to perform the activity'.[35] Fatigue after ABI was found to have a negative impact on physical, cognitive, and social functioning.[34,36] Young patients must adjust their lives to manage ABI-related fatigue, often resulting in reduced participation, for example by discontinued sports activities and limited school attendance. Fatigue is particularly prevalent during the transitions from childhood to adulthood.[34] Factors associated with being more tired include nTBI and older age i.e., adolescence or young adulthood.[36]

To date, the occurrence of fatigue and its multidirectional influence on participation restrictions have been explored among young patients with ABI, both cross-sectionally and longitudinally.[36-39] However, it is not known how severely fatigued young individuals (4-25 years old) with ABI referred to rehabilitation are, and there is a lack of knowledge regarding the persistence of fatigue over time after referral to rehabilitation and its longitudinal relationship with participation.

Activities and participation

According to the ICF, activities refer to the performance of tasks or actions by young individuals.[22] Limitations in mobility (walking, cycling) and self-care are commonly reported consequences of ABI in young individuals.[22,40-42] The ICF defines participation as 'involvement in a life situation'.[22] Participation can be operationalized using two key elements: attendance i.e., 'being present' and involvement i.e., 'active engagement'.[43] The ability to participate in valued life situations at home, school, work, and in the community is crucial for healthy development during the transitions from childhood to adulthood.[43] ABI in children, adolescents, and young adults can lead to significant participation restrictions, which are substantially higher compared to their healthy peers.[40,43] Studies on participation restrictions

in (Dutch) children and adolescents with disabilities, including TBI, have identified many limitations in social and educational activities.[40,44-46] Factors associated with greater participation restrictions include impaired motor, cognitive, behavioral, and sensory functioning.[40,45,46] With the exploration of participation, it is important to realize that perspectives on participation between young individuals and their parents may differ.[44]

Similar to the consequences on the level of body functions and structures, most studies on the impact of ABI on activities and participation have not encompassed the entire population of young patients (4-25 years old) with ABI in a rehabilitation cohort. Additionally, potential differences in perspectives on participation between patients and their parents have often not been considered. Therefore, knowledge regarding participation restrictions in young individuals with ABI referred to rehabilitation remains an under-researched topic.

Environmental factors: Impact on the family

The consequences of ABI among young individuals often have a significant impact on their families as well. This impact can be of emotional, social, or practical nature, e.g., consisting of increased stress, worries, or changes in family routines, roles, and responsibilities.[18,45,47,48]

Previous cross-sectional studies have emphasized the existence of family impact throughout all stages of recovery of young patients with both TBI and nTBI.[48-53] Its occurrence was found to be influenced by, among other aspects, the unexpected onset, the less visible consequences and the uncertain prognosis.[54-57] The full extent of the impact on the family often appears only in the phase of everyday life at home and community reintegration. Longitudinal studies among families of young individuals with TBI have found that significant family burden and stress, regardless of the cause or severity of the brain injury, may persist longer than 12 months after the onset of ABI.[54-58] However, these studies have mostly included patients with TBI,[54-57] or patients with more severe injuries,[54,56,58] or they have focused only on limited aspects of family functioning.[54,56]

Overall, research into the extent and course of the impact on the family and its determinants are scarce, in particular for the group of young individuals referred to rehabilitation after ABI.

Management of ABI in young individuals: the role of medical specialist rehabilitation

Regardless of the stage of recovery, the ultimate goal of rehabilitation is to enable the patient to fully participate in society.[22,59] When daily-life consequences persist after ABI in a young person between 4 and 25 years old, general practitioners or medical specialists often assess if there is an indication for medical specialist rehabilitation treatment. In the

Netherlands, most of the 16 specialized medical rehabilitation facilities (Medical Specialist Rehabilitation Centers, further designated as rehabilitation centers) provide inpatient or outpatient treatment for patients with ABI. In most cases patients are referred to outpatient rehabilitation care. Rehabilitation care in the Netherlands is typically delivered by professionals working in multidisciplinary teams.[12] The care is, apart from the nature and severity of the consequences of the ABI, tailored to the life stage of the young person and the family, considering their wishes and needs.[60]

In most rehabilitation centers in the Netherlands, the Dutch Care Standard for TBI in children and youth (Zorgstandaard traumatisch hersenletsel kinderen & jongeren, 2016) is used.[12] This standard is generally considered to be applicable to young individuals with nTBI as well.[12] In this standard,[12] it is described that young individuals between 4 and 25 years old with persisting daily life consequences after ABI could benefit from primary care or medical specialist rehabilitation care. Knowledge regarding the nature and severity of persisting daily-life consequences after ABI in young patients and their families at the time of referral to outpatient rehabilitation in the Netherlands is however limited. Research is needed to address this knowledge gap and further optimize rehabilitation treatment for this group.

Medical specialist rehabilitation aligns with the principles of value-based healthcare (VBHC).[61] VBHC states that the value in healthcare is the measured improvement in patient health outcomes relative to the costs, in order to optimize the value of care for patients and their families. One of the VBHC principles underlines the importance of providing outcomes that matter to all patients, putting patients at the center of healthcare and care standards are an operationalization of that statement.[61,62] The organization of care within multidisciplinary care pathways and the delivery of care across facilities are fundamental components of VBHC as well.[61,62] Therefore, it is crucial to ensure that prioritization extends beyond optimal care within the rehabilitation center itself, encompassing the seamless alignment of the referral process and potential follow-up treatments in primary care.

Regarding the delivery of rehabilitative care for young persons with ABI, age-appropriate care and the specific needs during transition moments of an individual are considered important elements.[25,26,31] The duration of rehabilitation can vary greatly, depending on the type and severity of the brain injury, as well as other factors such as the individual's age, overall health, and personal rehabilitation goals.[12,60]

A cohort of young patients and their families referred to outpatient rehabilitation: research project "Participate?!"

To gain more insight into the daily-life consequences of ABI for young patients who are referred to medical specialist rehabilitation and their families, the "Participate?!" project (in

Dutch: "Meedoen?!") was initiated. The project was approved by the Medical Ethical Committee of the Leiden University Medical Center (LUMC) (P15.165) and started in 2015 with funding from the Dutch Brain Foundation (Hersenstichting). The goals were to gain more insight into the consequences of ABI over the various domains of the ICF (body functions/structures, activities/participation, and environmental factors including HRQoL, fatigue, participation, and family impact) in a cohort of young patients with ABI between 4 and 25 years old and their families referred to an outpatient rehabilitation center in the Netherlands. This research project was conducted in collaboration with a Dutch national consortium, called "Brain Injury and Youth" (in Dutch: Hersenletsel en Jeugd, HeJ), which consisted of pediatric rehabilitation physicians.

The consortium initiated several projects to improve and monitor the current care and education for young patients with ABI and their parents, focusing on cognitive, physical, and emotional consequences.[7,19,36,63] In this project, a questionnaire was developed in consensus with the Brain Injury and Youth consortium. The questionnaire included parent and patient-reported outcome measures (PROMs) to assess HRQoL, fatigue, participation, and family impact.

The use of PROMs in (pediatric) rehabilitation practice is recommended to assess well-being and disability levels.[12,64-66] Additionally, the use of health outcomes data is promoted in line with VBHC principles to improve outcomes that are important to patients.[62] Similarly, outcome measurement for the patients' families, such as family impact, is crucial for VBHC as well.[62]

The road towards a national rehabilitation framework for young individuals with ABI: The research project "Participate?! Next Step"

As a follow-up to a successful collaboration between rehabilitation centers in the "Participate?!" project, rehabilitation professionals, including rehabilitation physicians, psychologists, physical therapists, occupational therapists, speech therapists, and social workers, showed a growing interest to identify potential variations in practice among rehabilitation centers and harmonizing the delivery of care for the population. This interest aligned with the principles of VBHC where the development of care pathways is advocated and was recommended in the literature on pediatric rehabilitation care.[12,25,62,66]

To take the "next step", the Participate?! project needed to continue, identifying differences, and strengthening collaborations among rehabilitation centers to further optimize care for young patients with ABI and their families. Consequently, in 2020, the "Participate?! Next Step" research project was initiated. This project was approved by the Medical Ethical

Committee of the LUMC (P15.165-addendum-1.0) and received funding from the Dutch Brain Foundation. A group of lead experts from participating rehabilitation centers was selected to support the project and strengthen collaboration. These lead experts represented their respective rehabilitation centers throughout the project and played a role in executing various parts of the project. Fourteen rehabilitation centers (Figure 2) committed to the project with the aim of strengthening collaborations and collectively optimizing the delivery of care for young individuals with ABI referred to medical specialist rehabilitation and their families.

The extent of potential variations among Dutch rehabilitation centers in the structure of care for young individuals with ABI, such as admission and discharge criteria, care organization, and aftercare, is currently unknown. Furthermore, as the commonly used standard of care does not specify exact structures and rehabilitation content,[12] it is expected that each rehabilitation center has its own approach to treating young individuals with ABI.

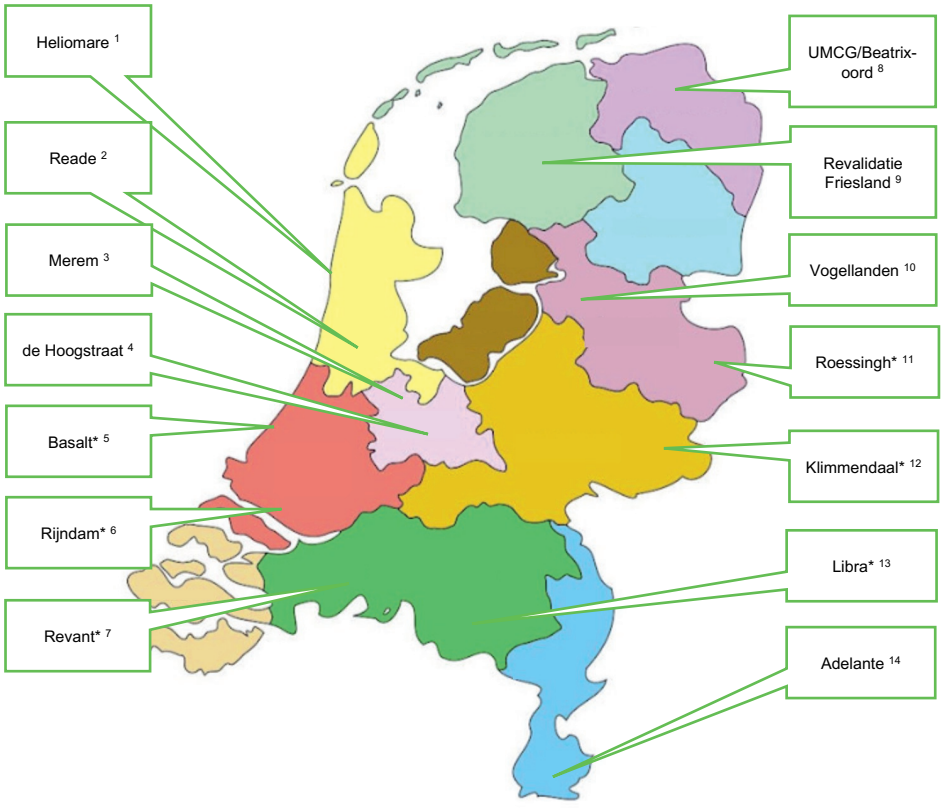

Figure 2. Participating rehabilitation centers that provide outpatient rehabilitation for young patients with ABI in the Netherlands.

Participating Rehabilitation Centers: [1] Heliomare, Wijk aan Zee; [2] Reade, Amsterdam; [3] Merem, Hilversum; [4] de Hoogstraat, Utrecht; [5] Basalt, The Hague; [6] Rijndam, Rotterdam; [7] Revant, Breda; [8] UMCG/Beatrixoord, Groningen; [9] Revalidatie Friesland, Beetsterzwaag; [10] Vogellanden, Zwolle; [11] Roessingh, Enschede; [12] Klimmendaal, Arnhem; [13] Libra, Eindhoven; [14] Adelante, Valkenburg.
* Centers with multiple locations: Only the primary/largest location is shown.

AIMS OF THIS THESIS

Section 1 presents the results of the "Participate?!" project regarding **persisting consequences of ABI in young individuals and families referred to outpatient rehabilitation in the Netherlands**. The aim of this section was to describe the course and/or severity of HRQoL, fatigue, participation, and family impact in young people with ABI and their families referred to outpatient medical specialist rehabilitation.

Chapter 2 introduces a new way to categorize and interpret fatigue severity levels among young patients with ABI based on scores from healthy age-matched peers. **Chapter 3** presents the results of a two-year follow-up study on fatigue and participation in children and young adults with ABI in the outpatient rehabilitation setting. **Chapter 4** comprises a study on participation restrictions in an outpatient rehabilitation cohort and explores the differences in participation perspectives between patients with ABI and their parents. **Chapter 5** describes parent-reported family impact at the time of referral to outpatient rehabilitation among families with a child with ABI and identifies factors that negatively influence family impact. **Chapter 6** focuses on the course of family impact and quality of life over a two-year period among parents of young patients with ABI. For the purpose of this thesis, patients' caregivers are also referred to as 'parents'.

Section 2 of this thesis presents the results of the "Participate?! Next Step" project concerning **joint collaborations between rehabilitation centers to optimize care for young individuals with ABI**. This section aims to describe and compare the structure and process of rehabilitation for young patients with ABI across Dutch rehabilitation centers. Furthermore, it aims to describe the development a national consensus-based framework for clinical practice, including preferred assessments, interventions, and psychoeducation, for young people with ABI across Dutch rehabilitation centers. **Chapter 7** describes potential variations among Dutch Rehabilitation Centers in the structure of rehabilitation care i.e., admission and discharge criteria, the organization of care, and the aftercare for young patients with ABI. **Chapter 8** concerns a Delphi study among healthcare professionals from 14 rehabilitation centers to reach a consensus on the content (assessments, interventions, and psychoeducational materials) of a national framework based on current practices for young people (4-25 years old) with ABI and their families in the Netherlands.

In **Chapter 9**, the findings of the studies in **Sections 1 and 2** are summarized and discussed.

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SECTION 1

Persisting consequences of ABI in young individuals and families referred to outpatient rehabilitation in the Netherlands

CHAPTER 2

Fatigue in young patients with acquired brain injury in the rehabilitation setting: categorizing and interpreting fatigue severity levels

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ABSTRACT

Purpose

Fatigue in patients with acquired brain injury (ABI) is common. However, to better target fatigue, clear ways to categorize/interpret fatigue-severity in individual patients are lacking. This study aims to determine/categorize fatigue severity among children, adolescents, and young adults with ABI.

Methods

This cross-sectional study included young patients admitted to outpatient rehabilitation and their parents. To determine fatigue, the PedsQL™Multidimensional-Fatigue-Scale was used (MFS, scores 0-100, lower scores=higher fatigue, patient-/parent-reported). Based on scores from a reference population, four categories were formed: "1=no/little fatigued" to "4=severely-more fatigued".

Results

All scores were lower than those from the reference population, with comparisons in the adolescent and young adult groups reaching statistical significance ($p < 0.05$). The proportions of patients in category 4 were: 9%/50%/58% among children/adolescents/young adults, showing that many patients were "severely-more fatigued"-than the reference population.

Conclusions

Measuring fatigue and categorizing fatigue severity looks promising for clinical practice and could help to better target fatigue.

INTRODUCTION

Fatigue is a common symptom with mental, emotional, and physical components among children, adolescents,[1] and young adults,[2] and it could influence their health-related quality of life (HRQoL).[1-4] Specifically in young patients (5-24 years old) with "irreversible damage to the brain" due to a traumatic (TBI) or a non-traumatic cause (nTBI) i.e., acquired brain injury (ABI),[5,6] fatigue was found to be one of the most reported symptoms.[7-20] Furthermore, fatigue is known for its persistence over time even years after onset of ABI.[21,22] Outpatient rehabilitation treatment could focus on fatigue-specific treatment to optimize HRQoL in young patients with ABI.[8,9,23] To date, the complex relationship between brain injury and fatigue is not entirely understood.[24] Only a few studies among adolescents and young adults with ABI (hospital and rehabilitation based) specifically addressed fatigue, concluding that it is relatively common,[8,25] even five years after onset.[20] In clinical rehabilitation practice, a measurement of fatigue is not always part of the standardized assessment at admission and thus remains under-recognized in assessment and treatment.

One Danish study compared the patient population to healthy age-matched peers, where adolescents and young adults with ABI reported considerably higher fatigue levels.[25] It is known that fatigue is measured and monitored with a broad variety of outcome measures, with different feasibilities, validities and internal consistencies.[3,13,26-28] For example, the previously described studies used the Multidimensional Fatigue Inventory-20 (MFI-20) and the Pediatric Quality of Life Inventory™ (PedsQL™) Multidimensional-Fatigue Scale (MFS).[8,20,25] The PedsQL™ MFS is the only outcome measure that has been translated in many languages, has been used among young patients with ABI (0-30 years old) and in rehabilitation-based studies.[1,2,8,20,25] Fatigue outcomes are often only presented on a linear scale e.g., 0-10 or 0-100, where higher scores indicate less fatigue or vice-versa.[3,13,26-28] Furthermore, when clinicians are interpreting 0-100 scores, based on Likert rating values (i.e., 100, 75, 50, 25, 0), this is not always suitable for treatment selection, nor does it automatically provide information in terms of how severe scores are compared to healthy peers. Therefore, in clinical practice, severity cut-off scores based on reference population scores[1,2] may be a more effective measure of fatigue severity than just pinpointing a score on a 0-100 scale.

One previous study compared fatigue (as measured with the PedsQL™ MFS) in patients with sickle cell disease to fatigue in healthy peers. They presented means, SDs, and effect sizes to compare both groups. Results of this study showed that patients were more fatigued than healthy peers (> 2 SDs below the mean of healthy peers, effect size: 1.28).[29] However, this study did not present clear cut-off scores to categorize fatigue severity. It

would be useful in clinical practice to differentiate between potential levels of fatigue severity by using cut-off scores based on outcomes from healthy peers to monitor changes in fatigue in individual patients with ABI.

Fatigue in young patients with ABI in a rehabilitation setting is commonly seen. However, a comparison of fatigue outcomes in young patients with ABI (5-24 years old) in an outpatient rehabilitation setting to fatigue outcomes in healthy peers is absent. A comparison with fatigue in healthy age-matched peers is available for patients with ABI that are older than 15 years old.[25] In this study, an outcome measure was used that is not suitable for patients under 15 years old (MFI-20).[25]

To gain further knowledge on fatigue in young patients with ABI this current study has three aims. First, to describe fatigue using the PedsQL™ MFS in 5- to 24-year-old patients with ABI that were admitted to outpatient rehabilitation. Second, to categorize the severity of fatigue in these patients using cut-off scores based on data obtained from healthy age-matched peers. Categorizing fatigue in severity cut-offs could support the interpretation of fatigue scores. Third, to examine the association between the severity of fatigue and HRQoL of patients, with the hypothesis that worse fatigue scores are associated with diminished HRQoL. Based on the nature and severity of fatigue, treatments such as psycho-education and/or physical fitness treatment and/or cognitive behavioral therapy could be better tailored to a patient's needs.[30-32] The insights from our study could support the interpretation of fatigue scores by clinicians, thereby enhancing its recognition and treatment in rehabilitation as well as increasing awareness of one of the major "invisible" problems after ABI in young patients: fatigue.

METHODS

Design and setting

This study was part of a larger, observational, longitudinal multi-center study on family impact, fatigue, participation, and quality of life in Dutch children, adolescents and young adults with ABI. The study was conducted from 2015-2019 in 10 rehabilitation centers in the Netherlands, all of which treat patients with ABI. The study protocol was reviewed by the medical ethics committee of the Leiden University Medical Center (P15.165), and an exempt from full medical ethical review was provided. In the current study, only data regarding patient and parent reported fatigue and HRQoL were used. The "Strengthening the Reporting of Observational studies in Epidemiology" (STROBE) guidelines were used for the reporting.[33]

Population/Participants

Patients with ABI: Children, adolescents, and young adults aged 5-24 years with a diagnosis of ABI, who were referred to a participating rehabilitation center and their parents were eligible for the study. If patients and/or parents were unable or limited to understand the Dutch language, they were not invited. Patients over the age of 16 years had to give permission for their parents to participate according to the Dutch law of healthcare decision making and vice-versa in patients below 16 years old.

Healthy Dutch peers: Dutch reference data regarding fatigue, as measured with the Pediatric Quality of Life Inventory™ (PedsQL™) Multidimensional-Fatigue Scale (MFS),[3] were previously reported by Gordijn et. al. and Haverman et. al.[1,2]

The study by Gordijn et.al. included 366 healthy 5- to 18-year-old children and/or their parents (n=497) from day care facilities and schools in the Netherlands. They divided the participants into age groups: children 5-7 years, children 8-12 years and adolescents 13-18 years[1]. The study by Haverman et.al. included 512 healthy 18- to 30- year-old young adults. The study was part of a larger Dutch study aimed at establishing normative data for several questionnaires measuring various psychosocial concepts, where young adults from the general population were invited by e-mail to participate.[2] For the present study, only published, aggregated results i.e., mean and SD per age group were used.

Assessments

The assessment comprised a set of (digital) questionnaires that were administered at admission and as part of routine care. Questionnaires were filled out either at home or at the outpatient clinic (digitally or on paper). Unique links to the digital questionnaires were sent to the participants by e-mail by the medical health professionals. Questionnaires that were filled out on paper were literally copied and transcribed into the digital database by the data manager. Thereafter, all data were recoded anonymously, and stored in a secured central digital database at Basalt Rehabilitation Center in The Hague, The Netherlands. For the present study on fatigue, only data gathered at admission were used.

Demographic and injury characteristics: patient demographics and injury-related characteristics were extracted from the medical records. Characteristics included: date of birth, sex, date of ABI onset, date of first appointment, and cause of the ABI. The time between ABI onset and referral to rehabilitation was presented per age group as numbers (%) and median (IQR) in months and divided into 2 groups: time between onset and referral less (<) and more (>) than 6 months. Age was determined at time of the first appointment and further divided into three groups: children (5-12 years), adolescents (13-17 years) and

young adults (18-24 years). ABI cause was divided in: TBI or nTBI and if known, the TBI severity level was reported as mild, or moderate/severe, based on the Glasgow Coma Scale at hospital admission.[34] NTBI causes were divided into; stroke/cerebrovascular accidents, brain tumors, meningitis/encephalitis, hypoxia/intoxication and other.

Outcome measures: fatigue: To assess patient fatigue (reported by patients, parents, or both), the 18-item PedsQL™ Multidimensional Fatigue Scale (MFS) was used as outcome measure. The PedsQL™ MFS is considered a feasible, valid and reliable tool to assess fatigue in patients with different age groups and diagnoses, including ABI.[3] It is translated and validated in Dutch.[1,2] The MFS yields a total scale score, and three domain-scores: general fatigue (GF, six items), sleep/rest fatigue (SRF, six items) and cognitive fatigue (CF, six items).

All scores are calculated as the sum of the items divided by the number of items answered. Items are answered on a Likert-scale (0=never to 4=almost always) and thereafter linearly transformed to a 0-100 scale (0=100, 1=75, 2=50, 3=25, 4=0). Lower scores indicate more fatigue.[3]

Reference data regarding fatigue: Self- and parent-reported Dutch reference data is available regarding fatigue among children and adolescents. For the young adult group, only self-reported data is available.[1,2] Regarding children and adolescents, mean total PedsQL™ MFS self-reported reference data scores were 76.8 (95% Confidence Interval, CI: 75.5–78.1) and for the domain scores: GF; 80.3 (95%CI: 78.81–81.77), SRF; 74.5 (95%CI: 72.88–76.09), and CF; 75.7 (95%CI: 73.83–77.56). Mean total PedsQL™MFS parent-reported reference data scores were 81.2 (95%CI: 80.1–82.3, and for the domain scores: GF; 81.3 (95%CI: 80.01–82.52), SRF; 83.8 (95%CI: 82.62–85.06), and CF; 78.5 (95%CI: 76.90–80.06). For the young adult group, the mean (SD) total score was 71.8 (14.56) and for the domain scores: GF; 70.4 (18.2), SRF; 68.6 (14.6), and CF; 76.3 (18.4).

HRQoL: The PedsQL™ Generic Core Scales-4.0 (PedsQL™ GCS-4.0, self- and parent-reported Dutch language version) was used to determine the HRQoL of young patients.[35,36] Only HRQoL total scores were used in this study. The scoring system of the The PedsQL™GCS-4.0 is similar to that of the above-described PedsQL™MFS.

Statistical analysis

Characteristics: All patient characteristics and fatigue outcomes were described per total and age group using descriptive statistics. These age-ranges correspond with the Dutch reference data from healthy peers.[1,2]

Fatigue: In this study, we compared fatigue outcomes (continuous variables) from patients with ABI with age-matched healthy children, adolescents which was both self- and parent-reported. Regarding young adults, only self-reported reference data was available. Mean fatigue scores and standard deviations from these healthy peers were used to determine how many standard deviations the patients in our cohort differ from the mean scores from healthy peers.

The study by Gordijn et.al. only reported 95% Confidence Intervals (95%CI) and SDs were calculated by taking the square root of the number of participants in this study (n) and multiplying it with the upper limit of the 95% CI minus the lower limit of the 95% CI and dividing it by 3.92 (normal distribution): SD= √N x (upper limit – lower limit) /3.92

For every (age)group, aggregated Z-scores (or standard scores) were calculated using the formula: "X" (the mean fatigue score from patients), minus "μ" (the mean fatigue score from healthy peers), divided by "σ" (the SD from the mean fatigue score in healthy peers). This method was also done for the parent-reported data.

$$Z = \frac{X - \mu}{\sigma}$$

X= mean fatigue score (patients with ABI)
μ= mean of the healthy peers
σ= SD of the healthy peers

To find corresponding probabilities, we used a Z-table/standard normal distribution table (a table for the values of Phi) to find *p*-values on the left of the mean to check whether the mean differences between the patients and the healthy peers were significant.

Negative scores in the Z-table correspond to the *p*-values which are less than the mean and vice-versa with positive scores.

Categorization of PedsQL™ MFS scores: The mean total PedsQL™ MFS scores and SDs from the reference data from Dutch healthy peers were used to create four categories of fatigue severity. The cut-offs for the categorization were age-group and patient/parent-reported specific. Further the categorization was calculated for the total and domain scores as presented below and specified in Figure 1.

Category 1: Fatigue score with more than +1SD difference compared to healthy peers: "less fatigued than healthy peers"
Category 2: Fatigue score between +1SD and -1SD compared to healthy peers: "fatigue comparable with healthy peers"
Category 3: Fatigue score between -1SD and -2SD compared to healthy peers: "moderately more fatigued"
Category 4: Fatigue score with more than -2SD difference compared to healthy peers: "severely more fatigued"

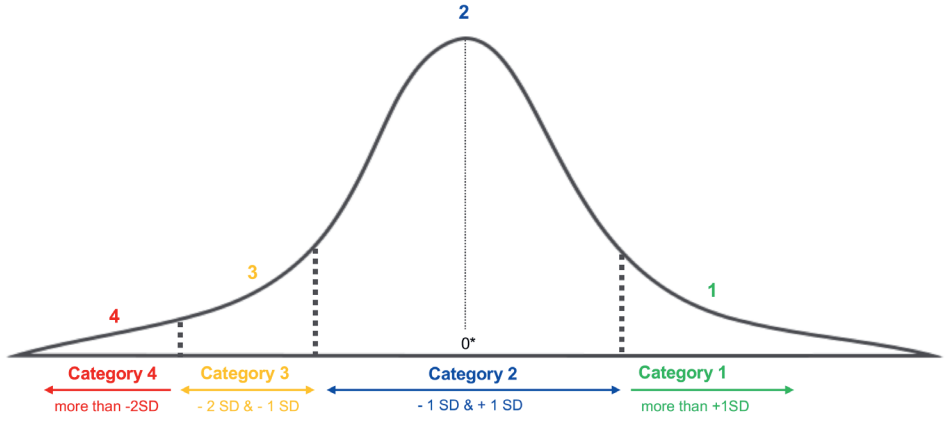

Figure 1. Fatigue severity classification in a normal distribution curve
** 0= equal to the mean score of the reference data*

This four-point categorization was discussed with a statistician (from the Leiden University Medical Center), and consensus was reached between the statistician and all authors before using this classification in the current analyses.

A Bonferroni correction was performed to account for multiple testing i.e., the α-value divided by the number of analyses on the dependent variable did not exceed 0.05. All *p*-values less than 0.05 in these analyses were considered statistically significant. All above-described analyses were performed using SPSS 25.0 for Windows (IBM, SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp).

RESULTS

Patient characteristics

Figure 2 shows the inclusion of the patients and/or parents who completed the questionnaires that were used in the analyses for the present study. Characteristics of the 260 participants are presented in Table 1. Seventy-six (29%) patients were children (5-12 years), 141 (54%) were adolescents (13-17 years), and 43 (17%) were young adults (18-24 years). Fifty-two percent of all patients were female and 74% of the patients had a traumatic brain injury. Regarding these patients with TBI, 78% had a mild TBI. Forty-two percent of patients were referred to the rehabilitation center more than six months after onset of brain injury. Regarding HRQoL, mean patient- and parent-reported total PedsQL™ GCS-4.0 mean (SD)scores of the whole population were 64.7 (17.4) and 61.4 (16.9), respectively.

Patient/parent-reported fatigue in young patients with ABI, versus healthy peers

In Table 2, the mean (SD) PedsQL MFS total and domain scores from all children/adolescents/young adults, (both self and parent-reported) are presented. The mean (SD) total PedsQL MFS patient and parent-reported fatigue scores were 50.1 (17.3) and 53.8 (19.2), respectively.

The lowest scores (i.e., more fatigue) were reported in the domain “cognitive fatigue” for all age groups, both patient- and parent-reported. The highest scores (i.e., less fatigue) were found in the domain sleep/rest fatigue for all groups. Considering the average total fatigue scores in the different age groups, the results show that overall, both the patient- and parent-reported fatigue scores decreased with age, indicating more severe fatigue in older children.

Total fatigue scores and almost all domain scores reported by patients with ABI and their parents were lower than those of healthy peers. Scores reported by adolescents (and their parents) and young adults were significantly lower than scores from healthy peers ($p < 0.05$), except for patient-reported sleep/rest fatigue ($p = 0.08$) and parent-reported cognitive fatigue ($p = 0.07$) in the adolescent group.

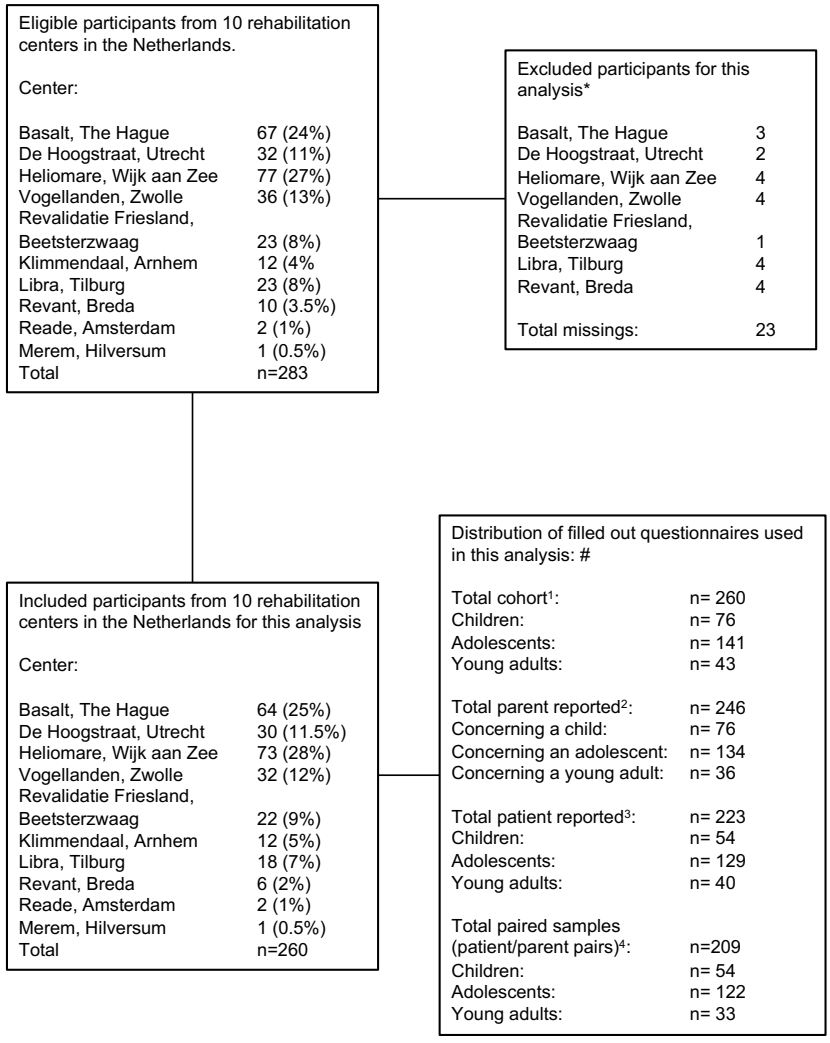

Figure 2. Distribution of participants from 10 Dutch rehabilitation centers.

*Missing participants: n=11 no official ABI diagnosis, n=12 incomplete questionnaires.
#1; number of questionnaires filled out by the patient, the parents or both in total and per age group (children, adolescents and young adults). 2; number of questionnaires filled out by parents only in total and per age group (children, adolescents and young adults). 3; number of questionnaires filled out by patients only in total and per age group (children, adolescents and young adults). 4; number of questionnaires filled out by patients and their parents (paired samples) only in total and per age group (children, adolescents and young adults).

Table 1. Patient, family and injury characteristics of children, adolescents, and young adults with acquired brain injury (ABI) referred to an outpatient rehabilitation center.

Patient characteristics	Children 5-12 years	Adolescents 13-17 years	Young adults 18-24 years	Total cohort 5-24 years
Age (years) at admission:				
Age group, number (%)	76 (29%)	141 (54%)	43 (17%)	260 (100%)
Mean (SD)	9 (2.1)	15 (1.4)	19 (2.1)	15 (3.5)
Sex				
Female, number (%)	40 (53%)	72 (51%)	23 (54%)	135 (52%)
Traumatic brain injury (TBI), number (%)	47 (62%)	110 (78%)	35 (81%)	192 (74%)
Severity level TBI (GCS*), number (%)				
Mild	41 (88%)	83 (76%)	27 (77%)	151 (78%)
Moderate/Severe	3 (6%)	12 (11%)	5 (14%)	20 (10%)
Unknown$	3 (6%)	15 (14%)	3 (9%)	21 (12%)
Non-traumatic brain injury, number (%)	29 (38%)	31 (22%)	8 (19%)	68 (26%)
Causes non-traumatic brain injury, number (%)				
Stroke	2 (7%)	9 (29%)	5 (63%)	18 (25%)
Brain tumor	13 (45%)	13 (42%)	2 (25%)	27 (41%)
Encephalitis/meningitis	6 (21%)	4 (13%)	1 (12%)	12 (18%)
Hypoxia/intoxication	0 (0%)	2 (6%)	0 (0%)	2 (3%)
Other	6 (21%)	3 (10%)	0 (0%)	9 (13%)
Time (months) between ABI onset and referral to rehabilitation				
Total: Median (IQR)	4 (1-21)	5 (1-18)	4 (2-19)	4 (1-18.5)
Group < 6 months				
Number (%)	47 (62%)	83 (59%)	26 (60%)	156 (60%)
Median (IQR)	2 (1-4)	2 (1-3)	2 (1-4)	2 (1-3)
Group > 6 months				
Number (%)	29 (38%)	58 (41%)	17 (40%)	104 (40%)
Median (IQR)	30 (14-54)	24 (10-64)	22 (11-58)	25 (12-57)
Health-related quality of life (HRQoL)#				
Mean (SD) patient-reported				64.7 (17.4)
Mean (SD) parent-reported				61.4 (16.9)

* GCS: Glasgow Coma Scale: "mild"13-15, "moderate" 9-12, "severe" < 8. If the GCS was unknown/not applicable for these patients, and if they had no history of consciousness loss at onset, the severity was equally considered as a "mild TBI". # PedsQL™ Generic Core Scales-4.0 for health-related quality of life (HRQoL) (Total score) 0-100, with lower scores indicating less quality of life.

Table 2. Patient- and parent-reported fatigue in children, adolescents, and young adults with ABI compared to healthy Dutch peers.

Patient-reported data, total group 5-24yr	Patients with ABI, n=223[$]	
	Mean	SD
Total fatigue	50.1	17.3
General fatigue	51.0	22.8
Sleep/rest fatigue	53.8	18.4
Cognitive fatigue	45.5	23.4

Parent-reported data, total group 5-24yr	Patients with ABI, n=246[$]	
	Mean	SD
Total fatigue	53.5	19.2
General fatigue	49.5	24.4
Sleep/rest fatigue	58.7	23.4
Cognitive fatigue	52.3	25.3

Patient-reported data, Children 5-12yr	Children with ABI, n=54[$]			Healthy Children, n=2111				
	Mean	SD	95% CI	Mean	SD	95% CI	Z	p-value
Total fatigue	57.5	14.0	53.7-61.2	77.6	20.4	74.9-80.4	-1.0	0.16
General fatigue	58.6	17.3	54.0-63.2	83.1	27.7	78.6-86.1	-0.9	0.19
Sleep/rest fatigue	64.3	15.2	60.2-68.3	76.8	26.0	72.3-79.3	-0.5	0.32
Cognitive fatigue	49.6	21.3	43.9-55.3	74.0	31.2	69.8-78.2	-0.8	0.22

Parent-reported data, children 5-12yr	Children with ABI, n=76[$]			Healthy Children, n=2321				
	Mean	SD	95% CI	Mean	SD	95% CI	Z	p-value
Total fatigue	59.9	18.0	55.9-64.0	82.1	17.8	79.8-84.4	-1.2	0.11
General fatigue	55.9	23.0	50.7-61.0	83.4	19.2	80.9-85.8	-1.4	0.08
Sleep/rest fatigue	69.7	19.1	65.4-74.0	86.6	18.6	84.2-89.0	-0.9	0.18
Cognitive fatigue	54.3	29.1	47.8-60.9	76.4	26.9	72.9-79.8	-0.8	0.21

Patient-reported data, Adolescents 13-17yr	Adolescents with ABI, n=129[$]			Healthy Adolescents, n=1551				
	Mean	SD	95% CI	Mean	SD	95% CI	Z	p-value
Total fatigue	50.1	17.1	47.1-53.0	75.2	12.1	73.3–77.1	-2.1	0.02*
General fatigue	51.1	23.9	47.0-55.2	76.7	14.2	74.4–78.9	-1.8	0.04*
Sleep/rest fatigue	52.5	16.9	49.6-55.4	71.9	14.3	69.6–74.1	-1.4	0.08
Cognitive fatigue	46.7	24.2	42.5-50.8	77.2	15.4	74.7–79.6	-2.0	0.02*

Table 2. Continued

Parent-reported data, Adolescents 13-17yr	Adolescents with ABI, n=134[$]			Healthy Adolescents, n=1611				
	Mean	SD	95% CI	Mean	SD	95% CI	Z	p-value
Total fatigue	51.7	18.7	48.6-54.9	79.2	14.1	77.0–81.4	-1.9	0.03*
General fatigue	47.4	24.7	43.2-51.5	77.7	16.1	75.2–80.2	-1.9	0.03*
Sleep/rest fatigue	55.6	22.3	51.8-59.3	80.9	15.2	78.5–83.2	-1.7	0.04*
Cognitive fatigue	52.3	23.8	48.3-56.3	78.9	18.1	76.1–81.7	-1.5	0.07

Patient-reported data, Young adults 18-24yr	Young adults with ABI, n=40[$]			Healthy Young adults, n=5122				
	Mean	SD	95% CI	Mean	SD	95% CI	Z	p-value
Total fatigue	40.2	17.5	34.8-45.6	71.8	14.6	70.5-73.0	-2.2	0.01*
General fatigue	40.6	22.3	33.7-47.5	70.4	18.2	68.9-72.0	-1.6	0.05
Sleep/rest fatigue	43.8	20.4	37.4-50.1	68.6	14.6	67.4-69.9	-1.7	0.04*
Cognitive fatigue	36.3	21.7	29.5-43.0	76.3	18.4	74.7-77.9	-2.2	0.01*

Parent-reported data,^ Young adults 18-24yr	Young adults with ABI, n=36[$]		
	Mean	SD	95% CI
Total fatigue	46.5	20.4	39.8-53.1
General fatigue	44.3	23.9	36.5-52.1
Sleep/rest fatigue	46.9	26.9	37.5-55.1
Cognitive fatigue	48.3	22.0	41.1-55.5

[$]Total: n=246 parents, n=223 patients. [1] Dutch reference data from healthy peers (self and parent-reported): ages 5-12 (children) and ages 13-17 (adolescents) years old. [2] Dutch reference data from healthy peers (self-reported): ages >18 (young adults) years old. ^No parent-reported reference data available. [#]PedsQL™ Multidimensional Fatigue Scale (MFS), 0-100, with lower scores indicating more fatigue. * $p < 0.05$: statistically significant.

Fatigue severity categorization of children, adolescents and young adults with ABI based on data from healthy peers

All results and the procedure regarding the categorization of fatigue severity levels in children/adolescents/young adults, based on Dutch reference data can be found in the supplementary table, Figure 2, Figure 3, and Figure 4. The supplementary table presents the calculated ranges regarding the four-group categorization based on the means and SDs from the reference data with the method described in Figure 2. Figure 3 shows the proportions of patients per fatigue severity categorization (Category 1 to 4). The proportion of children (n=54) assigned to categories 2 (50%) and 3 (41%) were higher than in categories 1 (0%) and 4 (9%). The proportions of children reported by their parents (n=76) assigned

to categories 2 (42%) and 3 (35%) were higher than in categories 1 (3%) and 4 (20%). The proportion of the adolescents (n=129) assigned to categories 2 (26%) and 4 (51%) were higher than in categories 1 (0%) and 3 (23%). The proportions of the adolescents reported by their parents (n=134) assigned to categories 3 (23%) and 4 (52%) were higher than in categories 1 (1%) and 2 (26%)-The proportion of young adults (n=40) assigned to categories 3 (28%) and 4 (60%) were higher than in categories 1 (10%) and 2 (12%).

Figure 4 presents the HRQoL total scores per fatigue severity category. Irrespective of age group or whether it concerned patient or parent reported scores, HRQoL scores decreased with each higher level on the fatigue severity category (i.e., more fatigue, lower QoL).

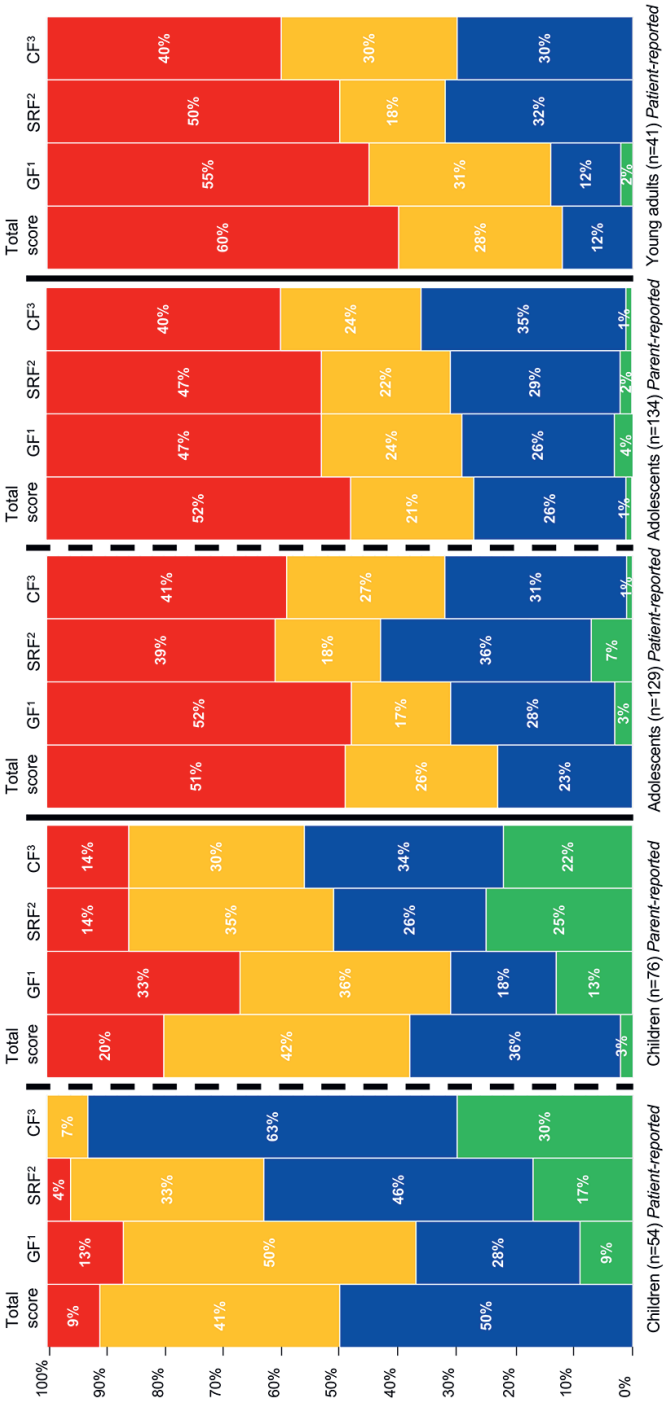

Figure 3. Percentages of children/adolescents/young adults with ABI per fatigue severity level category reported by patients and parents.

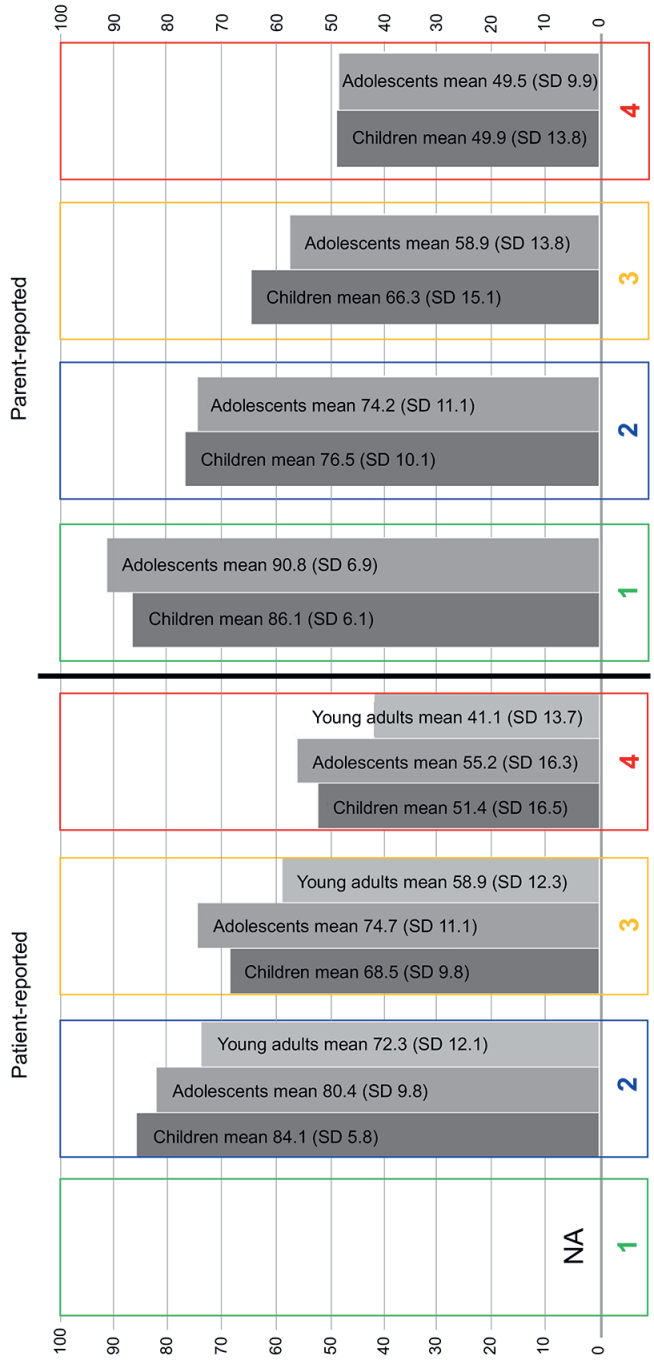

Figure 4. Patient-reported Mean HRQoL total scores# per fatigue severity category in children/adolescents/young adults with ABI.

DISCUSSION

Young patients with ABI, referred for outpatient rehabilitation treatment in The Netherlands, and their parents reported high levels of fatigue. Considerably higher fatigue levels were reported compared to healthy age-matched peers in the reference population. Moreover, a large number of patients were moderately more (category 3) or severely more fatigued (category 4) than healthy peers especially in the groups with adolescent and young adult groups. Finally, HRQoL scores were consistently lower when patients scored in a higher fatigue severity category.

Fatigue in children, adolescents and young adults with ABI in the rehabilitation setting

Considering the whole population of patients in our cohort, highest fatigue levels were found in the "cognitive fatigue" and "general fatigue" domain scales, which was in line with previous literature.[1,2,8,20,37] Higher fatigue levels were found in the groups of adolescents and young adults, which was in line with previous studies among patients with ABI,[8,20] as well as among healthy adolescents and young adults.[1,2]

HRQoL was also found to be lower in comparison with healthy populations, in line with previous studies.[8,20] The overall high levels of fatigue seen in patients with ABI (and their parents) and lower HRQoL warrant extra attention at admission and during outpatient rehabilitation treatment in the Netherlands.

Fatigue in young patients with ABI compared to healthy age-matched peers

Fatigue is known to be common among healthy adolescents and young adults and tends to increase over time in transition from childhood to early adulthood based on mean group scores.[1,2,21] The fatigue scores among young patients with ABI in the current study was on average approximately 20 points lower than scores of the healthy reference population.[1,2] Moreover, in the older age groups (adolescents and young adults), the differences were found to be even greater, which may probably indicate that these groups are at a higher at-risk for more problems in daily life functioning.

An explanation for the relationship between higher age and higher fatigue levels could be that adolescents and young adults are more capable of self-reflecting and are consistently comparing themselves with (healthy) peers.[1,2,21] Another explanation could be the increasing demands and responsibilities regarding daily life activities during the transition from childhood to adulthood.[11,21,22] Furthermore, the differences in scores between patients and parents increase per age group from children towards young adults, which was also seen among the healthy Dutch population.[1,2] An explanation for this tendency could be that

adolescents in transition to adulthood and young adults spend more time away from parents than younger children. Hence, parents have a limited perspective on their activities. Another reason could be that, despite the less overt signs of fatigue associated with cognitive fatigue, this could influence daily life functioning. Given the severity of fatigue in this rehabilitation-based population, measuring and monitoring fatigue can be an important focus at the start of- and during (rehabilitation) treatment, specifically for adolescents/ young adults that are in transition to adulthood.

Categorization of fatigue severity: improving usability for health care professionals

To better differentiate between fatigue severity, the fatigue scores from patients with ABI and their parents were categorized into four severity levels for both the total scores and all domain scores, allowing for an easier clinical interpretation of fatigue severity levels. Previous research only described comparisons with patients versus healthy peers with fatigue scores using means and SDs, where an interpretation of a score of -2SD's below the mean of a healthy peer could be made.[29] In the population in our cohort, a large proportion of patients (and parents) reported scores that fell into category 4, with scores more than -2SD below the mean score from healthy peers as well.[1,2]

Differences regarding the four-point categorization between the total and all domain scores (general fatigue, sleep/rest fatigue and cognitive fatigue) were found. Differentiating between domain scores could help to select specific approaches in treatment and to individualize treatment in clinical practice, since higher cognitive fatigue levels require different treatment approaches than those for higher sleep/rest fatigue during treatment.

Finally, HRQoL scores decreased with each level higher on the fatigue severity category (i.e., more fatigue, lower QoL). This trend is in line with the known multidirectional relation between fatigue and HRQoL and strengthens the fatigue severity categorization.[8]

A limitation of Likert scales, as well as that of interpreting 0-100 scores, is that these methods do not take scores from a reference population into account. Severity cut-offs based on scores of healthy peers are probably more suitable for evaluating treatment. Hence, shifting from severity category 4 to category two after treatment facilitates better interpretation of treatment outcome. It could also help select patients for fatigue-related therapy, i.e., a patient in a 'severely fatigued' category could benefit from different approaches than a patient in a less severely fatigued category.

Overall, the proposed fatigue severity cut-off classification may be used for research purposes to facilitate the comparisons of the severity of fatigue among different populations

of children, adolescents, and young adults. Nevertheless, it remains to be established if, and to what extent, the categorization is helpful to describe changes over time. The relatively high proportion of patients categorized in the moderate and severe fatigue categories in this rehabilitation-based population suggests that fatigue is a serious problem in these patients and needs a tailored rehabilitation treatment.

Limitations

There were some limitations to this study. First, we could not display a complete severity classification of TBI, since we only had access to GCS scores (and not in all cases, GCS scores were available). Only the GCS is commonly used in the Netherlands. Yet, it is not a foolproof predictor for the functioning of the child over time since it only gives a classification in the acute phase.[34,38] Future Dutch research should focus on collecting additional information regarding TBI severity (e.g., the length of coma (LOC) or the duration of post-traumatic amnesia (PTA)). Furthermore, for non-traumatic brain injuries there is no 'golden standard' for classification due to its complexity. Secondly, only self-reported reference data was available regarding the young adult age group.[1,2] Therefore, it was not possible to assign parent-reported scores in this group according to the four-level fatigue severity categorization. Third, the majority (74%) of the patients in the study had a traumatic brain injury, of which 78% was 'mild'. Moreover, it concerned a rehabilitation setting, where only patients with serious and/or persisting symptoms are admitted. It remains unclear if this specific selection of patients impacts the generalizability of the results. Even though the majority of the study population had a mild injury, the proportions with moderate to severe fatigue were substantial in our study, which is in line with other TBI population studies in The Netherlands[6,8] ruling in favor of the generalizability of our results. It cannot be ruled out, however, that the patients who were referred to a rehabilitation facility are distinct from those with similar severity of brain injury who are not treated or treated elsewhere. Finally, as is the case with every self-report measure, the results could be influenced by lack of comprehension or motivation, or (patients/parents) moment-bound stress and mood.

Directions for future research

A large part of young patients with ABI in the outpatient rehabilitation setting and their parents reported high levels of fatigue, specifically the patients that were in the age in transition to adulthood. Adolescents and young adults (and parents) reported significantly more fatigue than the healthy reference population. Taking fatigue into account in an early stage after ABI could possibly influence long-term persisting fatigue positively by appropriate interventions, based on specific domains regarding fatigue. However, future studies need to be undertaken to investigate fatigue outcomes over time and in evaluating these interventions.

Categorizing fatigue severity levels appears to be promising for use in the outpatient rehabilitation setting as a tool to better target fatigue at the start of rehabilitation treatment, and it can be used next to the initial linear 0-100 total and domain scores from the PedsQL™ MFS. We also expect that categorizing fatigue could help to give health care professionals as well as patients and their parents more insight regarding severity to optimize goal setting. The use of categorization levels and cut-off values is a first step in contextualizing and differentiating fatigue scores for research and clinical practice. The categorization could also be used as a tool to monitor fatigue over time and to evaluate the effect of (rehabilitation) treatment i.e., when a patient scores in the “severely fatigued” category at the start of treatment and in the category “comparably fatigued to healthy peers” after treatment. The next step would be to calculate the minimal clinically important difference (MCID) for this questionnaire and in this population to facilitate clinical use even more.

Disclosure Statement

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Supplementary table. Four-point classification based on Total and domain PedsQL MFS scores and SDs from the reference population.

Patient reported	**Categorization**				
		Total score mean (SD) 77.6 (20.4)	**GF[1] mean (SD) 74.0 (20.4)**	**SRF[2] mean (SD) 76.8 (26.0)**	**CF[3] mean (SD) 74.0 (31.2)**
Children, n=54	1	100 – 98.0	100 – 83.1	100 – 76.8	100 – 74.0
	2	98.0 – 57.3	83.1 – 55.4	76.8 – 50.8	74.0 – 42.8
	3	57.3 – 36.9	55.4 – 27.7	50.8 – 24.8	42.8 – 11.6
	4	Lowest through 36.9	Lowest through 27.7	Lowest through 24.8	Lowest through 11.6
		Total score mean (SD) 75.2 (12.1)	**GF[1] mean (SD) 76.7 (14.2)**	**SRF[2] mean (SD) 71.9 (14.3)**	**CF[3] mean (SD) 77.2 (15.4)**
Adolescents, n=129	1	100 – 87.3	100 – 90.9	100 – 86.2	100 – 92.6
	2	87.3 – 63.1	90.9 – 62.5	86.2 – 57.6	92.6 – 61.8
	3	63.1 – 51.0	62.5 – 48.3	57.6 – 43.3	61.8 – 46.4
	4	Lowest through 51.0	Lowest through 48.3	Lowest through 43.3	Lowest through 46.4
		Total score mean (SD) 71.8 (14.6)	**GF[1] mean (SD) 70.4 (18.2)**	**SRF[2] mean (SD) 68.6 (14.6)**	**CF[3] mean (SD) 76.3 (18.4)**
Young adults, n=40	1	100 – 86.4	100 – 88.6	100 – 83.2	100 – 94.7
	2	86.4 – 57.2	88.6 – 52.2	83.2 – 54.0	94.7 – 57.9
	3	57.2 – 42.6	52.2 – 34.0	54.0 – 39.4	57.9 – 39.5
	4	Lowest through 42.6	Lowest through 34.0	Lowest through 39.4	Lowest through 39.5
Parent reported	**Categorization**				
		Total score mean (SD) 82.1 (17.8)	**GF[1] mean (SD) 83.4 (19.2)**	**SRF[2] mean (SD) 86.6 (18.6)**	**CF[3] mean (SD) 76.4 (26.9)**
Children, n=76	1	100 – 82.1	100 – 83.4	100 – 86.6	100 – 76.4
	2	82.1 – 64.3	83.4 – 64.2	86.6 – 68.0	76.4 – 49.5
	3	64.3 – 46.5	64.2 – 45.0	68.0 – 49.4	49.5 – 22.6
	4	Lowest through 46.5	Lowest through 45.0	Lowest through 49.4	Lowest through 22.6
		Total score mean (SD) 79.2 (14.1)	**GF[1] mean (SD) 77.7 (16.1)**	**SRF[2] mean (SD) 80.9 (15.2)**	**CF[3] mean (SD) 78.9 (18.1)**
Adolescents, n=134	1	100 – 93.3	100 – 93.8	100 – 96.1	100 – 97.0
	2	93.3 – 65.1	93.8 – 61.6	96.1 – 65.7	97.0 – 60.8
	3	65.1 – 51.0	61.6 – 45.5	65.7 – 50.5	60.8 – 42.7
	4	Lowest through 51.0	Lowest through 45.5	Lowest through 50.5	Lowest through 42.7

[1] Domain score PedsQL MFS; General fatigue. [2] Domain score PedsQL MFS; Sleep/Rest fatigue. [3] Domain score PedsQL MFS; Cognitive fatigue. [1] Group 1: Less fatigued than healthy peers: more than (>) +1 SD, [2] Group 2: comparable to healthy peers: Between -1 SD & +1 SD, [3] Group 3: moderately more Fatigued: Between - 1 SD & -2 SD, [4] Group 4: severely more Fatigued: more than (>) -2 SD.

CHAPTER 3

Fatigue in young patients with acquired brain injury in the outpatient rehabilitation setting: a 2-year follow-up study

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ABSTRACT

Acquired brain injury (ABI) may cause fatigue and participation restrictions in young patients. However, knowledge regarding the course of these problems over time is lacking. This study aims to describe the course of fatigue and participation and their relationship over time in an observational two-year follow-up study among patients (5–24 years) with ABI referred for outpatient rehabilitation and their parents. Patients/parents completed the PedsQL™ Multidimensional-Fatigue-Scale (PedsQL™ MFS, totalscore/ 3-domains) and the Child/ Adolescent-Scale of Participation (CASP, totalscore/ 4-domains). Scores ranged from 0-100: lower scores = more fatigue/ participation problems. Linear mixed models and repeated measures correlations were used to determine the course over time (change-scores/ 95% CI) and correlations between fatigue/participation. At baseline, 223 patients/ 246 parents participated with 94/ 104 at either T1, T2 or both. Median age was 15 years (IQR: 12-17), 74% had a traumatic brain injury. Mean (SD) patient/parent-reported PedsQL™ MFS totalscores (baseline) were: 50.3 (17.3) and 53.8 (19.1), respectively. CASP totalscores were 78.0 (16.4) and 87.1 (13.6). Over time, patient-reported scores improved significantly (fatigue: +8.8 (2.9;14.7), $p < 0.05$)/ participation: +10.5 (6.3;14.7), $p < 0.05$). Similar results were found regarding parent-reported fatigue: +8.7 (3.4;13.9), $p < 0.05$ but not regarding participation. Two years later, fatigue was still considerable (patients: 59.1/ parents: 62.5). Moderate/fair correlations between fatigue/participation over time were found. Fatigue and participation in young patients with ABI improved two years after referral to rehabilitation. However, fatigue remained a considerable problem.

Keywords: fatigue, participation, rehabilitation, brain injury, young patients

INTRODUCTION

Acquired brain injury (ABI) refers to brain damage that occurs after birth and not relating to congenital disorders.[1] Two main causes can be distinguished: traumatic brain injury (TBI), caused by external trauma (e.g., traffic accidents, sports accidents, and violence); and non-traumatic brain injury (nTBI), caused by internal trauma (e.g., stroke, tumors, and brain inflammations).[1,2] The incidence rates of ABI among Dutch children, adolescents, and young adults are considerable; 290 per 100.000 for TBI, and 90 per 100.000 for nTBI.[3,4]

Approximately 30% of young patients with ABI do not fully recover after the acute and subacute phases.[5,6] These patients reach a chronic phase after ABI onset with persisting social and/or cognitive and/or physical and/or behavioral problems.[7-9] Fatigue is often reported by children, adolescents, and young adults with ABI, and/or their parents, and is known to negatively influence daily life functioning.[10-13] This also holds for patients with other chronic conditions and even for the healthy population.[14-18] In young patients with ABI, fatigue is often reported as a 'less-visible' long-lasting problem that is generally hard to treat due to its complexity and chronicity.[10,11,14-34] Furthermore, this population is known to be moderately more, to severely more fatigued compared to healthy age-matched peers.[10] After acquiring a brain injury, young patients with persisting problems have to adjust their lives to deal with multi-system impairments after the injury i.e., motor impairments, cognitive impairments impacting activities and participation (e.g., reducing/quitting (sport) activities, and not fully attending school/work). Fatigue could play a significant role, where rehabilitation-based cross-sectional studies found that more fatigue could result in limited participation in daily life.[11,20,21,34] Previous research has shown a multidirectional influence between fatigue and participation, where more fatigue is related to more participation restrictions in adults (aged 20-60 years) with TBI[35,36] and in young patients (aged 14-25 years) with ABI.[21]

To date, only a few studies investigated the course of fatigue over time.[37,38] These follow-up studies measured fatigue among young adults with stroke, adults with cerebral palsy, and children and adolescents with TBI and found that fatigue did not decrease significantly over time.[37,38] However, one of the studies, focused exclusively on patients with TBI,[37] while the other study[38] included participants with cerebral palsy rather than TBI. Furthermore, they did not specifically look at the course of fatigue, as reported by both patients and (their) parents, in the chronic phase in the young ABI population nor did they investigate associations with participation over time.[37,38]

Another important factor associated with fatigue after ABI is age, where more fatigue was

found in adolescents compared to children,[10,19-21] and young adults,[21] which was reported by both patients and their parents.[10,19-21] For these adolescents, fatigue could negatively affect the transition to adulthood. Having a nTBI and cognitive/behavioral (premorbid) problems before the onset of ABI were also found to have a relationship with fatigue.[20]

Due to the lack of knowledge described above for children and young adults with ABI, this study has two aims. First, to describe patient- and parent-reported fatigue and participation over 2 years in children, adolescents, and young adults (5-24 years old) with ABI referred for outpatient rehabilitation. Second, to describe the longitudinal associations between fatigue, participation, and potentially other related factors over time.

METHODS

Design and setting

This longitudinal study was part of an observational, multicenter cohort study on family impact, fatigue, participation, and quality of life among young Dutch patients (5-24 years old) with ABI in the outpatient rehabilitation setting. The study was conducted between 2015 and 2019 in ten rehabilitation centers (out of 16 in total in The Netherlands). The study protocol was reviewed by the medical ethical review board of the Leiden University Medical Center (P15.165), which provided an exemption from full medical ethical review. All local research committees from the participating centers approved the study. In the current study, only data regarding patient, injury, and family characteristics, as well as fatigue and participation outcomes were used, as reported by patients and/or (their) parents over 2 years.

Participants

In this study, young patients (5-24 years) diagnosed with ABI and their parents, referred by a general practitioner or medical specialist for outpatient rehabilitation care due to complex and/or persisting daily life problems after ABI were eligible to participate. Patients and parents who were unable/limited to write and/or understand the Dutch language were excluded from this study.

Procedure

Patients and parents filled out a digital questionnaire as part of regular care in the rehabilitation center. Patients and their parents received a digital link by email to complete the questionnaire (www.questback.nl). The questionnaire was filled in prior to the first appointment with the physiatrist to reduce the influence of the content of the appointment

in answering questions and formulating goals. One year (T1) and two years (T2) after the first appointment, the patients and their parents were invited voluntarily to complete the questionnaires again. Before completing the T1 and T2 questionnaires, participants (patients and/or parents, where appropriate) signed informed consent to participate in this study. For patients under the age of 8 years, only parents filled out the questionnaire. Patients over the age of 16 had to give permission to their parents to complete the questionnaires according to the Dutch law of healthcare decision-making. All data used in this study were anonymized before analysis and securely stored in a central database at Basalt Rehabilitation (The Hague, The Netherlands). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were used for presenting the results.[39]

Assessments

Information from medical records

Patient information was collected from medical records by the treating rehabilitation physician and included: sex (male/female), date of birth, date of referral to the rehabilitation center, age at the time of the first appointment (difference between the date of birth and the date of referral to rehabilitation). Furthermore, the time between the onset of ABI and referral to rehabilitation was calculated and divided into 2 groups: fewer than 6 months between onset and referral and more than 6 months. Injury characteristics were noted as well, where the categorization of ABI was divided into TBI/nTBI. If known, TBI severity levels were divided into either mild or moderate/severe (based on the Glasgow Coma Scale (GCS) at hospital admission[40]). If the GCS was not reported and there was no history of coma or loss of consciousness, TBI severity was considered 'mild'. Causes of nTBI were divided into stroke/cerebrovascular accidents, brain tumors, meningitis/encephalitis, hypoxia/intoxication, and 'other/unknown'. Due to the absence of valid instruments to measure nTBI severity, no nTBI severity levels were reported in this study. Finally, premorbid and current learning, behavior, and health-related problems were noted.

Outcome measures

To determine fatigue-related problems in young patients with ABI (reported by patients, parents, or both), the 18-item PedsQL™Multidimensional Fatigue Scale (MFS) was used.[41] The questionnaire is considered a feasible, valid, and reliable tool to assess fatigue in patients with different age groups and diagnoses (including ABI) and has been translated and validated in the Dutch language.[15,16,41] The 18 items yield a total scale score and contains questions in three domains (subscales, with 6 items each): general fatigue (e.g., "I feel too tired to do things that I like to do"), sleep/rest fatigue (e.g., "It is hard for me to sleep through the night"), and cognitive fatigue (e.g., "It is hard for me to keep my attention on things").

Items are answered on a Likert scale (0=never to 4=almost always) and thereafter linearly transformed to a 0-100 scale (0=100, 1=75, 2=50, 3=25, 4=0). Lower scores indicate more fatigue.[41]

The Child and Adolescent Scale of Participation (CASP) was used to measure participation restrictions in young patients with ABI (reported by patients, parents, or both) and has been translated in Dutch as well.[42,43] The CASP consists of 20 questions and yields a total score and 4 domain scores: Home Participation (6 items), Community Participation (4 items), School Participation (5 items), and Home and community living (5 items). Questions are answered on a 4-point Likert scale: 4 = age expected (full participation), 3 = somewhat limited participation, 2 = very limited participation, and 1 = unable to participate. Scores for each item are summed and divided by the maximum possible score based on the number of items rated. For both the total score and the domain scores the results, multiplied by 100, give a score between 0–100. Lower scores indicate more participation restrictions.[42,43]

Categorization of severity levels

Fatigue and participation severity level categorization, as proposed in previous studies, was used in the current study to see if fatigue and participation restriction severity changed over time.[10,15,16,22] To better categorize fatigue severity levels, we used data from two previous studies among healthy children/adolescents (4-18 years old) and young adults (18-30 years old).[15,16] These studies examined the psychometric properties of the PedsQL™ MFS that established Dutch norm data for this scale among children, adolescents, and young adults, enabling a comparison of fatigue levels in our study to the broader Dutch population from childhood to young adulthood.[15,16] In the current study, we distributed patients per age group in (children 5-12 years old, adolescents 13-17, and young adults 18-24).[15,16] Fatigue severity levels were based on scores from healthy age-matched peers and categorized as 1: 'less fatigued than healthy peers', 2: 'fatigue comparable with healthy peers', 3: 'moderately more fatigued than healthy peers', and 4: 'severely more fatigued than healthy peers'.[10,15,16] PedsQL™ MFS scores less than approximately 58.0 was considered 'severely more fatigued' for all age ranges (< 25 years old).[10] A 4-point categorization system to distinguish between levels of participation restrictions (CASP) was categorized as 1: 'full participation', 2: 'somewhat limited participation', 3: 'limited participation', and 4: 'very limited participation'.[22]

Statistical analysis

Descriptive statistics were used for all variables and outcomes. All continuous variables were expressed as medians with interquartile ranges (IQR) or means with standard deviations (SD), based on their distributions (Kolmogorov–Smirnoff test). Patient- and parent-reported data were analyzed and reported separately. Independent sample t-tests

or Mann-Whitney-U tests (based on their distribution) were performed to determine if there were significant differences between the TBI and nTBI groups regarding PedsQL™MFS scores at all time points.

Fatigue and participation over time

Before conducting analyses in the current study, the authors were aware of missing data at T1 and T2. Therefore, the procedure 'missing data evaluation' by Heymans et.al. (2019) to manage missing data was followed.[44] In line with this procedure, Little's-test to determine if data at the follow-up time points were 'missing completely at random' (MCAR), defined as a level of significance greater than 0.05 was performed.[44-46] When fulfilling this definition of MCAR, the data with repeated measures could be analyzed using a linear mixed model.[44-46]

If data were found to be MCAR, differences over time for the 2 groups were analyzed using linear mixed models (LMM) adjusted for age and sex. In these models, T1 and T2 were the fixed effects. At baseline, the outcomes were expressed as means with standard deviations (SD). Change scores (95% CI) were reported for the different time points (T1 and T2; differences between baseline and T1, and between T1 and T2). Fatigue and participation outcomes were visually interpreted and compared to the respective severity categorization that were previously described at all time points to see if severity categorization of fatigue/participation changes over time.[10,22]

Associations with fatigue

To determine longitudinal associations between fatigue (PedsQL™ MFS) and participation (CASP) scores repeated measures correlations were used.[47] With this method, the non-independence of repeated measures was considered by determining the correlation between two continuous variables (PedsQL™ MFS and CASP) where between-patient variance was being controlled.[47] Longitudinal correlations were noted as correlation coefficients (*r*), p-values, degrees of freedom (Df), and 95% CI. The correlation coefficients' strength was defined as: very strong = > 0.8; moderately strong = 0.6 to 0.8; fair = 0.3 to 0.5; and poor = < 0.3.[48] Univariate linear regression analyses were used to determine if the same factors that were associated in a previous cross-sectional study, were still associated with fatigue at one- and two-year follow-ups.[20] The PedsQL™ MFS total scores were the dependent variables. These possible factors (independent variables) were entered independently and one at a time i.e., age (continuous), older age groups (adolescents/young adults versus children), sex (female versus male), cause of ABI (nTBI versus TBI), premorbid problems (having one or more learning and/or behavioral and/or health-related problems versus none), current problems (having one or more learning and/or behavioral and/or health-related problems versus none) and the timing of referral to rehabilitation after the

onset of ABI (> 6 months versus < 6 months). Associations were presented as β-estimates, 95% Confident intervals (95%CI), and p-values.

To account for potential sex-based differences in scores, as well as the influence of age, we corrected for these variables in the LMM, the rmcorr, and the univariate linear regression analyses. By doing so, we aimed to control for their potential moderating effects and ensure a more accurate examination of the relationship between fatigue and other variables of interest.

Repeated measures correlations were performed in 'R' version 4.1.0, and module rmcorr version 0.5.2.[47] All other data were analyzed using SPSS software, version 28.0 (IBM SPSS Statistics for Mac, Armonk, NY: IBM Corp). The level of statistical significance was set at $p < 0.05$ for all analyses.

RESULTS

At baseline 223 patients and 246 parents (260 unique participants i.e., only patients, only parents, or both the same patients and their parents) participated in this study. Ninety-four patients and 104 parents participated either at T1, T2 or both time points (Figure 1).

Table 1 presents the patients' demographic and injury characteristics at baseline (for the patient-reported data, the parent-reported data, and all participants (patients and/or parents). More than half of the patients (52%) were female, and the median age was 15 years old (IQR 12-17). Seventy-four percent had a TBI, and 79% of them were classified as 'mild'. Finally, 40% of the patients were referred for outpatient rehabilitation more than six months after ABI onset. The patient- and parent-reported demographic and injury characteristics at the T1/T2 time points were generally consistent when compared to baseline data (Table 1). There were no significant differences found between patients with TBI and nTBI regarding patient/ parent-reported fatigue scores (normally distributed) at all time points, except for the sleep/rest fatigue domain at baseline (see Appendix).

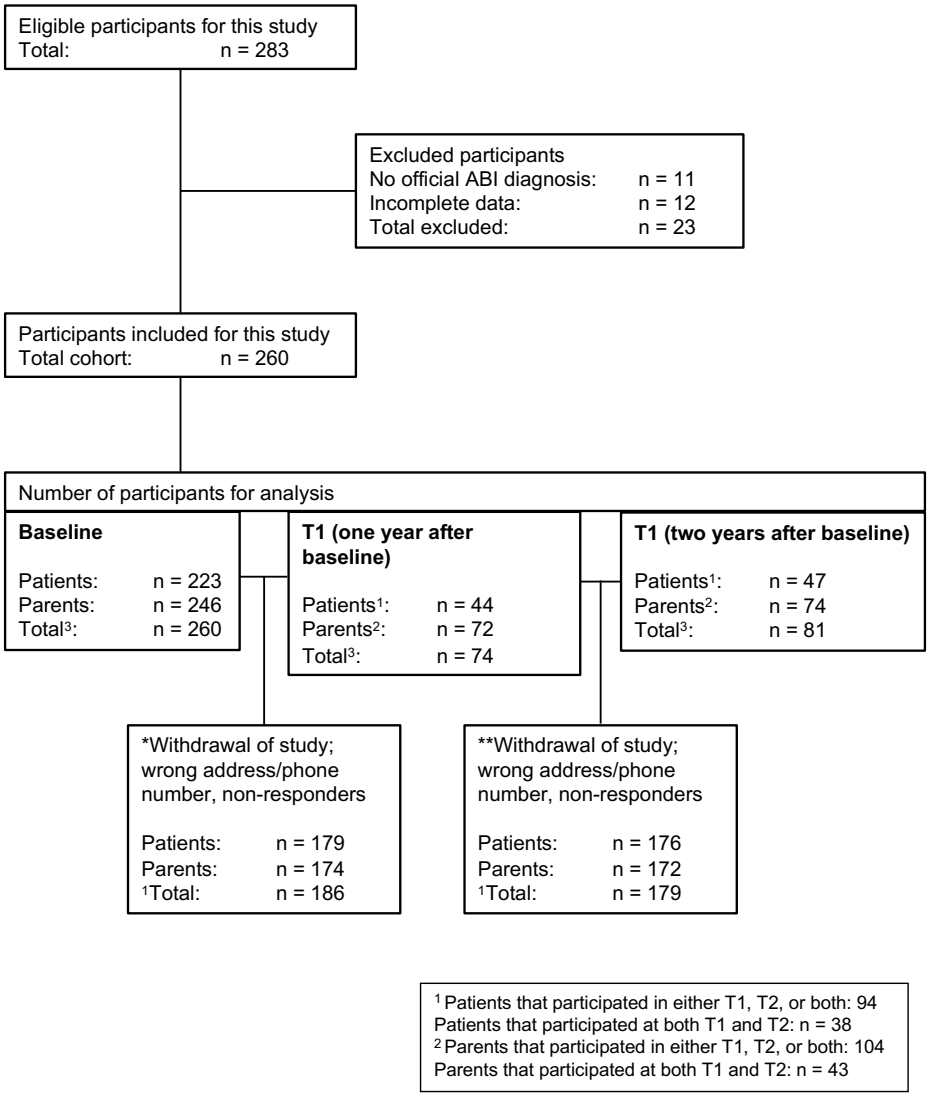

Figure 1. Flowchart of patients and parents that participated in the current study[1,2,3]: Number of unique participants (only patients, only parents, or both the same patients and their parents). In total at baseline, there were 260 unique participants, 223 patients, and 246 parents. * Between baseline and T1, ** between baseline and T2.

Table 1. Patient demographic and injury characteristics of, young patients with acquired brain injury (ABI) and their families referred to an outpatient rehabilitation center in The Netherlands.

Patient demographic and injury characteristics	Baseline			T1		T2	
	Total* n=260	Patient-reported n=223	Parent-reported n=246	Patient-reported n=44	Parent-reported n=71	Patient-reported n=47	Parent-reported n=72
Sex; Female, n (%)	135 (52%)	117 (53%)	127 (52%)	28 (64%)	45 (63%)	27 (57%)	45 (61%)
Age; Median (IQR)	15 (12-17)	15 (13-17)	14 (11-16)	15 (13-16)	14 (11-16)	14 (13-16)	14 (10-16)
- Children 5-12y, n (%)	76 (29%)	54 (24%)	76 (31%)	9 (20%)	25 (35%)	9 (19%)	25 (35%)
- Adolescents 13-17y, n (%)	141 (54%)	129 (57%)	133 (54%)	29 (66%)	38 (54%)	31 (66%)	36 (50%)
- Young adults 18-24y, n (%)	43 (17%)	40 (18%)	37 (15%)	6 (14%)	8 (11%)	7 (15%)	11 (15%)
Time (months) between onset and referral;							
Median (IQR)	4 (1-19)	4 (1-13)	4 (1-21)	5 (1-25)	4 (1-25)	4 (2-22)	4 (2-17)
> 6 months, n (%)	104 (40%)	83 (37%)	96 (39%)	17 (39%)	45 (63%)	16 (34%)	47 (64%)
TBI; n (%)	192 (74%)	167 (75%)	181 (74%)	29 (66%)	48 (69%)	35 (75%)	54 (74%)
Severity#; n (%)							
- Mild	151 (79%)	132 (79%)	143 (78%)	22 (76%)	41 (85%)	29 (83%)	46 (85%)
- Moderate/severe	20 (10%)	17 (10%)	18 (10%)	5 (17%)	6 (13%)	4 (11%)	2 (4%)
- Unknown	21 (11%)	18 (11%)	20 (12%)	2 (7%)	1 (2%)	2 (6%)	6 (11%)
nTBI; n (%)	68 (26%)	56 (25%)	65 (26%)	15 (34%)	23 (31%)	12 (26%)	19 (26%)
Cause; n (%)							
- Stroke	16 (24%)	15 (27%)	15 (24%)	3 (20%)	8 (35%)	3 (25%)	7 (37%)
- Tumor	27 (40%)	21 (38%)	25 (40%)	4 (27%)	4 (17%)	5 (42%)	4 (21%)
- Meningitis / Encephalitis	12 (18%)	11 (20%)	11 (18%)	3 (20%)	1 (4%)	2 (17%)	0 (0%)
- Hypoxia / Intoxication	2 (2%)	2 (2%)	2 (3%)	1 (7%)	5 (22%)	0 (0%)	3 (16%)
- Other	11 (16%)	7 (13%)	9 (15%)	4 (27%)	5 (22%)	2 (17%)	5 (26%)
Measured at baseline							
Patients with 1 or more premorbid problems^; n (%)	76 (29%)	68 (30%)	71 (29%)				
Patients with 1 or more current problems^; n (%)	246 (94%)	208 (93%)	230 (94%)				

* Total number of unique participants (260 patients and/or parents): 223 patients and 246 parents TBI: Traumatic brain injury. nTBI: non-traumatic brain injury. #Glasgow coma scale: "mild" 13-15, "moderate" 9-12, "severe" < 8. ^Learning/Behaviour/Health-related problems. Baseline: at time of referral; T1 = 1 year after referral; T2 = 2 years after referral.

The LMM was conducted using data from all participants at baseline (223 patients and 246 parents) and from those who participated either at T1, T2, or both i.e., 94 patients and 104 parents. Results of Little's-test showed a *p*-value of 0.07 (Chi-Square 22.4) which provides evidence that the missing data at T1/T2 were MCAR, as defined as a significance level greater than 0.05. Consequently, the data were analyzed in an LMM where missing repeated measures were corrected within the model.

Fatigue in young patients with ABI

PedsQL™ MFS (fatigue) mean (SD) scores reported by patients at baseline and change scores (95%CI, p-values) at T1 and T2 are presented in Table 2a.

Concerning the patient-reported baseline scores, a mean total PedsQL™ MFS score of 50.3 (SD 17.3) was found. When looking at fatigue severity categorization compared to healthy peers, patients scored in the categories 'moderately to severely more fatigued' compared to healthy peers (more than -1SD to more than -2 SD), depending on the age. The lowest score was found in the domain 'cognitive fatigue'; 45.5 (SD 23.4), and the highest in 'sleep/rest fatigue'; 54.0 (SD 18.4).

With respect to parent-reported fatigue at baseline (Table 2b), parents reported a mean (SD) total fatigue score for their children of 53.8 (SD 19.1). The lowest score (49.9, SD 24.2) was found in the domain 'general fatigue', and the highest (59.1, SD 23.2) in 'sleep/rest fatigue'. Patient-reported PedsQL™ MFS scores (Table 2a) improved significantly in the first year (baseline-T1): +9.8 (4.6;14.9) $p < 0.001$. In the second year, no significant change was found (T1-T2): -1.0 (-8.1;6.1) $p > 0.05$. The mean score of 59.1 at T2 (50.3 (baseline) + 9.8 (T1) -1.0 (T2)) indicates that patients were still 'moderately more fatigued' compared to healthy peers. The most improvement was found in the domain 'general fatigue' between baseline and T1: +14.1 (8.0;20.2) $p < 0.001$. Concerning the course of parent-reported fatigue over time (Table 2b), the PedsQL™ MFS change scores were in line with those reported by the patients: parents also reported scores that improved significantly in the first year (baseline-T1): +5.6 (0.6;10.6) $p < 0.05$, but not in the second (+3.1, (-3.3;9.5), $p > 0.05$).

Participation restrictions in young patients with ABI

CASP mean (SD) scores at baseline and change scores (95% CI, *p*-values) at T1 and T2 can be found in Table 2a (patient-reported) and Table 2b (parent-reported).

For participation scores at baseline, patients reported a mean CASP total score of 78.0 (SD 16.4) which fell in the range of the 'limited participation' category. The lowest score was found in the domain 'community participation', and the highest score in the domain 'home participation'.

With respect to participation scores at baseline reported by parents, a mean CASP total score for their children of 87.1 (SD 13.6) was reported, which falls in the range of the 'somewhat limited participation' category.

Regarding the changes of patient-reported participation over time, CASP total scores improved only significantly in the first year: +9.9 (6.2;13.6) $p < 0.001$. In the second year, no significant change was found (T1-T2): +0.6 (-4.1, 5.2) $p > 0.05$. The improvement over time from baseline (78.0 + 9.9 + 0.6 = 88.5) shows that patient-reported CASP scores changed from the 'limited participation' category to the 'somewhat limited participation' category.

Concerning the course of parent-reported participation over time, CASP total scores improved significantly in the first year as well: +3.1 (0.0;6.1) $p < 0.05$ but not significantly in the second (+0.8, (-2.5, 4.1), $p > 0.05$), thus, scores remained in the 'somewhat limited participation' category two years after baseline.

Factors related to fatigue at all time points

The associations between fatigue and participation over time from the repeated measures correlations can be found in Figures 2a and 2b. The repeated measures correlations (patient-reported) showed a moderately strong correlation between total fatigue (PedsQL™ MFS)

Table 2a. Patient-reported PedsQL™ MFS scores (fatigue) and Patient-reported and CASP (participation) scores at baseline and change over time

PedsQL™MFS: Patient-reported	**Baseline n=223 Mean (SD)**	**Baseline–T1 Change Score (95% CI) #**	**T1–T2 Change Score (95% CI) #**
Total score	50.3 (17.3)	+9.8 (4.6, 14.9) **	-1.0 (-8.1, 6.1)
General Fatigue	51.3 (22.8)	+14.1 (8.0, 20.2) **	-2.9 (-11.7, 5.9)
Sleep/rest fatigue	54.0 (18.4)	+8.6 (3.4, 13.9) *	-2.5 (-9.0, 4.0)
Cognitive fatigue	45.5 (23.4)	+6.5 (-1.7, 14.7)	+2.5 (-8.0, 13.0)
CASP: Patient-reported	**Baseline n=223 Mean (SD)**	**Baseline–T1 Change Score (95% CI) #**	**T1–T2 Change Score (95% CI) #**
Total score	78.0 (16.4)	+9.9 (6.2, 13.6) **	+0.6 (-4.1, 5.2)
Home & community living	73.6 (22.9)	+12.7 (7.7, 17.7) **	+2.5 (-3.0, 8.0)
Home participation	83.5 (13.9)	+7.2 (4.0, 10.4) **	-0.4 (-4.3, 3.4)
Community participation	70.2 (22.8)	+11.1 (5.4, 16.7) **	+1.7 (-5.6, 9.1)
School/work participation	72.6 (29.9)	+18.8 (13.9, 23.7) **	-2.3 (-8.7, 4.1)

PedsQL™ MFS: PedsQL™ Multidimensional Fatigue Scale. CASP: Child and Adolescent Scale for Participation. #Based on the linear mixed model, corrected for sex and age at admission. * p-value <0.05, ** p-value < 0.001; Baseline: at admission to rehabilitation; T1: 1-year follow-up; T2: 2-year follow-up; Outcomes at baseline were expressed as means with standard deviations (SD) and at T1 and T2 as change scores with 95% confidence intervals (95% CI).

Table 2b. Parent-reported PedsQL™ MFS scores (fatigue) and Parent-reported and CASP (participation) scores at baseline and change over time

PedsQL™MFS: Parent-reported	Baseline n=246 Mean (SD)	Baseline–T1 Change Score (95% CI) #	T1–T2 Change Score (95% CI) #
Total score	53.8 (19.1)	+5.6 (0.6, 10.6) *	+3.1 (-3.3, 9.5)
General Fatigue	49.9 (24.2)	+9.9 (3.7, 16.2) *	+0.3 (-7.4, 8.0)
Sleep/rest fatigue	59.1 (23.2)	+6.0 (0.9, 11.2) *	+3.6 (-2.6, 9.9)
Cognitive fatigue	52.3 (25.2)	+0.8 (-6.0, 7.6)	+5.3 (-3.2, 13.8)

CASP: Parent-reported	Baseline n=245 Mean (SD)	Baseline–T1 Change Score (95% CI) #	T1–T2 Change Score (95% CI) #
Total score	87.1 (13.6)	+3.1 (0.0, 6.1) *	+0.8 (-2.5, 4.1)
Home & community living	81.8 (21.8)	+3.9 (-1.0, 8.8)	+3.8 (-1.0, 8.7)
Home participation	90.2 (11.1)	+2.3 (-0.2, 4.8)	+0.3 (-2.5, 3.0)
Community participation	83.0 (20.5)	+3.0 (-1.6, 7.7)	+1.7 (-3.3, 6.7)
School/work participation	84.6 (24.5)	+9.3 (5.6, 13.0) **	-2.3 (-6.4, 1.8)

PedsQL™ MFS: PedsQL™ Multidimensional Fatigue Scale. CASP: Child and Adolescent Scale for Participation. #Based on the linear mixed model, corrected for sex and age at admission. * p-value <0.05, ** p-value <0.001; Baseline: at admission to rehabilitation; T1: 1-year follow-up; T2: 2-year follow-up; Outcomes at baseline were expressed as means with standard deviations (SD) and at T1 and T2 as change scores with 95% confidence intervals (95% CI).

and total participation (CASP) scores over time (*r* 0.7 (95% CI 0.6;0.8), p < 0.001). Regarding parent-reported data, a fair correlation was found over time (*r* 0.5 (95% CI 0.3;0.6) p < 0.001).

The univariate regression analyses (Table 3) showed that higher age (both continuously and according to age groups) was significantly associated with more fatigue (both patient- and parent-reported p < 0.05) at baseline but not at T1 and T2 follow-up. Significantly more fatigue (p < 0.05) was also seen in the specific age groups of adolescents (patient- and parent-reported)/young adults (patient-reported) versus children. One and two years after referral, having one or more premorbid learning/behavioral/health-related problems were significantly associated with more fatigue (p < 0.05) but not at baseline. Being female, the time of > 6 months between referral to the rehabilitation center and ABI onset, having nTBI, and having current learning/behavioral/health-related problems were not significantly associated with fatigue (p > 0.05).

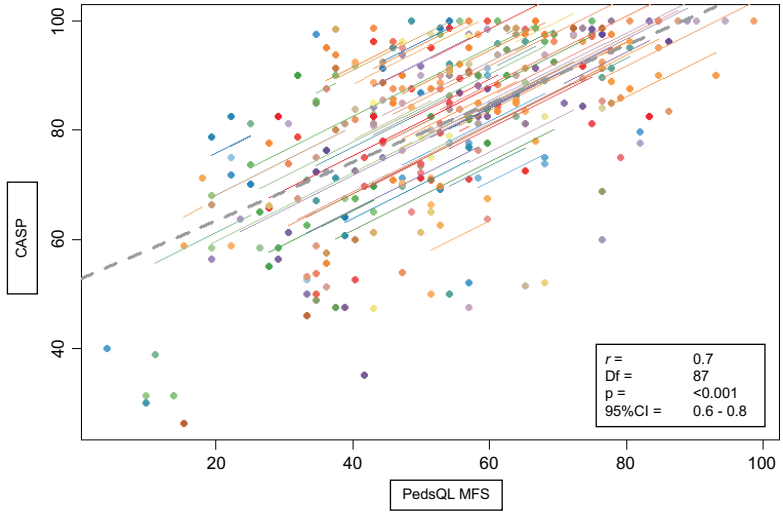

Figure 2a. Patient-reported longitudinal correlation between PedsQL™ MFS and CASP
PedsQL™ MFS: PedsQL™ Multidimensional Fatigue Scale. CASP: Child and Adolescent Scale for Participation. Patient-reported repeated measures correlation between PedsQL™MFS total score and CASP total score. r: correlation coefficient; Df: degrees of freedom; CI: 95% confidence intervals.

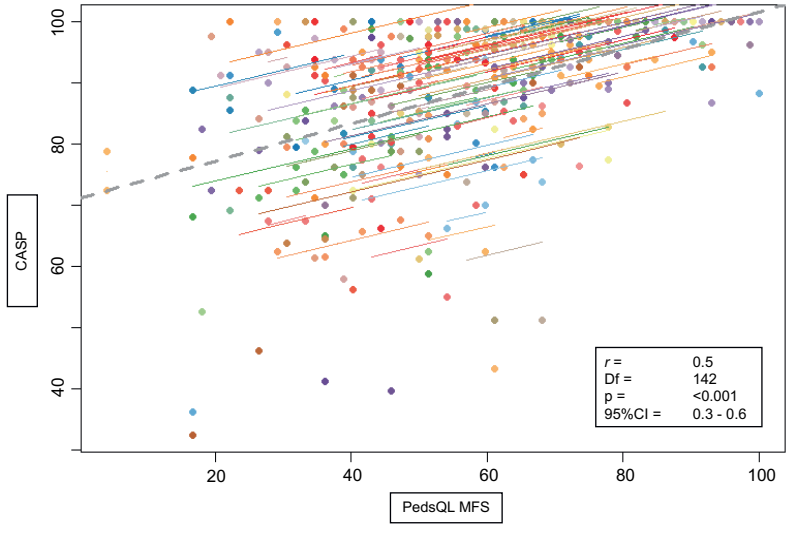

Figure 2b. Parent-reported longitudinal correlation between PedsQL™ MFS and CASP
PedsQL™ MFS: PedsQL™ Multidimensional Fatigue Scale. CASP: Child and Adolescent Scale for Participation. Parent-reported repeated measures correlation between PedsQL™MFS total score and CASP total score. r: correlation coefficient; Df: degrees of freedom; CI: 95% confidence intervals.

Table 3. Potential associated factors with fatigue reported by young patients with TBI/nTBI and their parents referred for outpatient rehabilitation treatment

PedsQL™MFS Patient-reported total scores n=223	**Baseline β (95% CI)**	**T1 β (95% CI)**	**T2 β (95% CI)**
Age (years)	-1.8 (-2.2; -1.1)**	-0.3 (-2.0; 1.4)	-0.1 (-2.0; 1.9)
Age group adolescents 13-17y[$]	-9.9 (-15.8; -4.0)**	-0.3 (-17.8; 12.2)	-4.7 (-21.8; 12.4)
Age group young adults 18-24y[$]	-17.3 (-24.1; -10.5)**	-0.03 (-17.2; 17.3)	-1.6 (-22.2; 19.0)
Sex (female)	-2.2 (-6.8; 2.4)	-3.7 (-13.3; 5.9)	6.3 (-4.3; 17.1)
Time between onset and referral > 6 months	1.2 (-3.5; 6.0)	3.0 (-6.5; 12.5)	-8.0 (-19.3; 2.9)
Having nTBI	4.3 (9.5; -0.1)	3.8 (-6.0; 13.5)	2.7 (-9.6; 14.0)
One or more premorbid problem(s)#	3.1 (-1.9; 8.1)	-11.4 (-21.7; -1.1)*	-16.4 (-27.7; -5.1)*
One or more current problem(s)#	-9.1 (-14.8; -3.4)*	-8.1 (-21.8; 4.6)	-9.4 (-26.1; 7.3)

PedsQL™MFS Parent-reported total scores n=246	**Baseline β (95% CI)**	**T1 β (95% CI)**	**T2 β (95% CI)**
Age (years)	-1.3 (-2.0; -0.7)**	-0.8 (-2.0; 0.4)	0.1 (-0.1; 1.3)
Age group adolescents 13-17y[$]	-3.3 (-10.7; 3.9)	0.6 (-14.2; 15.5)	8.3 (-22.2; 5.5)
Age group young adults 18-24y[$]	-10.7 (-18.9; -2.5)*	2.3 (-13.8; 18.4)	3.8 (-0.9; 18.0)
Sex (female)	-2.1 (-6.9; 2.7)	-2.6 (-11.9; 6.7)	2.4 (-7.1; 12.0)
Time between onset and referral > 6 months	3.7 (-1.2; 8.6)	-8.4 (-17.5; 0.7)	-8.9 9-18.5; 0.5)
Having nTBI	1.8 (-3.5; 7.2)	-1.9 (-11.5; 7.6)	-6.2 (-16.7; 4.3)
One or more premorbid problem(s)#	-2.5 (-7.8; 2.8)	-11.5 (-21.6; -1.5)*	-11.9 (-22.3; -1.4)*
One or more current problem(s)#	-11.2 (-17.2; -5.1)**	-5.8 (-19.4; 7.7)	0.4 (-14.3; 15.1)

Univariate regression analyses, data presented as β-estimates and 95% confidence intervals (95%CI). PedsQL™Multidimensional Fatigue Scale (MFS, 0-100, with lower scores indicating more fatigue). Fatigue total scores are the dependent variables and possible factors influencing fatigue are the independent variables.
#Premorbid/current learning/behavioral/health-related problems.
[$]Adolescents (13-17 years old) versus children (5-12 years old) and young adults (18-25 years old) versus children.
* $p < 0.05$, ** $p < 0.001$ Significant factors.

DISCUSSION

The results of this study showed that young patients aged 5 to 24 years with ABI, referred for outpatient rehabilitation, and their parents reported high levels of fatigue and limited participation. Fatigue and participation outcomes improved over the course of two years with the most improvement seen in the first year after referral. However, patients were still moderately to severely more fatigued compared to mean scores from healthy peers in previous studies by Gordijn et.al. (2011) and Haverman et.al. (2014)[15,16] and participation was still somewhat limited after two years. Significant associations were found between fatigue and participation over time where more fatigue was related to more participation restrictions.

Fatigue: a 'less visible' and persisting problem

Regarding fatigue, both patients and their parents reported considerably low PedsQL™ MFS scores (i.e., more fatigue-related problems) at the time of referral to rehabilitation and one and two years thereafter. Two years after referral, patients were still moderately to severely more fatigued than healthy peers.[10]

Over time, improvements in fatigue scores occurred within the first year after referral, and no significant improvement was reported in the second year. Two years after referral, the PedsQL™ MFS total fatigue score was comparable to fatigue scores reported by patients (11-17 years) with ABI 5 years after onset of ABI in a previous study (Total score current study: mean: 59.0 after two years versus between 47.9 and 62 after 5 years).[7] Despite the significant improvement in fatigue scores two years after referral, young patients with ABI in our cohort still experience more fatigue (mean: 59.0 SD: 18.7) in comparison to healthy Dutch peers aged 5-18 years (mean: 76.8 SD: 12.9) and aged 18-25 years (mean: 72.2 SD: 14.0).[10,15,16] The lowest scores (i.e., more fatigue) were found in the domain 'cognitive fatigue' in both the patient and parent-reported groups at baseline. Scores in this domain remained the lowest score found for fatigue-related problems two years after referral. This is in line with previous studies.[7,21] The persisting fatigue symptoms can possibly be explained by the presence of permanent neurological changes after ABI.[1] Additionally, cognitive fatigue is well known to be present after pediatric ABI and might be more pronounced due to the injury occurring during the developmental period of the brain in combination with external stressors such as performing demanding and increasingly more complex cognitive tasks at school.[7]

When comparing the results reported by patients to the results reported by parents, the largest differences were seen in the domains 'sleep/rest fatigue' and 'cognitive fatigue', where the parents reported fewer problems in these domains than patients did; especially

in the first year after referral. Similar results have been found in a cross-sectional rehabilitation-based study (with a smaller sample size) at the time of referral.[21] With this, it is essential to consider the potential influence of the source reporting fatigue, particularly as children mature and become more independent and spend less time in the direct vicinity of their parents. As children develop, their capacity to engage with assessment measures on their health status improves (and increases after the age of 7), allowing them to provide more detailed internal descriptions of their symptoms.[49] Clinicians should be aware of potential differences in perspectives between young patients and their parents concerning fatigue, as age-related changes may impact these perspectives.

Participation restrictions in the rehabilitation phase

The participation scores two years after referral are comparable to those found in patients with ABI (aged 6-22) two years post-injury and patients with severe TBI (aged 0-15) seven years post-injury.[6,25] Patient-reported participation scores changed from 'limited participation' to 'somewhat limited participation', whereas parent-reported scores remained in the same category.[22]

At one year after referral, the patients in this study reported an increase of 'school/work participation' almost twice as high as the increase in other domains. This was also seen in the parent-reported data. This might be explained by the outpatient rehabilitation treatment focusing on the resumption of school and/or work for these patients rather than activities outside of school/work as well as the priority patients and parents give to return to school/work above other activities. As found in previous cross-sectional research, there were differences in perspectives between patients and their parents regarding participation outcomes in all domains at the time of referral to rehabilitation.[21,22] However, the results in this longitudinal study showed that differences in perspectives are less one year after referral.[22] These results warrant collecting both patient and parent perspectives over time since parents' perspectives could reflect an outside perspective on progression during rehabilitation treatment.

Factors and participation associated with fatigue

We found that higher age was associated with fatigue, particularly in the adolescent and young adult age groups, consistent with our cross-sectional study within the same cohort.[10] A possible explanation includes that adolescents and young adults face increasing demands in daily life during their transition from childhood to adulthood.[15,16,35,36,50]

However, this association of increased fatigue in older age groups was only evident at baseline. Likely due to a high loss to follow-up at T1 and T2 this association was not found

one and two years after referral to rehabilitation. Consequently, these results must be interpreted with caution when interpreting these results over time.

Additionally, our findings showed that being female was not linked to higher fatigue levels at any time point. These results align with previous studies involving children, adolescents, and young adults with ABI, similar to our rehabilitation-based cohort, where sex was also found not to be associated with more fatigue.[7,20,51-54] However, other studies did report more fatigue levels within healthy young females,[14] females with physical disabilities,[17] and females with stroke or TBI in hospital-based cohorts.[55,56] Our results suggest that in the specific population of young individuals with ABI in the outpatient rehabilitation setting, sex plays a less prominent role. Clinicians should be equally aware of fatigue in male and female patients in rehabilitation practice.

Another factor associated with higher fatigue was having premorbid learning, behavioural, and health-related problems were associated with more fatigue at all time points. In line with the theory of the 'coping hypothesis',[57] it is known that after sustaining an ABI, the brain needs to work harder to compensate for impairments to cognitive functions, resulting in fatigue.[57,58] Young patients with ABI who had premorbid problems and then sustained an ABI could be presumed to experience even greater challenges post-injury,[57,58] potentially engaging in further compensation relative to typically developing peers who also sustained an ABI without premorbid problems. In clinical practice, it is thus important to be aware of the presence of premorbid problems in patients with ABI. Results also showed that patients in our cohort were fatigued at the time of referral, and one and two years later, regardless of the timing of referral or whether they had other current learning, behaviour, and/or health-related problems. This finding was only partly in line with a previous cross-sectional rehabilitation-based study, where having nTBI was associated with more fatigue.[20]

In patient-reported data, we found a moderately strong longitudinal correlation between fatigue and participation restrictions in individual patients, which implies that more fatigue is related to more participation restrictions. This correlation is in line with a previous follow-up study in an adult TBI population.[35] Whether fatigue influences participation or vice versa, with the former assumed more likely, and whether this is a causative relationship remains unanswered. Nonetheless, this knowledge indicates that more fatigue problems are related to more participation restrictions. Improving fatigue may therefore potentially lead to the ultimate goal of rehabilitation: helping patients achieve better participation in society after ABI.

Limitations

This study had several limitations. First, many participants were lost to follow-up. An explanation for this is that the questionnaires at baseline (T0) were completed in terms of routine care in preparation for the first appointment; something that is commonly asked from patients. At one (T1) and two (T2) years after referral the questionnaires were completed voluntarily, sometimes after contact with the rehabilitation center was terminated. Despite this, it is essential to note that the follow-up data were MCAR, as indicated by Little's test,[44,46] suggesting that missing data occurred randomly and were not related to specific factors i.e., the values at T1 and T2 are random sample from the dataset when it would have been complete.[44-46] We used LMM and repeated measure correlations which accounted for the repeated measures within each participant, thus effectively correcting for the missing follow-up values.[44-47] Second, our study concerned a rehabilitation setting, where only patients with persisting symptoms are referred to. It remains unclear if this specific patient selection impacts the results' generalizability.' Even though most of the study population had a mild injury, the proportions with moderate-to-severe fatigue were substantial in our study which is in line with the incidence rates of TBI and nTBI in The Netherlands ruling in favor of the generalizability of our results.[3,4] It cannot be ruled out though, that the patients who were referred to a rehabilitation center are distinct from those with similar severity of brain injury who are not treated at all or treated elsewhere. Third, the CASP is known for its 'ceiling effect'.[42,43] However, to date, the CASP is the only outcome measure that takes multiple domains of restrictions and the pediatric population into account.[27,42,43] Fourth, since there are no psychometric properties regarding CASP data from (healthy) Dutch young adults (older than 18 years) concerning participation, the results in our study should be interpreted with caution concerning this age group, although many young adults participate in similar activities to their younger generation. Furthermore, the suitability and sensitivity of this measure for the older age cohort in terms of parents' report as well as appropriateness of functioning and activities examined related to age should be considered. Future research should focus on examining suitability and possible adaptation according to age and gathering Dutch normative data regarding the CASP for the whole age range of children adolescents and young adults between 5-24 years old. Finally, as is the case with every self-report measure, the results could be influenced by lack of comprehension or motivation, or (patients/parents) moment-bound stress and mood.

CONCLUSIONS AND IMPLICATIONS

To conclude, fatigue and participation restrictions are commonly reported by young patients with ABI and their parents during the rehabilitation phase and despite the improvements two years after referral, patients are still moderately to severely more fatigued than healthy peers, and participation remains somewhat limited. Fatigue is significantly associated with participation restrictions over time, where more fatigue is related to more participation restrictions. Thus, improving fatigue-related problems may lead to better participation outcomes, making it a beneficial target for education, diagnostics, and interventions in rehabilitation practice. The improvements seen in scores between referral to rehabilitation and one year later do not follow through to the second year, which can even be seen in various outcomes. Targeting and monitoring these 'less visible' yet chronic problems in this population over a long period is important in clinical practice to enhance goalsetting before, during, and after rehabilitation.

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Conflicts of interest

The authors of this study have no conflicts of interest to declare.

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Appendix. Differences in patient- and parent-reported fatigue between patients with TBI and nTBI at baseline and one and two years later.

Fatigue* patient-reported	Cause	n	Baseline Mean (SD)	MD	p-value	n	T1 Mean (SD)	MD	p-value	n	T2 Mean (SD)	MD	p-value
Total score	TBI	167	49.0 (18.1)	4.3	0.06	29	58.6 (16.0)	3.8	0.22	35	58.5 (19.8)	2.7	0.29
	nTBI	56	53.3 (14.5)			15	62.4 (13.5)			12	61.2 (12.6)		
General	TBI	167	49.8 (23.3)	4.9	0.08	29	62.2 (19.1)	7.2	0.10	35	62.0 (25.1)	1.2	0.44
	nTBI	56	54.7 (21.0)			15	69.4 (15.2)			12	63.2 (20.1)		
Sleep/rest	TBI	167	51.8 (18.2)	7.8	0.007	29	60.0 (15.9)	7.2	0.09	35	58.9 (15.7)	5.7	0.12
	nTBI	56	59.5 (18.1)			15	67.2 (16.2)			12	64.6 (13.6)		
Cognitive	TBI	167	45.5 (24.5)	0.2	0.48	29	53.6 (26.6)	3.0	0.34	35	54.6 (27.3)	1.3	0.43
	nTBI	56	45.7 (20.1)			15	50.6 (21.3)			12	55.9 (18.4)		

Fatigue* parent-reported	Cause	n	Baseline Mean (SD)	MD	p-value	n	T1 Mean (SD)	MD	p-value	n	T2 Mean (SD)	MD	p-value
Total score	TBI	181	53.2 (19.8)	1.8	0.26	49	60.0 (20.3)	2.0	0.33	55	64.2(21.0)	6.2	0.09
	nTBI	65	55.0 (16.6)			23	58.0 (15.8)			19	58.0 (15.6)		
General	TBI	181	49.0 (24.8)	2.9	0.20	49	59.9 (24.4)	1.9	0.37	55	61.5 (24.2)	6.7	0.12
	nTBI	65	51.9 (22.7)			23	58.0 (22.7)			19	54.8 (19.9)		
Sleep/rest	TBI	181	57.2 (23.7)	6.5	0.02	49	64.4 (20.5)	2.4	0.31	55	69.2 (19.9)	0.1	0.49
	nTBI	65	63.7 (21.0)			23	66.8 (18.4)			19	69.1 (14.3)		
Cognitive	TBI	181	53.6 (26.6)	4.0	0.13	49	55.6 (27.0)	6.3	0.15	55	61.8 (27.0)	11.6	0.05
	nTBI	65	49.6 (23.5)			23	49.3 (22.0)			19	50.2 (23.1)		

* The Pediatric Quality of Life Inventory™Multidimentional Fatigue Scale (PedsQL™MFS) (patient- and parent-reported) MD: Mean difference. p-values in grey boxes are <0.05 and statistically significant. Family functioning ss= family functioning summary score, Parental HRQoL ss= parental HRQoL summary score.

CHAPTER 4

Participation restrictions among children and young adults with acquired brain injury in a pediatric outpatient rehabilitation cohort: the patients' and parents' perspective

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ABSTRACT

Improving participation is an important aim in outpatient rehabilitation treatment. Knowledge regarding participation restrictions in children and young adults with acquired brain injury (ABI) is scarce and little is known regarding the differences in perspectives between patients and parents in the outpatient rehabilitation setting. The aims are to describe participation restrictions among children/young adults (5–24 years) with ABI and investigating differences between patients' and parents' perspectives. At admission in 10 rehabilitation centers, patients and parents were asked to complete the Child and Adolescent Scale of Participation (CASP; score 0–100; lower score = more restrictions) and injury/patient/family-related questions. CASP scores were categorized (full/somewhat-limited/limited/very-limited participation). Patient/parent-reported outcomes were compared using the Wilcoxon signed-rank test. 223 patients and 245 parents participated (209 paired-samples). Median patients' age was 14 years (IQR; 11–16), 135 were female (52%), 195 had traumatic brain injury (75%). The median CASP score reported by patients was 82.5 (IQR: 67.5–90) and by parents 91.3 (IQR: 80.0–97.5) (difference = $p < 0.05$). The score of 58 patients (26%) and 25 parents (10%) was classified as 'very-limited'. Twenty-six percent of children and young adults referred for rehabilitation after ABI had "very-limited" participation. Overall, parents rated their child's participation better than patients themselves. Quantifying participation restrictions after ABI and considering both perspectives is important for outpatient rehabilitation treatment.

Keywords: participation; rehabilitation; acquired brain injury; pediatric; patient-report; parent-report

INTRODUCTION

Acquired brain injury (ABI) refers to irreversible damage to the brain which either has a traumatic cause; i.e., caused by external trauma (TBI) or a non-traumatic cause (nTBI); i.e., by internal causes.[1] It is a common diagnosis in children and young adults. The estimated yearly incidence rates in the Netherlands per 100,000 children and young adults are 288.9 (0–14 years) and 296.6 (15–24 years) for TBI and 108.8 (0–14 years) and 81.5 (15–24 years) for nTBI, respectively.[2] Due to natural brain adaptation, the majority of children and young adults with ABI will recover within the first year after brain injury.[3] However, on average, approximately 30% have persisting problems, and this group may benefit from rehabilitation treatment.[1-5] One of the ultimate goals of (outpatient) rehabilitation treatment is optimizing a patient's daily life participation.[2,6-10] However, despite its relevance, knowledge on participation restrictions of children and young adults with ABI referred for rehabilitation treatment is scarce. The currently available literature focuses on children (< 14 years) with TBI in hospital-based cohorts.[10-18]

Only a few studies focus on both patients' and parents' perspectives, and knowledge regarding outcomes on participation measuring both perspectives is even more scarce.[9,12,14,19,20] Moreover, for the pediatric rehabilitation-based population, and in the context of family-centered care, the question is whether the severity and nature of participation restrictions can best be rated by patients, parents or both, which is still an under-researched area.[20-24]

Two relevant studies (a study in the United States (US) and a Dutch study) found strong internal structure validity and internal consistency between the patient and parent reported versions of the outcome measures i.e., the Child and Adolescent Scale of Participation (CASP).[9,20] Yet, discrepancies between patients' and parents' perspectives were found, where parents reported lower scores than the patients.[9,20] However, the study conducted in the US only focused on youth aged 11–17 years and with chronic conditions/disabilities, and making comparison to patients with ABI difficult.[20] The Dutch study focused on patients with ABI a small age range (14–25 years), and used a relatively small sample size (n=49) from only one rehabilitation center.[9] This rehabilitation-based study in which the primary focus was on fatigue outcomes, investigated participation as well and found multidirectional relationships between participation and fatigue as well as considerable participation restrictions among patients with ABI as measured with the CASP (median 82.5, IQR 68.8, 92.3).[9]

Other studies based on hospital-based cohorts, report that 25–80% of children and young adults with either TBI (mild/moderate/severe) or nTBI (i.e., stroke, tumor) experience participation restrictions after ABI.[2,6,7,9,10,14,16,17,20-36] This wide range is due to differences in definition of participation, outcome measures, inclusion criteria (i.e., age, type and severity, hospital based) and time points (i.e., time since onset of ABI) used in these studies.[36] In both children and young adults, participation restrictions after ABI tend to persist for a long time which negatively influences life development.[37]

Negative consequences could affect the development of physical, psychological and social emotional skills and competencies, as well as the shaping of identity, health and wellbeing in adulthood.[2,7,9,14,16,17,25,30-36,38-40] Regarding the factors associated with participation restrictions, several studies found that more participation restrictions after pediatric ABI were associated with (among others), diminished health-related quality of life (HRQoL), and negative patient and environmental influences i.e., more patient's motor, cognitive, behavioral and emotional consequences.[7,12,16,22,23,36,41,42] To date, these influences were not investigated among children and young adults with ABI who were referred for outpatient rehabilitation treatment.

The present study aims to investigate among children and young adults with ABI (5–24 years with TBI or nTBI) who were referred for outpatient rehabilitation treatment (not having received any prior rehabilitation treatment):

1. the nature and severity of participation restrictions;
2. differences regarding patients' and parents' perspectives on patients' participation restrictions;
3. the association between HRQoL and patient- and environmental factors on the one side and participation restrictions on the other side.

MATERIALS AND METHODS

Design

Data from patients with ABI (and/or their parents) that were referred for outpatient rehabilitation treatment on the basis of continuing and/or expected problems, related to their brain injury were analyzed. These patients had not received any outpatient rehabilitation treatment yet. This study was part of a larger multi-center study on family impact, fatigue, participation and quality of life and associated factors in the Dutch ABI population (children and young adults). The study was started in 2015 in 10 Dutch rehabilitation centers, using a consensus-based set of patient/parent-reported outcome measures (PROMs) at

admission as part of routine care. The reports of these PROMs were used for clinical goal setting in rehabilitation practice. The protocol for this study was reviewed by the medical ethics committee of the Leiden University Medical Center (P15.165), and an exempt from full medical ethical review was provided. For the current article the 'Strengthening the Reporting of Observational studies in Epidemiology' (STROBE) guidelines were used.[43]

Patients

All children and young adults aged 5–24 years with a diagnosis of ABI, who were referred for outpatient rehabilitation treatment to a participating rehabilitation center and their parent(s) were eligible to participate. If patients and/or parents were unable/limited to write and/or understand the Dutch language, they were not invited by the center's health care professionals to complete the questionnaires. Patients over the age of 16 years had to give their parents' permission for completing the questionnaires according to the Dutch law of healthcare decision making.

Data Collection

Demographic and injury characteristics were extracted from the medical records by health professionals employed by the rehabilitation centers where patients had their appointment. For the outcomes related to participation, quality of life and child and environmental outcomes a (digital) questionnaire was administered to patients and/or their parents. Patients and parents were given the opportunity to complete this questionnaire prior to the first appointment during their visit at the outpatient rehabilitation clinic. If a patient (in case of a young adult) came without parents to the appointment, parents were asked to complete the questionnaires either on paper or digitally within one week after the first appointment. Unique links to the digital questionnaires were sent to the participants by e-mail by the medical health professionals working at the rehabilitation centers. Data were recoded, and thereafter anonymously stored in a central database at Basalt rehabilitation center in The Hague (The Netherlands). Finally, after analyzing the data, the centers received the results to use for clinical practice.

Assessments

Demographic and Injury Characteristics: Information regarding demographics and injury-related characteristics included: date of birth, date of injury, date of referral to rehabilitation, age at the start of the first appointment i.e., the difference between date of birth and date of referral to rehabilitation and gender i.e., male/female. Time between onset of ABI and referral to rehabilitation was calculated and thereafter divided into 2 groups: referred for rehabilitation within 6 months, and after 6 months after ABI onset. The categorization of ABI was divided in: TBI/nTBI. If known, the TBI severity levels were divided into either mild,

or moderate/severe (based on the Glasgow Coma Scale at hospital admission[44]). NTBI causes were divided into stroke/cerebrovascular accidents, brain tumors, meningitis/encephalitis, hypoxia/intoxication, and other.

Participation Outcome Measure: The Child and Adolescent Scale of Participation (CASP) was administered to patients and parents to measure participation restrictions of the patient. The CASP is part of the "Child and Family Follow-up Survey" (CFFS).[45] The CFFS, including CASP was validated for children, young adults and youth with ABI, was translated in the Dutch language, and is considered feasible and reliable tools to assess participation restrictions.[2,17,20,25,45-48] Patient-report (both children and young adults) and parent-report versions of the CASP were available and used both in the present study.[17,20,47] The CASP is a 20-item questionnaire, yielding a total score, and 4 domain scores including: home & community living activities; 5 items, home participation; 6 items, community participation; 4 items, and school/work participation; 5 items. Activities regarding participation are rated on a 4-point scale: 4 = age expected (full participation), 3 = somewhat limited, 2 = very limited, and 1 = unable. Items marked as "not applicable" do not receive a score. Scores for each item are summed and divided by the maximum possible score based on the number of items rated. The results, multiplied by 100, give a final score between 0–100, which counts for both the total score and the domain scores. The higher the scores, the closer a patient is participating to age-expected participation levels in daily life.

Four-Level Categorization: For the present study, a 4-level categorization system was developed to distinguish between levels of participation restrictions of patients for use in clinical practice. First, a draft version of a 4-level categorization was created by five of the authors based on preliminary analysis of the CASP data gathered for the present study and consensus discussions (F.A., A.d.K., M.H., G.B. and T.V.V.). We thereafter presented the categorization to a group of physicians and psychologists in the field, and to the remaining authors who are all experts in the field. Together, consensus was reached on the categorization and it was agreed to use it for further analyses in the present study. The 4-level categorization was made as follows:

- Category 1, CASP score 100–97.5: Full participation; participating in activities the same as or greater than peers, with or without assistive devices or equipment.
- Category 2, CASP score 97.5–81.0: Somewhat limited participation; participating in activities a bit less than peers. The patient may also need occasional supervision or assistance.
- Category 3, CASP score 81.0–68.5: Limited participation; participating in activities less than peers. The patient may also need supervision or assistance.

- Category 4, CASP score 68.5 or less: Very limited participation; participating in activities much less than peers, the patient may also need a lot of supervision or assistance.

Secondary Outcome Measures: When assessing participation restrictions, patient (i.e., children and young adults) factors, environmental factors as well as health related quality of life were described using the following outcome measures:

- Child/young adults' factors: The Child and Adolescent Factors Inventory (CAFI). The 15-item CAFI is a parent-report outcome measure consists of a list of problems or impairments related to the patients' health, cognitive, physical and psychological functioning. The CAFI is also part of the CFFS. Each item is rated on a 3-point scale: 1 = No problem; 2 = Little problem; 3 = Big problem. The final score is the sum of all item ratings divided by the maximum possible score of 54 (e.g., 36/54 = 0.67). This score then was multiplied by 100 to create an outcome on a 0–100-point scale. Higher scores indicate a greater extent of problems.[45]

- Environmental factors: Child and Adolescent Scale of Environment (CASE): The 18-item CASE is a parent-reported outcome measure and is designed to assess the frequency and impact of environmental barriers experienced by children and young adults with disabilities. The CASE is also part of the CFFS. Similar to the CAFI, each item is rated on a 3-point scale: 1 = No problem; 2 = Little problem; 3 = Big problem and the final score is calculated in the same way. Again, higher scores indicate a greater extent of problems.[45]

- Health-related Quality of Life (HRQoL): The 23-item Pediatric Quality of Life Inventory™ Generic Core Scales 4.0 (PedsQL™ GCS 4.0) is a patient-reported and parent-reported outcome measure and is used to determine the patients' HRQoL.[49] It is available in a Dutch language version and is validated for different age ranges and diagnoses (also for the pediatric TBI population).[50] It yields a total-score and 4 dimension scores i.e., physical functioning (8 items), emotional functioning (5 items), social functioning (5 items), school/work functioning (5 items).[49] Items are answered on a Likert-scale (0 = never to 4 = almost always) and thereafter linearly transformed to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0). The results, items summed and divided by the number of items answered gives a final score between 0–100, with lower scores indicating diminished HRQoL.[49,51]

Statistical Analysis

Characteristics: Patients' injury, demographic and family related characteristics were described using descriptive statistics. All continuous variables were expressed as medians

with interquartile ranges (IQR) and means with standard deviations (SD), based on their distributions (Kolmogorov-Smirnoff (K-S) test). Characteristics were presented for the total group and for the group of children (5–17 years) and the group of young adults (18–24 years) separately. The age categorization for children and young adults is in line with the Committee on Improving the Health, Safety, and Well-Being of Young Adults (Washington DC, 2015) and previous Dutch studies in patients with ABI.[50,52-54]

Primary/Secondary Outcome Measures: Regarding the primary (CASP) and secondary outcome measures (CAFI, CASE, PedsQL™ GCS-4.0), descriptive statistics were used to describe both the patient-report and the parent-report total scores of the CASP and the PedsQL™ GCS-4.0 and, if applicable, the domain scores. The CAFI and CASE were described similar as the CASP and the PedsQL™ GCS-4.0 but were only parent-report outcome measures. All outcomes were expressed as medians with IQRs (K-S test). To assess the potential correlation between the total scores of the CASP, PedsQL™ GCS-4.0 for HRQoL (patient/parent-report) and the CAFI/CASE (parent-report), Spearman correlations were calculated (Rho; ρ) and were considered: very strong, if > 0.70; strong, if 0.40–0.69; moderate, if 0.30–0.39; weak, if 0.2–0.29; and negligible, if < 0.19.[55]

Four-Level Group Categorization (CASP): To interpret how limited the patients' participation restrictions were (patient-report and parent-report), the 4-level group categorization was used i.e., "full participation"/ "somewhat limited"/"limited"/"very limited" participation. The CASP median (IQR) total scores are presented for all 4 group category levels. Per group (1 to 4), patient characteristics i.e., age, gender, time between administration to rehabilitation and ABI onset (< 6 months or 6 months between onset and referral), cause; TBI/nTBI; and severity levels TBI; mild/moderate-severe, were reported (using descriptive statistics). Finally, within-group median (IQR) total scores of the CAFI/CASE/PedsQL™ GCS-4.0 were reported.

Comparing Patients' and Parents' Perspectives: To compare outcomes, data from the patient-report and parent-report CASP versions, Wilcoxon signed-rank tests were used, for children and young adults separately. To test agreement between patients and parents additionally the Intraclass Correlation Coefficients (absolute agreement, single measures; ICC's) were calculated both for the CASP total and CASP domain scores. ICC scores were considered poor, if < 0.40; moderate, if 0.41–0.60; good, if 0.61–0.80; excellent, if > 0.81.[56] Regarding the results obtained by using the 4-level categorization system, Weighted kappa (Kw) with linear weights was used to assess agreement between patients' and parents' scores.[57,58] The Strength of agreement is considered: poor, if < 0.20; fair, if 0.21–0.40; moderate, if 0.41–0.60; good, if 0.61–0.80; very good, if 0.81–1.00.[57-59] A Bonferroni

correction was performed to account for multiple testing (the *p*-value divided by the number of analyses on the dependent variable did not exceed 0.05). Outcomes were described for the total group, for children (5–17 years), and for young adults (18–24 years) separately. Descriptive statistics were used to describe the CASP median (IQR) total scores, domain scores and categorization (counts, percentages).

Differences/similarities in participation restriction categorization were described as follows: patients scoring in the same category as their parents, patients scoring themselves 1 to 3 categories lower than their parents, and patients scoring themselves 1 to 2 categories higher than their parents.

All analyses were performed using SPSS 24.0 for Windows (IBM, SPSS Statistics for Windows, Version 24.0. IBM Corp, Armonk, NY, USA). The level of significance was set at $p < 0.05$ for the Spearman Rho correlation, Wilcoxon signed rank and ICC tests.

RESULTS

Characteristics

Patient, family and injury related characteristics are described in Table 1. The flow of all eligible participants for the current analyses can be found in Figure 1. The data of two-hundred- sixty patients, (217 children (83%) and 43 young adults (17%)) and/or their parents was analysed. In total, there were 223 patient- and 245 parent-reported questionnaires completed and there were 209 patient-parent pairs (see Table 1 and Figure 1). One hundred and ninety-five (75%) patients had TBI of which 151 were mild TBI (77%). One hundred and thirty-five patients were female (52%). Ninety-six patients (39%) were referred to the rehabilitation center more than six months after brain injury onset. The median age of the patients in the group of children (5–17 years) was 14 years (IQR 11–16), and 18 (IQR 18–19) in the 18-year-old age group.

Table 1. Patient, family and injury characteristics of children and young adults with acquired brain injury (ABI) referred to an outpatient rehabilitation center.

Patient Injury and Demographic Related Characteristics	**Children 5–17 y, n = 217**	**Young Adults > 18 y, n = 43**	**Total Cohort 5–24 y, n = 260**
Gender:			
• Female n (%)	112 (52%)	23 (54%)	135 (52%)
Age (years) at admission			
• median (IQR)	14 (11–16)	18 (18–20)	14 (11–16)
Time (months) between ABI onset and referral to rehabilitation			
• median (IQR)	4 (1–18)	4 (2–19)	4 (1–18)
• >6 months n (%)	87 (40%)	17 (40%)	104 (40%)
Traumatic brain injury (TBI) n (%)	160 (74%)	35 (81%)	195 (75%)
Severity levels TBI * n (%)			
• Mild	124 (78%)	27 (77%)	151 (77%)
• Moderate-severe	15 (9%)	5 (14%)	20 (10%)
• Unknown	21 (13%)	3 (9%)	24 (13%)
Non-traumatic brain injury (nTBI) n (%)	57 (26%)	8 (19%)	65 (25%)
Causes nTBI n (%)			
• Tumor	25 (44%)	2 (25%)	27 (41%)
• Stroke	11 (19%)	5 (63%)	16 (25%)
• Encephalitis/meningitis	10 (17%)	1 (12%)	11 (17%)
• Hypoxia/intoxication	2 (4%)	0 (0%)	2 (3%)
• Other/unknown	9 (16%)	0 (0%)	9 (14%)

Family Related Characteristics	**Children 5–17 y, n = 209**	**Young adults 18 y, n = 36**	**Total Cohort 5–24 y, n = 245**
Living in a single-parent household n (%)	34 (16%)	8 (22%)	42 (17%)
Cultural background parents:			
• non-Dutch n (%)	16 (8%)	2 (6%)	18 (7%)
Educational level parent** number (%)			
• Low	7 (3%)	3 (8%)	10 (4%)
• Intermediate	41 (20%)	6 (17%)	47 (19%)
• High	162 (77%)	27 (75%)	188 (77%)

* Based on Glasgow Coma Scale at hospital admission: “mild”—13–15, “moderate”—9–12, “severe” < 8; ** Educational level parent: low—prevocational practical education or less, intermediate—prevocational theoretical education and upper secondary vocational education, high—secondary education, higher education and/or university level education.

Participation Outcomes

Regarding participation outcomes in our population, as seen in Table 2, the median CASP total score reported by patients (n=223) was 82.5 (IQR: 67.5–90.0), and by parents (n = 245) was 91.3 (IQR: 80.0–97.5). As seen in Table 2, Figure 2a,b, the lowest scores were found in the domain score ”community participation” i.e., median patient-report score 75.0 (IQR: 56–92), median parent-report score 87.5 (IQR: 75–100). The highest median scores were found in the 'home participation' domain score for patients (87.5, IQR: 75–96), and in the "school/work participation" domain score for parents (95.0, IQR: 83–100).

Secondary outcome measures are also presented in Table 2. Regarding HRQoL, the median PedsQL™GCS-4.0 patient-report total score was 65.2, (IQR: 53–78), and the median parent-report score was 60.9 (IQR: 48–75). The parent-report median scores in the CAFI (child/young adult factors) and CASE (environmental factors) were: 56.9 (IQR: 49–65) and 39.0 (IQR: 33–51), respectively. Spearman's rho correlations between the CASP scores and the CAFI/CASE and HRQoL were significant ($p < 0.01$) and strong ranging between: 0.53–0.67.

Four-Level CASP Categorization

Table 3 shows within-group (patient/injury-related) characteristics, and CASP/CAFI/ CASE/ HRQoL scores of participation restrictions (patient-report and parent-report where applicable) in our cohort, organized by the 4-level CASP participation restrictions categorization.

Eighty-nine percent of the patients, and 73% of the parents reported patients' participation restrictions in more than one CASP domain. Forty-three percent (patient-reported) and 45% (parent-reported) reported CASP total scores that fell in the "somewhat limited" category. Twenty six percent (patient-report) and 10% (parent-report) reported CASP total scores that fell in the "very limited" category. In this "very limited" category, median CASP scores were 57.9 (IQR: 50–64) for patient-report data, and 61.4 (IQR: 49–65) for parent-report data.

Patients who fell in this 'very limited' category, had a median age of 15 years (both in the patient and parent-reported category), 45–52% were female, 64–78% had a TBI and 33–40% were referred for rehabilitation more than 6 months after ABI onset.

Lower participation CASP scores, i.e., category levels up to category 4, also showed lower (diminished) patient and parent report HRQoL scores, and higher (more problems) parent report CAFI/CASE scores.

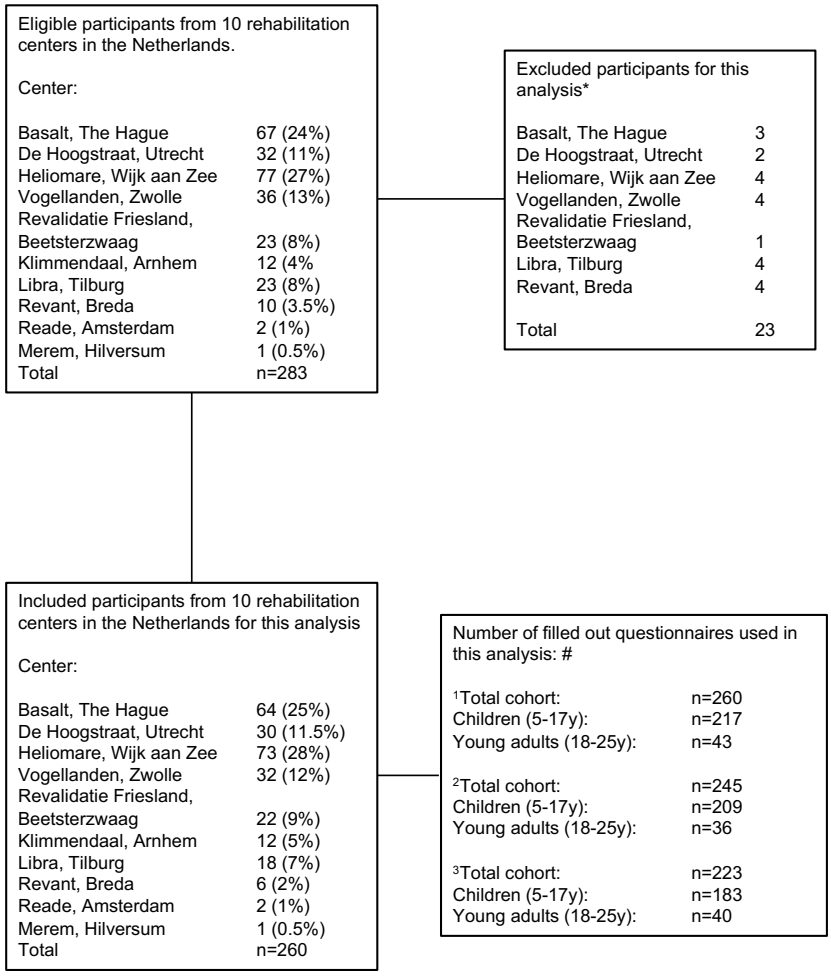

Figure 1. Flow of children and young adults with ABI admitted for rehabilitation and eligible for the present analysis

* Missing participants: n=11 no official ABI diagnosis, n=12 incomplete questionnaires.
# Number of filled out questionnaires used in this analysis (total/patient-reported/parent-reported): [1] number of questionnaires filled out by the patient, the parents or both in total and per age group (children, adolescents and young adults).
[2] number of questionnaires filled out by parents only in total and per age group (children, adolescents and young adults).
[3] number of questionnaires filled out by patients only (self-reported) in total and per age group (children, adolescents and young adults).

Table 2. Total and domain scores on the CASP, CAFI, CASE and PedsQL™ GCS-4.0 (HRQoL) of children and young adults with acquired brain injury (ABI) and mutual correlations.

Outcome Measure	Domain Scores/Total Scores	Patient Report n = 223 Median (IQR)	Parent Report n = 245 Median (IQR)
CASP [1]	Total Score	82.5 (68–90)	91.3 (80–98)
	Home/community living activities	80.0 (63–90)	90.0 (75–100)
	Home participation	87.5 (75–96)	91.7 (83–100)
	Community participation	75.0 (56–92)	87.5 (75–100)
	School/work participation	85.0 (67–95)	95.0 (83–100)
PedsQL™ GCS-4.0 (HRQoL) [2]	Total score	65.2 (53–78)	60.9 (48–75)
	Physical health	68.8 (50–86)	68.8 (47–81)
	Emotional functioning	65.0 (45–85)	60.0 (40–75)
	Social functioning	80.0 (65–90)	75.0 (60–95)
	School/work functioning	50.0 (35–65)	50.0 (30–60)
CAFI [3]	Total Score	NA	56.9 (49–65)
CASE [3]	Total Score	NA	39.0 (33–51)

Correlations [$]		Patient Report n = 223 Rho	Parent Report n= 245 Rho
CASP total score	HRQoL total score	0.67 **	0.62 **
CASP total score	CAFI total score	NA	0.60 **
CASP total score	CASE total score	NA	0.53 **

[1] CASP: Child and Adolescent Scale of Participation, 0–100 with lower scores indicating more participation restrictions.

[2] PedsQL™ Generic Core Scales 4.0 for Health-related quality of life (HRQoL): 0–100 with lower scores indicating lower HRQoL.

[3] CAFI: Child and Adolescent Factors Inventory (CAFI), and CASE: Child and Adolescent Scale of Environment, 0–100 with higher scores indicating more problems.

[$] ρ = Spearman's rho (ρ) correlation.

** $p < 0.001$.

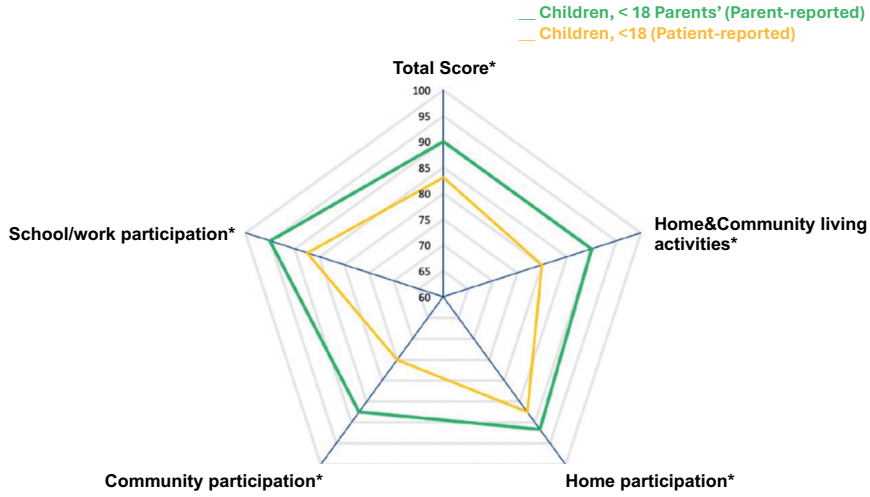

Figure 2a. Differences in CASP scores between Patients and Parents in children (5-17 years) with ABI.

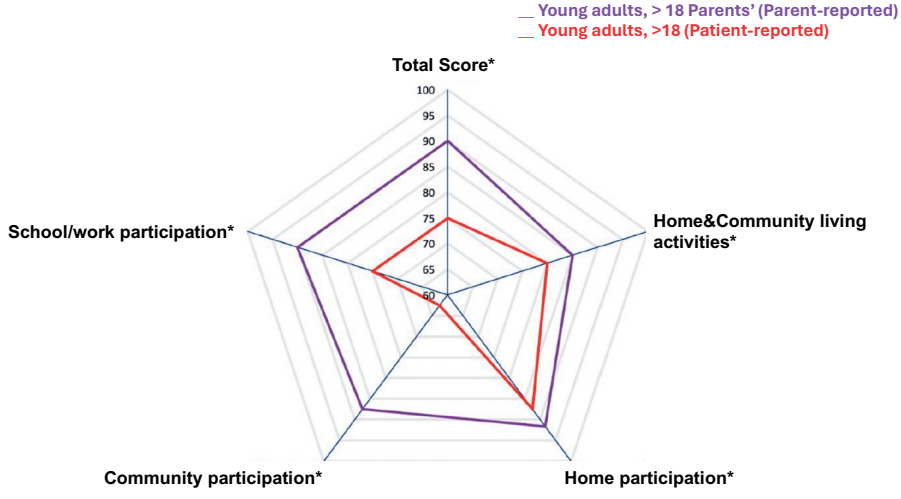

Figure 2b Differences in CASP scores between Patients and Parents in young adults (18-24 years) with ABI.

*2a and 2b CASP: Child and Adolescent Scale of Participation, 0–100 with lower scores indicating more participation restrictions.

Table 3. Within group characteristics of children and young adults with acquired brain injury (ABI) based on CASP participation restriction categorization.

Patient-Report (CASP) n = 223 (100%)								
Category	n (%)	CASP Totalscore# Median (IQR)	Age: Median (IQR)	Gender Female: n (%)	$ Admin to Rehab ≥6 m: n (%)	Cause TBI: n (%)	Severity TBI Mild: n (%)	[a] HRQoL Median (IQR)
[1] Full participation	25 (11%)	98.7 (98–99)	15 (12–16)	12 (48%)	13 (52%)	18 (72%)	14 (88%)	80.4 (75–86)
[2] Somewhat limited participation	95 (43%)	86.8 (84–91)	14 (12–16)	50 (53%)	35 (37%)	72 (76%)	55 (86%)	75 (63–82)
[3] Limited participation	45 (20%)	75 (71–78)	15 (11–17)	29 (64%)	15 (33%)	32 (71%)	24 (83%)	62 (52–68)
[4] Very limited participation	58 (26%)	57.9 (50–64)	15 (13–16)	26 (45%)	15 (33%)	45 (78%)	39 (97%)	47.3 (38–58)

Parent-Report (CASP) n = 245 (100%)										
Category	n (%)	CASP Totalscore # Median (IQR)	Age: Median (IQR)	Gender Female: n (%)	$ Admin to Rehab ≥6 m: n (%)	Cause TBI: n (%)	Severity TBI Mild: n (%)	[a] HRQoL Median (IQR)	[b] CAFI Median (IQR)	[b] CASE Median (IQR)
[1] Full participation	67 (27%)	100 (98–100)	15 (11–16)	33 (49%)	24 (36%)	58 (87%)	45 (92%)	75 (63–83)	47.1 (43–57)	34.4 (33–36)
[2] Somewhat limited participation	111 (45%)	91.3 (88–94)	13 (10–15)	59 (53%)	43 (39%)	79 (71%)	62 (86%)	64.1 (54–77)	56.9 (51–63)	39.8 (33–50)
[3] Limited participation	42 (17%)	76.3 (73–80)	14 (10–16)	23 (55%)	19 (45%)	28 (67%)	24 (89%)	47.8 (41–55)	63.7 (55–71)	48.8 (43–62)
[4] Very limited participation	25 (10%)	61.4 (49–65)	15 (12–17)	13 (52%)	10 (40%)	16 (64%)	12 (92%)	42.4 (35–48)	64.7 (59–74)	53.2 (41–67)

CASP: Child and Adolescent Scale of Participation, 0–100 with lower scores indicating more participation restrictions. Categories: 1 Full participation: Group 1, Between 97.5–100: Participating in activities the same as or more than other peers, 2 Somewhat limited participation: Group 2, Between 97.5–81: Participating in activities somewhat less than other peers, 3 Limited participation: Group 3: Between 81–68.5: Participating in activities less than other peers, 4 Very limited participation: Group 4, Below (<) 68.5: Participating in activities much less than other peers.45 $ Time (months) between administration to rehabilitation and ABI onset (more than 6 months). a Patient and parent-report PedsQL™ Generic Core Scales 4.0 for health-related quality of life (HRQoL), 0–100 with lower scores indicating lower HRQoL. b Parent-report CAFI: Child and Adolescent Factors Inventory, and Parent-report CASE: Child and Adolescent Scale of Environment, 0–100 with higher scores indicating more problems.

Differences in Patients' and Parents' Perspectives

In Table 4, the differences in participation outcomes between patients and parents (paired samples) is reported. Regarding the total paired-sample group (n= 209), there was moderate agreement in participation total CASP and domain outcomes between patients and their parents i.e., ICC = 0.42–0.57, all p < 0.001. In the group of children (5–17 years, n=176) moderate agreement was found between patients' and their parents' total CASP and domain scores (ICC = 0.43–0.55, all p < 0.001). In the young adult (≥ 18 years, n= 33) group, there was poor-moderate patient/parent agreement between patient- and parent report scores on all CASP domains (ICC = 0.37–0.59, all p < 0.001). Regarding the categorical data on the 4-level categorization system, a fair to moderate agreement was found between the patients and parents; "moderate" in children; Kw: 0.42 (95%CI 0.32–0.52, p < 0.001), and "fair" in young adults; Kw: 0.27 (95%CI 0.08–0.46, p < 0.05). Regarding the differences in categorization between patients and their parents, in the total paired-sample group, 38% of the patients scored themselves in a lower CASP level category than their parents. In the group of children, the same percentage was found (38%), while in the young adult group 51% scored themselves in a lower category than their parents.

Table 4. Differences and similarities between patient and parent CASP participation scores and categories.

Paired Samples Total Group (5–24 Years) n = 209				
CASP	**Patient Report Median (IQR)**	**Parent Report Median (IQR)**	**Wilcoxon Z #**	**ICC $**
Total Score	82.5 (68–90)	90.0 (80–97)	-8.2 **	0.54
Home/community living activities	80.0 (63–90)	90.0 (75–100)	-5.9 **	0.51
Home participation	87.5 (75–96)	91.7 (83–100)	-5.9 **	0.42
Community participation	75.0 (56–92)	87.5 (75–100)	-8.5 **	0.51
School/work participation	85.0 (66–90)	95.0 (80–100)	-6.2 **	0.57

CASP Categorization	**Patient report Number (%)**	**Parent Report Number (%)**	**Patient/Parent Categorization ^**	**Number (%)**
- Full	23 (11%)	51 (24%)	Same as parents	110 (53%)
- Somewhat limited	92 (44%)	98 (47%)	Different from parents	99 (47%)
- Limited	41 (20%)	37 (18%)	a:1 category worse	54 (26%)
- Very Limited	53 (25%)	23 (11%)	b: 2 categories worse	15 (7%)
Kw: 0.40 (95% CI 0.31–0.49), p < 0.001			c: 3 categories worse	10 (5%)
			d: 1 category better	18 (9%)
			e: 2 categories better	2 (1%)

Table 4. Continued

Paired Samples Children (5–17 Years) n = 176				
CASP	**Patient Report Median (IQR)**	**Parent Report Median (IQR)**	**Wilcoxon Z #**	**ICC $**
Total Score	83.1 (69–90)	90.0 (80–97)	-7.4 **	0.54
Home/community living activities	80.0 (63–90)	90.0 (75–100)	-5.2 **	0.51
Home participation	87.5 (75–96)	91.7 (83–100)	-5.4 **	0.43
Community participation	75.0 (56–92)	87.5 (75–100)	-7.4 **	0.52
School/work participation	87.5 (70–96)	95.0 (82–100)	-5.6 **	0.55

CASP Categorization	**Patient report Number (%)**	**Parent Report Number (%)**	**Patient/Parent Categorization ^**	**Number (%)**
- Full	20 (11%)	41 (23%)	Same as parents	99 (53%)
- Somewhat limited	83 (47%)	86 (49%)	Different from parents	77 (47%)
- Limited	30 (17%)	31 (18%)	a:1 category worse	42 (24%)
- Very Limited	43 (24%)	18 (10%)	b: 2 categories worse	11 (6%)
Kw: 0.42 (95% CI 0.32–0.52), p < 0.001			c: 3 categories worse	8 (5%)
			d: 1 category better	14 (8%)
			e: 2 categories better	2 (1%)

Paired Samples Young Adults (18–24 Years) n = 33				
CASP	**Patient Report Median (IQR)**	**Parent Report Median (IQR)**	**Wilcoxon Z #**	**ICC $**
Total Score	75.0 (65–86)	90.0 (78–99)	-3.6 **	0.56
Home/community living activities	80.0 (66–90)	85.0 (75–100)	-2.8 *	0.52
Home participation	87.5 (75–90)	91.7 (79–100)	-2.3 *	0.37
Community participation	62.5 (50–84)	87.5 (75–100)	-4.0 *	0.48
School/work participation	75.0 (55–90)	90.0 (74–100)	-2.8 *	0.59

CASP Categorization	**Patient report Number (%)**	**Parent Report Number (%)**	**Patient/Parent Categorization ^**	**Number (%)**
- Full	3 (9%)	10 (30%)	Same as parents	12 (37%)
- Somewhat limited	9 (27%)	12 (36%)	Different from parents	21 (63%)
- Limited	11 (33%)	6 (18%)	a:1 category worse	11 (33%)
- Very Limited	10 (30%)	5 (15%)	b: 2 categories worse	4 (12%)
Kw: 0.27 (0.08–0.46), p < 0.05			c: 3 categories worse	2 (6%)
			d: 1 category better	4 (12%)
			e: 2 categories better	0 (0%)

[1] CASP: Child and Adolescent Scale of Participation, 0–100 with lower scores indicating more participation restrictions. # Z scores for Wilcoxon signed-rank test for nonparametric data outcomes * p < 0.05, ** p < 0.001; $ ICC; Intraclass Correlation Coefficients rated: < 0.40: poor; 0.41–0.60: moderate; 0.61–0.80 good; >0.81: excellent. Kw: Weighted Kappa interpretation (categorical CASP score): < 0.20: poor, 0.21–0.40: fair, 0.41–0.60: moderate, 0.61–0.80: good, 0.81–1.00: very good agreement. ^Patient categorization compared to parents' categorization: The differences in categorized participation between patients and their parents, a: Patients that scored 1 category worse than their parents, b: Patients that scored 2 categories lower than their parents, c: Patients that scored 3 categories lower than their parents, d: Patients that scored 1 category better than their parents, e: Patients that scored 2 categories better than their parents.

DISCUSSION

According to data gathered before/on the first appointment for routine outpatient rehabilitation for children and young adults with ABI and their parents in multiple rehabilitation centers, 88% (patient-reported) and 73% (parent-reported) of the patients have participation restrictions that can be classified as "somewhat limited" to "very limited", with a considerable number of patients (25, parent reported and 58, patient reported) that can be classified as "very limited". The large majority was classified in the "somewhat limited" category. Overall, patients consistently reported more severe participation restrictions than parents. There was a greater discrepancy in the levels of participation restrictions between patients and parents in the young adult group compared to the children group.

Participation Restrictions

These results confirm that experiencing participation restrictions is common in pediatric patients with brain injuries (TBI/nTBI).[2,6,7,9,12,16,17,25,30-36,41] Furthermore, the results we found, pointed out that the rehabilitation referred group had more participation restrictions compared to a Dutch hospital-based cohort. In the current analyses of data among patients referred to an outpatient rehabilitation center, the vast majority reported participation restrictions in one or more domains of the CASP. This proportion was relatively high as compared to the 25–80% reported in a systematic review of studies on participation restrictions in children and youth with ABI including in hospital-based cohorts[7]. The current analyses found that the majority of patients was classified as "somewhat limited". These patients could also be "at risk" regarding restricted participation.

In clinical practice it could also be important to monitor the patients that score relatively better than patients with more limited participation. However, future research must confirm this hypothesis by further looking into the "somewhat limited" patients. Concerning the prevalence of participation restrictions in young adults, some differences with the literature were found. A previous rehabilitation-based study, with patient and parent-reported data that focused on patients with ABI in the age group of 14–25, reported similar participation restrictions when compared to the results of the total sample from the current analyses.[9] However, more participation restrictions were found in the young adult group in the current analyses.[9] Differences could possibly be explained by differences in age inclusion. Results suggest that young adults experience more participation restrictions than children. This could be explained by the greater appeal made on for example independence, planning and coping in this transitional age group.

Community Participation

For both patient-report and parent-report CASP outcomes and in all (age) groups (< 18 years/ > 18 years/total), the lowest scores were found in the domain 'community participation' which includes participation related to e.g., social play/leisure activities with friends, events, sports, doing groceries, communicating with others in the neighborhood.[45,47] Restrictions in community participation could also be related to the fact that children and young adults with ABI often have difficulties in social functioning, emotional functioning, and processing sensory stimuli (after ABI onset). These competences are needed when participating in the community.[7,37] However, other factors (e.g., environmental resources, stigma, family support, as well as time allocation), may also influence community participation.[14,42]

Correlations with the CASP and CAFI/ CASE/ HRQoL

In comparison to a previous Dutch study in a hospital cohort with a higher CASP total score, the mutual correlations of the CASP with the CAFI, and CASE (parent-report), were higher in this rehabilitation-based population.[2] Regarding HRQoL, in line with previous literature participation was found to be highly correlated with HRQoL (patient-report and parent-report).[9,16,35] These results underline the interdependence of limitations on the level of participation (CASP), child/young adult factors e.g., body functions and structures (CAFI), environmental factors (CASE), and HRQoL (PedsQL™ GCS-4.0). These findings also support the assumption that the CASP, PedsQL™ GCS-4.0, CAFI, and CASE are more suitable among patients that were administered to outpatient rehabilitation (and filled out the questionnaires at admission) than in patients that were in a hospital (hospital-based).

Notable Results Found in the Current Rehabilitation-Based Population

Notable results were found in the current analyses among the outpatient rehabilitation-based population, which were not found in previous studies.[36,41]

Firstly, the majority of children and young adults with a mild TBI reported scores in the "very limited" category. These results suggest that the TBI population experience participation restrictions no matter the initial TBI severity. Therefore, targeting and monitoring these restrictions for all TBI severities is relevant at admission to rehabilitation treatment.

Secondly, late referral (over 6 months) to outpatient rehabilitation was common across all participation category groups based on the CASP total scores, in example; "somewhat limited participation category"–"very limited participation category". "One-third up to 45% of the patients in the different participation categories were referred for rehabilitation more than 6 months after ABI onset. This was also common among more than one-third of the patients in the "very limited" category. Several explanations can be given for a delay in referral. Medical specialists and general practitioners could potentially underestimate (long-

term) problems/restrictions of patients or simply do not recognize them and/or they may not be familiar with pediatric ABI care pathways. Parents and patients do not know what signals or problems to be alert of, may tend to choose a "wait and see" approach before seeking help and/or are not familiar with ABI support pathways.[5]

These findings should be discussed with professionals in acute care to increase awareness of possible consequences of later rehabilitation referral and to ultimately improve referral policies and procedures.

Differences in Perspectives

Regarding patients' and parents' perspectives, moderate agreement between patient and parent reported CASP (total and domain) scores were found. Previous studies underlined the importance of measuring both patients' and parents' perspectives to assess outcomes.[20,36] One Dutch study regarding adolescents and young adults with ABI found a difference between the patients and the parents CASP total score outcomes, similar to what we found in the results of the analyses.[9] Parents tend to report less participation restrictions for their children than the patients themselves, which is in contrast to previous studies with other outcomes (e.g., HRQoL; where parents usually report lower scores than their children).[9,16,17,25,30-33,35,40] This was also found in our analyses. A large part of the patients in our cohort scored themselves in another CASP level category than their parents did. These discrepancies in reporting outcomes may be explained due to the fact that most participation activities (of the children and young adults) occur outside of the home environment where parents are not present and also, young adults spend more time away from parents than children. Our results suggest that assessing both patients' and parents' perspectives is important in order to identify differences and similarities. By using both perspectives, a broader view on overall functioning is attained, providing health care professionals the opportunity to consider both patients' and parents' perspectives when collaborating on rehabilitation goals, and make sure parents play an active role in today's often proposed family-centered care.[14]

Categorization of Severity of Participation Restrictions

In the currently analyzed data, a 4-level categorization was created that correspond to specific CASP score ranges to reflect the overall degree of participation restriction. This categorization was based on previously identified levels of participation suggested by one of the authors (G.B.). To date, CASP outcomes were described as just a score between 0 and 100 (lower score = more participation restrictions). To facilitate a better interpretation of the score in clinical practice, we proposed a categorization of the total score into four levels. This 4-level categorization can be used next to the original 0–100 score) to compare

and report CASP outcomes. The use of cut-off values may help to contextualize and differentiate the scores for clinical practice (i.e., indication for rehabilitation, evaluation of intervention) and research. All statistical comparisons of patients' and parents' scores in the present study consistently demonstrated a considerable discrepancy. Poor agreement was also seen using the proposed 4-level categorization, substantiating the validity of that division. Regarding the 4 categories, the majority of the patients and their parents reported CASP scores in the 'somewhat limited', the "limited" and 'very limited' categories. A quarter of the children and almost one-third of the young adults scored in the most restricted, i.e., "very limited" category. Parent and patient-report scores differed in participation restriction category in almost half of the of cases, with parent scores and categories demonstrating lower levels of participation restriction as previously described. Future longitudinal studies could use this new categorization to further evaluate its utilization, and/or to investigate recovery outcomes over time (e.g., moving to higher category level of participation) during rehabilitation treatment related to interventions.

Limitations

Describing analyses and results among rehabilitation referred patients resulted in a number of limitations. First, there was a relatively small sample of young adults compared to the sample of children (43 vs. 217). The explanation is merely organizational: most rehabilitation centers have a separate pediatric (< 16 or < 18 years) and adult (> 18 years) department where only the pediatric department was involved. Only two centers had a separate department for young adults (18–25 years) and included young adults. However, the number of included young adults was large enough to analyze and report outcomes for separately. Since, due to age and life phase, in the young adult group is a different group of patients it is recommended to include this group of patients in transition fully in future pediatric studies. Secondly, not for all patients paired sample data was available, making the analysis for the differences/similarities between patients' and parents' perspectives only possible for a portion of our analyses (n = 209). However, since we had paired sample data available for the majority of patients, we believe that outcomes are generalizable. Third, the CASP is known to have a ceiling effect.[17,47] Nonetheless, in contrast to other studies reporting ceiling effects in children and young adults with ABI, these were less evident in the present analyses making the CASP a more suitable instrument for use in rehabilitation cohorts (versus patients that are hospitalized) of patients with ABI.[2,17,20,47] Furthermore, an alternative instrument that also focusses on the ABI population is lacking.[17] Finally, results of patient/parent rated outcome measures could be biased, i.e., by limitations in motivation or patients' and/or parents' moment bound 'stress and mood'.

Directions for Future Research

Interesting follow up projects could be longitudinal studies monitoring participation over time and evaluative studies using the CASP to explore the effect of rehabilitation programs for children and young adults with ABI and their families, since optimizing participation is an important rehabilitation goal. In these studies, the newly developed categorization of participation outcomes could be used and further investigated on its usefulness and robustness. Future studies should include the search for the best available participation outcome measures particularly given the number of promising participation-focused, multi-setting interventions that recently have been developed to improve participation outcomes for individual children, youth, and families.[21-24] The next challenge is to drive implementation of participation-based interventions on a larger scale, and research should be focused on enabling strategies and on cost-effectiveness of these interventions. The CASP and our newly proposed categorization of participation restrictions could support this process.

CONCLUSIONS

A substantial portion of patients (ages 5–24 years) with acquired brain injury referred to an outpatient rehabilitation center in The Netherlands had “limited” to “very-limited” participation. Patients reported greater participation restrictions than their parents and disparities between patient-reported and parent-reported participation restrictions were greater in young adults than in children. Furthermore, a strong correlation was found between patient and environmental factors (CAFI and CASE), HRQoL (PedsQL™ GCS-4.0), and participation (CASP). Most restrictions were found in the ‘community participation’ domain. A large part of the patients with a late referral (> 6 months) to rehabilitation after ABI onset reported “very limited” participation. Early referral is important as this may reduce participation restrictions. Taking into account both patients’ as well as parents’ perspectives is important in outpatient rehabilitation treatment in order to guide both patients and their parents appropriately during treatment. Furthermore, the categorization of CASP scores into 4 categories might be useful for clinical practice and research, but more study is needed to understand how this can be applied and inform participation focused clinical and practical decisions.

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Institutional Review Board Statement

The protocol for this study was reviewed by the medical ethics committee of the Leiden University Medical Center (P15.165), and an exempt from full medical ethical review was provided.

Data Availability Statement

Data used in this study is stored in a central database at Basalt Rehabilitation center, The Hague in the office of innovation, quality and research and can be available when requested.

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Conflicts of Interest

The authors declare no conflict of interest.

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CHAPTER 5

Parent-reported family impact in children and young adults with acquired brain injury in the outpatient rehabilitation setting

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ABSTRACT

Purpose

To increase knowledge/awareness on family impact (FI) after acquired brain injury (ABI) in rehabilitation settings, it is essential to investigate the associations between patient-functioning and impact on families. This has been explored in hospital-based cohorts, but not in rehabilitation settings.

Methods

A cross-sectional, multi-center study among parents of children/ young adults (aged 5–24 years) with ABI referred to rehabilitation was performed. Patient/injury/family-characteristics were noted, and parents completed the PedsQL™ Family-Impact-Module (FIM) and PedsQL™ generic-core-4.0 to assess FI and health-related quality of life (HRQoL). Univariate- and multivariable-regression analyses were performed to investigate associations between HRQoL/ patient/ injury/ family-related factors and FI.

Results

246 families participated; patients' median age was 14 years (IQR 11–16), 65 had non-traumatic-brain-injury (nTBI) (26%), 127 were female. FI was found to be considerable (median FIM-score 71.9, IQR:60–85). Especially referral to rehabilitation > 6 months after onset, diminished patients' mental/ emotional health and HRQoL (child/ family factors), and premorbid problems were associated with higher FI.

Conclusions

In this rehabilitation cohort, pediatric ABI caused considerably higher FI than in hospital-based studies with referral to rehabilitation > 6 months, diminished child/family factors and presence of premorbid problems increasing FI. Assessing and monitoring FI and its associated factors enables professionals to individualize treatment, psychoeducation, support and follow-up.

Keywords: Family impact; acquired brain injury; rehabilitation; pediatric

INTRODUCTION

Acquired brain injury (ABI) refers to any damage to the brain that occurs after birth and can be categorized in traumatic brain injuries (TBI) and non-traumatic brain injuries (nTBI).[1] TBI is caused by external trauma (e.g., traffic accidents, sports accidents, abuse), while nTBI results from internal causes (e.g., stroke, tumors, infections, hypoxia).[1] The estimated yearly incidence rates in the Netherlands are: 288.9 (0–14 years) and 296.6 (15–24 years) per 100.000 for TBI and 108.8 (0–14 years) and 81.5 (15–24 years) for nTBI.[2] ABI may cause a variety of long-term deficits for patients including motor, communication, cognitive, and behavioral impairments.[2–6]
It is well known that due to natural brain adaptation a majority of the patients with ABI will recover within the first year after brain injury.[7–9] However, a group of patients (approximately 30% [2,8,10]) with ABI will remain with persisting daily life problems. These problems can have a considerable negative impact on functioning, participation and health-related quality of life (HRQoL) for the patient, as well as the family.[8,9,11–14]

Previous studies regarding family impact in patients (either TBI and/or nTBI) mostly concern hospital-based cohorts.[12,15–29] Hospitalization of a child after ABI may influence the impact on families negatively, mainly due to a shift in routines, roles and responsibilities, worrying, flawed communication and increased stress.[15,16,28] In 40–45% of the families this negative impact lasts longer than 12 months.[16–18,28,30]

A Dutch hospital-based study among children and young adults with ABI (75%TBI) found considerable impact in families after pediatric ABI.[19] In other (hospital based) studies, several factors were found to increase family impact, like higher age at ABI onset, premorbid problems of the child (e.g., behavioral problems), a non-traumatic brain injury (e.g., stroke or brain tumor) and severity of limitations.[2,8,19,22,31] However, in these studies the variation in age groups, setting, the time point of assessments and questionnaires used to assess family impact, makes it difficult to compare results.[15–21,30,32,33]

Knowledge gained on family impact in the group of patients with ABI during the later phase of recovery (at the start of rehabilitation treatment) is scarce. In the previous literature, only one rehabilitation-based study was found. This study found that parents experienced significant emotional distress and a high burden of care. However, this study only focused on patients with TBI, it used a small sample size (n = 10) and was interview-based (no valid outcome measures were used).[25]

The present study aims to further increase knowledge/awareness on family impact after acquired brain injury (ABI) in outpatient rehabilitation settings and investigate the associations between patient functioning and impact on families. Since referral to rehabilitation means there are persisting problems in functioning, activities, and participation we expect greater family impact in a rehabilitation cohort compared to a hospital cohort.

Results of this study may help to better tailor and utilize (family centered [34,35]) rehabilitation treatment to improve and personalize help and meet the wishes and needs for both the patient and his/her family.

METHODS

Study design

This study was part of a larger multicenter, prospective cohort study on family impact, fatigue, participation and HRQoL in children and young adults with ABI, referred to a rehabilitation center for outpatient treatment. Inclusion started in 2015 in 10 rehabilitation centers in The Netherlands, i.e., Basalt, The Hague; De Hoogstraat, Utrecht; Heliomare, Wijk aan Zee; Vogellanden, Zwolle; Klimmendaal, Arnhem/Apeldoorn; Revalidatie Friesland, Beetsterzwaag; Libra, Tilburg; Revant, Breda; Reade, Amsterdam and Merem, Hilversum. This study was approved by the medical ethics committee of the Leiden University Medical Center (P15.165) which provided an exempt from full medical ethical review since data was collected as part of regular care (assessing possible problems and restrictions for discussion during rehabilitation intake). All local research committees of the participating centers approved the study. This study concerns parent-reported data gathered at admission, collected between September 2015 and December 2018. For presenting the results, the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines were used.[36]

Participants

For this study, all parents of patients who were diagnosed with ABI and referred by a general practitioner or medical specialist to 1 of the 10 participating rehabilitation centers, between 2015 and 2018 were eligible to participate. Participants were excluded if: parents and/or patients were unable/limited to write and/or understand the Dutch language and were therefore unable to complete the questionnaires.

Procedure and assessments

Prior to the first appointment, parents received a link to the digital questionnaires

(www.Questback.nl), requesting parents to complete the questionnaires before the first appointment, after gaining permission of the patient (when over 16 years old).

Information from medical records: Information regarding the patient's demographics and injury related characteristics was obtained from the medical records by the treating physician, and included: gender (male/female), date of injury, date of birth. Furthermore, the causes of ABI were noted as follows: TBI with, if known, severity levels (i.e., mild, moderate/severe based on the Glasgow coma scale[37]). Finally, nTBI, including cause (i.e., stroke/, (brain) tumors, meningitis/encephalitis, hypoxia/intoxication, and other). Since there is no valid instrument to assess the severity levels of nTBI due to the wide variety of causes and expected outcomes, severity levels for nTBI were not reported in this study. Time between onset (date of injury) and referral to rehabilitation was calculated and categorized in less than 6 months or more than 6 months after onset.

Outcome measures

Family impact: The Pediatric Quality of Life Inventory™ Family Impact Module (PedsQL™ FIM) was used to measure family impact.[33] This 36-item questionnaire is considered to be a valid tool to assess impact on families with a child with a (chronic) disability and has been used in an ABI study previously.[19] Items in the PedsQL™ FIM are answered on a 0–4 Likert-scale (0 = never to 4 = almost always) and thereafter linearly transformed to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0). The PedsQL™ FIM yields a total score (the sum of the 36 items, divided by the number of items answered) and 4 scale scores: a parental Quality of Life (QoL) summary score (20 items, divided over physical, emotional, social, and cognitive functioning subscales), a family functioning summary score (8 items, divided over "daily activities" and "family relationships" subscales), a worrying score (5 items), and a communication score (3 items). The scale scores range from 0 to 100 where lower scores indicate higher parent-reported family impact.[22,25]

Health-related quality of life (HRQoL): The Dutch version of the Pediatric Quality of Life Inventory™ Generic Core Scale 4.0 (PedsQL™ GCS 4.0) was used to measure HRQoL.[31,32] This questionnaire is considered to be a valid tool to assess HRQoL and it has been validated for the ABI (both TBI and nTBI) population.[38–40] The questionnaire consists of 23 items and yields a total score (the sum of the 23 items, divided by the number of items answered) and 4 scales; physical functioning (8 items), emotional functioning (5 items), social functioning (5 items), school functioning (5 items).[39] Items in the PedsQL™ are answered on a 0–4 Likertscale (0 = never to 4 = almost always) and thereafter linearly transformed to a 0–100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0). Lower scores indicate diminished HRQoL.[39]

Child and family functioning: To gather a broad perspective on family functioning we wanted to investigate if it is necessary to use added questions (from another validated outcome measure regarding child and family functioning) on the same construct as the used validated outcome measures (PedsQL™ FIM and PedsQL™ GCS 4.0) to and strengthen findings. Poor to moderate correlation between added validated questions and an outcome measure could mean that added questions are needed to gather a broader perspective. Therefore, we added seven additional questions regarding both the patients' and their family's potential disabilities in daily life from the validated Child and Family Functioning Scale–Dutch language version (CFFS-DLV) questionnaire.[41,42] Parents were asked about (Question [Q] 1 and 2) the presence of premorbid problems (i.e., learning and/or behavioral and/or health-related, yes/no) and the presence of current problems (i.e., learning and/or behavioral and/or health-related, yes/no). They were also asked (Q3 and 4) to rate their child's current physical and mental/emotional health using a Likertscale (1 = a lot of problems to 5 = no problems), their child's current quality of life (Q5: QoL, 1 = bad to 5 = excellent), and the QoL of the whole family (Q6:1 = bad to 5 = excellent). For questions 3–6, answers were further divided into two categories: good health or QoL (Likert scores 3–5) or diminished health or QoL (Likert scores 1–2). Finally, (Q7) parents were asked if they currently experienced a lack of support or guidance related to their child's ABI (yes/no).

Parent and family questions: Parents also completed questions regarding family-related characteristics; does the patient live in a single parent household (yes/no), are there siblings present (yes/no), does the patient live without his/her parents (yes/no), and the parents' educational levels (low [prevocational practical education or less]/intermediate [prevocational theoretical education and upper secondary vocational education]/high [secondary education, higher education and/or university level education]).[2,42] For this study, only data from parents who completed all questionnaires and outcome measures (PedsQL™ FIM and the PedsQL™ GCS 4.0) was used.

Hypotheses related to family impact

Previous literature, merely pertaining to patients with ABI in hospital-based cohorts, studied patients' demographics, injury and family-related characteristics influencing family impact cause, severity, social economic status (based on educational level parents), and single-parent households.[12,15–29] In our study, we examined whether these findings also hold for patients with an ABI in an outpatient rehabilitation cohort. Furthermore, we added four hypotheses to investigate other factors possibly influencing outcomes in our cohort:

- Parents of patients with a higher age will report higher family impact after ABI compared to parents of patients with a younger age (i.e., the higher the patient's age, the higher the

parent reported family impact), due to the transitional age phase and expected roles and responsibilities in society of older patients.
- Patient and family functioning factors (i.e., premorbid and current learning/behavioral/ health problems; diminished quality of life of the patient; diminished quality of life of the whole family; diminished physical health of the patient; diminished mental/ emotional health of the patient) are related to higher family impact.
- Shorter time between onset of ABI and referral to rehabilitation is associated with higher family impact, since early referral is mostly due to more problems in daily life directly after ABI onset.
- Diminished pediatric health-related quality of life (HRQoL) is related to higher family impact.

Statistical analysis

Descriptive statistics were used for all variables and outcomes. All continuous variables were expressed as medians with interquartile range (IQR) or means with standard deviation (SD), based on their distributions (Kolmogorov–Smirnoff test). To assess the correlation between the outcome measure (PedsQL™ GCS 4.0 for HRQoL) and the added (CFFS-DLV) questions, Pearson correlations were used (poor to fair agreement below 0.40: poor; between 0.41 and 0.60: moderate; between 0.61 and 0.80 good; above 0.81: excellent [43]).

To investigate which factors (independent variables) were related to family impact (PedsQL™ FIM total score and scale scores: dependent variables), univariate linear regression analyses were used. Thereafter (after checking for multicollinearity), multivariable linear regression analyses were used to further assess risk-factors regarding family impact.

Univariate linear regression analyses: The following factors were entered independently, one at the time: Demographic/injury/family related: cause of ABI (TBI/nTBI), severity levels of TBI (mild or moderate/severe), timing of referral to rehabilitation after onset of ABI (< 6 months/ > 6 months), educational levels parent (low/medium-high), single-parent household (yes/no), living with parents (yes/no), the absence of siblings (yes/no), age (continuous), patient/family functioning: pre-morbid problems (learning and/or behavioral and/or health-related problems, yes/no), more than 2 pre-morbid problems (yes/no), having more than 2 current learning and/or behavioral and/or health related problems (yes/no), quality of life of the whole family (diminished/good), quality of life of the patient (diminished/good), physical health (diminished/good), mental/emotional health (diminished/good), and parents experiencing a lack of support regarding their child's ABI (yes/no). Finally, the PedsQL™ GCS 4.0 for HRQoL (independent variable) was entered as continuous variable.

Multivariable linear regression analysis: Multivariable linear regression analysis was performed with only those variables with p-values < 0.20 in the univariate analysis.

Outcomes (for both univariate and multivariable regression) were expressed as β-estimates with 95% confidence intervals (95% CI) and p-values (level of significance $p < 0.05$). All data were analyzed using SPSS software, version 22.0 (IBM SPSS statistics for Windows, Armonk, NY: IBM Corp).

RESULTS

Patients' demographic/injury/family-related characteristics

Families of 246 patients with ABI participated in this study (Figure 1). The patients' median age was 14 years (IQR 11–16), with 127 (52%) being female. There were 181 patients (74%) with TBI, of whom 143 had a mild injury (78%). Of the 65 patients with nTBI, 25 (40%) had a brain tumor. One-hundred and-forty-seven (60%) patients were referred to a rehabilitation center less than 6 months after onset of ABI. The largest percentage of patients lived with their parent(s) (97%), with 17% (42) living in a single-parent household. Twenty-eight of the parents (11%) had a low educational level (Table 1).

Patient/family functioning (CFFS-DLV)

Seventy-one (29%) patients had premorbid learning/behavioral/health-related problems, 200 patients (81%) currently have more than 2 learning/behavioral/health-related problems. One-hundred-seventy-seven parents (72%) reported both diminished mental/emotional and physical health of their child, and 64 (26%) reported diminished quality of life of the whole family. Finally, 122 parents (50%) currently experience a lack of help and guidance related to their child's injury (Table 2).

Family impact scores and parent reported HRQoL

In Table 3 the results regarding the parent-reported family impact and patient HRQoL are presented. The total median PedsQL™ FIM score was 71.9 (IQR 60–85). The lowest scores (i.e., more problems) were found on the worrying scale (median 65.0, IQR 50–80). The highest scores (i.e., fewer problems) were found on the communication scale (median 83.3, IQR 58–100). For the parent-reported patients' HRQoL, the total median score was 60.9 (48–75). The lowest scores were found on the school/work functioning scale (median 50.0, IQR 30–60) and the highest on the social functioning scale (median 75.0, IQR 60–95).

Correlations between different measures of parent reported HRQoL

A poor–moderate correlation (0.38–0.51) was found between the PedsQL™ GCS 4.0 (total score and both mental/emotional and physical scale scores) and the additional questions from the CFFS-DLV (parent-reported questions about their child's quality of life and mental/emotional and physical problems) (Appendix).

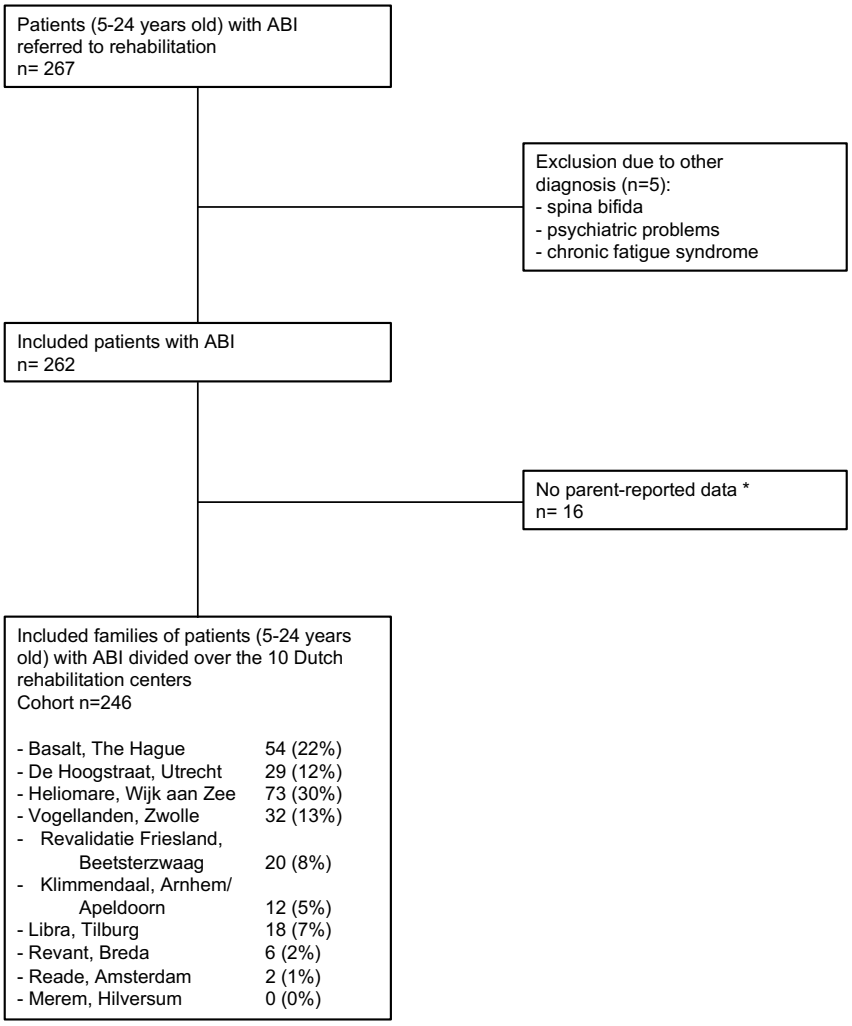

Figure 1. Flow diagram of the 246 patients and their families eligible to participate in this study
*In the Netherlands, children ≥ 16 years old have the legal right to exclude their parents from healthcare decision making.

Table 1. Patients' demographic/injury/family characteristics of 246 children and young adults with acquired brain injury (ABI) referred for outpatient rehabilitation treatment

	Cohort n= 246
Demographic characteristics	
Sex: female; number (%)	127 (52%)
Age (years) at referral; median (IQR)	14 (11-16)
- 5-11 years old; number (%)	76 (29%)
- 12-17 years old; number (%)	134 (56%)
- 18-24 years old; number (%)	36 (15%)
Time(months) between the onset & referral to rehabilitation;	
- Less than (<) 6 months; number (%)	147 (60%)
Injury characteristics	
Traumatic brain injury (TBI); number (%)	181 (74%)
Severity levels of TBI (based on GCS*); number (%)	
- Mild	143 (78%)
- Moderate-severe	18 (10%)
- Unknown	20 (12%)
Non-traumatic brain injury (nTBI); number (%)	65 (26%)
Causes nTBI; number (%)	
- Brain tumor	25 (40%)
- Stroke	15 (24%)
- Hypoxia/intoxication	2 (3%)
- Encephalitis/meningitis	11 (18%)
- Other	9 (15%)
Family characteristics	
Living with their parents; number (%)	238 (97%)
Living in a single-parent household; number (%)	42 (17%)
Having (a) sibling(s); number (%)	214 (87%)
Educational level parents; n (%) #	
- Low	28 (11%)
- Intermediate	108 (44%)
- High	110 (45%)

* Glasgow Coma Scale # Educational level parent: low; prevocational practical education or less, intermediate; prevocational theoretical education and upper secondary vocational education, high; secondary education, higher education and/ or university level education.

Demographic/illness/family factors related to family impact

In the univariate regression analyses (Tables 4a and 4b) the cause of ABI (nTBI), a single-parent household and lower parental educational levels were significantly associated with higher family impact (lower PedsQL™ FIM scores, $p < 0.05$). Furthermore, the time between referral to rehabilitation and the onset of ABI more than 6 months (> 6 months) was significantly associated with higher family impact (lower FIM scores).

Table 2. Child and family functioning in 246 families of children and young adults, aged 5–24 years old, with acquired brain injury (ABI) referred for outpatient rehabilitation treatment.

	Cohort n= 246
*Child and family functioning**	
Patients with Pre-morbid problems; number (%)	71 (29%)
- Learning-related	37 (15%)
- Behaviour-related	28 (11%)
- Health-related	33 (13%)
- More than 2 premorbid problems reported	20 (8%)
Patients with current problems; number (%)	230 (94%)
- Learning-related	207 (84%)
- Behaviour-related	160 (65%)
- Health-related	179 (73%)
- More than 2 current problems reported	200 (81%)
Child functioning; number (%)	
- Diminished physical health	111 (45%)
- Diminished mental/emotional health	158 (64%)
- Both diminished mental/emotional and physical health	177 (72%)
- Diminished quality of life	119 (48%)
Family functioning; number (%)	
- Diminished quality of life of the whole family	64 (26%)
- Experiencing a lack of help and/or guidance related to the child's ABI	122 (50%)

*Parent-reported questions, from the Dutch version of the Child and Family Functioning Scale (CFFS-DLV).[2,3]

Patient/family functioning factors related to family impact

In the univariate regression analyses (Tables 4a and 4b), currently having either mental/emotional or physical, or both mental/emotional and physical health problems, the presence of pre-morbid problems, and parent-reported diminished QoL of the whole family were significantly associated with higher family impact (lower PedsQL™ FIM scores, $p < 0.05$).

Demographic/illness/family and patient/family functioning related factors in the multivariable regression model

After checking for multicollinearity (there were none) all the variables with $p < 0.20$ (demographic/illness/family and patient/family functioning related factors) from the univariate analyses were used in the multivariable regression analyses (marked as Bold values in Tables 4a and 4b). NTBI, parent-reported patients' diminished mental/emotional health, and diminished quality of life for the whole family remained significantly associated with higher family impact (lower PedsQL™ FIM scores).

Table 3. Family Impact and health related quality of life of 246 children and young adults, aged 5-24 years old with acquired brain injury (ABI) referred for outpatient rehabilitation treatment

			Median	Interquartile range (IQR)
PedsQL™ Family impact module (FIM)	Total score*		71.9	(60-85)
	Scale scores*	Worrying	65.0	(50-80)
		Communication	83.3	(58-100)
		Family functioning summary scale	75.0	(59-94)
		- Daily activities	75.0	(50-100)
		- Family relations	75.0	(60-95)
		Parental health-related quality of life	72.5	(60-86)
		- Physical Functioning	66.7	(50-83)
		- Emotional Functioning	70.0	(55-90)
		- Social functioning	81.3	(63-100)
		- Cognitive functioning	85.0	(60-100)
PedsQL™ Generic Core Set 4.0	Total score*		60.9	(48-75)
	Scale scores*	- Physical and social health summary score	68.6	(47-82)
		- Physical Functioning	60.0	(47-17)
		- Emotional Functioning	60.0	(40-75)
		- Social functioning	75.0	(60-95)
		- School/work functioning	50.0	(30-60)

*For all outcomes 0 to 100, lower scores indicate higher parent-reported family impact (PedsQL™ FIM) and poorer health-related quality of life (PedsQL™ Generic Core set).

Family impact related to HRQoL

In the univariate analyses diminished parent-reported HRQoL was significantly associated with higher family impact on the total score and almost all scale-scores ($p < 0.05$, except for physical functioning [$p < 0.20$]). All outcomes can be found in Table 4c.

Table 4a. Demographic/injury/family factors associated with family impact in a cohort of 246 children and young adults, aged 5–24 years old with acquired brain injury (ABI) referred for outpatient rehabilitation treatment.

PedsQL™ Family Impact Module	Total score β (95% CI)	Worrying β (95% CI)	Communication β (95% CI)	Family functioning summary scale β (95% CI)	Parental health-related quality of life (HRQoL) β (95% CI)
Demographic related factors					
Age at onset of ABI	-0.2 (-0.8, 0.3)	0.1 (-0.6, 0.7)	0.3 (-0.5, 1.0)	-0.2 (-0.9, 0.5)	-0.4 (-1.0, 0.2)
Referral to rehabilitation < 6 months	5.5 (1.3, 9.6) **	6.4 (1.5, 11.3) **	12.4 (6.7, 18.0) ***	4.2 (-0.8, 9.2) *	4.7 (-0.1, 9.3) *
			7.4 (12.9, 1.9)		
Injury related factors					
nTBI	-7.9 (-3.4, -12.5) **	-10.4 (-5.0,-15.8)***	-10.9 (-4.6, -17.4)**	-8.2 (-2.6,-13.7)**	-6.8 (-1.8, -11.8) **
	-4.8 (-8.9, -0.7)	**-8.1 (-13.4, -2.8)**			
Moderate/severe TBI	3.6 (-11.5, -4.3)	-0.01 (9.4, -9.4)	-5.4 (5.5, -16.3)	-8.0 (-17.3, 1.3) *	-4.1 (-12.9, 4.8)
Family related factors					
Single parent household	-7.6 (-2.2, -12.9) **	-5.9 (0.5, -12.4) *	- 7.5 (0.1, -15.1) *	-8.9 (-2.4,-15.4)**	-7.4 (-1.5, -13.3) *
Lowest educational level parent	-20.7 (-39.4, -2.0)**	-23.2 (-45.3, -0.9) **	-28.4 (-54.4, -2.5)**	-16.2 (-38.7, 6.4)*	-20.7 (-41.2, -0.3)**
Absence of siblings	-5.7 (11.8, -0.4) *	-2.4 (-9.6, 4.9)	-13.3 (-21.7, 4.8) **	-4.9 (-12.2, 2.4) *	-5.6 (-12.3, 1.0) *
			-8.4 (-0.7, -15.9)		

Linear regression analyses, data presented as β-estimates, 95% confidence interval (95% CI). PedsQL™ Family Impact Module (FIM, 0-100, with lower scores indicating more parent-reported family impact.): dependent variables and possible factors influencing family impact: independent variables.
* p < 0.20; ** p < 0.05, *** p < 0.001 Significant factors, and included in the multivariable regression analyses (done with only factors entered which were significantly associated (*p* <0.2) with FIM scales according to the univariate analysis).
Multivariable regression: **Bold scores:** p < 0.05 significant variable in the multivariable regression analyses.
health/learning/behavioural problems.

Table 4b. Child and family functioning factors associated with family impact in a cohort of 246 children and young adults, aged 5–24 years old with acquired brain injury (ABI) referred for outpatient rehabilitation treatment.

PedsQL™ Family Impact Module	Total score β (95% CI)	Worrying β (95% CI)	Communication β (95% CI)	Family functioning summary scale β (95% CI)	Parental health-related quality of life (HRQoL) β (95% CI)
Related child functioning factors					
Premorbid problems #	-6.2 (-1.7, -10.7)**	-6.9 (-1.7, -12.3)**	-6.7 (-0.4, -13.0)**	-7.0 (-1.7,-12.4)**	-5.6 (-0.7, -10.5)**
				-7.9 (-14.8, -1.1)	
More than 2 premorbid problems	-11.6 (-4.2,-19.0)***	-14.8 (-6.1, -23.6)**	-12.9 (-2.5, -23.3)**	-6.2 (-16.3, 3.8)*	-11.1 (-2.9, -19.2)**
	-6.3 (-12.6, 0.01)	-8.2 (-19, -14.3) **	-5.8 (1.5, -13.2)*	-1.5 (4.9, -7.8)	-4.7 (1.0, -10.5)*
More than 2 current problems #	-13.9 (-10.0,-17.9)***	-13.4 (-8.6,-18.2)***	-16.0 (-10.4,-21.7)***	-13.8 (-8.9,-18.6)***	-13.9 (-9.6,-18.3)***
Diminished mental/emotional health	**-10.6 (-17.5, -3.6)**		**-11.2 (-21.4, -1.1)**		**-13.5 (-21.5, -5.6)**
	-8.0 (-4.0, -12.0)***	-9.9 (-5.2, -14.7)***	-7.8 (-2.0, -13.5)**	-7.9 (-3.1, -12.8)**	-7.6 (-3.2, -12.0)**
Diminished physical health	-13.3 (-9.0, -17.5)***	-14.8 (9.7, 19.9)***	-14.8 (-8.6, -21.0)***	-14.4 (-9.2, -19.6)***	-12.2 (-7.4, -16.9)***
Diminished mental/emotional and physical health					
Related family functioning factor					
Diminished QoL of the whole family	-17.9 (-13.8, -22.1)***	-13.4 (-8.1, -18.7)***	-20.5 (-14.5, -26.6)***	-20.9 (-15.9,-25.9)***	-17.6 (-12.9,-22.2)***
	-12.9 (-17.2, -8.5)	**-6.4 (-11.9, -0.7)**	**-12.6 (-19.1, -6.2)**	**-17.9 (-24.6, -10.9)**	**-12.8 (-17.8, -7.7)**

Linear regression analyses, data presented as β-estimates, 95% confidence interval (95% CI). PedsQL™ Family Impact Module (FIM, 0-100, with lower scores indicating more parent-reported family impact.): dependent variables and possible factors influencing family impact: independent variables.
* $p < 0.20$; ** $p < 0.05$, *** $p < 0.001$ Significant factors, and included in the multivariable regression analyses (done with only factors entered which were significantly associated ($p < 0.2$) with FIM scales according to the univariate analysis).
Multivariable regression: **Bold scores:** $p < 0.05$ significant variable in the multivariable regression analyses.
health/learning/behavioural problems.

Table 4c. Patients' health related quality of life associated with family impact (FIM) in a cohort of 246 children and young adults, aged 5–24 years old with acquired brain injury (ABI) referred for outpatient rehabilitation treatment.

PedsQL™ Family Impact Module	Total score β (95% CI)	Worrying β (95% CI)	Communication β (95% CI)	Family functioning summary scale β (95% CI)	Parental health-related quality of life (HRQoL) β (95% CI)
PedsQL™ generic core-4.0 (HRQoL)					
Total score	0.6 (0.5, 0.7) ***	0.6 (0.4, 0.7) ***	0.4 (0.3, 0.6) ***	0.6 (0.4, 0.7) ***	0.6 (0.5, 0.7) ***
Physical functioning	0.2 (0.2, 0.3) ***	0.3 (0.1, 0.4) ***	0.1 (-0.04, 0.2) *	0.3 (0.2, 0.4) ***	0.3 (0.2, 0.3) ***
Emotional functioning	0.5 (0.4, 0.5) ***	0.5 (0.4, 0.6) ***	0.4 (0.3, 0.5) ***	0.4 (0.3, 0.5) ***	0.5 (0.4, 0.5) ***
Social functioning	0.4 (0.3, 0.5) ***	0.4 (0.3, 0.5) ***	0.5 (0.3, 0.6) ***	0.4 (0.3, 0.5) ***	0.4 (0.2, 0.4) ***
School/work functioning	0.3 (0.2, 0.3) ***	0.2 (0.1, 0.3) ***	0.2 (0.04, 0.3) **	0.2 (0.1, 0.3) ***	0.3 (0.2, 0.4) ***

Univariate regression analyses, data presented as β-estimates, 95% confidence interval (95%CI). PedsQL™ Family Impact Module (FIM, 0-100, with lower scores indicating more parent-reported family impact.): dependent variables and possible factors influencing family impact: independent variables.

* $p < 0.20$; ** $p < 0.05$, *** $p < 0.001$ Significant factors.

DISCUSSION

In this cross-sectional study including 246 families of children and young adults (aged 5–24 years old) with ABI, referred to rehabilitation for outpatient treatment, we found a substantial parent reported family impact (median; 71.9 IQR; 60–85). Associated factors related to higher family impact were having nTBI, referral to rehabilitation > 6 months after onset, diminished mental/emotional health, diminished HRQoL of the whole family, and the presence of premorbid learning/behavioral/health-related problems. Family impact was specifically greater when a patient had nTBI, when parents reported that mental/emotional health and HRQoL of the whole family was diminished. Finally, a diminished parent-reported HRQoL was significantly associated with higher family impact on all domains of the PedsQL™ FIM.

Family impact

Until now, knowledge regarding family impact of families with patients (children/young adults) with ABI who were referred for rehabilitation treatment remained scarce. Only one study (with a small sample size of only 10 patients with TBI, and no outcome measures) reported that pediatric TBI affects the whole family and that parents experienced emotional distress and worrying as was in line with our study.[25] It is generally acknowledged that five stages are recognizable in every emotional response to personal trauma and change: denial – anger –bargaining – sadness/depression – acceptance (Kübler-Ross model). However, this is not as a linear process that everyone goes through step by step, nor will everyone go through all steps. Several factors determine the impact of pediatric ABI on a family of which time is one. We found in our cross-sectional study that a longer time since onset was related to higher family impact. How families move through the different phases of emotional response, how family impact truly changes over time and what the possible influence of cognitive and personality changes of the patient have on this needs to be investigated in future longitudinal studies. When compared to a Dutch hospital-based ABI cohort (in children and young adults), the family impact scores in our study are consistently lower, meaning more impact:[19] median total PedsQL™ FIM score; 71.9 (our study) versus mean; 82.9 (hospital-based cohort). For the scale scores regarding our cohort versus hospital-based cohort: parental HRQoL; 72.5 versus 85.4, family functioning; 75.0 versus 81.7, communication; 83.3 versus 100, worrying; 65.0 versus 90.0.[19] These results were in line with our expectations that parents in our rehabilitation-based cohort report higher family impact than those in other (hospital-based) cohorts. This could be due to the persisting problems in patients' functioning, activities, and participation, at time of referral in our cohort for which they were referred to a rehabilitation center. Compared to an American cohort with parents of children with healthy children and children with a chronic condition we found

similar family impact (mean total PedsQL™ FIM score: 80.4 [SD 16.1] for healthy children, and 70.8 [SD 14.5] for children with a chronic condition,[21] respectively, while 2 hospital-based studies in patients with nTBI (in a brain tumor and stroke population) found higher family impact than we found (mean total PedsQL™ FIM scores 58.8 [SD 16.9] and 53.4 [SD 17.4], respectively).[18,22] Nonetheless, due to small sample sizes, differences in health care systems (in the Netherlands and in the USA), and differences between subjects and causes (TBI, nTBI and/or both), these similarities have to be interpreted with caution.

Factors related to family impact, outcomes in hospital-based cohorts compared to a rehabilitation-based cohort

Previously found factors influencing family impact in hospital-based cohorts (i.e., cause, severity, educational levels of parents, and single parent households) were tested in our rehabilitation cohort with pediatric patients with ABI as well and we found generally the same influence.[12,15-29] This study confirmed that having nTBI results in higher family impact than having TBI. This can possibly be explained by the wide variety of causes, and outcomes of nTBI. These patients with nTBI probably faced a more complex and longer hospital treatment and uncertain prognosis than the patients with TBI in our cohort (with similar severity).[18,22] Lower educational levels of parents and patients living in single-parent households also resulted in significantly higher family impact, which confirmed both our expectations and findings in previous studies.[23,24,26]

A systematic review containing hospital-based cohorts only and patients with moderate-severe (based on Glasgow coma scale) TBI showed that higher injury severity levels in patients with moderate-severe TBI resulted in higher family impact.[15] The differences in outcome between our study and previous studies can be partially explained by difference in type of patient included, and our relatively small sample size of the moderate/severe group (n = 18) compared to the mild group (n = 143). In future studies, the family impact should be monitored over time as the impact may persist over time, also for the group of patients with mild TBI. Furthermore, almost half of the parents in our study were experiencing a lack of help/information concerning their child's ABI. This could result in worrying about the child's future or frustration toward health care professionals. It is thus important that patients and parents receive the appropriate information in a timely manner as this could decrease the family impact.

Age related to family impact

Regarding age, this study found that age is not a significant factor related to family impact. These results differ from previous studies, where age was presented as an associated factor.[15,19] In the whole age range in this cohort there is a substantial impact on the family after a child suffered from ABI, no matter the age.

Patient and family functioning factors related to family impact (CFFS-DLV)

This study also supports the use of specific questions regarding child/family functioning (CFFS-DLV questions).[41,42] All additional questions on functioning had a poor-moderate correlation with the PedsQL™ GCS 4.0 (on the total score and the emotional functioning scale).[39] A poor correlation suggests that questions, additional to standardized outcome measures are probably needed to create a broader perspective on QoL and child/family functioning. Next to the standardized outcome measures, we used the above-described additional questions and as we assumed (more than 2) premorbid health and/or learning and/or behavioral related problems was significantly related to higher family impact in our study. This was also reported in previous studies.[19,31] It could be explained by the fact that premorbid existing problems already caused family impact before the onset of the brain injury. Patients who were having (more than 2) current health- and/or learning and/or behavioral related problems (n = 230, 94%) also related to higher family impact, confirming that almost all patients referred for rehabilitation treatment perceive daily life problems at that point. Diminished mental/emotional or physical problems (or both) in daily life also related to significantly higher family impact, which also confirmed our expectations. Finally, parents reporting diminished quality of life of the whole family was significantly related to higher family impact. These findings underline the importance of involving the families in the rehabilitation treatment programs. This could for example be done by providing tailor-made psychoeducation, follow-up and support for parents, brothers and sisters and/or by including families in home-based therapy activities. To what extent this could contribute to reducing family impact must be further examined.[34,35]

Time between onset and referral related to family impact

Referral to (one of the 10 participating) rehabilitation centers less than 6 months after the onset of ABI was significantly associated with less family impact (i.e., higher scores) on the PedsQL™ FIM total score, worrying scale and communication scale. An explanation could be that the earlier the referral, the sooner parents felt that they were being helped and heard by healthcare professionals, which could positively influence family impact contrary to late referral (> 6 months). Furthermore, a large portion of recovery after ABI occurs in the first months after onset, when parents tend to worry less.[2,10] Despite the late referral to rehabilitation (> 6 months), 54 families (44.3%) of patients that were referred to the rehabilitation after 6 months still experienced a lack of help/information regarding their child's ABI diagnosis, worry more about their child's future (mean FIM worrying scale: for < 6 months; 67.0 SD; 18.3, for > 6 months; 60.0 SD; 21.0), or see less reduction of symptoms (due to natural adaptation/recovery of the brain) than they expected. In hospital-based cohorts of pediatric patients with ABI, it is known that the long-term outcome is related to family and environmental factors (including family cohesion, resources, social support,

socioeconomic status) and persisting parental stress.[5,16,28] Families in rehabilitation-based cohorts are presumably in another stage of grief at the time of referral to rehabilitation, and parental stress may still be present. Helping parents cope with this stress may influence outcomes in terms of family impact. However, we did not study this, and future research should focus on longitudinal outcomes of family impact and how this relates to parental stress in rehabilitation-based cohorts. We hypothesized that a longer time between the onset of the ABI and referral to rehabilitation would result in lower family impact. However, the opposite was true. Findings in our study underline the importance of assessing and monitoring family impact on the long-term and timely referral to rehabilitation programs for children and young adults so that treatment can begin before family impact increases.

HRQoL related to family impact

This study confirmed the assumption that diminished HRQoL was significantly associated with higher family impact. We found one study (in patients with ADHD) with similar results.[31] Aiming to positively influence health-related quality of life during (family centered) rehabilitation treatment could possibly decrease family impact.[34,35]

PedsQL™ FIM

This study used the PedsQL™ FIM to measure parent-reported family impact. Neither cutoff scores nor minimal clinically important differences (MCID) are available for the FIM. The PedsQL™ FIM has been proven to be a valid and reliable tool to measure family impact in families of patients with a (chronic) disease or impairment.[19,21,33] Furthermore, it has been used previously in patients diagnosed with ABI and it has been translated and validated into the Dutch language.[19] Therefore, we recommend using the PedsQL™ FIM in future ABI studies to further investigate the psychometric properties (including cutoff scores and MCIDs) in this patient population.

Study limitations

This study had a number of limitations. We collected only parent-reported data. It needs to be considered whether only the parents' perspective on family impact is enough to measure family impact,[27] i.e., the siblings or professional perspective regarding family impact were not taken into account. Future research should consider including other perspectives to investigate family impact in children and young adults with ABI. Furthermore, the results of questionnaires could be biased by limitations of language comprehension, motivation, or parental stress and mood at the moment of completing the questionnaire. For 20 patients with TBI (12%), although registered by healthcare professionals as TBI, no Glasgow Coma Scale (GCS) score to classify the severity was available. Finally, our population was rather diverse in terms of cause and severity of ABI which may have influenced outcomes as well.

CONCLUSIONS

Acquired brain injury in children and young adults results in a substantial impact on families. The most significant risk factors related to higher family impact were: time of referral to rehabilitation more than 6 months after the onset of ABI, presence of premorbid (health/learning/behavioral) problems, diminished mental/emotional health of the patient. Diminished health-related quality of life of the patient was also significantly associated with higher family impact. The patient's age was found to be a non-significant factor related to family impact. This study underlines the importance of measuring and monitoring family impact in the outpatient rehabilitation setting. Future longitudinal follow-up studies are needed to further decrease the knowledge gap on family impact in rehabilitation after pediatric ABI.

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Appendix. Correlations between the PedsQL™ GCS 4.0 and the parent-reported questions as part of the CFFS-DLV in 246 families of children and young adults, aged 5–24 years old with acquired brain injury (ABI) referred for outpatient rehabilitation treatment.

Assessed correlations

PedsQL™ GCS 4.0	CFFS-DLV	Correlation#
PedsQL™ GCS 4.0 Total Score[1]	Parent-reported Quality of life	0.44 (moderate)
PedsQL™ GCS 4.0 Physical functioning scale score[2]	Parent-reported physical health problems	0.38 (poor)
PedsQL™ GCS 4.0 Emotional functioning scale score[3]	Parent-reported mental/ emotional health problems	0.51 (moderate)

Pearson Correlation: poor to fair agreement below 0.40: poor; between 0.41 and 0.60: moderate; between 0.61 and 0.80 good; above 0.81: excellent.[43]
[1] Correlations between parent reported quality of life and PedsQL™ GCS 4.0 for HRQoL.
[2] Correlations between parent reported physical health and PedsQL™ GCS 4.0 Physical functioning scale score.
[3] Correlations between parent-reported mental/emotional health and PedsQL™ GCS 4.0 Emotional functioning scale score.

CHAPTER 6

A longitudinal follow-up study of parent-reported family impact and quality of life in young patients with traumatic and non-traumatic brain injury

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ABSTRACT

Purpose

Brain injuries (traumatic-/nontraumatic, TBI/nTBI) in young patients may lead to problems e.g., decreased health-related-quality of life (HRQoL), and causes family impact. Knowledge regarding family impact and the relationship with patients' HRQoL over time is scarce. This follow-up study describes family impact/HRQoL and their mutual relationship in young patients (5–24 years) after TBI/ nTBI.

Materials&methods

Parents of patients that were referred to outpatient rehabilitation completed the PedsQL™ Family-Impact-Module questionnaire to assess family impact and the parent-reported PedsQL™ Generic-core-set-4.0 to assess patients' HRQoL (lower scores: more family impact/worse HRQoL). Questionnaires were completed at time of referral to rehabilitation (baseline) and one/two years later (T1/T2). Linear-mixed-models were used to examine family impact/HRQoL change-scores, and repeated-measure correlations (*r*) to determine longitudinal relationships.

Results

Two-hundred-forty-six parents participated at baseline, 72 (at T2), median patient's age at baseline was 14 years (IQR: 11-16), and 181 (74%) had TBI. Mean (SD) PedsQL™ Family-Impact-Module score at baseline was 71.7 (SD: 16.4) and PedsQL™ Generic-core-set-4.0: 61.4 (SD: 17.0). Over time, PedsQL™ Family-Impact-Module scores remained stable, while PedsQL™ Generic-core-set-4.0 scores improved significantly ($p < 0.05$). A moderately strong longitudinal correlation was found between family impact & HRQoL ($r = 0.51$).

Conclusions

Family impact does not tend to decrease over time but remained a considerable problem, although patients' HRQoL improved. Next to focusing on patients' HRQoL, it remains important to consider family impact and offer family-support throughout rehabilitation.

Keywords: Rehabilitation; family impact; quality of life; young patients; traumatic brain injury; nontraumatic brain injury

INTRODUCTION

Acquired brain injury (ABI) is common among children, adolescents, and young adults under the age of 25 years and can be categorized into traumatic brain injury (TBI; caused by external trauma) and non-traumatic brain injury (nTBI; internal causes).[1,2] Due to natural brain adaptation, it is expected that in approximately 70% of all ABI cases, most problems experienced by patients reduce within the first year after onset.[3-11] However, about 30% remain with persistent problems that could considerably affect daily life functioning, where the severity of the problems is often related to the type and severity of the initial injury.[3-11] These problems can have a significant negative impact on the patient's daily life functioning, participation, health-related quality of life (HRQoL) and it can have an impact on the whole family as well.[3-11] TBI or nTBI is a critical and often acute life event in young people and may lead to a considerable impact on the family. The impact can be emotional, social, or financial and include consequences such as increased stress, worrying, and changes in the families' routines, roles, and responsibilities.[8,11] The impact on the family may be particularly substantial in patients with persistent problems, a subgroup of about 30% of all patients.[3-11] Some of these patients are referred to multidisciplinary rehabilitation, mostly provided in an outpatient rehabilitation setting.[12-15]

Previous literature has emphasized the existence of family impact during all stages of recovery of young patients with both TBI and nTBI, i.e., in the acute, subacute, and rehabilitation stages.[3,8,11,16-22] One of those studies described various factors that negatively influenced family impact at the time of referral to rehabilitation. These factors included the time between brain injury onset and referral to rehabilitation of more than six months and the presence of pre-morbid problems in the child.[3] Furthermore, having nTBI resulted in more family impact compared to having TBI.[3] Previous studies also described the relationship between higher parent-reported family impact and a decreased patients' HRQoL in young patients with chronic diseases, including both TBI and nTBI.[3,16,17,20,23,24] However, most of these studies only reported cross-sectional relations,[3,20] only studied an adult population,[16] or only assessed this relationship in patients with either only general chronic health conditions,[24] or only severe TBI and/or nTBI.[17,23,24] Longitudinal studies, among young children with TBI, found that families experience a long-lasting impact related to their child's injury for more than 12 months.[25-28] This was also found in two studies among adult patients with TBI.[29,30] However, these studies only included patients with TBI, and patients with more severe injuries only considered a limited age range of patients (only children or only adults), or only looked at limited aspects of family functioning.[25-30]

To date, knowledge regarding the course of family impact and patients' HRQoL over time in families of young patients in the rehabilitation phase is scarce. Therefore, this study aims to describe differences between patients with TBI and nTBI regarding the family impact and patients' HRQoL, to describe the course of parent-reported family impact, as well as parent-reported patients' HRQoL over time in young patients with TBI or nTBI (5-24 years old), referred for outpatient rehabilitation. Furthermore, this study aims to determine the longitudinal relationship between family impact and patients' HRQoL.

We hypothesize that family impact has decreased and patients' HRQoL has improved two years after referral to rehabilitation. Furthermore, we hypothesize that family impact decreases less in patients with nTBI compared to TBI. Finally, we hypothesize that there is a longitudinal relationship between a decrease in family impact and an improvement in patients' HRQoL.

METHODS

Design

This longitudinal study was part of a Dutch observational multicentre cohort on family impact, fatigue, participation, and quality of life among young patients (5-24 years) with ABI and their families in the outpatient rehabilitation setting.[3,31] The multicentre study was carried out between 2015 and 2019 in ten rehabilitation centers in the Netherlands that were specialised in treating young patients with acquired brain injury. The multicentre study protocol was reviewed by the medical ethical review board of the Leiden University Medical Centre (P15.165), with an exemption from full medical ethical review being provided as the data were collected as part of routine care. All local research committees from the participating centers approved the study as well. All data used in the multicentre study were anonymised before analysis and securely stored in a central database by a data manager at Basalt Rehabilitation (The Hague, The Netherlands). In the current study, only parent-reported data were used. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were used for the reporting of the results.[33]

Participants

Participants in the current study were parents of young patients (5-24 years) with ABI that were referred by a family practitioner or medical specialist to one of the ten outpatient rehabilitation centers. Participants were not eligible if they were unable and/or limited to write and/or understand the Dutch language. The current study included 246 parents with a child with either a TBI or nTBI between 5-24 years old admitted for rehabilitation in one

of the participating centres. More than half of the patients (52%) were female and 74% of the patients had a diagnosis of TBI, which provided us with a good cross-section of the general Dutch ABI population.[1,34]

Assessments

Patient and family characteristics: At baseline, the patient's demographics- and injury characteristics were collected from their medical records by the treating physician i.e., sex (male/female/other), age, and the cause of brain injury, which was divided into a TBI group, a nTBI group, and a total group. TBI severity levels were divided into three groups: mild and moderate/severe/'unknown' (based on the Glasgow coma scale [35]). If the GCS was unknown but there was no history of conscious loss, the severity level was also considered 'mild'. Causes of nTBI were divided into stroke, brain tumours, meningitis or encephalitis, hypoxia or intoxication, and 'other'. Since there are no valid/commonly used instruments to measure nTBI severity, no nTBI severity levels were noted. The time between TBI/nTBI onset (date of injury) and referral to the rehabilitation centre was calculated and divided into 'less than six months' or 'more than six months' after onset (< 6 months/ > 6 months). The family characteristics included: single-parent household/two parents, siblings/no siblings, the cultural background of the parents (Dutch/non-Dutch), and parents' educational levels (low (prevocational practical education or less)/intermediate (prevocational theoretical education and upper secondary vocational education)/high (secondary education, higher education, and university level education)).

Outcome measures: To measure family impact and HRQoL the Pediatric Quality of Life Inventory™ Family Impact Module (PedsQL™ FIM),[36] and the Pediatric Quality of Life Inventory™ Generic Core Scales-4.0 (PedsQL™ GCS-4.0) were used.[37-39] These instruments have good psychometric properties, and they have previously been validated and used among young patients with TBI and nTBI. Dutch language versions for both outcomes were available.[3,21,36,40-42]

- Family impact: The 36-item PedsQ™ FIM questionnaire was used to assess family impact. A four-point Likert scale from 'never' to 'almost always' was used to answer the questions. It yields a total score and four domain scores. The four domains were: 'parental quality of life summary score' (e.g., "I have trouble getting support from others") with twenty items, a 'family functioning summary score' (e.g., "Stress or tension between family members") with eight items, the domain 'worrying' (e.g., "I worry about my child's future") with five items, and the domain 'communication' (e.g., "It is hard for me to talk about my child's health with others") with three items. After completion, the scores were linearly transformed on a scale from 0 to 100 (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0). The total and

domain scores were calculated by the sum of the items answered, divided by the number of items answered, resulting in a score ranging from 0 to 100, where lower scores indicate more (i.e., worse) parent-reported family impact.[36]

- Health-related Quality of Life (HRQoL): The 23-item parent-reported PedsQL™ GCS-4.0 was used to measure patients' HRQoL. It yields a total score and four domain scores, i.e., physical functioning (eight items), emotional functioning (five items), social functioning (five items), and school/work functioning (five items). Scores are calculated in the same manner as with the PedsQL™ FIM. It is also resulting in a score ranging from 0-100 with lower scores indicating lower HRQoL.[37-39]

Procedure

Participants filled out an online questionnaire that contained the above-described outcome measures (PedsQL™ FIM and PedsQL™ GCS-4.0). Before completing the questionnaire, parents (and/or patients where appropriate) signed an informed consent to participate. Prior to the first appointment with the rehabilitation physician (baseline), parents received a link by email to complete an online questionnaire (via www.questback.nl). One year (T1) and two years (T2) after the first appointment, parents were invited to complete the questionnaire again voluntarily.

Statistical Analysis

All data were analysed for the TBI group, the nTBI group, and the total group separately and at the three time points (baseline, T1, and T2). Descriptive statistics were used for all characteristics and variables. Continuous variables were expressed as medians (with interquartile ranges; IQR) or means (with standard deviations; SD), based on their distributions (Kolmogorov–Smirnoff test). Independent sample T-tests were performed to determine differences in outcomes between the TBI and the nTBI groups at all time points and presented as t-values (t), degrees of freedom (Df), and p-values.

To check if the known missing data at T1/T2 were 'missing completely at random' (MCAR) and therefore suitable to use in a linear mixed model (LMM), Little's-test was performed.[43] Results of this test showed that cases were MCAR (Chi-Square of 22.4, p 0.07), allowing analysis in a LMM where missing repeated measures are being corrected within the model.[44] In the LMM, the follow-up time points were the fixed effects, and the participants were the random effects. The PedsQL™ FIM and the PedsQL™ GCS-4.0 scores were expressed as means with standard deviations (SD) at baseline. Change scores (with 95% confidence intervals; 95% CI) were computed between baseline and T1, between T1 and T2, and between baseline and T2. All analyses in the LMM were corrected for age and sex. All

above-described data were analysed using SPSS software, version 28.0 (IBM SPSS Statistics for Mac, Armonk, NY: IBM Corp).

To determine longitudinal correlations between the PedsQL™ FIM and the PedsQL™ GCS-4.0, repeated measures correlations (rmcorr) were used. With this method, the non-independence of repeated measures was considered by determining the relationship between two continuous variables (the PedsQL™ MFS and the PedsQL™ GCS-4.0) where between-patient variance is being controlled.[45] All analyses in the repeated measure correlations (rmcorr) were corrected for age and sex as well. The results were noted as correlation coefficients (*r*), 95% Confidence Intervals (95%CI), and p-values. The correlation coefficients' strength can be considered: > 0.8 = very strong; 0.6 up to 0.8 = moderately strong; 0.3 to 0.5 = fair; and < 0.3 = poor.[46] For this method, 'R' version 4.1.0, and the rmcorr module version 0.5.2 were used.[45] The level of statistical significance was set at $p < 0.05$ for all analyses.

RESULTS

In total, 246 parents of young patients with TBI or nTBI participated in this study. At the one- and two-year follow-ups (T1/T2), 71 and 72 parents completed the questionnaires, respectively (Figure 1). Table 1 presents the demographic, injury, and family characteristics at baseline. The median age of the patients in the total group was 14 years (IQR 11-16). Seventy-four percent (n=181) had a TBI, of which 78% were classified as 'mild'. In the nTBI group (n=65, 26%), 40% had a brain tumor, and 24% had a stroke. Ninety-six (40%) of the patients were referred for outpatient rehabilitation more than six months after the onset of the brain injury and 17% of the patients were living in a single-parent household.

Family impact and HRQoL: TBI versus nTBI

As seen in Table 2, the total mean (SD) PedsQL™FIM score in the TBI group at baseline was 73.8 (SD 19.2), and 65.6 (SD 15.7) in the nTBI group. For all groups at baseline, the lowest scores, i.e., more family impact, were found on the 'worrying' domain and the highest on the domain 'communication'.

A significant difference was found between the TBI group and the nTBI group concerning family impact total and almost all domain scores at baseline (total score; t=3.6, Df=116, $p < 0.001$), at T1 (total score; t=2.1, Df=54, $p = 0.04$), and at T2 (total score; t=2.4, Df=32, $p = 0.02$), except for the domain 'parental-HRQoL summary score' at T1 (t=1.4, Df=57, $p = 0.08$) and T2 (t=1.5, Df=36, $p = 0.07$). The total mean (SD) PedsQL™GCS-4.0 score at

baseline was 61.9 (SD 16.9) for the TBI group and 60.0 (SD 17.3) for the nTBI group. For all groups, the lowest scores were found on the 'School/work functioning' domain and the highest on the 'social functioning' domain. Regarding HRQoL scores between the TBI group and the nTBI group, significant differences were only found on the domains 'emotional functioning' ($p < 0.05$ at baseline) and 'social functioning' ($p < 0.05$ at all time points).

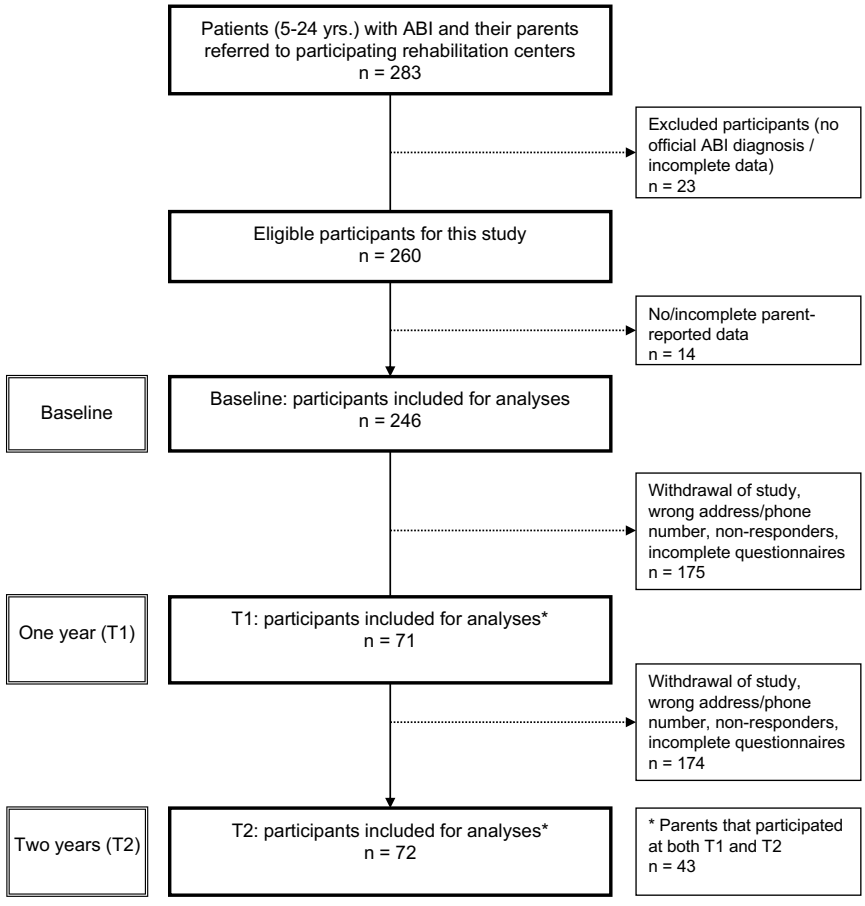

Figure 1. Flow chart of the participants in this study

Table 1. Demographic, injury, and family characteristics in children, adolescents, and young adults with TBI/nTBI, referred to outpatient rehabilitation, at baseline

Demographic characteristics	**Total Group n= 246**	**TBI group n= 181 (74%)**	**nTBI group n= 65 (26%)**
Sex; n (%)			
Female	127 (52%)	99 (54%)	29 (45%)
Age (years) at referral; median (IQR)	14 (11-16)	15 (12-16)	13 (10-16)
5-11 years old; n (%)	76 (29%)	48 (24%)	32 (43%)
12-17 years old; n (%)	134 (56%)	103 (59%)	27 (48%)
18-24 years old; n (%)	36 (15%)	30 (17%)	6 (9%)
Time(months) between the onset & referral to rehabilitation;			
Median (range)	4.0 (1-21)	3.0 (1-10)	16.0 (3-46)
More than (>) 6 months; n (%)	96 (40%)	56 (31%)	25 (40%)

Injury characteristics	**TBI group n= 181 (74%)**	**nTBI group n= 65 (26%)**
Severity levels of TBI (based on GCS*); n (%)		
Mild	143 (78%)	
Moderate-severe	18 (10%)	
Unknown**	20 (12%)	
Causes nTBI; n (%)		
Brain tumor		25 (40%)
Stroke		15 (24%)
Hypoxia/intoxication		2 (3%)
Encephalitis/meningitis		11 (18%)
Other		9 (15%)

Family characteristics	**Total Group n= 246**	**TBI group n= 181 (74%)**	**nTBI group n= 65 (26%)**
Single-parent household; n (%)			
Yes	42 (17%)	28 (15%)	15 (23%)
Having (a) sibling(s); n (%)			
Yes	214 (87%)	160 (88%)	54 (84%)
Cultural background parents; n (%)			
Non-Dutch	28 (11%)	20 (11%)	8 (12%)
Educational level parents; n (%) #			
Low	28 (11%)	20 (11%)	8 (12%)
Intermediate	108 (44%)	79 (43%)	29 (44%)
High	110 (45%)	81 (46%)	29 (44%)

TBI = traumatic brain injury; nTBI = non-traumatic brain injury. *Glasgow Coma Scale (GCS).
**If the GCS was unknown but there was no history of conscious loss (which was the case), the severity level was also considered 'mild'. # Educational level parents, low: prevocational practical education or less, intermediate: prevocational theoretical education and upper secondary vocational education, high: secondary education, higher education, and university level education).

Table 2. Differences in parent reported family impact and patients' Health related quality of life between patients with TBI and nTBI at baseline and one and two years later.

Family impact*	Cause	n	Baseline Mean (SD)	MD	t-value (Df)	p-value	n	T1 Mean (SD)	MD	t-value (Df)	p-value	n	T2 Mean (SD)	MD	t-value (Df)	p-value
Total score	TBI	181	73.8 (16.2)	8.2	3.6 (116)	<0.001	48	74.5 (16.5)	7.6	2.1 (55)	0.04	53	75.9 (14.8)	9.4	2.4 (32)	0.02
	nTBI	65	65.6 (15.7)				23	66.8 (12.8)				19	66.5 (14.8)			
Worrying	TBI	181	66.9 (18.8)	10.7	3.8 (110)	<0.001	48	66.0 (18.5)	7.1	1.7 (49)	0.04	53	69.1 (14.3)	9.8	2.5 (30)	0.01
	nTBI	65	56.2 (19.5)				23	58.9 (16.1)				19	59.2 (15.2)			
Communication	TBI	181	80.7 (21.9)	11.3	3.3 (103)	0.001	48	81.9 (23.3)	16.3	2.8 (43)	0.004	53	84.4 (19.9)	21.7	3.7 (28)	<0.001
	nTBI	65	69.4 (24.3)				23	65.6 (23.5)				19	62.7 (22.8)			
Family functioning ss	TBI	181	75.3 (19.1)	8.4	3.0 (113)	0.003	48	76.3 (18.5)	10.3	2.4 (49)	0.01	53	78.8 (17.7)	12.1	2.3 (29)	0.01
	nTBI	65	66.9 (19.1)				23	66.0 (16.2)				19	66.6 (19.9)			
Parental HRQoL ss	TBI	181	73.9 (18.0)	7.1	2.9 (121)	0.004	48	74.8 (18.8)	5.5	1.4 (57)	0.08	53	75.1 (17.4)	6.3	1.5 (36)	0.07
	nTBI	65	66.8 (16.7)				23	69.3 (13.7)				19	68.8 (15.2)			

HRQoL*	Cause	n	Baseline Mean (SD)	MD	t-value (Df)	p-value	n	T1 Mean (SD)	MD	t-value (Df)	p-value	n	T2 Mean (SD)	MD	t-value (Df)	p-value
Total score	TBI	181	61.9 (16.9)	1.9	0.8 (110)	0.21	48	72.5 (16.5)	5.3	1.4 (47)	0.09	53	73.8 (18.4)	6.3	1.5 (37)	0.08
	nTBI	65	60.0 (17.3)				23	67.2 (12.8)				19	67.5 (15.4)			
Physical functioning	TBI	181	64.6 (20.9)	0.7	0.2 (93)	0.42	48	77.4 (17.5)	3.0	0.7 (43)	0.25	53	77.1 (22.9)	3.4	0.6 (31)	0.29
	nTBI	65	63.9 (26.8)				23	74.4 (16.8)				19	73.7 (15.2)			
Emotional functioning	TBI	181	60.4 (22.9)	5.5	1.8 (123)	0.04	48	66.2 (20.3)	6.7	1.1 (36)	0.14	53	68.5 (24.1)	7.4	1.3 (37)	0.10
	nTBI	65	54.9 (20.9)				23	59.5 (24.7)				19	61.1 (20.4)			
Social functioning	TBI	181	74.9 (20.8)	5.5	1.8 (112)	0.04	48	82.0 (21.2)	10.0	2.0 (50)	0.02	53	81.6 (18.7)	11.9	2.1 (27)	0.02
	nTBI	65	69.4 (20.9)				23	72.0 (17.4)				19	69.7 (22.0)			
School/work functioning	TBI	181	46.2 (25.2)	2.7	-0.8 (136)	0.19	48	61.6 (21.8)	3.2	0.6 (45)	0.28	53	66.2 (23.8)	4.4	0.9 (47)	0.19
	nTBI	65	48.9 (20.7)				23	58.4 (20.0)				19	61.8 (15.2)			

* The Pediatric Quality of Life Inventory™ Family Impact Module (PedsQL™ FIM) and the Pediatric Quality of Life Inventory™ Generic Core Scales-4.0 (PedsQL™ GCS-4.0). MD: Mean difference. t-value (Df): values of independent sample t-tests and degrees of freedom. p-values in grey boxes are <0.05 and statistically significant. Family functioning ss= family functioning summary score, Parental HRQoL ss=parental HRQoL summary score.

Family Impact over time

PedsQL™ FIM change scores, analysed with the linear mixed model (LMM) between baseline and T1, between T1 and T2, and between baseline and T2 are presented in Table 3.

The total group: In the total group, the total change score between baseline and T1 was: +2.2 (95% CI -2.3;6.7, p > 0.05), and in the second year (between T1 and T2); +1.7 (95% CI -4.1;7.5, p > 0.05). Only significant improvement was found in the 'worrying' domain, between baseline and T1: +6.9 (95% CI 1.5;12.3), p < 0.05, and between baseline and T2: +9.9 (95% CI 4.5;15.3), p < 0.001. Scores on the 'communication' domain decreased in 2 years over time (baseline-T2) yet, not significantly: -1.2 (95% CI -8.1;5.8), p > 0.05.

The TBI group: In the TBI group, the improvement of the total score in the first year (baseline-T1) was: +2.8 (95% CI -2.6;8.2, p > 0.05) and +0.4 (95% CI -6.6;7.5, p > 0.05) between T1 and T2. In line with the results from the total group, significant improvement between baseline and T2 was seen on the domain 'worrying' (p < 0.05) and a (non-significant) decrease in the domain 'communication' between baseline and T2.

The nTBI group: Regarding the nTBI group, improvements of PedsQL™ FIM total scores in the first year and the second were: +2.3 (95% CI -5.3;9.9), and +3.2 (95% CI 6.8;13.2) yet both were non-significant (p > 0.05). In almost all domain scores more improvements were seen in the second year, except on the 'worrying' domain where most improvement was seen between baseline and the first year: +10.0 (95% CI 1.0;18.9, p < 0.05).

Table 3. Parent-reported family impact over the course of time

Total group				
PedsQL™ FIM[1]	**Baseline n= 246 Mean (SD)**	**Baseline–T1 Change Score (95% CI)[#]**	**T1–T2 Change Score (95% CI)[#]**	**Baseline–T2 Change Score (95% CI)[#]**
Total score	71.7 (16.4)	+2.2 (-2.3, 6.7)	+1.7 (-4.1, 7.5)	+3.9 (-0.9, 8.7)
Worrying	64.1 (19.5)	+6.9 (1.5, 12.3) *	+3.0 (-9.8, 3.8)	+9.9 (4.5, 15.3) **
Communication	77.7 (23.0)	-3.5 (-9.8, 2.8)	+2.3 (-6.0, 10.7)	-1.2 (-8.1, 5.8)
Family functioning summary score	73.1 (19.4)	-0.1 (-5.7, 5.4)	+2.9 (-4.2, 10.1)	+2.8 (-2.9, 8.6)
Parental HRQoL summary score	72.0 (17.9)	+2.8 (-1.9, 7.4)	+0.8 (-5.1, 6.7)	+3.6 (-1.3, 8.5)

Table 3. Continued

TBI group				
PedsQL™ FIM[1]	**Baseline n= 181 Mean (SD)**	**Baseline–T1 Change Score (95% CI) #**	**T1–T2 Change Score (95% CI) #**	**Baseline–T2 Change Score (95% CI) #**
Total score	73.8 (16.2)	+2.8 (-2.6, 8.2)	+0.4 (-6.6, 7.5)	+3.2 (-2.6, 9.0)
Worrying	66.9 (18.8)	+6.4 (-0.3, 13.1)	+2.2 (-6.1, 10.6)	+8.6 (2.1, 15.1) *
Communication	80.7 (21.9)	-3.4 (-11.0, 4.1)	+0.5 (-9.7, 10.6)	-2.9 (-11.3, 5.4)
Family functioning summary score	75.3 (19.1)	+1.2 (-5.4, 7.9)	+1.9 (-6.6, 10.4)	+3.1 (-3.6, 9.9)
Parental HRQoL summary score	73.9 (18.0)	+3.4 (-2.2, 9.0)	-0.6 (-7.7, 6.5)	+2.8 (-3.1, 8.7)

nTBI group				
PedsQL™ FIM[1]	**Baseline n= 65 Mean (SD)**	**Baseline–T1 Change Score (95% CI) #**	**T1–T2 Change Score (95% CI) #**	**Baseline–T2 Change Score (95% CI) #**
Total score	65.6 (15.7)	+2.3 (-5.3, 9.9)	+3.2 (6.8, 13.2)	+5.5 (3.3, 13.2)
Worrying	56.2 (19.5)	+10.0 (1.0, 18.9) *	+3.6 (-7.8, 14.8)	+13.6 (3.6, 23.5) *
Communication	69.4 (24.3)	-1.6 (-12.8, 9.6)	+5.3 (-8.8, 19.5)	+3.7 (-8.9, 16.3)
Family functioning summary score	66.9 (19.1)	-1.7 (-11.3, 7.9)	+2.9 (-10.2, 15.9)	+1.2 (-10.3, 12.7)
Parental HRQoL summary score	66.8 (16.7)	+2.6 (-5.3, 10.6)	+2.9 (-7.3, 13.2)	+5.5 (-3.4, 13.2)

[1]: Pediatric Quality of Life Inventory™ Family Impact Module (FIM). #Based on the linear mixed model, corrected for age and sex. * p-value <0.05, ** p-value <0.001; Baseline: at referral to rehabilitation; T1: 1-year follow-up; T2: 2-year follow-up. Outcomes at baseline are expressed as estimated means with standard deviations (SD) and at T1 and T1 as change scores with 95% confidence intervals for difference (95% CI). Lower total scores (and domain scores) mean more family impact.

HRQoL in young patients over time

PedsQL™ GCS-4.0 change scores between all time points are presented in Table 4.

The total group: The changes scores for the total score in the total group were +9.6 (95% CI 4.9;13.8, p < 0.001) in the first year and +1.4 (95% CI 4.2;7.2, p > 0.05) in the second. Similar results were found in all domain scores with the largest overall improvement on the domain school/work functioning (baseline-T2): +17.7 (95% CI 11.7;23.7, p < 0.001).

The TBI group: Significant improvement in PedsQL™ GCS-4.0 total scores in the first year were found: +10.8 (95% CI 5.2;16.4), p < 0.001. Change scores were non-significant in the second year: +1.1 (95% CI -5.9;8.1), p > 0.05. Significant improvements were found between baseline and T1 in all domain scores (p < 0.05).

Table 4. Parent-reported Health-Related Quality of Life (HRQoL) for their child over the course of time

Total group				
PedsQL™ GCS-4.0[1]	**Baseline n= 246 Mean (SD)**	**Baseline–T1 Change Score (95% CI) #**	**T1–T2 Change Score (95% CI) #**	**Baseline–T2 Change Score (95% CI) #**
Total score	61.4 (17.0)	+9.6 (5.1, 14.0) **	+1.4 (-4.3, 7.0)	+11.0 (6.3, 15.6) **
Physical functioning	64.4 (22.6)	+12.4 (7.3, 17.4) **	-0.3 (-6.9, 6.4)	+12.1 (6.0, 18.0) **
Emotional functioning	58.9 (22.5)	+5.2 (-0.8, 11.3)	+2.6 (-4.9, 10.1)	+7.8 (1.7, 13.9) *
Social functioning	73.4 (20.9)	+5.7 (0.1, 11.4) *	-0.2 (-6.9, 6.6)	+5.5 (0.2, 10.9) *
School/work functioning	46.9 (24.1)	+13.2 (7.3, 19.2) **	+4.5 (-2.8, 11.7)	+17.7 (11.7, 23.7) **
TBI group				
PedsQL™ GCS-4.0[1]	**Baseline n= 181 Mean (SD)**	**Baseline–T1 Change Score (95% CI) #**	**T1–T2 Change Score (95% CI) #**	**Baseline–T2 Change Score (95% CI) #**
Total score	61.9 (16.9)	+10.8 (5.2, 16.4) **	+1.1 (-5.9, 8.1)	+11.9 (6.4, 17.5) **
Physical functioning	64.6 (20.9)	+13.3 (7.2, 19.3) **	-0.6 (-8.7, 7.5)	+12.7 (5.7, 19.6) **
Emotional functioning	60.4 (22.9)	+5.9 (-1.1, 12.9)	+2.2 (-6.7, 11.1)	+8.1 (0.9, 15.5) *
Social functioning	74.9 (20.8)	+7.5 (0.4, 14.6) *	-0.5 (-8.6, 7.5)	+7.0 (1.1, 12.8) *
School/work functioning	46.2 (25.2)	+14.9 (7.6, 22.2) **	+4.5 (-4.6, 13.7)	+19.4 (11.9, 27.0) **
nTBI group				
PedsQL™ GCS-4.0[1]	**Baseline n= 65 Mean (SD)**	**Baseline–T1 Change Score (95% CI) #**	**T1–T2 Change Score (95% CI) #**	**Baseline–T2 Change Score (95% CI) #**
Total score	60.0 (17.3)	+7.6 (0.1, 15.0) *	+0.5 (-9.0, 10.0)	+8.1 (-0.6, 16.7)
Physical functioning	63.9 (26.8)	+10.8 (1.1, 20.5) *	-0.6 (-13.3, 12.2)	+10.2 (-2.4, 22.9)
Emotional functioning	54.9 (20.9)	+4.6 (-7.5, 16.7)	+1.5 (-12.9, 15.9)	+6.1 (-5.1, 17.3)
Social functioning	69.4 (20.9)	+3.2 (-5.7, 12.2)	-1.8 (-14.6, 10.9)	+1.4 (-10.6, 13.4)
School/work functioning	48.9 (20.7)	+9.6 (-0.6, 19.8)	+3.5 (-7.9, 14.0)	+13.1 (3.8, 22.5) *

[1]: The Pediatric Quality of Life Inventory™ Generic Core Scales-4.0 (PedsQL™ GCS-4.0). #Based on the linear mixed model, corrected for age and sex. * p-value <0.05, ** p-value <0.001; Baseline: at referral to rehabilitation; T1: 1-year follow-up; T2: 2-year follow-up. Outcomes at baseline are expressed as estimated means with standard deviations (SD) and at T1 and T1 as change scores with 95% confidence intervals for difference (95% CI). Lower total scores (and domain scores) mean lower HRQoL.

The nTBI group: Overall less improvement was found in the nTBI group regarding the HRQoL outcomes compared to the TBI group (in the total score and all domain scores).

Relationship between family impact and HRQoL

The longitudinal correlations between PedsQL™ FIM (family impact) and PedsQL™ GCS-4.0 (HRQoL) over time for the total/TBI/nTBI groups can be found in Figure 2a, Figure 2b, and

Figure 2c. Regarding the total group a fair longitudinal correlation was found over time: r = 0.51 (95% CI: 0.38-0.68, p < 0.001). A fair longitudinal correlation between family impact and HRQoL in the TBI group r = 0.48 (95%CI: 0.31-0.62, p < 0.001). A moderately strong correlation was found in the nTBI group r = 0.64 (95% CI: 0.40-0.79, p < 0.001) for nTBI, respectively.

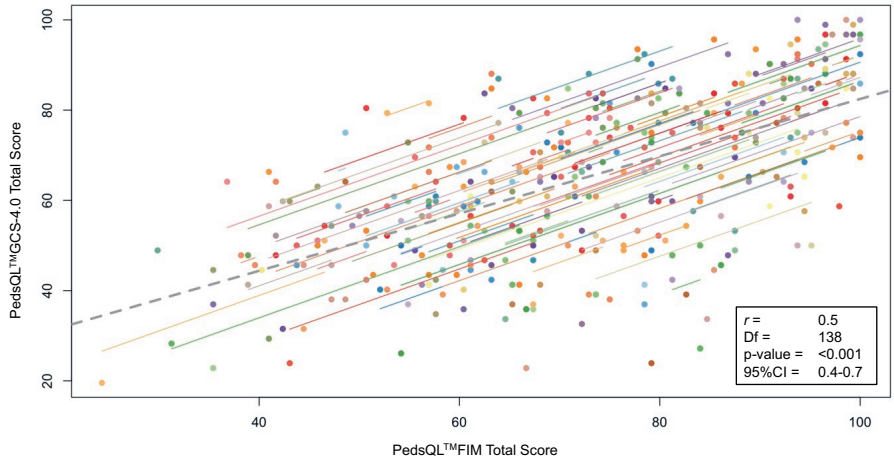

Figure 2a. Longitudinal correlation between Family impact (PedsQL™ FIM) and HRQoL (PedsQL™ GCS-4.0) in the total group.
PedsQL™ FIM: Pediatric Quality of Life Inventory™ Family Impact Module. PedsQL™ GCS-4.0: Pediatric Quality of Life Inventory™ Generic Core Scales-4.0. * Correlation coefficient (*r*): very strong = > 0.8; moderately strong = 0.6 to 0.8; fair = 0.3 to 0.5; and poor = < 0.3. # p-value <0.05 = statistically significant. Df = Degrees of freedom, 95%CI = 95% Confidence Interval. Analyses were corrected for age and sex.

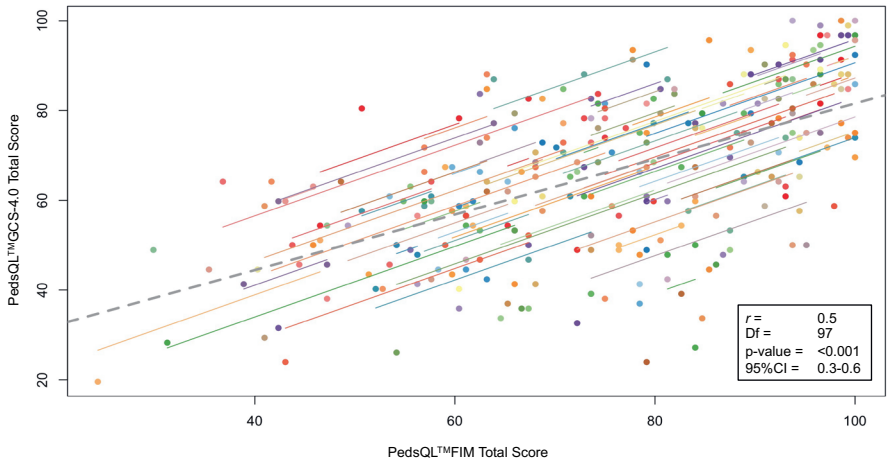

Figure 2b. Longitudinal correlation between Family impact (PedsQL™ FIM) and HRQoL (PedsQL™ GCS-4.0) in the TBI group.
PedsQL™ FIM: Pediatric Quality of Life Inventory™ Family Impact Module. PedsQL™ GCS-4.0: Pediatric Quality of Life Inventory™ Generic Core Scales-4.0. TBI: Traumatic brain injury.
* Correlation coefficient (*r*): very strong = > 0.8; moderately strong = 0.6 to 0.8; fair = 0.3 to 0.5; and poor = < 0.3. # p-value <0.05 = statistically significant. Df = Degrees of freedom, 95% CI = 95% Confidence Interval. Analyses were corrected for age and sex.

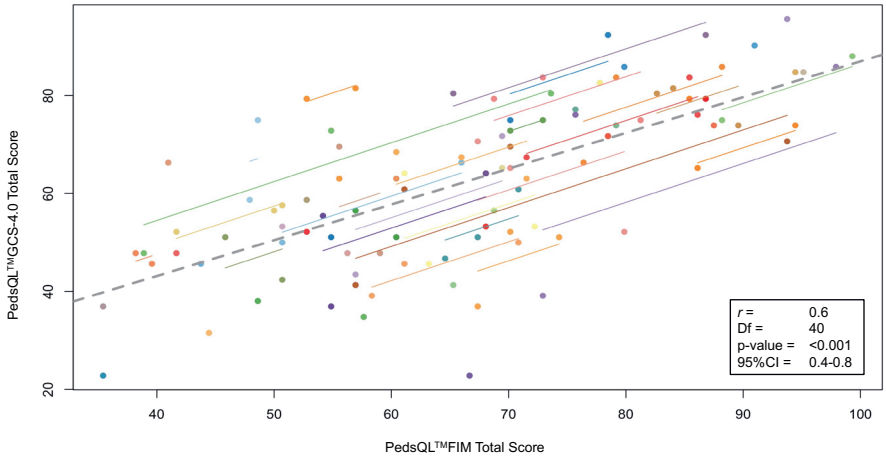

Figure 2c. Longitudinal correlation between Family impact (PedsQL™ FIM) and HRQoL (PedsQL™ GCS-4.0) in the nTBI group.
PedsQL™ FIM: Pediatric Quality of Life Inventory™ Family Impact Module. PedsQL™ GCS-4.0: Pediatric Quality of Life Inventory™ Generic Core Scales-4.0. nTBI: Non-traumatic brain injury.
* Correlation coefficient (*r*): very strong = > 0.8; moderately strong = 0.6 to 0.8; fair = 0.3 to 0.5; and poor = < 0.3. # p-value <0.05 = statistically significant. Df = Degrees of freedom, 95% CI = 95% Confidence Interval. Analyses were corrected for age and sex.

DISCUSSION

This longitudinal multicentre study among parents of young patients (5-24 years) with TBI or nTBI found considerable family impact and decreased patients' HRQoL at the time of referral to outpatient rehabilitation (baseline). Significant differences in family impact were found between the TBI and nTBI groups with more family impact in the nTBI group. Contrary to what we hypothesized, only a slight decrease of family impact in both the TBI and the nTBI groups over two years after referral to rehabilitation was found and was non-significant (in the total and almost all domain scores). This was a large contrast with patients' HRQoL, which improved significantly over time in both groups. A fair longitudinal relationship between decreased family impact and an improvement in patients' HRQoL was found in the TBI group, whereas moderately strong relationships were found in the nTBI group.

Results showed a significant difference in family impact scores between the TBI and nTBI groups at all time points, whereas the nTBI group had significantly lower scores both at baseline and almost all time points. When looking at the change scores, the course of family impact over time differed among the TBI and nTBI groups as well. Family impact in the TBI group tended to decrease the most in the first year after referral to rehabilitation, while in the nTBI group, family impact decreased more between the first and second year after referral. This could be explained by the fact that nTBI has a less predictable prognosis compared to TBI, which could require more time for family adjustment. This rehabilitation-based study revealed more family impact in both the TBI and nTBI groups at the time of referral to rehabilitation compared to a Dutch hospital-based study (our TBI group: 73.8 SD 16.2, our nTBI group: 65.6 SD 15.7 versus TBI: 83.6 SD 16.2, nTBI: 70.8 SD 19.6 in the hospital study).[21] This can be explained by the fact that patients in our cohort were referred for rehabilitation due to persisting TBI- or nTBI-related daily life problems that cause considerable impact on families compared to a hospital cohort where patients may have improved considerably in the acute of subacute phase after their brain injury. In conclusion, family impact persists in both groups with a different trajectory over time but is always higher than in a hospital cohort.[21] These results underline the importance of measuring the impact on families over time and taking the cause of brain injury into account during the different stages of recovery.

Until now, knowledge on parent-reported family impact over time in families with a child with persisting problems after a TBI or nTBI is scarce. The findings of our study suggest that in the two years after referral to rehabilitation only the aspect 'worrying' decreased significantly within families in both the TBI and nTBI groups. This contrasts with our hypothesis that family impact would decrease over time in all domains among families

with a child that suffered from a brain injury. This finding is in line with previous hospital- or community-based studies in families of children with TBI, that did not find a decrease of family impact one year after brain injury onset as well.[25-30] Comparisons of our results with those from previous studies must be done with caution as studies are different with respect to age, causes, daily life functioning and presence of persisting problems.[25-30] The reasons for the persistence of family impact remain unclear, but it could be hypothesized that factors such as suboptimal long-term care, lack of information or unrealistic expectations regarding the prognosis could play a role. During rehabilitation, the focus lies on the patient by improving HRQoL and participation abilities and there might be less focus on their families which could overshadow the potential still-existing family problems that are not fully considered. These results and considerations underline the importance of focusing on the patients' families in all phases of recovery and over time.

Contrary to the results of the course of family impact over time, almost no significant differences were found regarding patients' HRQoL between the TBI and nTBI groups at all time points. In both the TBI and nTBI groups, the patients' HRQoL mean scores reported by parents were considerably low at baseline compared to scores from healthy peers i.e., between 82.1 (SD: 8.9) and 83.9 (SD: 13.1) depending on the age, versus 61.4 (SD: 17.0) in our total group of young patients with TBI/nTBI.[40,41] Furthermore, even though HRQoL improved significantly over time in both groups, scores remained considerably lower compared to healthy peers.[40,41] Furthermore, in line with family impact scores in our study, HRQoL scores are lower compared to scores in the hospital-based study by de Kloet et al. (despite the similarities between the populations).[21] This can be explained by the fact that patients in our cohort were all referred to outpatient rehabilitation with persisting daily life problems after TBI/nTBI while we assume that only a subpopulation of the hospital cohort needed a referral to outpatient rehabilitation. The results of our study underline the importance of measuring and monitoring patients' HRQoL over time in clinical practice to monitor improvement or decrease in patients' functioning.

Regarding the relationship between family impact and HRQoL results showed that family impact and HRQoL had a moderately strong correlation when measuring individual patients over time in the total group. However, significant differences between de TBI and nTBI groups were found, where a moderately strong longitudinal correlation between family impact and patients' HRQoL was found in the nTBI group yet, only a 'fair' correlation in the TBI group. These results were contrary to the expectation of strong correlations between family impact and HRQoL over time for both the TBI and nTBI groups. Only a few previous studies have described associations between patients' diminished HRQoL and a higher parent-reported family impact among patients with chronic diseases (including TBI and

nTBI).[3,16,20,23,24] However, these studies did not include patients older than 18 years of age or did not measure these associations over time.[3,16,20,23,24] Furthermore, these studies found only investigated correlations between family impact and HRQoL on the group level (and did not consider individual repeated measurements on the same patients). The current study can be considered the first that investigated the correlation between FI and HRQoL over time using a method that takes into account the individual non-independence of repeated measurements on the same patients. To conclude, strong correlations between outcome measures at one time point in a whole group do not automatically seem to correlate as strongly in the individual patient over time. Therefore, these results suggest looking into the individual patient and his/her family when measuring FI and HRQoL is important for using these measures in clinical practice.

Strengths and limitations

This study had several limitations. First, only parent-reported data were analysed, while siblings or perspectives from other family members were not included. However, to date, the PedsQL™ FIM is the only outcome measure that assesses the impact on the family in several domains. Future research should focus on developing outcome measures and/or modifying the PedsQL™ FIM to consider including perspectives of other important people in the lives of patients with TBI/nTBI. Furthermore, there is no normative data for the general population in The Netherlands; this data would give insight into the course of family impact during the development of healthy children and could help to better interpret outcomes of studies in TBI/nTBI. Second, many participants were lost to follow-up. An explanation for this is that the questionnaires at the time that a patient was referred for rehabilitation were completed in terms of routine care, while one and two years later, parents were asked to complete the questionnaires voluntarily, often after the patient no longer had visits to the clinic. The relatively high non-response (even after a significant number of reminders) could be decreased by sharing the results directly after the administration of the questionnaires and involving the patient and parents in the results and the importance of testing over time. Nevertheless, missing data were missing completely at random, meaning that missing data in the dataset happened by coincidence (the observed values at T1 and T2 in the dataset are a random sample from the dataset when it would have been complete). Furthermore, we used two statistical methods that took repeated measures into account within the same participant, and we thereby corrected for missing observations (a linear mixed model to determine change over time and repeated measure correlations to determine correlations over time). Third, there were 20 patients in the TBI (12%) group with unknown TBI severity levels (based on the GCS). However, in all these patients there was no history of conscious loss, and therefore the severity level could be also considered ‘mild’, which was confirmed by all treating rehabilitation physicians in all participating

rehabilitation centers. This may suggest that some patients designated as having a mild injury might be young patients with concussions, which may have influenced outcomes. However, even in these patients persisting problems were found for which they had been referred for rehabilitation. Fourth, in our study, we found differences in family impact between the TBI and the nTBI group, whereas in the nTBI group greater family impact was found. This could possibly be explained by the initial between-sample differences in the severity of injury-related disability and the expected duration of symptoms. To outline these differences, we chose to report outcomes for both groups separately as well. Fifth, the authors acknowledge the lack of additional (parental) information e.g., parental mental and physical health, disability status, extra-family support potential, and patients' needed care from parents to look into additional potential correlations with the PedsQL™ FIM. We recommend collecting more detailed data on characteristics of parental functioning in future research. Finally, the results of the questionnaires could be biased by the parents' motivation, stress, and mood at the time of completion.

CONCLUSIONS

This study showed that family impact in families with a child who suffers from a TBI or nTBI referred for rehabilitation treatment is considerable, especially in patients with a nTBI. In general, the impact on the family remains stable over time, even though patients' HRQoL improved. The findings of this study underline the importance of measuring and monitoring family impact and HRQoL over time. Furthermore, it is important to investigate family impact separately for patients with TBI and patients with nTBI as both groups follow a different course over time. Future studies should focus on selecting and evaluating approaches during rehabilitation treatment that both increases the HRQoL of the patient and reduces family impact after a child has either TBI or nTBI.

Clinical Message

Next to focusing on the patient's HRQoL, it is important to monitor the wishes and needs of the family and support them throughout the rehabilitation process since the improvement of the patient's HRQoL does not always automatically lead to reduced family impact.

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Disclosure statement

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SECTION 2

Joint collaborations between rehabilitation centers to optimize care for young individuals with ABI

CHAPTER 7

The structure of rehabilitation care for young patients with acquired brain injury: Similarities and differences among Dutch rehabilitation centers

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ABSTRACT

Purpose

To describe similarities and differences in rehabilitation care for young patients with acquired brain injuries (ABI) aged between 4 and 25 years among Dutch outpatient rehabilitation centers (RCs). Due to differences between RCs in terms of history/culture, team composition/expertise, and cooperation with network partners, variations between RCs are expected.

Methods

In this cross-sectional survey-study, professionals from RCs were invited to complete a 21-item questionnaire on the structure of rehabilitation for young patients with ABI (12 yes/no & 9 corresponding open-ended-questions). There were three topics: admission/discharge criteria (n=2&2), the organisation of rehabilitation (n=7&5), aftercare (n=3&2). Answers to yes/no questions were described and open-ended questions were thematically analyzed/categorized. The similarity in rehabilitation practice was defined as an item being present/described in ≥ 75% of the RCs.

Results

Rehabilitation professionals from 12 RCs participated. Similarities and differences were found regarding the structure of rehabilitation. Concerning the admission criteria (present in all RCs), "having a diagnosis of ABI" was seen as an important criterium in all RCs, where all other admission criteria were described differently. The discharge criterium "attainment of goals" was the only criterium found in ≥ 75% of the RCs. Regarding the organisation of rehabilitation, all RCs described the presence of specialized teams and diagnosis-specific consultation appointments. Differences were also found: the presence of "transition-teams" for young adults, and presence of general treatment programs (< 75% of the RCs). Concerning aftercare, similarities were found in the presence of structural end-reports, standard consults with rehabilitation physicians at discharge, and follow-up appointments. However, differences were seen in the timing between discharge and follow-up (six weeks-twelve months).

Conclusions

Despite similarities between RCs, differences were found in admission/discharge criteria, organisation of rehabilitation, and aftercare. Gaining insights into practice variation across RCs may help to reach consensus regarding 'best practice' on the structure of rehabilitation care for young patients with ABI.

Keywords: Rehabilitation Services; Health Care Organizations and Systems; Child and Adolescent Health; Comparative Health Systems/International Health

INTRODUCTION

Acquired brain injury (ABI) refers to any brain damage that occurs after birth and is worldwide a common condition, both in adults as well as in children and youth under the age of 25.[1,2] ABI can be divided into traumatic brain injury (TBI) and non-traumatic brain injury (nTBI).[1,2] In young patients (< 25 years old), TBI is the most common type (75% of all ABI) and is caused by external causes e.g., sports/traffic accidents and violence, whereas nTBI is the result of internal causes e.g., brain tumors and meningitis.[1,2] Young patients with ABI form a heterogeneous population concerning types of injury, severity, and long-term consequences.[3-5]

The care for patients with ABI, and more specifically young patients with ABI strongly depends on the severity and complexity of the brain injury.[6-9] When severe and more complex problems due to ABI are present, young patients initially receive care in the hospital, whereafter they are often admitted for either inpatient or outpatient rehabilitation treatment (depending on complexity of remaining problems).[7,10-12] Young patients with minor problems after ABI are often not hospitalized and usually receive treatment (i.e., physical therapy/ psychology) in primary care if indicated e.g., by general practitioners and/or medical specialists.[10,12,13] However, in case of persistent, more complex, or progressive problems, patients with a mild ABI are referred by medical specialists or general practitioners to outpatient rehabilitation services as well.[8-10,12,14,15]

In the Netherlands, care for young patients with TBI is described on its main features in a standard of care for children and adolescents (0-18 years old).[6] However, this standard of care does not specify the exact structures of rehabilitation care and leaves substantial room for variation, which may lead to differences in the delivery of care between rehabilitation centers (RCs).[16-19] Additionally, due to differences between RCs in terms of history and culture, composition and expertise team, and cooperation with network partners, variation between RCs is expected as well.

Such practice variation has been observed in the provision of rehabilitation in previous studies (adult stroke/arthritis rehabilitation) [20-22] but to date, it has not been studied in pediatric ABI rehabilitation in the Netherlands. If not explained by the case mix, practice variation could possibly be a signal of suboptimal care for patients (as described in previous studies).[20-22]

With the description and comparison of the provision of care across organizations, it is important to consider the context, structure, process, and outcome of care. Based on such

insights, specifically for the rehabilitation setting, frameworks and quality of care indicators were developed to evaluate quality of care for patients for several diagnoses.[16-24] Regarding the structure of rehabilitation care, regional differences were found in admission and discharge criteria for rehabilitation treatment, differences in care pathways, experience/knowledge of professionals, and referrals to other care facilities.[20-22]

It is not known whether and to what extent there are differences among RCs in the Netherlands in the structure of care for the population of young patients with ABI. Investigating potential similarities and differences could reinforce collaborations between RCs and targeting and reducing unwanted practice variations (if any) could be beneficial for the young ABI population in the Netherlands. Therefore, the aim of this study is to explore similarities and differences (variations) in the structure of care for young patients with ABI (4-25 years old) across Dutch RCs.

METHODS

Design

A cross-sectional survey study on the structure of outpatient rehabilitation for young patients with ABI.

Setting

The current study was part of a multicenter project: "Participate?! Next Step" (2021-2023) among Dutch RCs. This project aimed to optimize care for young patients (aged 4-25 years old) with ABI in the Netherlands among Dutch RCs. It was initiated by a project group, consisting of a PhD candidate (first author), and four senior researchers (second, third, and the last two authors) from Basalt Rehabilitation Center (The Hague, The Netherlands). The Medical Ethics Committee of the Leiden University Medical center (P15.165-addendum-1.0) and all local research committees of participating RCs approved the study.

Procedure

To provide an overview of the structure of rehabilitation care for young patients with ABI, the project group formulated an online questionnaire that was based on questionnaires from previous studies that investigated practice variation in terms of admission/discharge criteria, organization of rehabilitation, and aftercare.[20,21] Questions were adjusted and specified to focus on the structure of care for young patients with ABI in the outpatient rehabilitation setting. The questionnaire was formulated in Dutch and was first pilot tested by the project group (and adjusted where necessary). Thereafter, it was sent to participants

through an e-mail-link, using 'Castor' (Electronic-Data-Capture). It consisted of 21 questions (see Appendix 1). Twelve questions could be answered with: 'yes'/'no' and nine 'open answer questions' to request more details on the topics of interest. Questions were divided into 3 topics: the availability of admission/discharge criteria for rehabilitation treatment (n=2 yes/no questions & 2 open-ended questions), the organization of rehabilitation (n=7&5), and aftercare (n=3&2).

Participants

All RCs participating in the project were asked to appoint one or two of their healthcare professionals currently working with children with ABI to function as representatives in the project "Participate?! Next Step". Representatives were healthcare professionals:

- with experience with the target group,
- who were well informed about the way the care for the target group is organized in their team,
- that were willing to answer an online questionnaire.

The representatives were invited by e-mail to answer the online questionnaire. The project group encouraged them to involve their colleagues to answer all questions adequately on behalf of their RC (they mandated their RC as a whole).

Data Collection/Analyses

After the questionnaires were filled out by the participants, the completeness of the answers was verified. The first author asked participants to supply more information in case of incomplete answers. The 12 questions that could be answered with 'yes/no' were analyzed using descriptive statistics (presented as numbers (n) and percentages (%)). The nine 'open-ended answers' were qualitatively analyzed using thematic-analyses-methods.[25] First, open-ended answers were visually screened and merged into tables by the first author. When no additional information was given in an open-ended answer, it was noted as not applicable (NA) and not further analyzed. Thereafter, homogeneity of descriptions was noted per question, and thematic syntheses were formed.[25] The project group individually reviewed these syntheses, and after reaching consensus, they noted the numbers/percentages of themes per open-ended answer, enabling the objective identification of common themes.

Since levels of agreement in studies regarding 'similarities' are not clearly defined, the project group set these a priori at ≥ 75% in this study.[26] In case of < 75% agreement, it was considered a difference in structure (a practice variation). Finally, to present the results, all questions and answers were translated into English (and checked by a native-English speaker).

RESULTS

Fourteen representatives from 12 RCs in the Netherlands (Figure 1) answered the questionnaire on behalf of their RC. All representatives stated that they filled out the questionnaire with the help of their colleagues, resulting in the minimization of the chance of a response bias. These representatives were healthcare professionals, including one rehabilitation physician, one physical therapist, four psychologists, six occupational therapists, and two speech therapists.

Figure 1. Participating rehabilitation centers that provide outpatient rehabilitation for young patients with ABI in the Netherlands.

Participating Rehabilitation Centers: [1]Heliomare, Wijk aan Zee; [2]Reade, Amsterdam; [3]de Hoogstraat, Utrecht; [4]Basalt, The Hague; [5]Rijndam, Rotterdam; [6]Revant, Breda; [7]Revalidatie Friesland, Beetsterzwaag; [8]Vogellanden, Zwolle; [9]Roessingh, Enschede; [10]Klimmendaal, Arnhem; [11]Libra, Eindhoven; [12]Adelante, Valkenburg.

Admission/discharge criteria in pediatric ABI rehabilitation

All RCs (n=12, 100%) reported the presence of admission criteria in pediatric ABI rehabilitation treatment (see Table 1a, and Table 1b). However, differences were seen in four out of five descriptions of admission criteria, where the only similarity (> 75%) was seen regarding the criteria of "A diagnosis of ABI must be present" for starting treatment. Differences were seen regarding criteria that described that "participation restrictions had to be present in daily life" (n=5, 42%), "the patient/parents needed to have clear guiding-questions" (n=5, 42%), "patients/parents had to be in need of multidisciplinary rehabilitation treatment" (n=5, 42%), and "patients had to have sufficient mental and/or physical capacity before starting treatment" (n=3, 25%).

Table 1a. Similarities and differences in the presence of admission and discharge criteria in rehabilitation treatment in 12 Dutch ABI specialized Rehabilitation Centers

Presence of:	Answer (closed)	n (%)	Similarity#
Q1. Admission criteria	Yes	12 (100%)	Yes
	No	0 (0%)	
Q3. Discharge criteria	Yes	12 (100%)	Yes
	No	0 (0%)	

Q: Question. n: number. #similarities between centers: 'Yes' meaning that more than 75% of the centers provided the same answer and 'No' (differences) meaning that less than 75% of the centers provided the same answer.

Table 1b. The description of admission and discharge criteria in rehabilitation treatment in 12 Dutch ABI specialized Rehabilitation Centers

Description	Answer (open-ended*)	n (%)	Similarity#
Q2. Description of admission criteria	A diagnosis of ABI	12 (100%)	Yes
	Patients must have participation restrictions in daily life	5 (42%)	No
	Patients/parents need to have clear guiding questions	5 (42%)	No
	Requirement/need for multidisciplinary rehabilitation treatment	5 (42%)	No
	Mental and/or physical capacity of the patient needs to be sufficient	3 (25%)	No
Q4. Description of discharge criteria	Attainment of rehabilitation goals	10 (83%)	Yes
	Insufficient progress or no progress at all in achieving goals	3 (25%)	No
	Aftercare needs to have been arranged	5 (42%)	No

Q: Question. n: number. #similarities between centers: 'Yes' meaning that more than 75% of the centers provided the same answer and 'No' (differences) meaning that less than 75% of the centers provided the same answer. *Theme of description/explanation: synthesis through answers provided by the healthcare professionals from the 12 participating RCs.

All RCs (n=12, 100%) mentioned the presence of discharge criteria in paediatric ABI rehabilitation treatment. Across RCs, similarity was seen in the description of one discharge criterium i.e., ten RCs used the criterium "attainment of rehabilitation goals" (83%). Differences were seen across RCs regarding the criterium that patients had to stop treatment when they had "insufficient progress/no progress at all in achieving goals" (n=3, 25%) and that "aftercare needs to have been arranged" (n=5, 42%).

Organization of rehabilitation treatment

Regarding the organization of rehabilitation (Table 2a, and Table 2b), all RCs (n=12, 100%) described the presence of a team specialized in pediatric ABI treatment consisting of rehabilitation physicians, psychologists, physical therapists, occupational therapists, speech therapists, and social workers. Ten RCs (83%) also described other disciplines (e.g., nurses, creative therapists) being part of the team.

There were similarities found in the presence of an ABI-specific consultation appointment for new patients with a (suspected) ABI (n=10, 83%), carried out by a rehabilitation physician specialized in (pediatric) ABI (n=10, 83%).

All RCs (n=12, 100%) used age cut-off points for allocating patients to pediatric or adult rehabilitation teams, yet there were no unanimous cut-off points across RCs. The following age cut-off points were used: 4-18 years old (n=7, 58%) and 4-20 years old (n=5, 42%).

Table 2a. Similarities and differences in the presence of the organization of treatment in 12 Dutch ABI specialized Rehabilitation Centers

Presence of	Answer (closed)	n (%)	Similarities#
Q5. Specialized teams	Yes	12 (100%)	Yes
	No	0 (0%)	
Q7. Consultation appointments	Yes	10 (83%)	Yes
	No	2 (17%)	
Q9. Age cutoff points for pediatric versus adult treatment	Yes	12 (100%)	Yes
	No	0 (0%)	
Q11. Teams or programs for young adults	Yes	8 (67%)	No
	No	4 (33%)	
Q13. General ABI treatment program	Yes	8 (67%)	No
	No	4 (33%)	
Q15. Standard last consults	Yes	12 (100%)	Yes
	No	0 (0%)	
Q16. Structural end reports	Yes	11 (92%)	Yes
	No	1 (8%)	

Q: Question. n: number. #Similarities between centers: 'Yes' meaning more than 75% of the centers provided the same answer and 'No' (differences) meaning less than 75%.

Four RCs (33%) described the presence of 'transition teams' where adult patients between 18-25 years old receive age-appropriate care with a focus on their transition from childhood to adulthood.

Furthermore, differences were seen in the presence of a general ABI treatment program where only 8 (67%) described having such a program for the young adult age group (18-25 years old) and 8 (67%) for the whole population of young patients (4-25 years old) with ABI (n=8, 67%).

Table 2b. The description of the organization of treatment in 12 Dutch ABI specialized Rehabilitation Centers

Description		Answer (open-ended*)	n (%)	Similarities#
Q6.	Description of disciplines	Rehabilitation physicians, Psychologists, Physical therapists, Occupational therapists, Speech therapists, social workers	12 (100%)	Yes
		Other disciplines[1]	10 (83%)	Yes
Q8.	Consultation with whom	With a specialized rehabilitation physician	10 (83%)	Yes
Q10.	Description of age cutoff points	18 years old[2]	7 (58%	No
		20 years old[2]	5 (42%)	No
Q12.	Specification of teams programs	A program for young adults is being developed	1 (8%)	No
		A 'transition team' for adolescents/young adults exists	3 (25%)	No
Q14.	Description of availability[3]	NA[3]	NA[3]	NA[3]

Q: Question. n: number. *Theme of description/explanation: synthesis of answers by participants. #Similarities between centers: 'Yes' meaning more than 75% of the centers provided the same answer and 'No' (differences) meaning less than 75%.
[1] Nurses, music therapists, psycho-motor therapists, teachers specialized in youth with ABI, cognitive trainers, movement agoges, psycho-diagnostic staff members, rehabilitation technicians, exercise instructors, creative therapists, pedagogues, dieticians, clinical linguists, mental health /cognitive therapists, activity therapists, and psychiatrists.
[2] Young adults >18 or 20 sometimes receive pediatric rehabilitation when appropriate and/or when indicated.
[3] In case of the description of availability, no additional information was given after Q13: the presence of a general ABI treatment program.

Aftercare in pediatric ABI rehabilitation

Many similarities were found between RCs in the aftercare (Table 3a, and Table 3b) where RCs mentioned the presence of standard last consults with rehabilitation physicians before ending the rehabilitation program (n=12, 100%) and the presence of structural end reports (n=11, 92%).

All RCs (n=12, 100%) mentioned the presence of a structural follow-up appointment for the patient/parents after the rehabilitation program has ended. However, variations were seen regarding the time between discharge and follow-up ranging from 6 weeks-12 months, as well as regarding the frequency of follow-up: either annually or at 'transition moments' e.g., change of schools, from school to work.

All RCs (n=12, 100%) mentioned structural referrals to regional (care) facilities that support follow-up for the patient when indicated, yet the description of the actual reasons for referral, as well as structural cooperation with regional (care) facilities (e.g., primary care) in the follow-up process for the patient/parents, varied between RCs.

Table 3a. Similarities and differences in the presence of aftercare in 12 Dutch ABI specialized Rehabilitation Centers

Presence of	Answer (closed)	n (%)	Similarities#
Q16. Structural follow-up appointments	Yes	12 (100%)	Yes
	No	0 (0%)	
Q19. Structural referral to primary care[1]	Yes	12 (100%)	Yes
	No	0 (0%)	
Q21. Structural cooperation with primary care[1]	Yes	6 (50%)	No
	No	6 (50%)	

Q: Question. n: number. #Similarities between centers: 'Yes' meaning more than 75% of the centers provided the same answer and 'No' (differences) meaning less than 75%.
[1]When aftercare is indicated/appropriate.

Table 3b. The description of aftercare in 12 Dutch ABI specialised Rehabilitation Centers

Description	Answer (open-ended*)	n (%)	Similarities#
Q17a. Follow-up appointment with whom	Rehabilitation Physician	12 (100%)	Yes
	Psychologist	2 (17%)	No
Q17b. Time between discharge and follow-up	After 6 weeks[1]	2 (17%)	No
	After 3 months[1]	3 (25%)	No
	After 6 months[1]	3 (25%)	No
	After 12 months[1]	4 (33%)	No
Q17c. Frequently of follow-up	At transition moments (e.g., change of schools, from school to work)[1]	2 (17%)	No
	Once a year[1]	6 (50%)	No
Q20. Reasons for referral to primary care[2]	If treatment can be addressed by one discipline (no more need for multidisciplinary care)	6 (50%)	No
	If treatment/support is desirable closer to home	6 (50%)	No

Q: Question. n: number. *Theme of description/explanation: synthesis of answers by participants. #Similarities between centers: 'Yes' meaning more than 75% of the centers provided the same answer and 'No' (differences) meaning less than 75%.
[1]The timing and continuation of follow up appointments is in accordance with the patient/parents.
[2]When aftercare is indicated/appropriate.

DISCUSSION

This study found both similarities and variations among 12 Dutch RCs offering rehabilitation for young patients with ABI. Similarities regarding the presence of admission and discharge criteria, specialized teams, and structural follow-up were present in all RCs. Considerable differences were found as well, specifically regarding the description of the structure of rehabilitation care. Insights into similarities and differences may help reduce practice variation and optimize the quality of care for young patients with ABI. Here we discuss the implications of similarities and variations found in our study and provide recommendations for clinical practice and future research.

The description and use of admission and discharge criteria is considered important in clinical practice. Such criteria optimize resource allocation, ensure consistent patient treatment, promote patient safety, and enhance communication among healthcare professionals. Adhering to these criteria could enhance the quality of care within RCs. The importance of the description and use of admission and discharge criteria was also underlined in previous research.[6,16-18,20] Although all RCs in our study reported the presence of admission and discharge criteria, substantial differences in their actual descriptions were found. This is in line with previous studies.[21,22] A large variation (i.e., only mentioned by 5 RCs) was found in the admission criterium that "patients need to have participation restrictions in daily life". This variation is remarkable because optimizing participation is considered one of the ultimate goals of pediatric rehabilitation.[27,28]

The lack of generalized admission criteria that could be used in all RCs that provide pediatric ABI rehabilitation could be due to the heterogeneity of the population, although we have not investigated the cause of this variation. In addition, the attainment of rehabilitation goals, which is highlighted in the literature,[29] was considered an important discharge criterion among most RCs as expected, although this was not mentioned by all RCs. In line with previous literature that found variations in admission and discharge criteria in rehabilitation (adult stroke/arthritis populations),[21,22] we recommend reaching national consensus on clear and explicit criteria.

Regarding the organization of rehabilitation, the data collected among Dutch RCs show similarities and considerable differences as well. RCs were consistent in the need for specialized teams, with a wide variety of ABI-specific expertise. All RCs noted that they had a permanent team specialized in pediatric ABI. Yet, a remarkable finding was that despite the specialized teams being present in all RCs, not all teams had a general treatment program with specific outcome measures and interventions that would suit the target group

present. The absence of treatment program protocols could not only result in variations between RCs but also between team members within an RC. The lack of treatment program protocols in some RCs was also in line with the findings of previous studies that investigated practice variation.[21,22] Access to a treatment program protocol or guideline could reduce variation within teams and between RCs, whilst keeping the individual needs and wishes of patients (and their families) in mind. However, a national treatment program that could be used in all RCs when treating this population is lacking to date. Therefore, the creation of a national treatment program/guideline for the target group in outpatient rehabilitation is recommended.

While all RCs used age cut-offs to determine whether a young patient should be treated in a pediatric-appropriate or adult-appropriate rehabilitation setting, results showed variations in the cut-off-points across RCs (58% used 4-18 years as cut-off-point, 42% 4-20 years old). This could be due to the fact that some patients between 18 and 20 could better fit in a pediatric setting and some in an adult setting, based on their current needs and goals or purely based on age regardless of needs and goals.

Some RCs have “transition-teams”, to emphasize age-appropriate care for young adults where the focus lies on their transition from childhood to adulthood in relation to their ABI. Despite the importance of delivering age-appropriate care,[30] this was only seen in four RCs. Even though we do recognize that some RCs might not have the team/treatment capacity to organize this, we recommend focusing on more age-appropriate care.

All RCs reported that there are standard consults where treatment is being evaluated before ending rehabilitation and that there are structural follow-up appointments with rehabilitation physicians. These physicians discuss with patients/parents if and which form of aftercare is appropriate. Some RCs mentioned that referring to care facilities closer to home was considered important. National standards of care/guidelines also describe that providing sufficient aftercare for patients (also young patients with TBI/ABI) is important.[6,19] Our results showed differences between RCs in terms of the timing and frequency of aftercare, as well as the place where this is provided. This could be due to the current focus of pediatric rehabilitation care lies on individual patients, where every ABI, family, and system of patients is unique. This is important to consider in decision-making. In line with previous research,[16-24] setting clear criteria regarding the place, timing, and frequency of aftercare based on age and type of injury instead of only looking at individual patients could help to optimize aftercare for this pediatric ABI population. Due to regional differences in care pathways across RCs in the Netherlands, it is important to first look into possibilities to strengthen criteria regarding the place, timing, and frequency of aftercare within each RC separately before reaching national agreements on this matter.

Strengths and limitations

To date, this is the first (Dutch) study that investigated similarities and differences (practice variation) between RCs regarding the care for young patients with ABI on a considerably large scale (12 out of 16 RCs in the Netherlands). A structured approach was used for identifying similarities and differences among RCs. The recommendations that were provided in this study provide useful insights whilst keeping differences in care pathways between regions in mind. This 'look behind the curtains' in 12 RCs could enable collaborations between RCs and could eventually help reaching consensus on rehabilitation structures that currently vary across RCs that provide care for young patients with ABI.

This study also had some limitations. In this study, we explored the way rehabilitation care for children with ABI is organized in different RCs in The Netherlands. Therefore, we asked healthcare professionals how care is organized in the RC they work in. We have chosen to ask healthcare professionals because they have the role in the delivery of care. This may be a limited perspective since actively involving managers and policymakers might have resulted in a broader view. Future research could, for instance, use focus groups to potentially obtain a broader view per RC. Focus groups are a valuable research method that provides deeper insights and diverse perspectives, involving patients and relatives to enhance understanding of interventions' impact and outcomes. Furthermore, only Dutch RCs were included in the present study, thereby limiting outcomes in terms of generalizability for the care for young patients around the globe. However, this study provides information on how to obtain information regarding similarities and differences between RCs which could be useful for other countries/regions to look into their own possible practice variations.

Second, the answers that were provided by the participants could possibly be influenced by factors that were beyond the boundaries of their profession such as the financial influence of insurance companies and admission criteria of other care facilities in the aftercare process. The interplay between these factors should be further investigated.

CONCLUSION

If not explained by the case mix due to the heterogeneity of the population, exploring differences (variations) among RCs could help in reaching the goal of providing the best possible care for young patients with ABI. If RCs uniformly adhere to the same criteria and structure of treatment, this can support effective and timely referrals to RCs by medical specialists and general practitioners if indicated. Acknowledging differences that were

found among RCs in this study can be considered the first step to further optimize care. Focusing on reaching national consensus among RCs to reduce variations and uniform treatment in terms of content to optimize rehabilitation care for young patients with ABI should be the next step. Finally, joint frameworks about the organization and content of rehabilitation treatment can help clinicians/researchers with clinical reasoning and decision-making.

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Conflicts of interest

The authors of this study have no conflict of interest to declare.
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Appendix 1. Questionnaire to study the structure of ABI rehabilitation for young patients divided into topics, questions, and the way they could be answered

Topic 1	**Admission/discharge criteria for rehabilitation treatment**		
Question (Q)		**Closed answer (yes/no)**	**Open-ended (description)**
Q1.	Are there admission criteria before starting the rehabilitation treatment program?	X	
Q2.	Give a description of which admission criteria.		X
Q3.	Are there discharge criteria for ending the rehabilitation program present?	X	
Q4.	Give a description of which discharge criteria.		X
Topic 2	**The structure of rehabilitation treatment**		
Question (Q)		**Closed answer (yes/no)**	**Open-ended (description)**
Q5.	Is there a team specialized in pediatric ABI treatment present?	X	
Q6.	Give a description of which disciplines are in these teams (if any).		X
Q7.	Is there a specific consultation appointment for new pediatric patients with ABI present?	X	
Q8.	Give a description with whom the specific consultation hour is (if any).		X
Q9.	Does the RC use age cutoff points* in age groups for patients with ABI?	X	
Q10.	Give a description of which age cutoff points (if any).		X
Q11.	Is there a general program for the young adult age group (18-25 years)?	X	
Q12.	Give a specification of this program (if any).		X
Q13.	Is there a general ABI treatment program?	X	
Q14.	Give a description of availability (if any).		X
Q15.	Is there a standard last consult with the rehabilitation physician before ending the rehabilitation program?	X	
Q16.	Is there a structural end report with outcomes from the start and throughout the whole rehabilitation program/trajectory?	X	
Topic 3	**Aftercare**		
Question (Q)		**Closed answer (yes/no)**	**Open-ended (description)**
Q17.	Is there a structural follow-up appointment for the patient/parents after the rehabilitation program has ended?	X	
Q18a.	Give a description of with whom the patient/parents are receiving a structural follow-up appointment (if any).		X
Q18b.	Give a description of how much time this usually takes place after discharge (if any).		X
Q18c.	Give a description of how frequently this usually takes place (if any).		X
Q19.	Is there a structural referral to regional (care) facilities that support follow-up for the patient?	X	
Q20.	Give a description of reasons for referral to regional (care) facilities that support follow-up for the patient (if any).		X
Q21.	Is there structural cooperation with regional (care) facilities present in the follow-up process?	X	

* The use of age cutoff points for patients to differentiate from

CHAPTER 8

A national consensus-based framework on preferred assessments and interventions in current treatment for young people with acquired brain injury in Dutch rehabilitation centers

Submitted

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ABSTRACT

Purpose

To create a consensus-based framework with preferred assessments, interventions, and psychoeducational materials (PE-materials) to be used in pediatric ABI-rehabilitation to optimize the delivery of comparable care.

Methods

For this three-round Delphi study, healthcare professionals (physiatrists, psychologists, social workers, physical/occupational/speech/language therapists) from RCs providing care for young people with ABI were invited to participate. In the first two (online) rounds, currently used assessments/interventions/PE-materials were collected, stepwise-prioritized, subsequently listed per discipline, and classified per International-Classification-of-Functioning (ICF)-domain. Results from rounds one/two were discussed in a consensus meeting (in person), aiming to reach agreements on assessments/interventions/PE-materials in the national framework and how to use this in current practice.

Results

Seventy-four healthcare professionals from 14 rehabilitation centers (RCs) participated. After Delphi round one, 163 assessments, 39 interventions, and 64 PE-materials were collected. After round two, the selection was narrowed down to n=51/n=34/n=28, respectively. After round three, consensus was reached on 37 assessments, 25 interventions (divided over all disciplines/classified per ICF-domain), 27 PE-materials, as well as consensus on the use of the framework by all participating RC to enhance clinical reasoning in current practice.

Conclusions

A consensus-based national framework in ABI rehabilitation has been developed which is now available to optimize the delivery of care for young people with ABI across Dutch RCs.

Keywords: Health Care Organizations and Systems, Pediatrics, Clinical Practice Patterns/Guidelines/Resource Use/ Evidence Based Practice

INTRODUCTION

Acquired brain injury (ABI) is a comprehensive term for brain damage that occurs after birth including traumatic brain injury (TBI) and non-traumatic brain injury (nTBI).[1] ABI is prevalent in young people under the age of 25.[2,3] ABI can lead to significant disruptions in the development of a young person and it is known to be a leading cause of disability in this age group, worldwide,[2,3] as well as in the Netherlands.[4] Young people with ABI constitute a heterogeneous population in terms of age, type of injury, injury severity, and impairment levels, as well as in perceived limitations in activities and restrictions in participation.[5-7] For persisting problems in daily life young patients may at some point require rehabilitation treatment in specialized multidisciplinary rehabilitation teams.[8-11]

Several studies on the effectiveness of rehabilitation treatment for individuals with disabilities, including young patients with ABI, reported that the ultimate goal of rehabilitation treatment is optimal participation in society. The actual focus and content of rehabilitation treatment appeared to vary across these studies despite similarities in populations.[8,9,12-14] Variability in the provision of rehabilitation treatment for young patients with ABI is not only observed in the literature,[8,9,12-14] but also in daily practice. Despite the existence of a Dutch standard for quality of care for children (0-18 years) with TBI in The Netherlands,[15] exact structures or rehabilitation content is lacking. Therefore, substantial room for variation in rehabilitation treatment across rehabilitation centers (RCs) is possible.[15] Assessments (e.g., physical and cognitive) are considered particularly important in rehabilitation treatment and are widely used to determine the patient's current functioning, goalsetting,[16-18] and to evaluate interventions.[16,17] It is likely that the variation in assessments and interventions may in part be related to the scarcity of practice guidelines or recommendations on the rehabilitation treatment of young patients with ABI. Practice variations described in the literature and observed in daily practice may be signalizing suboptimal care, as was described in previous studies on rehabilitation treatment in adult populations (stroke/arthritis rehabilitation).[19,20]

The literature regarding the content of rehabilitation treatment for children and adolescents with ABI is scarce. Several studies give an overview of assessments and interventions for rehabilitation populations.[13,21-25] These studies focused on specific populations i.e., adults with stroke and ABI,[21] children with stroke,[22] and children with ABI in the acute phase.[23] However, these studies did not focus on multidisciplinary rehabilitation treatment for the population of young patients (4-25 years) with ABI as a whole.[13,23-25] Furthermore, psychoeducation (PE) is considered an important element of treatment interventions in pediatric ABI rehabilitation and many materials are available.[10,26] However, a list specific for the population of young patients with ABI in the rehabilitation setting is lacking to date.

Rehabilitation professionals (e.g., physiatrists, psychologists, physical therapists, occupational therapists, speech/language therapists, and social workers) in the Netherlands show a growing interest in harmonizing assessments and interventions used in pediatric rehabilitation treatment. Creating structured rehabilitation frameworks describing assessments and interventions are also in line with the principles of value-based healthcare (VBHC) to provide the best possible care for each individual child and their family.[27]

A national framework containing assessments, interventions, and psychoeducational materials (PE-materials) could decrease undesired practice variation and enhance the offering of comparable care for young patients with ABI regardless of where they live in the Netherlands. Further, it could stimulate collaborations and joint research projects across RCs in terms of (cost)-effectiveness and efficacy, which is also in line with the principles of VBHC.[27] Therefore, the goal of the current study was to create a national consensus-based framework on preferred assessments, interventions and PE in current outpatient rehabilitation treatment for young people, aged 4 to 25 years, with acquired brain injury in Dutch RCs.

METHODS

Design

In the current study, a three-round Delphi method was used to collect assessments and interventions used in rehabilitation treatment for children with ABI and to reach consensus among physiatrists and healthcare professionals across RCs regarding these assessments and interventions. In this study, the guidelines for the Delphi Survey Technique by Hasson et.al. were used.[28] In line with these guidelines,[28] two Delphi rounds addressed preferred assessments and interventions using online questionnaires (e-Delphi method [29]), followed by a consensus meeting using a nominal group technique (group-brainstorming through writing down, sharing, and voting on topics).[30] A list of PE-materials used in current practice was also collected during the Delphi rounds.

Setting

The current study was part of the multicenter project “Participate?! Next Step” (2021-2023) in which 14 Dutch RCs providing rehabilitation treatment for young patients between 4-25 years old with ABI participated. The project was led by a project group that consisted of a PhD candidate FA), and four senior researchers (AdK, FvM, TVV, and MvdH), all of whom are authors of the current study. The project also had an advisory board consisting of physiatrists, psychologists, and senior researchers (n=8). Their task was to advise and

assist in designing and conceptualizing the project as well as the outlines of the current Delphi study. Six members of the advisory board have contributed as authors in the current study (IR, SL, KH, PdK, StW, and CR). The project and study protocol were reviewed and approved by the medical ethical review board of the Leiden University Medical Center (P15.165-addendum-1). The local research committees from all participating RCs approved the project, including the current study.

Recruitment of participants

The physiatrists and healthcare professionals that were involved in the project "Participate?! Next Step" within the participating RCs were asked to propose up to 12 of their colleagues (physiatrists/healthcare professionals, up to two per discipline) to participate in the Delphi study. Potential participants were eligible to participate when they were (1) a physiatrist or a healthcare professional from one of the following disciplines: psychology, physical therapy (PT), occupational therapy (OT), speech/language therapy (SLT), or social work (SW); (2) when they were working with children and/or adolescents and/or young adults (4-25 years old) with ABI in daily practice; and (3) when they were willing to participate in all three rounds of the Delphi study. Subsequently, the project group provided information regarding the procedure, and planning of the Delphi study to potential participants by e-mail.

First Delphi round: In the first round of the Delphi study, participants received a unique link (by e-mail) to access an online questionnaire containing five questions. The first two questions were general, i.e., the RC of employment, discipline, and years of experience working with young patients with ABI (< 5 / ≥ 5 years). The other three questions were discipline-specific questions, concerning which assessments, interventions, and PE-materials they use within their discipline in current practice. Participants were asked to provide any information available on the description and/or validity of the assessments, interventions, and PE-materials. The participating physiatrists monitored and complimented the assessments, interventions, and PE-materials that were proposed by the healthcare professionals in their own RCs. The project group combined data from all completed questionnaires. The assessments, interventions, and PE-materials in daily practice across RCs in the first round were filtered for repeated listings. The surveys were conducted using Castor EDC. In line with the current Dutch standard of practice-based care,[15] assessments and interventions used in two or more of the participating RCs were included in the list for the second round. Thereafter, they were categorized by discipline (where applicable) and classified by the International Classification of Functioning (ICF) domains (body functions (b), activities and participation (d), environmental factors (e), and body structures (s)),[31] through ICF linking rules.[32] All described PE-materials were included in the list and proposed for the second Delphi round.

Second Delphi round: The participants who filled out the questionnaire in the first round were asked to participate in the second round. For every assessment and intervention that was selected after analyzing the first round, participants were asked whether they thought it should be included in the national framework on current practice (yes/no). After collecting the results of the second round, the project group used a level of agreement to reach consensus.

- When ≥ 75% of the respondents answered 'yes' to a proposed assessment/intervention the item was included in the concept framework.
- If 75% or more (≥) of the answers per assessment/intervention were answered by 'no' the assessment/intervention was rejected.
- If 25-75% of the answers per item were answered by 'yes', the assessment/intervention was put on a list to be discussed in the third Delphi round.

The concept framework for the discussion in the third round contained the items that were selected after the second round (assessments/interventions with ≥ 75% 'yes') and the items that had to be discussed were highlighted (items with 25-75% 'yes'). During the second round participants were asked to check the completeness/appropriateness of the PE-materials.

Third Delphi round: The third Delphi round consisted of an in-person meeting of approximately 4 hours to discuss and reach consensus on the results of the first two rounds. Prior to the meeting (approximately two weeks), all participants from the RCs received the concept framework in preparation for the meeting. One rehabilitation physiatrist and one other healthcare professional (either a psychologist, PT, OT, SLT, or SW) from each RC were allowed to be present due to national restrictions during the COVID-19 pandemic at the time. They were asked to represent their RC as a whole. The project group was present as well. The meeting was divided into two parts.

In the first part of the meeting, the way in which the national framework should be used for individual patients with ABI and their families in rehabilitation treatment was discussed. The aim of the discussion was to reach consensus regarding the best suitable and discipline-specific techniques for selecting assessments and interventions in clinical practice within the national framework for an individual patient with ABI.

In the second part of the consensus meeting, the 'concept framework' was discussed. Participants voted for acceptance/rejection per assessment/intervention that was listed in the category '25-75% yes'. Again, ≥ 75% agreement among RCs that were represented by physiatrists and healthcare professionals was used to include assessment/intervention. Less than 75% agreement between RCs meant no consensus was reached and therefore,

the assessment/intervention would not be included in the national framework. Thereafter, the list with assessments and interventions that were already accepted in the second Delphi round (i.e., with more than 75% answering 'yes') were presented and the participants had the opportunity to discuss these items prior to 'final acceptance'.

The list of PE-materials was proposed as well, for a final check of completeness. After the consensus meeting, the project group made a final list of assessments and interventions per discipline, and PE-materials (generic) that reached consensus in the Delphi process.

Analyses

All analyses were done using SPSS (IBM SPSS Statistics for Mac, version 28, Armonk, NY: IBM Corp). Descriptive statistics were used for the characteristics of the participants. Descriptive statistics were used to present responses from the first round and were expressed as numbers (n) and percentages (%). The dichotomous (yes/no) answers in the second round and the final accepted items in the third round are presented as numbers and frequencies, as well.

RESULTS

From 14 RCs in the Netherlands, 84 healthcare professionals were invited to participate. Of those, 76 (90%) responded stating that they were willing to participate in the study and completed the first round. The flow of included participants in this study is presented in Figure 1. Table 1 shows the characteristics of the participants. Eleven physiatrists (14.5%), 15 psychologists (20%), 10 PT (13%), 19 OT (25%), 12 SLT (16%), and 9 SW (11.5%) participated. In the second round, 56 participants responded (74% of 76 responders in total). Finally, 28 physiatrists and/or healthcare professionals that represented their RC and the project group (n=5) participated in the in-person consensus meeting for the third round (total participants 33).

First and second online Delphi rounds

After the first Delphi round, a total of 136 unique assessments were listed. During the first Delphi round, the psychologists, representing all participating RCs, proposed a battery for neuropsychological testing, which was listed throughout the Delphi rounds as one assessment. Fifty-one assessments were considered to be related to the field of PT, 45 for OT, 38 for SLT, and two for SW (Table 2). Concerning the interventions, 39 were listed after the first round; 9 for psychology, 8 for PT, 13 for OT, 6 for SLT and 5 for SW (Table 3). Twenty-seven PE-materials were collected and included in the list (Table 4).

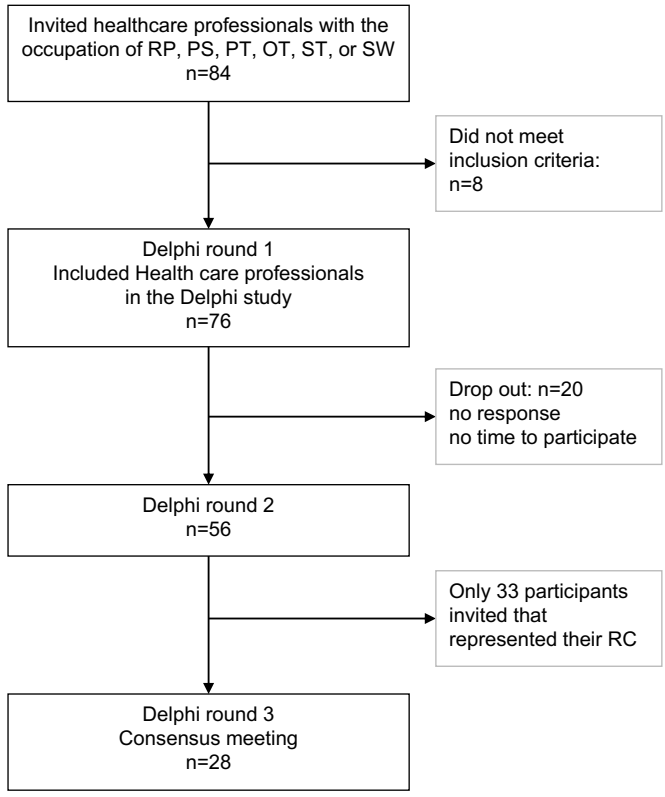

Figure 1. Flow diagram of participants in the Delphi study on assessments, interventions, and psychoeducation materials used in outpatient rehabilitation treatment of young patients with ABI.
RP: Rehabilitation physiatrists, PS: Psychologists, PT: Physical Therapists, OT: Occupational Therapists, ST: Speech Therapists, SW: Social Workers.

For the second Delphi round, the number of assessments narrowed down from 136 to 45 and interventions from 39 to 34, PE-materials remained at 27.

Consensus meeting (third Delphi round)

In the first part of the meeting, consensus was reached on the underlining importance of working in a multidisciplinary and interdisciplinary team due to the heterogeneity and complexity of the target group where the expertise of each discipline complements the other. For example, physical therapists and occupational therapists could combine their expertise when using an intervention to enhance the best possible care for an individual. Consensus was also reached on how to select appropriate assessments and interventions from the framework to use with the individual patient. A majority of participants (> 75%)

Table 1. Characteristics of participating health care professionals in the three-round Delphi study.

Characteristics of participants n=76	Number (%)
Rehabilitation center, n (%)	
· Adelante, Valkenburg	4 (5%)
· Basalt, The Hague	9 (11.5%)
· de Hoogstraat, Utrecht	5 (7%)
· Heliomare, Wijk aan Zee	4 (5%)
· Klimmendaal, Apeldoorn	8 (10%)
· Libra, Eindhoven	4 (5%)
· Merem, Hilversum	5 (7%)
· Reade, Amsterdam	5 (7%)
· Revalidatie Friesland, Beetsterzwaag	8 (10%)
· Revant, Breda	9 (11.5%)
· Roessingh, Enschede	5 (7%)
· Vogellanden, Zwolle	8 (10%)
· Rijndam, Rotterdam	1 (2%)
· UMCG/Beatrixoord	1 (2%)
Discipline, n (%)	
· Physiatrists	11 (14.5%)
· Psychologists	15 (20%)
· Physical therapists	10 (13%)
· Occupational therapists	19 (25%)
· Speech language therapists	12 (16%)
· Social workers	9 (11.5%)
Years of working experience with the target group, n (%)	
· < 5 years	23 (30%)
· > 5 years	53 (70%)

agreed that clinical reasoning was important when selecting assessments and interventions for individual patients. Participants suggested to adjust a previously developed flowchart (Swinkels et.al.) for facilitating the selection of the most appropriate assessments and interventions from the framework to be suitable for the individual patient with ABI. After the consensus meeting the project group developed this flow chart (Figure 2), which participants approved (by email).

During the second part of the meeting, consensus was reached on a list of 37 assessments to be included in the national consensus-based framework across the disciplines: 9 for PT, 10 for OT, 15 for SLT, and 2 for SW. The psychologists present during the meeting confirmed the battery for neuropsychological testing was to be listed as one assessment in the national framework. Furthermore, consensus was reached on a total of 25 interventions: 5 for psychology, 6 for PT, 7 for OT, 4 for SLT, and 3 for SW. The listed assessments and

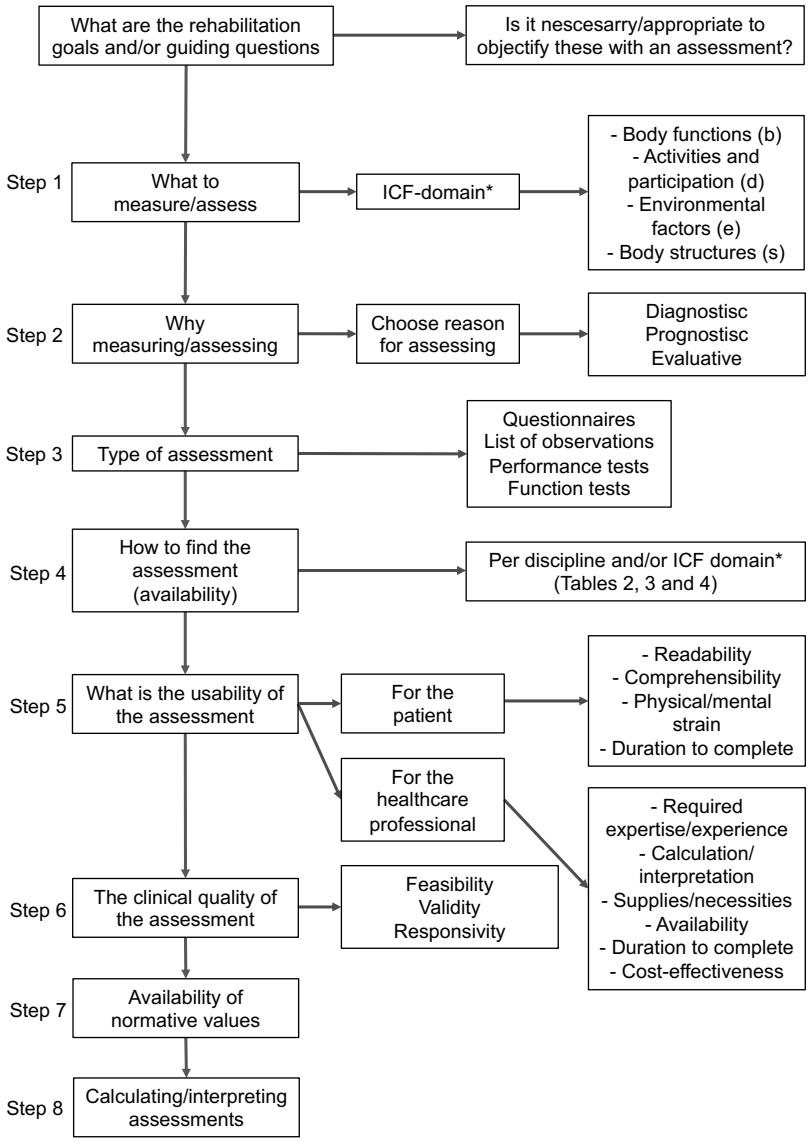

Figure 2. Flowchart for selecting appropriate assessments in clinical practice from the national consensus-based framework.
Based on: "Raamwerk klinimetrie voor evidence-based products", Swinkels et.al. 2016.33
* Body functions (b), activities and participation (d), environmental factors (e), and body structures (s): domains and sub-domains of the International Classification of Functioning, Disability and Health (ICF).

interventions corresponded with all ICF domains including body functions and structures (n=25 assessments, n=15 interventions), activities and participation (n=30 assessments, n=19 interventions), environmental factors (n=8 assessments, n=11 interventions), and body structures (n=20 assessments, n=10 interventions). Finally, all listed PE-materials were confirmed by the group and included in the national framework.

All assessments, interventions, and PE-materials that were confirmed during the consensus meeting were added and merged by the project group to create the national consensus-based framework. Approximately two months after the meeting, the framework was sent to the participating physiatrists and healthcare professionals for a final check. This did not result in any alterations in the list.

See Table 2, Table 3, and Table 4 for the list of all accepted assessments, interventions, and PE-materials in the national consensus-based framework.

Table 2. Assessments per ICF-domain after the three-round Delphi study among healthcare professionals from fourteen Dutch rehabilitation centers.

Discipline	Delphi round 1	Delphi round 2	Result after consensus meeting	
			Accepted assessment	
Psychology	n=1	n=1	n=1	Battery for Neuropsychological testing *
Physical therapy	n=51	n=17	n=91	Two-point discrimination test
				Six-minute walking test (6MWT)
				Standaard lichamelijk onderzoek *
				Gait analysis
				Acquired Brain Injury Challenge Assessment (ABI-CA)
				Visual Analogue Scale (VAS)
				Shuttle run test (SRT)
				Hand-held Dynamometer (HHD)
				Functional Strength Measurement (FSM)
Occupational therapy	n=45	n=10	n=10	"Systematische Opsporing Schrijfproblemen (SOS-2-NL)" writing test *
				Jamar meter / pinch meter
				Nine Hole Peg Test
				AssistingHand Assessment (AHA)
				"Activiteitenweger" *
				Sensory Profile (SP)
				Daily activities observation list ("ADL observatielijst") *
				Canadian Occupational Performance Measure (COPM)
				Perceive, Recall, Plan Perform (PRPP)
				The Beery-Buktenica Developmental Test of Visual-Motor Integration, 6th Edition (Beery VMI 6TH edition)
Speech therapy	n=38	n=15	n=15	"Nederlandstalig Dysartrieonderzoek – Kinderen (NDO-K) *
				Token Test
				Peabody Picture Vocabulary Test
				Clinical Evaluation of Language Fundamentals (CELF-5)
				Schlichting test *
				Computer-Based Instrument for Low Motor Language Testing (C-BiLLT)
				Boston naming Task (BNT) *
				Renfrew Expressive Vocabulary Test (REV-T)
				Analysis of spontaneous language production
				90ml swallow test
				Cervical auscultation *
				The Radboud Dysarthria Assessment
				Sunnybrook
				Drooling quotient
				Diagnostic instrument for apraxia (DIAS) *
Social work	n=2	n=2	n=2	Family Questionnaire *
				Questionnaire focused on burden of care *
TOTAL	n=136	n=45	n=37	

* Outcome measure only available and/or only developed in Dutch. # body functions (b), activities and participation (d), environmental factors (e), and body structures (s): domains and sub-domains of the International Classification of Functioning, Disability and Health (ICF). 1 additional physical therapy assessments (n=6) that can be used as alternatives for the accepted assessments: Medical Research Council (MRC)-scale test, Functionele spierkracht test*, Steep Ramp Test, Bruce test, Movement-ABC-2 Test, Gross motor function measure (GMFM).

	ICF (sub)domain#			
	b	**d**	**e**	**s**
	b1	d1/d2	e3/e4	s1
	b256/b280			
	b450	d420/d450		s770/s730
	b735	d420		s730/s730
		d420/d450		s770/s730
	b450/b7300	d420/d450		s770/s730
	b280			
	b450/b740	d420/d450		s770/s730
	b7300/b740			
	b450/b7300	d420/d450		s770/s730
	b147/b760	d440		s750
	b7300	d440		s750
	b147/b760	d440		s750
	b147/b760	d440		s750
		d2303		
		d2303/d710-d779	e310-e399	
		d2303/d710-d779	e310-e399	
		d2303/d710-d779	e310-e399	
	b147	d2303/d710-d779	e310-e399	
	b147	d2303		s750
	b167/b310-b330			
	b167/b310-b330			
	b167/b310-b330			
	b167/b310-b330			
	b167/b310-b330	d330		s310-s340
	b167/b310-b330	d330		
	b167/b310-b330	d330		
	b167/b310-b330	d330		
	b167/b310-b330	d330	e310-e399	s310-s340
		d330/d550-d560		s310-s340
		d330/d550-d560		s310-s340
		d330/d550-d560		s310-s340
		d330/d550-d560		s310-s340
		d330/d550-d560		s310-s340
	b167/b310-b330	d330		s310-s340
		d710-d799	e310-e399	
		d710-d799	e310-e399	

Table 3. Interventions per ICF-domain after the three-round Delphi study among healthcare professionals from fourteen Dutch rehabilitation centers.

Discipline	Delphi round 1	Delphi round 2	Result after consensus meeting	
			Accepted intervention	
Psychology	n=9	n=7	n=5	Cognitive behavior Therapy (CBT)
				Eye Movement Desensitization & Reprocessing (EMDR)
				Family meetings
				Acceptance & Commitment Therapy (ACT) [1]
				Strategy training *
Physical therapy	n=8	n=8	n=6	Graded activity / graded exposure [1]
				Fitness training
				Functional training
				Mindfulness
				Training through the "frequency, intensity, time, and type" (FITT)-factors
				Advice regarding sports
Occupational therapy	n=13	n=8	n=7	Strategy training *
				Wheelchair training *
				Graded activity /graded exposure [1]
				Constrained- Induced Movement Therapy (CIMT)
				Independence training *
				Niet Rennen Maar Plannen *
				Errorless learning method
Speech therapy	n=6	n=6	n=4	Prompts Restructuring Oral Muscular Phonetic Targets
				Language therapy*
				Assistive communication training*
				Logo Art Online
Social work	n=5	n=5	n=3	Family meetings
				Acceptance and Commitment Therapy (ACT)[1]
				Therapy focused on the whole social system*
TOTAL	n=39	n=34	n=25	

* Intervention only available and/or only developed in Dutch. # body functions (b), activities and participation (d), environmental factors (e), and body structures (s): domains and sub-domains of the International Classification of Functioning, Disability and Health (ICF). 1Test applicable for multiple disciplines.

	ICF (sub)domain#			
	b	**d**	**e**	**s**
		d250		
		d250		
			e310-e399	
	b1	d160-d179	e310-e399	s110
	b1	d160-d179		s110
	b740		e3/e4	
	b450/b740	d450		s730/s770
	b450/b740	d420/d450		s730/s770
	b735			
	b450/b740/b7300	d420/d450		s730/s770
			e3/e4	
	b1/b147	d160-d179		s110
	b147/b740/b760	d440		s750
	b740		e3/e4	
	b147/b760	d2303/d440/d710-d779	e330-e399	s750
			e330-e399	
		d2303/d440/d710-d779		
		d2303/d440/d710-d779		
	b167/b330	d330	s310-s340	
	b167/b310/b330	d330	s310-s340	
	b167/b310/b330	d330	e330-e399	
	b167/b330	d330		
		d710-d799	e310-e399	
		d710-d799	e310-e399	
		d710-d799	e310-e399	

Table 4. Psychoeducational materials after the three-round Delphi study among healthcare professionals from fourteen Dutch rehabilitation centers.

Result after consensus meeting		
Accepted psychoeducation		
Total number	**Specification of type**	**Name/title**
n=27	Book n=13	"Ik hou nog steeds van appeltaart" *
		"Brainstars" *
		"Speels brein" *
		"Mag ik ook ff" *
		"NAH niet altijd handig" *
		"Waarom heeft een krokodil zo'n platte kop" *
		"Elvin het vergeetachtige olifantje" *
		"Er lijkt niets met ons aan de hand maar dat is niet zo. Ons hoofd moet heel hard werken" *
		"De puzzel van nah" *
		"Bordje vol" *
		"Omgaan met hersenletsel" *
		"De Zorgzame Giraffe, autobiografisch verhaal over Niet Aangeboren Hersenletsel" *
		"Volle Hoofden Boek (werkboek voor kinderen/ jongeren)" *
	Folder n=4	"Hoe verder na traumatisch hersenletsel bij kinderen en jongeren" *
		"Slaaptips voor kinderen en pubers" *
		"Het NAH boekje voor onderwijs" *
		Brains ahead! study
	Internet Site n=7	Breinstraat.nl *
		hersenletseluitleg.nl *
		Kinderneurologie.eu *
		Overprikkeling.com *
		"Afasienet.com" *
		"Brain Blocks"
		"Methode RIK (Revalidatie En Ik)" *
	Movie n=1	"Ze zeggen dat ik zo veranderd ben" *
	Standard of care n=1	Traumatisch Hersenletsel Kinderen & Jongeren *
	Application n=1	Energie/activiteitenweger *

* Psychoeducation only available and/or only developed in Dutch.

DISCUSSION

In the current study, the process of developing a national consensus-based framework on preferred assessments, interventions, and PE-materials for young patients with ABI (4-25 years old) and their families was described. This is the first known study to describe the consensus-building process on a national scale across physiatrists and healthcare professionals to optimize and harmonize rehabilitation treatment for the pediatric ABI population.

Prior to the consensus meeting of this study, 136 different assessments and 39 interventions were used in the rehabilitation treatment of young patients with ABI and their families in the Netherlands, many of which were only used by a few healthcare professionals across RCs. Many of the assessments and interventions were generic and not specifically developed for the target group. This necessitates employing assessments to pinpoint the specific ICF domains where daily life problems occur.[31] Selecting the best suitable assessments to evaluate treatment outcomes for specific daily life problems in young patients with ABI can facilitate this need.

In terms of assessments in the field of psychology, only the 'battery for neuropsychological testing' (in Dutch: neuropsychologisch onderzoek, NPO) was proposed in the Delphi rounds by the participating psychologists. A national consortium of psychologists and physiatrists had already reached consensus on the use of this testing battery which contains tests to assess cognitive and mental functioning for the population of young patients with ABI in rehabilitation. This test battery was also described and recommended in the Dutch standard of care,[15] which was also the only specific assessment that was described in this standard of care.

Through the Delphi study consensus was reached on 37 assessments that covered all domains of the ICF model.[31] It is expected that this set is suitable for measuring the complete range of possible daily life problems and patient functioning and evaluating interventions in the ABI patient population. Many of these listed assessments were psychometrically tested and used among young patients with a wide variety of diagnoses in general pediatric rehabilitation.[16,17] However, most assessments were not psychometrically tested for the specific pediatric ABI patient population in rehabilitation. Nevertheless, a consensus-based framework of assessments can be used as a tool to potentially diminish practice variation and to help healthcare professionals with selecting the best suitable assessments for the target group. With confirmation of all participating Dutch RCs, this framework will be used in the future continuously which provides the opportunity to gather evidence on the use of the assessments not specifically designed for ABI.

In line with the assessments, interventions focusing on ABI-related consequences that align with diagnosis- and age-specific treatment are crucial for effective rehabilitation treatment.[13,21-25] The use of evidence-based interventions by healthcare professionals in various patient groups, including children with moderate/severe TBI and adult stroke, has been documented in the literature (e.g., cognitive behavior therapy, graded activity training, and the ABI-challenge assessment).[13,23,25] Prior to the current study, healthcare professionals used a wide variety of treatment interventions, and a large variation was seen across RCs in the Netherlands. The Delphi study resulted in a consensus on 25 interventions that covered the whole range of ICF domains.[31] Consequently, future research should investigate the optimal fit of currently proposed interventions for patients with specific ABI-related problems (e.g., cognitive fatigue, participation restrictions or social/emotional problems) and in specific age groups (e.g., adolescents that are in transition from childhood to adulthood).

The benefits of psychoeducation have been emphasized in earlier research and standards of care as being an important intervention to help young patients and their families to optimize functioning in daily life by better understanding the sequelae of ABI.[15,26,31] Psychoeducation is known to be effective before and during rehabilitation treatment for patients and their parents by for example enhancing knowledge on brain injury.[10] The Delphi study identified a list of PE-materials that can be used in rehabilitation treatment. Nevertheless, many of these materials were not specifically developed for the rehabilitation population of young people with ABI and their families. Additionally, a few of the PE-materials on the list included movies, apps, and websites, all of which are inherently transient and subject to change. It is crucial to continue developing and editing this list of materials in accordance with new insights into recovery and functioning after ABI of young patients in the rehabilitation setting.

Recommendations

To harmonize rehabilitation treatment across RCs in the Netherlands, consensus was reached on the implementation process of this national consensus-based framework by all the participating RCs (with their teams of physiatrists and healthcare professionals) that provide care for young patients with ABI and their families which is in line with the principles of VBHC.[27]

It is recommended that this framework is used as a tool during rehabilitation treatment to enhance selecting appropriate assessments in clinical practice. This was partly based on the flowchart by Swinkels et.al.[33]

Another recommendation arising from this Delphi study is that all disciplines involved during rehabilitation treatment should work together and look further than their own discipline to optimize the best possible multidisciplinary care for the young patient with ABI.

In line with VBHC principles,[27] as well as with literature in pediatric cerebral palsy rehabilitation,[18] a final recommendation is that the needs, wishes, and goals of individual patients with ABI and their families are important to consider when using this national consensus-based document as a healthcare professional.

Future research and development should focus on gathering evidence on the listed assessments, interventions, and PE-materials (in terms of psychometric properties and effectiveness) to make the consensus-based national framework more evidence-based.

Limitations

This study had a number of limitations. First, not all Dutch RCs providing rehabilitation treatment for young people with ABI participated in either the project "Participate?! Next Step" or the current Delphi study (14 out of 16 in total), which may have resulted in an incomplete picture/missed assessments, interventions, and PE-materials.

Secondly, most of the results of the Delphi study were applicable to the age group of 4-18 years. Only a few RCs that participated in the current study have a separate transition outpatient clinic through 25 years, in which the transitions from childhood and adolescence to adulthood get specific attention. Assessments, interventions, and PE-materials specifically for the age group of 18 to 25 years should be explored further, in line with recommendations to focus on age-appropriate care.[15,34]

Third, the care pathways, methods, and treatment offer in healthcare differs between countries making the results of this study less generalizable to ABI populations in other countries. Nevertheless, the outlines, procedures, recommendations, and limitations from the current study could be an example for similar research in other countries.

Fourth, when collecting assessments, interventions, and PE-materials for this framework, only healthcare professionals participated. In line with VBHC principles,[27] perspectives of patients and their parents on the content of rehabilitation treatment would also be important to take into account when optimizing the current national consensus-based framework.

CONCLUSION

This study developed a national consensus-based framework with preferred assessments, interventions, and PE-materials in outpatient rehabilitation treatment of young patients with ABI and their families in The Netherlands. This provides a valuable contribution to optimizing the care and support for these patients and their families. The framework can be used in clinical practice as a tool to enhance selecting appropriate assessments and setting goals at the start before, during, and after outpatient rehabilitation. The consensus-building process described in this study can be used as a blueprint by other research groups to create similar frameworks for other diagnoses. Future research should focus on substantiating and improving the current 'practice-based' national framework into an evidence-based guideline in terms of psychometric properties and effectiveness on the listed assessments, interventions, and PE-materials for the pediatric ABI population.

Declarations

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CHAPTER 9

Summary and general discussion

SUMMARY

Acquired Brain Injury (ABI) refers to any damage to the brain that occurs after birth caused by either Traumatic Brain Injury (TBI) or Non-Traumatic Brain Injury (nTBI).[1] ABI is a relatively common condition in Dutch children, adolescents, and young adults aged between 4 and 25 years old.[2,3] It can have significant and persisting consequences across various health domains.[2,4-7] When the impact of ABI is substantial, it may necessitate inpatient or outpatient medical specialist rehabilitation in a rehabilitation center.[2,8-10] This thesis aimed to enhance the understanding of ABI-related consequences and optimize the quality of rehabilitation provided to young individuals with ABI in the Netherlands by addressing the following overarching research questions:

First, to describe the course and/or severity of Health-related Quality of Life (HRQoL), fatigue, participation, and family impact in young people with ABI and their families referred to outpatient medical specialist rehabilitation between referral and one and two years later.

Second, to describe and compare the structure and process of rehabilitation for young patients with ABI across Dutch rehabilitation centers and develop a national consensus-based framework for clinical practice, including preferred assessments, interventions, and psychoeducation, for young people with ABI across Dutch rehabilitation centers.

Chapter 1 provides a general, comprehensive overview of ABI in young individuals aged 4-25 years. It covers key aspects, such as definitions, epidemiology, consequences, and stages of recovery, and current management, with a focus on medical specialist rehabilitation.

Furthermore, this chapter introduces the background of two research projects that have contributed data to the studies within this thesis. The first project, entitled “Participate?!”, concerned a cohort study conducted in ten Dutch rehabilitation centers. This project systematically collected data from consecutive patients with ABI and their parents on various domains of functioning over time. The second project, “Participate?!” Next Step included a mixed-methods study among healthcare professionals from 14 Dutch rehabilitation centers. This multifaceted project utilized a cross-sectional survey study to investigate the occurrence of practice variation across rehabilitation centers and to develop a national framework with preferred assessments, interventions, and psycho educational materials in pediatric ABI rehabilitation practice.

Section 1. Persisting consequences of ABI in young individuals and their families referred to outpatient rehabilitation in the Netherlands

In this thesis the persisting consequences after ABI among young individuals are described, specifically focusing on the International Classification of Functioning, Disability and Health (ICF) domains *'body functions and structures'* (**Chapters 2 and 3**), *'activities and participation,* (**Chapter 4**), and '*environmental factors'*, (**Chapters 5 and 6**). The data used in the studies described in **Chapters 2-6** were gathered by means of a multicenter cohort study (Project "Participate?!"). Over a four-year period, ten rehabilitation centers gathered data from consecutive patients with ABI between 5-24 years old and their parents at admission (baseline) and one and two years later. Patient-Reported Outcome Measures (PROMs) were used to assess various health domains, including Health-Related Quality of Life (HRQoL), fatigue, participation restrictions, and family impact. Specifically, the following PROMs were employed: the Pediatric Quality of Life Inventory™ Generic Core scales-4.0 (PedsQL™ GCS-4.0),[11-13] the PedsQL™ Multidimensional Fatigue Scale (PedsQL™ MFS),[14-16] the Child and Adolescent Scale of Participation (CASP),[17,18] and PedsQL™ Family Impact Module (PedsQL™ FIM).[19] In addition to these PROMs, a questionnaire was administered to collect data on demographics, injury specifics, patient characteristics, and family related factors. At baseline 223 young patients and 246 parents were included. From 94 patients and 104 parents, data was available at follow-up at either one year (T1), two years (T2), or both. The number of patients and parent may vary for the different analyses as the proportions of patients and parents completing specific instruments varied both within and across time points.

Chapter 2 described the extent of fatigue in young patients with ABI following outpatient rehabilitation using the PedsQL™ MFS as completed by patients and parents at baseline. For this cross-sectional analysis, the total score and subdomain scores to capture general fatigue, sleep/rest, and cognitive fatigue from the PedsQL™ MFS were used (scores ranging from 0 to 100, lower scores indicating higher fatigue levels). Additionally, the severity of fatigue was categorized using previous data from two studies with healthy Dutch peers to create cut-off scores. The mean fatigue scores and their corresponding standard deviations (SD) from healthy peers were used to quantify the number of standard deviations by which the patients in our cohort deviated from the mean scores of healthy peers. Based on the total scores of the study participants and the data from healthy peers four severity categories of fatigue scores were distinguished:

1: scores more than +1SD difference (less fatigued compared to healthy peers),
2: scores between +1SD and -1SD (fatigue comparable with healthy peers),
3: scores between -1SD and -2SD (moderately more fatigued),
4: scores with more than -2SD difference (severely more fatigued than healthy peers).

Findings showed that patients with ABI and their parents reported considerable fatigue, with mean (SD) patient-/parent-reported PedsQL™ MFS total scores of 51.0 (17.3)/ 53.5 (19.2), respectively. These scores were significantly lower than those of healthy peers, which ranged between 71.8 (14.6) and 82.1 (17.8). Fifty to 88% of the young patients with ABI either scored in the "moderately more fatigued" or the "severely more fatigued" categories. It was concluded that categorizing fatigue severity cut-off scores appeared to be a suitable tool for monitoring fatigue. This categorization could be used next to the linear scores from the PedsQL™ MFS.

In **Chapter 3**, the course of fatigue and participation and their relationship over time were assessed. For this longitudinal observational study, the PedsQL™ MFS and CASP from the same cohort were used. Linear mixed models were used to assess the changes in fatigue and participation scores over time (change scores, (95% CI), p-values) and repeated measures correlations were used to describe correlations (r_{rm}, (95% CI), p-values) between fatigue and participation over time. 223 patients and 246 parents completed the questionnaires at baseline, whereas 94 patients and 104 parents completed the same questionnaire at T1, T2, or both time points. Patient-reported fatigue and participation scores improved significantly between baseline and T2 (+8.8, (2.9-14.7), $p < 0.05$ and +10.5, (6.3-14.7), $p < 0.05$). Comparable results were found regarding parent-reported fatigue (+8.7, (3.4-13.9), $p < 0.05$), but not for participation (+3.9, (1.1-7.7), $p > 0.05$). Fatigue scores were relatively low at baseline and fatigue remained considerably present two years after referral to rehabilitation. A moderately strong longitudinal correlation between patient-reported PedsQL™ MFS and CASP scores over time (r_{rm}=0.7, (0.6;0.8), $p < 0.001$), and a fair correlation for parent-reported data (r_{rm}=0.5, (0.3;0.6), $p < 0.001$) was found. These findings suggest that increased fatigue can lead to more participation restrictions at all time points. Despite the improvements over time, patients were still more fatigued than their healthy peers, and participation remained limited.

Participation restrictions among young patients with ABI and the differences between the patients' and parents' perspectives are described in **Chapter 4**. For the purpose of this cross-sectional study using data from the same cohort that was described in previous chapters, CASP scores were classified into four categories:
1: scores between 100–97.5 (full participation),
2: scores between 97.5–81.0 (somewhat limited participation),
3: scores between 81.0–68.5 (limited participation),
4: scores below ≤ 68.5 (very limited participation).

Considerable participation restrictions were found. Parents -reported significantly less participation restrictions compared to patients (91.3 (IQR: 80.0-97.5) vs 82.5 (IQR: 67.5-90), $p < 0.05$). In particular young adults tended to rate their participation worse than parents. A notable proportion of patients (n=58, 26%) and parents (n=25, 10%) reported scores reflecting "very limited" participation. It was concluded that measuring participation restrictions following ABI and accounting for both the perspectives of patients and parents is important in outpatient rehabilitation treatment. Furthermore, categorizing the CASP scores appears to be useful in clinical practice.

Chapter 5 focused on the impact of ABI in a child on families at the time of referral to rehabilitation and factors associated with that impact. Parents of patients participating in the same cohort study as described previously completed the PedsQL™ FIM to assess family impact (scores 0-100, with lower scores indicating a higher family impact). For this cross-sectional analysis parent-reported data at baseline were used. Univariate and multivariate regression analyses were conducted to explore the factors associated with family impact. Parents reported substantial family impact (median total score 71.9, IQR 60-85), particularly in the "worrying" domain (65.0, IQR 50-80). Factors associated with higher family impact included the presence of nTBI, referral to rehabilitation longer than six months after ABI onset, worse mental/emotional health, worse HRQoL of the entire family, and the presence of premorbid learning/behavioral/health-related problems. Higher age and TBI severity did not seem to have a significant effect on family impact. These results emphasize the necessity of measuring the impact on families within the population of young patients with ABI.

In **Chapter 6**, the course of family impact over time and its relationship with patients' HRQoL was investigated This longitudinal study used the PedsQL™ FIM and the parent-reported PedsQL™ GCS-4.0 (to assess patients' HRQoL) at the time of referral and one and two years later. The group of patients were split into TBI and nTBI groups. Linear mixed models were used to examine family impact and HRQoL over time (change scores (95% CI), p-values). Repeated measure correlations were used to find correlations between family impact and patients' HRQoL (r_{rm}, p-values). Baseline data from 181 parents of patients with TBI and 65 with nTBI were used for this analysis. The results showed that family impact did not change over time in the TBI group (+2.1, (-1.9, 6.2), $p > 0.05$) and was still considerable after two years (mean score 77.0). Only worrying improved significantly in the TBI group (+8.6, (2.1, 15.1), $p < 0.05$). In contrast with TBI, family impact improved statistically significantly in the nTBI group (+5.8, (0.2, 11.4), $p < 0.05$). A statistically significant improvement was also seen for all domains of the patients' HRQoL over the same period ($p < 0.05$) in both the TBI and nTBI groups. A moderately strong longitudinal correlation between family impact and

patients' HRQoL (r_{rm}=0.51, p < 0.001) was observed. These results indicate that apart from HRQoL, family impact should be monitored before, during, and after rehabilitation in young patients with ABI.

Section 2. Joint collaborations between rehabilitation centers to optimize care for young individuals with ABI

Next to describing persistent consequences of ABI, the provision of appropriate care to address these consequences is very important. For this purpose, it is important to gain insight into the current delivery of rehabilitative care, which can be described in terms of its structure, and outcomes.[20] Regarding the studies in **Chapters 7 and 8**, fourteen Dutch rehabilitation centers (out of sixteen in total) that provide medical specialist rehabilitation for young individuals with ABI participated in project "Participate?! Next Step". Each rehabilitation center proposed one (or two) lead experts who assisted throughout the project on behalf of their rehabilitation center. Regarding the structure of rehabilitation for this population, similarities and differences across rehabilitation centers were identified in **Chapter 7**. With respect to the outcomes and content of treatment, the consensus-building process of a national treatment framework is described in **Chapter 8**.

Chapter 7 comprises a cross-sectional survey study, where rehabilitation professionals completed a 21-item questionnaire on the structure of outpatient ABI rehabilitation. The topics were related to the admission/discharge criteria, organization of rehabilitation, and aftercare. The similarity in rehabilitation practice was defined as ≥ 75% concordance of responses among rehabilitation centers. Twelve rehabilitation centers participated. All rehabilitation centers reported the use of admission and discharge criteria, however their content varied. Differences were also observed in the presence of 'transition teams' for young adults (present in four out of twelve rehabilitation centers (33%)) and general ABI-treatment programs in terms of the organization of rehabilitation (present in eight out of twelve rehabilitation centers (67%)) stated they used such a program. For aftercare, differences were observed in the timing of discharge and follow-up. This study highlighted variations in the delivery of care for patients with ABI across Dutch rehabilitation centers, suggesting the need for the development of a national framework to enhance the provision of comparable care for young individuals with ABI.

The consensus-building process of a national framework for healthcare professionals including preferred assessments, interventions, and PE-materials for young individuals with ABI in the rehabilitation setting is described in **Chapter 8**. This study comprised a three-round Delphi study involving healthcare professionals from 14 Dutch rehabilitation centers with different disciplines (physiatrists, psychologists, social workers, physical therapists, occupational therapists, and speech therapists). In the first two online rounds, currently

used assessments, interventions, and psycho educational materials (PE-materials) were collected, stepwise prioritized, and listed per occupation discipline according to ICF domains. Results from the first two rounds were discussed in a live consensus meeting to reach consensus on all three aspects of the framework and its implementation and usability in current practice. A total of 74 healthcare professionals from 14 rehabilitation centers participated in this study. After all Delphi rounds, consensus was reached on the use of 37 preferred assessments, 25 interventions, and 27 preferred PE materials. Additionally, consensus was reached on how to use the framework to enhance the selection of appropriate assessments and interventions in current practice. The developed consensus-based national framework aids in uniforming and optimizing the delivery of care for young individuals with ABI across Dutch rehabilitation centers.

GENERAL DISCUSSION

Identifying, targeting, evaluating and monitoring the consequences of Acquired Brain Injury (ABI) in children, adolescents and young adults (4-25 years old) are essential elements of medical specialist rehabilitation care for this patient group. Currently, there are a number of knowledge gaps regarding the occurrence and severity of consequences and the delivery of rehabilitation care, hindering the optimalization of care. This thesis addressed the specific characteristics of ABI in young individuals and their families who were referred for rehabilitation, examined the consequences of ABI in terms of various aspects of health status (**Section 1**), as well as the current and desired delivery of medical specialist rehabilitation for this patient population (**Section 2**).

This General discussion reflects on this thesis in the context of the available knowledge from existing literature, highlights methodological considerations, provides insights into potential areas for future research, and discusses implications for rehabilitation practice.

Section 1. Persisting consequences of ABI in young individuals and families referred to outpatient rehabilitation in the Netherlands

The studies in **Chapters 2 to 6** of his thesis showed that the majority of young individuals who were referred to a rehabilitation center due to persisting ABI-related consequences had mild injuries. Nevertheless, it was found that the whole population described in this thesis experienced severe and long-lasting consequences from their ABI on multiple domains of the World Health Organization International Classification of Functioning, Disability and Health (ICF).[21]

Impairments in body functions and structures: Fatigue in young patients with ABI

Two studies in this thesis found that young patients with ABI referred for outpatient rehabilitation treatment had problems on the level of the ICF domain Body functions and structures (**Chapters 2 and 3**). In this domain, fatigue was reported to be a severe problem in more than half of the population at referral to rehabilitation (prevalence depending on age, i.e., higher age, more problems). Two years after referral, fatigue remained a prominent problem for most patients. Individuals with higher fatigue levels consequently reported a lower Health Related Quality of Life (HRQoL). Furthermore, in these young individuals, more participation restrictions were seen on the level of the ICF domain Activities and Participation. These findings are consistent with previous studies conducted in young patients with severe neurological disorders, including TBI.[22,23] Not unexpectedly, the patients in our studies had higher fatigue levels compared to hospital-based cohorts of young patients with ABI.[7,24-26] These findings suggest that persistent fatigue may be one of the reasons for admission to medical specialist rehabilitation and underscore the need to consider this group to be a specific subgroup within the general ABI population.

The findings in this thesis emphasized the importance of measuring fatigue in young patients with ABI in the rehabilitation setting. In this thesis, the Pediatric Quality of Life Inventory™ Multidimensional Fatigue Scale (PedsQL™ MFS) was used as measurement instrument for fatigue.[14-16] This patient/parent-reported outcome measure (PROM) comprehensively evaluates fatigue on various domains, including general fatigue, sleep/rest fatigue and cognitive fatigue. It is specifically designed for use in children, adolescents, and young adults with various conditions,[14-16] and reference data is available from Dutch healthy individuals.[14,15] There are other PROMs available to measure fatigue, such as the Fatigue Scale-Child,[27] Patient-Reported Outcomes Measurement Information System (PROMIS)-Pediatric Fatigue,[28] Multidimensional Fatigue Inventory,[29] and Fatigue Impact Scale,[30] however these may be less suitable in the pediatric rehabilitation setting. The reasons for these instruments to be less appropriate are that they either do not cover all fatigue domains[28,30] or only cover a limited age range,[27-30] or are too diagnosis specific for the heterogeneous character of ABI.[27,29] Moreover, for some instruments no reference data are available to compare scores with those of healthy peers.[27-30] PedsQL™ MFS domain scores are each expressed on a 0-100 scale, where lower scores indicate more fatigue. However, the interpretation of these scores in order to make clinical decisions is difficult. To enhance the understanding of PedsQL™ MFS scores, we proposed a fatigue severity categorization system, based on reference data from healthy, age-matched peers,[14,15] which can be used next to the conventional 0-100 score range. This proposed categorization system allows for a quick comparison of fatigue outcomes in relation to healthy individuals. While this system seemed promising, further research into its applicability in clinical practice

is required. Apart from interpreting the scores at admission in order to set treatment goals and assign and execute interventions, the interpretation of changes of the scores over time is also important. For that purpose, the Minimally Clinically Important Differences (MCIDs)[31] of the various domains of the PedsQL™ MFS should be established in this population, preferably by using the patient perspective on perceived changes in health status. By using the proposed categorization system, either or not refined based on future studies, and established MCIDs, clinicians and researchers in rehabilitation are enabled to better measure fatigue and evaluate its changes over time.

As is mentioned above, in addition to measuring fatigue it is essential to initiate proven effective treatment interventions to support young patients with ABI with coping with, or reducing fatigue. However, the effectiveness of such treatments has not yet been described in the literature for young individuals with ABI. Furthermore, the studies in this thesis did not evaluate specific fatigue-related treatment in children and youth with ABI either. Nonetheless, effective treatment interventions for fatigue have been evaluated in other populations, such as adolescents and young adults with chronic fatigue syndrome,[32-37] and chronic pain.[38,39] These interventions typically involve either cognitive behavioral therapy (CBT) to improve coping with fatigue in daily life or graded activity training (GAT) to enhance physical fitness.[32-39] For ABI in adults specifically, a study in patients with stroke demonstrated the effectiveness of combining CBT and GAT to improve both coping with fatigue and physical fitness.[40] In future research, it would be of added value to explore the feasibility and the (cost) effectiveness of these interventions in young individuals with ABI in the rehabilitation setting.

Restrictions in participation

A large proportion of young individuals with ABI described in this thesis were found to have daily life problems on the ICF level 'Activities and Participation' as measured with the Child and Adolescent Scale for Participation (CASP) (**Chapters 4 and 6**). Persistent participation restrictions were reported at time of referral to rehabilitation. One and two years thereafter, participation restrictions decreased, but remained prevalent in almost all patients. Participation restrictions were found across various domains, including at home, in school/at work, and in society. Moreover, a clear association with the severity of fatigue was found. It was also seen that parents tended to report less participation restrictions of their children than the children themselves. Participation restrictions have previously been described across various pediatric ABI populations, including patients with severe TBI, other neurological conditions and pediatric oncology.[5,41-46] Our rehabilitation-based cohort showed more severe participation restrictions compared to young patients with ABI seen only in a Dutch hospital.[2]

In the studies in this thesis we used the CASP, which is an often-used PROM that measures participation restrictions in children and adolescents with disabilities, including ABI.[17,18,47] Over the last decade, other assessments for measuring participation have been developed, such as the Children Participation Questionnaire, and the Questionnaire of Young People's Participation.[48,49] However, according to two relatively recent systematic reviews on investigating PROMs that measure participation, the CASP was considered the most suitable PROM to assess participation restrictions on multiple domains in ABI to date, despite its known ceiling effect.[50,51] However, when looking at the population of young individuals with ABI specifically, no normative data for comparison is available, and MCIDs are lacking. To enhance both the scientific and clinical relevance of this instrument, addressing these knowledge gaps for the rehabilitation setting is recommended.

Reducing participation restrictions is one of the most important goals in rehabilitation treatment.[52-55] For the provision of appropriate care for young people with ABI, it is essential to consider environmental factors, such as social environment, as highlighted in the existing literature.[56,57] Currently, several interventions specifically addressing participation restrictions in young individuals are available, such as Social Participation and Navigation (SPAN) developed by Bedell et.al.[58,59] and the Pathways and Resources for Engagement and Participation (PREP) by Anaby et.al.[60,61] SPAN is an app-based intervention aimed at improving social participation,[58,59] and PREP focuses on identifying and implementing strategies to remove environmental barriers that may hinder participation.[60,61] Both interventions were proven effective in children and adolescents with physical disabilities, including those with ABI.[56,57,61,62] Despite their relevance and potential, there are no Dutch versions of either SPAN or PREP. It could therefore be considered to cross-culturally translate and adapt the SPAN and PREP interventions, and evaluate them in the Dutch rehabilitation setting.

Environmental factors: Impact on the family

Impact of ABI on the family concerns the domain of environmental factors of the ICF framework, and is an important aspect to consider in rehabilitation (**Chapters 5 and 6**). In the cohort described in these Chapters, a considerable proportion of the parents reported a severe impact on their families. The observed family impact in our study was notably higher than in a hospital based pediatric ABI cohort,[63] and remained present over time in most families. Regarding factors associated with family impact, a lower HRQoL of the affected child was significantly associated with higher family impact. Our findings are in line with previous research demonstrating a considerable impact of ABI on families as well.[63-67]

In the studies described in **Chapters 5 and 6**, the PedsQL™ Family Impact Module (PedsQL™ FIM) was used. It has been demonstrated previously that this instrument provides valuable insights into the complex parent-reported family impact in the pediatric ABI population.[19] Multiple studies have used this PROM,[65-67] including a Dutch study in a hospital based pediatric ABI cohort,[63] and found the PedsQL™ FIM to be able to adequately detect family impact.[63,65-67] Other studies in pediatric ABI patients investigating family impact have predominantly used qualitative interviews.[68-71] However, despite the valuable insights derived from such studies, in clinical practice it can be challenging for clinicians to quickly interpret the impact on families. The use of a quantitative instrument such as the PedsQL™ FIM enables researchers to compare family impact across study populations, both with ABI and with other conditions. Furthermore, it also enables rehabilitation, physiatrists, psychologists and social workers to make a fast and adequate assessment of family functioning.[19] This can facilitate the detection of family impact and possibly timing of the initiation of interventions throughout all stages of the rehabilitation process. However, to date, no reference data for the PedsQL™ FIM is available to interpret severity compared to the healthy population, and no MCIDs are available to adequately interpret change over time. This hampers clinical decision making, and it is recommended to enhance the clinical relevance of the PedsQL™ FIM in pediatric ABI rehabilitation by addressing these knowledge gaps through future research.

Beyond measuring and monitoring family impact it is important to actively address this impact in rehabilitation practice. Research has demonstrated that involving the family as active participants in the child's rehabilitation process using holistic approaches can lead to improved recovery outcomes.[5,72-77] Specific studies found that family impact can be effectively addressed in various pediatric conditions in Dutch rehabilitation settings, such as physical disabilities and cerebral palsy using family centered interventions.[78,79] However, these interventions were not specifically developed for the pediatric ABI population. Such interventions may also be of added value in the Dutch pediatric ABI rehabilitation context, however their (cost) effectiveness and feasibility must first be established in this specific population.

Transitional stages

In the studies in this thesis, the group of adolescents (aged 13-17 years) and young adults (18-24 years) with ABI reported more severe ABI-related problems in terms of HRQoL, fatigue, and participation compared to children (4-12 years). These problems could potentially have an impact on healthy development on all ICF domains in older patients.[80-82] Therefore, it is crucial to acknowledge the significance of transitional stages where young individuals transition from childhood to adolescence and from adolescence to adulthood,[5,7,81,83,84] in the delivery of age-appropriate rehabilitation care and in research.

Using patient/parent-reported outcome measures in project "Participate?!": Lessons learned

To our knowledge, no other (inter)national projects, besides project "Participate?!" have measured ABI-related consequences in terms of HRQoL, fatigue, participation, and family impact on such a large scale in rehabilitation cohorts of young individuals with ABI and their parents over time. To measure these consequences across multiple domains of functioning, the PedsQL™ Generic Core Scales-4.0 (GCS-4.0),[11-13] the PedsQL™ MFS,[14-16] the CASP,[17,18] and the PedsQL™ FIM[19] were used which are the most valid, reliable, and widely accepted PROMs to date. These PROMs provided valuable insights into the less visible consequences of ABI in young individuals and their families in the rehabilitation setting (**Section 1** of this thesis) and aided in optimizing care across rehabilitation centers for this population.

To strengthen the applicability of the PROMs used in project "Participate?!" for clinical practice, MCIDs should be established, preferably by using the patient perspective on perceived changes in health status. Furthermore, they should be used in conjunction with objective tools such as physical activity and cognitive assessments to improve goal setting and enable informed decisions on interventions.

A downside of the use of PROMs in project "Participate?!" were the high dropout rates (**Chapters 3 and 6**). At time of referral to rehabilitation, the completion of PROMs was part of routine care opposed to one to two years after referral where participants were asked to complete the PROMs again for research purposes. At that time, participants may have passed the most challenging phase of their recovery, which could have diminished their motivation to invest time and energy in filling out questionnaires. Research has shown that PROMs can be time-consuming which could be experienced as burdensome and difficult for some patients, and lengthy questionnaires can cause higher dropout rates.[85-87] To address dropout rates in follow-up projects, various strategies can be investigated.

First, a two-stage approach could be considered where in stage one a generic questionnaire that screens all relevant ICF domains is used, whereafter in stage two specific PROMs may be used based on relevant outcomes in stage one. For this, pre-defined scores indicating the need for further detailed and personalized examination of daily life consequences after ABI could be used. This approach aligns with value-based healthcare (VBHC) principles, which prioritize high-value care by considering patient/parent-reported outcomes.[88,89] This new approach should be studied in future research, which could lead to a reduction of the burden for both patients and parents and clinicians. Second, PROMs should be seamlessly integrated into the healthcare process, with participants gaining immediate access to their

results. Follow-up assessments should occur at the end of rehabilitation treatment instead of one or two years after referral to immediately provide patients and their parents with insights into their treatment progress and goal attainment. Finally, healthcare professionals should be made more aware of the benefits and usability of PROMs in clinical practice. They should actively encourage patients and their parents to complete follow-up PROMs to be able to effectively evaluate treatment.

Section 2. Joint collaborations between rehabilitation centers to optimize care for young individuals with ABI

Over the past few years, a Dutch consortium of healthcare professionals called 'Brain injury and Youth' (in Dutch: Hersenletsel en Jeugd; HeJ) has facilitated collaborative efforts from rehabilitation centers and network partners to enhance the treatment of and support for young individuals with ABI and their families. In the studies described in **Chapters 7 and 8** of this thesis, the network partners contributed to the investigation of practice variation between rehabilitation centers and the creation of a national consensus-based framework for rehabilitation treatment for young individuals with ABI and their families (project "Participate Next Step").

Differences and similarities in Dutch rehabilitation care

In **Chapter 7** of this thesis, practice variation (differences and similarities) regarding the structure of rehabilitation care for young individuals with ABI and their families in the Netherlands was studied. Despite the identification of similarities, differences were found in terms of admission and discharge criteria, treatment content and aftercare, which was in line with previous research in stroke and arthritis rehabilitation.[10,90,91] The occurrence of practice variation is relevant, as indeed the recognition and reduction of differences in health delivery were found to be significant steps towards the optimization of care delivery across healthcare practices.[92-94] In that light, our findings may feed the discussion among rehabilitation professionals from different rehabilitation centers on structural aspects of care delivery, such as specific admission/discharge criteria, treatment content and dosage and the provision of aftercare. Due to the national nature of our study, findings are limited regarding their generalizability to other countries. However, the research design and method used could serve as a blueprint for studies on an international scale, allowing for broader perspectives and comparisons.

Creating a national consensus-based treatment framework

Chapter 8 of this thesis outlined the development of a national consensus-based treatment framework, using a Delphi method.[95-97] This development was initiated based on the clinical observation that healthcare professionals in rehabilitation used a broad range of

assessments, interventions, and psycho educational materials, in the absence of guidelines or other forms of consensus statements on the delivery of specialist rehabilitation care for young individuals with ABI. In other areas, including arthritis, adult ABI and pediatric cerebral palsy rehabilitation, frameworks for the assessments and/or interventions that are important during treatment of these specific populations are available.[98-101] Such a framework did not exist for young individuals with ABI and through the Delphi study described in **Chapter 8**, this was addressed. Consensus was reached on what assessments, interventions and psychoeducational materials were most suitable to use in the rehabilitation of young individuals with ABI. Healthcare professionals can use this framework as a resource to make tailored choices based on the ICF domains in terms of assessments, goal setting, assignment of treatments, and treatment evaluation to create a personalized program.[102,103]

With respect to the framework that eventually resulted from the study in **Chapter 8**, it must be noted that not all assessments, interventions and psychoeducational materials that were agreed upon in the framework were specifically developed for the population of young individuals with ABI. Despite the fact that many assessments and interventions included in the framework are generic and are used in other pediatric rehabilitation populations they may be suitable to be used in young individuals with ABI as well. However, it is worth exploring if they fully meet the needs and wishes of this specific population in order to further optimize care. Moreover, future research should involve the exploration of the usability and the content of the framework in rehabilitation practice. Gaps in knowledge on cut-off points and/or MCIDs of assessments should be addressed to enhance the usability of these specific outcome assessments in evaluating treatment in clinical practice. Furthermore, usability of interventions, and psycho educational materials in current rehabilitation practice should be investigated as well. This enables a transition from practice based to evidence based treatment for the target group.

Project "Participate Next Step": lessons learned and steps to be taken

The primary goal of project "Participate Next Step" was to optimize rehabilitation care for young individuals with ABI and their families. In this project cooperative efforts across rehabilitation centers led to valuable insights on similarities and differences across centers and the creation of a national framework for the provision of rehabilitation care in this specific patient group. Joint collaborations between healthcare facilities are essential to optimize care for specific populations. "Participate Next Step" project strengthened the collaborative network within and beyond the Brain injury and Youth (HeJ) consortium, involving 14 out of 16 centers, delivering rehabilitation care for young individuals with ABI across the Netherlands. Additionally, lead experts (1 to 2 per center) from the 14 participating centers played a crucial role as connectors within their own center and between participating

centers. They delivered valuable assistance throughout the project by describing the structural aspects of rehabilitation processes and providing their expert perspective on the rehabilitation of this specific population and the future implementation of the national framework.

Experiences in this project can be used as an example for other commonly seen health conditions in outpatient rehabilitation care. However, several limitations for this project must be noted as well. First, only 14 out of 16 rehabilitation centers that provide outpatient rehabilitation care for young individuals with ABI participated. Additionally, we relied on healthcare professionals' perspectives only, which may not represent all viewpoints on the optimization of care among young individuals with ABI. Second, even though a user group comprising young individuals with ABI and parents of children with ABI was involved in the project "Participate Next Step", they did not actively participate in the Delphi study. Therefore, their perspectives on what they consider important during rehabilitation were not included. Future research should proactively engage all stakeholders when conducting studies, also including healthcare professionals, management professionals and young individuals with ABI and their families, aligning with literature recommendations,[104-106] and principles of VBHC.[88,89] For instance, patient involvement and engagement should be considered in research which could be addressed by including patients as active participants in research groups[107,108] to comprehensively understand their needs and preferences in further optimizing rehabilitation for this population.

Directions for future research and implications for clinical practice

With the knowledge and insights acquired from this thesis, we are on the road to optimize rehabilitation care for young individuals with ABI and their families. Along this journey suggested directions for future research are as follows:

- Continuous research on measuring and monitoring ABI-related consequences such as diminished HRQoL, fatigue, restricted participation, and family impact in young individuals and their families.
- Development of, and research into the effectiveness and cost effectiveness, of specific interventions to reduce fatigue, participation restrictions and family impact.
- Establishing MCIDs for the PedsQL™ GCS-4.0, the PedsQL™ MFS, the CASP, and the PedsQL™ FIM PROMs to quantify clinically meaningful progress.
- Evaluating the content of the developed framework by conducting both qualitative and quantitative evaluations with input from healthcare professionals and the target group in order to create a more well-founded and concise framework.
- Extend the participation of young individuals with ABI and their families in future research and further incorporating their (unmet) needs and wishes.

For rehabilitation practice in the Netherlands, the following implications could be considered:

- The studies in this thesis and clinical practice suggest that the systematic use of PROM outcomes not only for goal setting, but also to monitor and evaluate treatment throughout the whole rehabilitation process should be optimized. A proper evaluation will facilitate the transition to, for example, primary care.
- Differences in admission/discharge criteria, and aftercare across rehabilitation centers should be further analyzed and consensus should be reached on which criteria to use and how aftercare should be provided.
- Age-appropriate rehabilitation transition care and follow-up should be further integrated into rehabilitation care.
- Joint collaborations between rehabilitation centers should be continued and strengthening collaborative networks across, hospitals, and primary care providers should be considered. For this, lead experts should serve as valuable connectors.

This thesis emphasizes the importance of a holistic approach to rehabilitation and lays the foundation for future initiatives aiming to further optimize the right rehabilitation treatment at the right time, at the right place for young individuals with ABI and their families.

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CHAPTER 10

Nederlandse samenvatting en discussie

SAMENVATTING

Bij Niet-Aangeboren Hersenletsel (NAH) is er sprake van schade aan de hersenen die ontstaan is na de geboorte. NAH kan, afhankelijk van de oorzaak, worden onderverdeeld in traumatisch hersenletsel (THL) en niet-traumatisch hersenletsel (nTHL).[1] NAH komt relatief vaak voor bij kinderen, adolescenten en jongvolwassenen tussen de 4 en 25 jaar oud (verder aangeduid als kinderen en jongvolwassenen).[2,3] De impact van NAH kan ingrijpend en langdurig zijn voor deze kinderen en jongvolwassenen, en kan verschillende aspecten van hun dagelijks functioneren beïnvloeden.[2,4-7] Wanneer de gevolgen van NAH tot langdurige beperkingen leiden, kan medisch-specialistische revalidatiebehandeling in een revalidatiecentrum noodzakelijk zijn.[2,8-10] Het doel van dit proefschrift was enerzijds de kennis over de gevolgen van NAH bij kinderen en jongvolwassenen op het gebied van vermoeidheid, participatie, kwaliteit van leven (KvL) en impact op de familie te vergroten en anderzijds een bijdrage te leveren aan het optimaliseren van de kwaliteit van revalidatiezorg voor deze doelgroep in Nederland.

In **Hoofdstuk 1** wordt een uitgebreid overzicht van de mogelijke gevolgen van NAH bij kinderen en jongvolwassenen van 4 tot 25 jaar gegeven, aan de hand van hun situatie bij aanmelding in de medisch-specialistische revalidatie (MSR). Dit hoofdstuk behandelt verder de definities, epidemiologie, beschrijft de herstelfasen en de huidige zorgverlening, met name de MSR. Bovendien worden in dit hoofdstuk twee onderzoeksprojecten geïntroduceerd die de basis vormden voor dit proefschrift: de projecten 'Meedoen?!' en 'Meedoen Next Step'.

Het project 'Meedoen?!' richtte zich op de langdurige gevolgen na NAH en het beloop van daarvan, zowel bij aanmelding voor revalidatie als één en twee jaar later (**Sectie 1** van dit proefschrift).

In het project 'Meedoen Next Step' werden de structuur en de zorgprocessen van revalidatie voor kinderen en jongvolwassenen met NAH in Nederlandse revalidatiecentra onderzocht en onderling vergeleken. Vervolgens werd een nationaal, op consensus gebaseerd behandelraamwerk ontwikkeld, waarin de meest gebruikte en vrij beschikbare klinimetrie, interventies en psycho-educatieve materialen voor de dagelijkse praktijk in de MSR voor kinderen en jongvolwassenen met NAH in Nederland werden vastgelegd (**Sectie 2** van dit proefschrift).

Sectie 1. Blijvende gevolgen van NAH bij kinderen en jongvolwassenen die poliklinisch behandeld worden in de Nederlandse MSR, en hun familie

Deze sectie van het proefschrift beschrijft langdurige gevolgen van NAH bij de doelgroep, aan de hand van domeinen 'Lichaamsfuncties en anatomische eigenschappen' (**Hoofdstuk 2 en 3**), 'Activiteiten en participatie' (**Hoofdstuk 4**), en 'Omgevingsfactoren' (**Hoofdstuk 5 en 6**) van de International Classification of Functioning, Disability and Health (ICF).

Om in het project 'Meedoen?!' de kwaliteit van leven, vermoeidheid, participatieproblemen en gezinsimpact van NAH bij kinderen en jongvolwassenen te bepalen, werden patiënt gerapporteerde uitkomstmaten (Patient-Reported Outcome Measures: PROMs) gebruikt. Daarnaast werden demografische- en patiënt gerelateerde gegevens verzameld. In **Hoofdstuk 2-6** wordt gebruik gemaakt van een naar de MSR verwezen groep kinderen en jongvolwassenen met NAH en hun ouders. Op het moment van verwijzing naar de MSR (T0) werden 223 patiënten en 246 ouders geïncludeerd. Van 94 patiënten en 104 ouders waren longitudinale follow-up data beschikbaar (een jaar later (T1) en/of twee jaar later (T2)). De beschikbaarheid van gegevens van patiënten en/of ouders voor analyse varieerde per meetmoment omdat niet alle patiënten en ouders op alle momenten de vragenlijsten hadden ingevuld.

In **Hoofdstuk 2** wordt de mate van vermoeidheid beschreven bij kinderen en jongvolwassenen met NAH bij aanmelding voor poliklinische MSR, gemeten met de PedsQL™ Multidimensional Fatigue Scale (PedsQL™ MFS). Deze PROM belicht verschillende domeinen van vermoeidheid, waaronder algemene vermoeidheid, slaap/rust, en cognitieve vermoeidheid, waarbij scores variëren van 0 tot 100 (lagere scores geven meer vermoeidheid aan). Voor deze cross-sectionele studie werden zowel de totaalscore als de domeinscores van de PedsQL™ MFS gebruikt. Om de ernst van vermoeidheid te beoordelen, werden afkapwaarden bepaald met behulp van gegevens uit eerdere studies met de PedsQL™ MFS onder gezonde Nederlandse leeftijdsgenoten. Hierbij dienden de gemiddelde scores en bijbehorende standaarddeviaties (SD) van deze gezonde populatie als referentie om te bepalen in welke mate de patiënten in het NAH-cohort daarvan verschilden. Op basis hiervan werden vier categorieën gemaakt om de mate van vermoeidheid uit te drukken:

1. Minder vermoeid dan gezonde leeftijdsgenoten (scores met meer dan +1SD verschil),
2. Vermoeidheid vergelijkbaar met gezonde leeftijdsgenoten (scores tussen de +1SD en -1SD),
3. Meer vermoeid dan gezonde leeftijdsgenoten (scores tussen de -1SD en -2SD),
4. Veel meer vermoeid dan gezonde leeftijdsgenoten (scores met meer dan -2SD verschil).

Uit de resultaten bleek dat zowel kinderen en jongvolwassenen met NAH als hun ouders substantiële vermoeidheid rapporteerden. De gemiddelde patiënt- en ouder gerapporteerde PedsQL™ MFS-scores waren respectievelijk 51.0 (SD17.3) en 53.5 (SD19.2). Deze scores waren significant lager dan die van gezonde leeftijdsgenoten, die tussen de 71.8 (SD14.6) en 82.1 (SD17.8) lagen. Vijftig tot 88% van de kinderen en jongvolwassenen met NAH (afhankelijk van leeftijd) hadden een score die overeenkwam met de categorieën "meer vermoeid dan gezonde leeftijdsgenoten" of "ernstig meer vermoeid dan gezonde leeftijdsgenoten". Naast het gebruik van de lineaire 0-100 scores van de PedsQL™ MFS, kan het categoriseren van de ernst van vermoeidheid mogelijk nuttig zijn voor het monitoren van vermoeidheidsklachten in de klinische praktijk.

In **Hoofdstuk 3** wordt het beloop van vermoeidheid en participatie over de tijd beschreven bij kinderen en jongvolwassenen met NAH die poliklinische MSR ontvingen. Vermoeidheid en participatie werden bij aanmelding en 1 en 2 jaar later gemeten, waarbij ook de onderliggende relatie tussen beide aspecten werd onderzocht. Deze longitudinale, observationele studie maakte gebruik van de PedsQL™ MFS voor vermoeidheid en de Child & Adolescent Scale of Participation (CASP) voor participatie. Om de veranderingen in vermoeidheids- en participatiescores over de tijd vast te stellen werden linear mixed models gebruikt (uitkomsten uitgedrukt in veranderingsscores met 95% betrouwbaarheidsintervallen, p-waarden). Daarnaast zijn er repeated measures correlations gebruikt om de relatie tussen vermoeidheid en participatie over de tijd te onderzoeken (r_{rm}, uitgedrukt in 95% betrouwbaarheidsinterval, p-waarden).
Op T0 vulden 223 patiënten en 246 ouders de vragenlijsten in. Van 94 patiënten en 104 ouders waren vervolg vragenlijsten beschikbaar (T1, T2 of beide). De gemiddelde door de patiënten gerapporteerde PedsQL™ MFS- en CASP-scores lieten een significante verbetering zien tussen T0 en T2 (+8.8, 2.9-14.7, $p < 0.05$ respectievelijk +10.5, 6.3-14.7, $p < 0.05$). De door ouders gerapporteerde PedsQL™ MFS score toonde een vergelijkbare gemiddelde verbetering (+8.7, 3.4-13.9, $p < 0.05$), dit gold echter niet voor de gemiddelde CASP-score (+3.9, 1.1-7.7, $p > 0.05$). Er werd een gemiddeld sterke longitudinale correlatie gevonden tussen de door patiënten gerapporteerde PedsQL™ MFS- en CASP-scores (r_{rm}=0.7, (0.6;0.8), $p < 0.001$). Daarentegen werd slechts een matige correlatie gevonden voor de door ouders gerapporteerde scores (r_{rm}=0.5, (0.3;0.6), $p < 0.001$). Deze bevindingen laten zien dat meer vermoeidheidsklachten geassocieerd zijn met meer participatieproblemen op alle meetmomenten. Ondanks de verbeteringen in de loop van de tijd bleven patiënten vermoeidheid en beperkingen in hun participatie ervaren.

Hoofdstuk 4 beschrijft een cross-sectioneel onderzoek naar de beperkingen op het gebied van participatie van kinderen en jongvolwassenen met NAH bij aanmelding voor poliklinische

MSR en de eventuele verschillen in perspectieven op participatie tussen patiënten en hun ouders. Om de mate van participatie beter te kunnen beschrijven werden de CASP-scores in deze studie onderverdeeld in vier categorieën, op basis van consensus met de auteur van de CASP: 1. volledige participatie (scores tussen de 100–97.5), 2. enigszins beperkte participatie (scores tussen de 97.5–81.0), 3. beperkte participatie (scores tussen de 81.0–68.5), 4. ernstig beperkte participatie (scores onder of gelijk aan ≤ 68.5).
In de resultaten werden aanzienlijke beperkingen op het gebied van participatie gevonden. De gemiddelde door de ouders gerapporteerde CASP score waren significant hoger dan die de patiënten zelf (91.3 (IQR: 80.0-97.5) versus 82.5 (IQR: 67.5-90), $p < 0.05$). Dit verschil was het meest uitgesproken bij de jongvolwassenen. Een kwart van de patiënten (n=58, 26%) en een minder groot deel van de ouders (n=25, 10%) rapporteerde scores onder of gelijk aan ≤ 68.5 die vielen binnen categorie 4: "ernstig beperkte participatie". Een conclusie die getrokken kan worden uit deze studie is dat het in de MSR belangrijk is om participatieproblemen na NAH zowel vanuit het perspectief van kinderen en jongvolwassenen als van hun ouders te meten. Verder lijkt dat het categoriseren van CASP-scores nuttig zou kunnen zijn bij het interpreteren en uitleggen van metingen in de dagelijkse revalidatiepraktijk.

In **Hoofdstuk 5** wordt de impact op het gezin van NAH bij kinderen en jongvolwassenen beschreven, aan de hand van de PedsQL™ Family Impact Module (PedsQL™ FIM). De scores van dit instrument lopen van 0-100, waarbij lagere scores meer gezinsimpact aanduiden. Om te onderzoeken welke factoren geassocieerd zouden kunnen zijn met de gezinsimpact en hoe de relatie met KVL was, werden univariate en multivariate regressieanalyses toegepast.
Op grond van de gemiddelde PedsQL™ FIM score bleek de gezinsimpact aanzienlijk te zijn (mediane totaalscore: 71.9, IQR 60-85), en het hoogst (laagste score) binnen het domein "Zich zorgen maken" (65.0, IQR 50-80).
Factoren die gerelateerd waren aan een hogere mate van gezinsimpact, waren: nTHL, langere tijd tussen het ontstaan van het letsel en aanmelding in de MSR, slechtere mentale/emotionele gezondheid, een lagere KvL en pre-morbide problemen op het gebied van leren, gedrag en/of gezondheid. Leeftijden de ernst van het hersenletsel bleken in deze studie geen significante relatie te hebben met de impact op het gezin. Deze bevindingen onderstrepen het belang om de gezinsimpact bij gezinnen van jonge patiënten met NAH te monitoren.

Hoofdstuk 6 beschrijft het beloop van gezinsimpact over een periode van twee jaar waarbij ook naar de relatie met de KvL van de patiënten werd gekeken. Deze longitudinale studie maakte gebruik van PedsQL™ FIM en de PedsQL™ Generic Core Scales (GCS)-4.0 (voor KvL van de patiënt). De vragenlijsten werden ingevuld op het moment van aanmelding bij de

MSR (T0), en één en twee jaar later (T1 en T2). De patiëntengroep werd verdeeld in een groep met THL (n=181 op T0) en een groep met nTHL (n=65 op T0). Er werden linear mixed models gebruikt om het beloop van de gezinsimpact en de KvL over de tijd te meten (verschilscores met 95% betrouwbaarheidsinterval, *p*-waarden). Om de correlaties tussen gezinsimpact en KvL van de patiënt te onderzoeken, werden repeated measures correlations gebruikt (r_{rm}, p-waarden).
De resultaten toonden aan dat de gezinsimpact gedurende de tijd niet significant veranderde in de THL-groep (+2.1, (-1.9, 6.2), $p > 0.05$) en na twee jaar nog steeds aanzienlijk was (gemiddelde score van 77.0). Alleen in het domein "Zich zorgen maken" was er een significante verbetering te zien in deze groep (+8.6, (2.1, 15.1), $p < 0.05$). In tegenstelling tot de THL-groep, verbeterde de gezinsimpact wel significant in de nTHL-groep (+5.8, (0.2, 11.4), $p < 0.05$). Ten aanzien van KvL werd er gedurende dezelfde tijdsperiode in beide groepen een statistisch significante verbetering gevonden ($p < 0.05$) op alle domeinen van de KvL van de patiënten. Er werd een gemiddeld sterke longitudinale correlatie gevonden tussen de gezinsimpact en de KvL van de patiënt (r_{rm}=0.51, $p < 0.001$). Deze bevindingen benadrukken dat naast het monitoren van de KvL van de patiënt, het van groot belang is de gezinsimpact voor, tijdens en na de MSR van kinderen en jongvolwassenen met NAH ook te monitoren.

Sectie 2. Samenwerkingsverbanden tussen revalidatiecentra voor het optimaliseren van revalidatiezorg voor kinderen en jongvolwassenen met NAH

Naast het beschrijven van de beperkingen als gevolg van NAH bij aanmelding in de MSR, is het van belang om een optimaal aanbod in de MSR na te streven. Om dit te bereiken is het essentieel om inzicht te krijgen in structuur en processen van MSR voor kinderen en jongvolwassenen met NAH.[11] In de studie 'Meedoen?! Next Step', beschreven in **Hoofdstuk 7 en 8** participeerden veertien Nederlandse revalidatiecentra die MSR voor kinderen en jongvolwassenen met NAH aanbieden. Elk revalidatiecentrum werd vertegenwoordigd door één of twee lokale studievertegenwoordigers (kartrekkers) die het project ondersteunden vanuit hun eigen centrum.

Hoofdstuk 7 beschrijft een cross-sectioneel onderzoek waarbij zorgprofessionals werkzaam in 12 verschillende centra voor MSR een vragenlijst met 21 items invulden over de structuur van poliklinische NAH-revalidatiezorg. Deze items betroffen het hanteren van aanmeld- en ontslagcriteria, de organisatie van revalidatiebehandelingen en de nazorg. vereenkomsten in de revalidatiezorg werden gedefinieerd als een eensluidend antwoord van 75% of meer van de respondenten op een bepaald onderwerp.
Hoewel alle centra gebruik maakten van aanmeld- en ontslagcriteria, waren er verschillen met betrekking tot de omschrijving van deze criteria. Vier van de twaalf centra (33%) hadden

een 'transitieteam' voor jongvolwassenen (14-25 jaar). Verder waren er verschillen in de organisatie van revalidatie, waarbij er in acht van de twaalf centra (67%) specifieke NAH-behandelprogramma's werden aangeboden. Wat betreft nazorg waren er verschillen in het moment van ontslag en de timing van follow-upmomenten. Deze studie toonde naast overeenkomsten ook verschillen in het aanbieden van revalidatiezorg voor jonge NAH-patiënten tussen revalidatiecentra aan. De gevonden verschillen onderstrepen de noodzaak om een landelijk behandelraamwerk te ontwikkelen om overal in Nederland vergelijkbare zorg voor kinderen en jongvolwassenen met NAH te kunnen bieden.

Tot slot beschrijft **Hoofdstuk 8** het proces van het bereiken van consensus over een landelijk behandelraamwerk voor zorgprofessionals, waarin de meest gebruikte en vrij beschikbare klinimetrie, interventies en psycho-educatieve materialen voor kinderen en jongvolwassenen met NAH in de revalidatiesetting zijn opgenomen. Dit onderzoek betrof een Delphi-studie bestaande uit drie rondes, waaraan zorgprofessionals vanuit verschillende disciplines (revalidatieartsen, psychologen, fysiotherapeuten, ergotherapeuten, logopedisten en sociaal werkers: n=74) uit 14 revalidatiecentra deelnamen.

In de eerste twee (online) Delphi-rondes werden de meest gebruikte klinimetrie, interventies en psycho-educatieve materialen verzameld, stap voor stap geprioriteerd en per discipline gecategoriseerd op basis van de ICF-domeinen. De resultaten van deze rondes werden vervolgens besproken tijdens een fysieke bijeenkomst (ronde 3), met als doel consensus te bereiken over de drie pijlers van het behandelraamwerk, de implementatie en het gebruik in de revalidatiepraktijk.
Na drie Delphi-rondes werd consensus bereikt over het opnemen van 37 verschillende vormen van klinimetrie, 25 interventies en 27 psycho-educatieve materialen. Ook werd overeenstemming bereikt over hoe de verschillende vormen van klinimetrie, interventies en psycho-educatieve materialen het best in de revalidatiepraktijk kunnen worden ingezet. Dit op consensus gebaseerde behandelraamwerk draagt bij aan het verder uniformeren en optimaliseren van het zorgaanbod voor kinderen en jongvolwassenen met NAH binnen Nederlandse MSR.

DISCUSSIE

Het identificeren, evalueren en monitoren van de gevolgen van niet-aangeboren hersenletsel (NAH) bij kinderen, adolescenten en jongvolwassenen (4-25 jaar oud) vormen belangrijke aspecten binnen de medisch specialistische revalidatiezorg (MSR) voor deze doelgroep. Er waren echter verschillende kennishiaten met betrekking tot de prevalentie en ernst van

NAH-gerelateerde gevolgen en het huidige en gewenste aanbod van MSR voor deze doelgroep. Daarom zijn de gevolgen van NAH onderzocht op verschillende domeinen van functioneren (**Sectie 1**) en het huidige en gewenste aanbod van MSR voor deze patiëntenpopulatie is in kaart gebracht (**Sectie 2**). In deze discussie wordt gereflecteerd op de uitkomsten van de onderzoeken die zijn beschreven in dit proefschrift, alsmede op de methodologische implicaties ervan, en worden suggesties voor toekomstig onderzoek, en aanbevelingen voor de praktijk gedaan.

Sectie 1. Blijvende gevolgen van NAH bij kinderen en jongvolwassenen die poliklinisch behandeld worden in de Nederlandse MSR, en hun familie

Twee studies in dit proefschrift (**Hoofdstukken 2 en 3**) toonden aan dat kinderen en jongvolwassenen met NAH, die verwezen werden naar de MSR, gemiddelde genomen aanzienlijke vermoeidheidsproblemen hadden. Deze vermoeidheid bleek ook twee jaar na verwijzing naar de MSR nog aanwezig, waarbij kinderen en jongvolwassenen met meer vermoeidheidsklachten een lagere kwaliteit van leven (KvL) rapporteerden en meer participatieproblemen ondervonden. Kinderen en jongvolwassenen met NAH in onze studies vertoonden meer vermoeidheid dan gezonde kinderen,[12-15] maar in vergelijking met de literatuur ook meer dan kinderen en jongvolwassenen met NAH in ziekenhuiscohorten.[7,16-20] Het meten en monitoren van verschillende aspecten van vermoeidheid in de MSR doelgroep bij aanvang en tijden en na de behandeling is daarom ook noodzakelijk. Om vermoeidheidsklachten te verminderen zijn behandelingen zoals cognitieve gedragstherapie (CGT) en graded activity training (GAT), of een combinatie van beide effectief gebleken in andere populaties.[21-29] Echter, de effectiviteit hiervan is bij kinderen en jongvolwassenen met NAH in de MSR nog niet onderzocht. Het is daarom van belang om de toepasbaarheid en effectiviteit van deze interventies voor deze doelgroep te verder te onderzoeken.

Naast vermoeidheidsklachten werden in **Hoofdstukken 4 en 6** door een groot gedeelte van de kinderen en jongvolwassenen met NAH aanhoudende participatieproblemen gerapporteerd. Ons revalidatiecohort vertoonde meer participatieproblemen dan kinderen en jongvolwassenen met NAH in een ziekenhuiscohort.[2] Het verminderen van participatieproblemen is één van de belangrijkste doelen binnen de MSR wat op velerlei verschillende manieren aangepakt wordt.[30-35]

Er zijn een aantal specifieke behandelinterventies beschikbaar om participatieproblemen bij kinderen met een chronische aandoening te verminderen, zoals Social Participation and Navigation (SPAN)[36,37] en de Pathways and Resources for Engagement and Participation (PREP).[38,39] Beide interventies bleken effectief te zijn bij kinderen en adolescenten met fysieke aandoeningen, waaronder NAH.[34,35,39,40] Echter, ondanks deze resultaten bestaan er

nog geen Nederlandse versies van deze interventies. Het zou daarom waardevol zijn om ze te vertalen, waar nodig aan te passen en te evalueren voor gebruik in de Nederlandse MSR.

Uit de resultaten uit **Hoofdstukken 5 en 6**, kwam naar voren dat een groot aantal ouders van kinderen en jongvolwassenen met NAH een aanzienlijke gezinsimpact rapporteerde. De gemiddelde gezinsimpact was hoger dan in een ziekenhuiscohort van kinderen met NAH,[41] en bleek twee jaar na aanmelding in de MSR in de meeste gevallen nog aanwezig. Dit onderstreept het belang van specifiek meten en volgen van gezinsimpact en het gericht ondersteunen van het gezin binnen de MSR. Onderzoek heeft aangetoond dat het betrekken van ouders, en hen een actieve rol te geven in het revalidatieproces van hun kind, het herstel ten goede kan komen.[5,42-47] Een aantal internationale studies binnen verschillende doelgroepen hebben aangetoond dat gezinsgerichte behandelinterventies gezinsimpact effectief kunnen verminderen,[48,49] Het verdient sterk aanbeveling om deze interventies in Nederland op toepasbaarheid en effectiviteit te onderzoeken.

Naast het project 'Meedoen?!' (**Sectie 1**) zijn er geen andere grootschalige nationale of internationale projecten bekend die de problemen van kinderen en jongvolwassenen met NAH en hun ouders in de MSR en op het gebied van KvL, vermoeidheid, participatie en gezinsimpact structureel en over de tijd in kaart hebben gebracht. De gebruikte patiënt gerapporteerde uitkomstmaten (Patient-Reported Outcome Measures: PROMs), waaronder de PedsQL™ Generic Core Scales-4.0 (GCS-4.0),[14,15,50] de PedsQL™ MFS,[12,13,51] de CASP,[52,53] en de PedsQL™ FIM,[54] hebben waardevolle inzichten opgeleverd in de eerder genoemde NAH-gerelateerde problemen en hebben geholpen bij het optimaliseren van revalidatiezorg voor deze doelgroep. Hoewel er meerdere methoden en meetinstrumenten bestaan om domeinen van functioneren in kaart te brengen, zijn deze vaak minder geschikt voor in de MSR, met name vanwege het ontbreken van Nederlandse normdata. Vaak zijn ze enkel beschikbaar voor beperkte leeftijdsgroepen, of brengen ze niet volledig alle domeinen, die voor kinderen en jongvolwassenen met NAH van belang zijn, in kaart.[55-64] Om de toepasbaarheid en waarde van PROMs te versterken is het essentieel om ook de verandering van scores in de loop van de tijd te kunnen interpreteren, bij voorkeur door het vaststellen van Minimally Clinically Important Differences (MCIDs).[65] Er is echter vervolgonderzoek nodig om dergelijke stappen te kunnen zetten. Het is ook van belang om PROMs samen met objectieve metingen van zorgprofessionals in te zetten en te integreren in het zorgproces, niet alleen voor de individuele patiëntenzorg maar ook ten behoeve van het monitoren en verbeteren van de kwaliteit van zorg. Zorgprofessionals moeten worden aangemoedigd om patiënten actief te betrekken bij het gezamenlijk evalueren van behandelingen, onder andere met behulp van het invullen van PROMs, in lijn met de principes

van waardegedreven zorg.[66,67] Zo wordt beter aangesloten bij de wensen en eigen regie van de patiënten en hun ouders.

Sectie 2. Samenwerkingsverbanden tussen revalidatiecentra voor het optimaliseren van revalidatiezorg voor kinderen en jongvolwassenen met NAH

In **Hoofdstuk 7** van dit proefschrift is onderzocht of er sprake is van praktijkvariatie (identificatie van verschillen en overeenkomsten) in de MSR voor kinderen en jongvolwassenen met NAH en hun families in Nederlandse revalidatiecentra. Ondanks overeenkomsten in werkwijze zijn er vele verschillen waargenomen op het gebied van aanmeld- en ontslagcriteria, de organisatie van de zorgprocessen de nazorg. Dit kwam overeen met verschillen in de structuur van de zorg die eerder waren gevonden in onderzoeken naar revalidatie van patiënten met andere aandoeningen zoals een beroerte en reumatoïde artritis.[10,68,69] Het onderzoeken van praktijkvariatie is relevant, omdat gebleken is dat het (h)erkennen en verminderen van praktijkvariatie binnen de gezondheidszorg een stap kan zijn naar zorgoptimalisatie.[70-72] Onze bevindingen kunnen bijdragen aan de discussie onder zorgprofessionals binnen de MSR over de optimalisatie van de structuur en het proces van de zorgverlening zoals het hanteren van aanmeld- en ontslagcriteria, de indicatiestelling voor en inhoud en dosering van behandelingen = en het aanbod van nazorg.

De totstandkoming van het behandelraamwerk (**Hoofdstuk 8**) was gebaseerd op observaties uit de revalidatiepraktijk. Hieruit bleek dat, onder andere vanwege het ontbreken van behandelrichtlijnen voor poliklinische MSR voor kinderen en jongvolwassenen met NAH, zorgprofessionals een breed scala aan klinimetrie, interventies en psycho-educatieve materialen gebruikten. Voor andere aandoeningen, zoals artritis, volwassen NAH- en cerebrale parese, zijn raamwerken voor revalidatie beschikbaar waar klinimetrie en/of interventies die belangrijk zijn tijdens de behandeling van deze specifieke populaties beschreven staan.[73-76] Een dergelijk raamwerk ontbrak echter voor kinderen en jongvolwassenen met NAH. Daarom is door middel van een Delphi-methode[77-79] consensus bereikt over welke klinimetrie, interventies en psycho-educatieve materialen het meest geschikt waren voor gebruik in de revalidatie van kinderen en jongvolwassenen met NAH, zodat een revalidatie raamwerk voor deze doelgroep ook ontwikkeld werd. Zorgprofessionals kunnen dit raamwerk gebruiken als een hulpmiddel om keuzes te maken met betrekking tot behandeldoelen, het inzetten van behandelingen en de evaluatie daarvan, om zo een programma op maat aan te kunnen bieden.[80,81] Echter, niet alle klinimetrie, interventies en psycho-educatieve materialen die zijn opgenomen in het raamwerk zijn voldoende onderbouwd en/of specifiek ontwikkeld voor de populatie van kinderen en jongvolwassenen met NAH. Hierdoor is het met toekomstig onderzoek belangrijk om te onderzoeken of de inhoud van het huidige behandelraamwerk volledig voldoet aan de behoeften en wensen

van deze specifieke populatie om daarmee de zorg voor de doelgroep verder te optimaliseren. Voor zorgevaluatie op individueel niveau moeten kennishiaten over afkapwaarden en/of MCIDs van klinimetrie en interventies en de bruikbaarheid van psycho-educatieve materialen worden onderzocht. Hiermee zou de nu op praktijk gebaseerde behandeling beter onderbouwd, meer 'evidence-based', gemaakt kunnen worden voor de doelgroep.

Om de behandeling en zorg voor kinderen en jongvolwassenen met NAH en hun families te verbeteren, heeft het Nederlandse consortium Hersenletsel en Jeugd (HeJ) in de afgelopen jaren samenwerkingen versterkt tussen centra voor MSR en met verschillende netwerkpartners. Het project 'Meedoen Next Step' (**Sectie 2**) heeft gezorgd voor het versterken van het samenwerkingsnetwerk binnen en buiten dit consortium. Veertien van de 16 revalidatiecentra in Nederland waren betrokken bij het project 'Meedoen Next Step'. Samenwerking tussen revalidatiecentra is essentieel om de zorg voor specifieke populaties te optimaliseren. Lokale studievertegenwoordigers, de zogenaamde kartrekkers, van de 14 deelnemende centra speelden een cruciale rol als verbinders binnen hun eigen centrum en tussen de deelnemende centra. Ook speelden zij een belangrijke rol in de implementatie van het landelijk raamwerk. De stappen die zijn genomen in dit project kunnen als voorbeeld dienen voor andere doelgroepen binnen de poliklinische MSR. Er zijn echter ook een aantal beperkingen van dit project naar voren gekomen. Ten eerste namen niet alle revalidatiecentra die poliklinische zorg bieden voor kinderen en jongvolwassenen met NAH deel (14 van de 16), wat de generaliseerbaarheid van de bevindingen kan beïnvloeden. Bovendien richtte het onderzoek zich uitsluitend op de perspectieven van zorgprofessionals, waardoor het perspectief van kinderen en jongvolwassenen met NAH en hun ouders wellicht onvoldoende werd gerepresenteerd. Hoewel een gebruikerscommissie, bestaande uit kinderen en jongvolwassenen met NAH en hun ouders, bij het project betrokken was, waren zij niet actief betrokken bij de Delphi-studie, waardoor hun inzichten en prioriteiten met betrekking tot de optimalisatie van zorg niet werden meegenomen. Toekomstig onderzoek zou daarom een meer inclusieve benadering moeten volgen, waarbij alle belanghebbenden - zorgprofessionals, management, kinderen en jongvolwassenen met NAH en hun families - actief worden betrokken. Deze aanpak sluit niet alleen aan bij de aanbevelingen in de literatuur,[82-84] maar ook bij de principes van waardegedreven zorg.[66,67] Het opnemen van kinderen en jongvolwassenen met NAH en hun ouders als actieve deelnemers in onderzoeksgroepen kan een effectieve manier zijn om hun behoeften, voorkeuren en ervaringen nauwkeurig te begrijpen, wat uiteindelijk de revalidatiezorg voor deze specifieke populatie ten goede kan komen.

Aanbevelingen en implicaties

Met de kennis en inzichten verworven in dit proefschrift wordt de MSR voor kinderen en jongvolwassenen met NAH en hun families geoptimaliseerd. Om dit proces te continueren en versterken, worden de volgende aanbevelingen voor toekomstig onderzoek voorgesteld:

- Meer onderzoek naar NAH-gerelateerde gevolgen, zoals verminderde KvL, vermoeidheid, beperkte participatie bij kinderen en jongvolwassenen en gezinsimpact, over de tijd.
- Het kwalitatief en kwantitatief evalueren van de inhoud van het ontwikkelde behandelraamwerk met input van zorgprofessionals en de doelgroep om uiteindelijk een goed gefundeerd en beknopt raamwerk te creëren.
- Het betrekken van kinderen en jongvolwassenen met NAH en hun families in vervolgonderzoek om zo hun (onvervulde) behoeften en wensen beter te identificeren en te ondersteunen.
- Ontwikkeling van, en onderzoek naar de effectiviteit en kosteneffectiviteit van specifieke interventies om vermoeidheid, participatiebeperkingen en impact op het gezin te verminderen.
- Vaststellen van MCIDs voor de PedsQL™ GCS-4.0, de PedsQL™ MFS, de CASP en de PedsQL™ FIM PROMs om klinisch betekenisvolle vooruitgang te kunnen bepalen.

Voor de MSR in Nederland kunnen de volgende implicaties worden overwogen:

- De studies in dit proefschrift en de klinische praktijk suggereren dat het optimaliseren en systematisch gebruiken van PROM-uitkomsten niet alleen belangrijk is voor het stellen van doelen, maar ook voor het monitoren en evalueren van behandeling in de MSR en de eigen regie van jongere en ouders. Een juiste evaluatie vergemakkelijkt de overgang naar bijvoorbeeld eerstelijnszorg.
- Verschillen in aanmeld- en ontslagcriteria en nazorg tussen revalidatiecentra zouden verder kunnen worden geanalyseerd. Vervolgens kan er consensus bereikt worden over welke criteria te gebruiken en hoe de nazorg vorm te geven.
- Samenwerking tussen revalidatiecentra onderling en met regionale netwerkpartners behoeft continuering. Hierbij kunnen lokale studievertegenwoordigers (kartrekkers) als waardevolle verbinders fungeren.

Dit proefschrift benadrukt het belang van een holistische benadering van MSR. Het legt de basis voor toekomstige initiatieven die tot doel hebben om de revalidatiebehandeling voor kinderen en jongvolwassenen met NAH en hun families verder te optimaliseren, op het juiste moment en op de juiste plaats.

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CHAPTER 11

List of publications
Curriculum vitae
Dankwoord

LIST OF PUBLICATIONS

Peer-reviewed articles

International publications:

Allonsius F, van Markus-Doornbosch F, de Kloet A, Opschoor D, Vliet Vlieland T, van der Holst M. Fatigue in children and young adults with acquired brain injury in the outpatient rehabilitation setting a 2-year follow-up. Neuropsychological Rehabilitation. 2024 Jan 4:1-23 [Epub ahead of print].

Allonsius F, de Kloet A, van Markus-Doornbosch F, Vliet Vlieland T, van der Holst M. A longitudinal follow-up study of parent-reported family impact and quality of life in young patients with traumatic and non-traumatic brain injury. Disability and Rehabilitation. 2023 Jun 9:1-11.

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Allonsius F, de Kloet A, van Markus-Doornbosch F, Meesters J, Kromme C, Vliet Vlieland T, van der Holst M. Parent-reported family impact in children and young adults with acquired brain injury in the outpatient rehabilitation setting. Brain Injury. 2021 Apr 16;35(5):563-573.

Allonsius F, de Kloet A, Bedell G, van Markus-Doornbosch F, Rosema S, Meesters J, Vliet Vlieland T, van der Holst M. Participation Restrictions among Children and Young Adults with Acquired Brain Injury in a Pediatric Outpatient Rehabilitation Cohort: The Patients' and Parents' Perspective. International Journal for Environmental Research and Public Health. 2021 Feb 8;18(4):1625.

Publication in Dutch:

Allonsius F, de Kloet A, van Markus-Doornbosch F, van der Holst M. Behandelprogramma voor kinderen en jongvolwassenen met niet-aangeboren hersenletsel in de medisch-specialistische revalidatie. 2023 Feb.

Curriculum vitae

Florian Allonsius werd geboren op 4 september 1992 in Terneuzen. In 2011 behaalde hij zijn HAVO-diploma aan het Zeldenrust-Steelantcollege in Terneuzen en werd hij ingeloot voor de studie Fysiotherapie aan de Avans Hogeschool Breda. Tijdens zijn studie kwam hij tijdens verschillende stages in aanraking met de kinderrevalidatie. In 2015 behaalde hij de Bachelor Fysiotherapie. Vanwege de gewekte interesse in de kinderrevalidatie heeft Florian aansluitend de master Pediatric Physical Therapy (kinderfysiotherapie) gedaan aan Avans+ te Breda, die hij In 2019 heeft afgerond. Van 2015 tot 2024 heeft Florian als kinderfysiotherapeut gewerkt. Eerst in verschillende fysiotherapiepraktijken in Breda en omstreken (2015-2017) en vanaf 2017 tot 2023 in de kinderrevalidatie, onder andere bij het VU-Medisch Centrum Amsterdam (2017-2018), bij Basalt revalidatie Leiden (2018-2020) en het Leids Universitair Medisch Centrum (2023-2024).

In augustus 2018 is Florian, naast zijn werkzaamheden als kinderfysiotherapeut bij Basalt revalidatie Leiden, gestart als junior onderzoeker bij het multicenter project 'Meedoen?!' bij Basalt. Eerst heeft hij in het kader van de master kinderfysiotherapie in 2018 (afstudeer) onderzoek gedaan naar de gezinsimpact van niet-aangeboren hersenletsel bij kinderen en jongvolwassenen in de medisch specialistische revalidatie. Dit gebeurde onder leiding van dr. Arend de Kloet en dr. Menno van der Holst. Hierna is in 2020 het vervolg op het project 'Meedoen?!', genaamd 'Meedoen Next Step', gestart waarbij Florian werd aangesteld als promovendus (2021). Dit resulteerde in het proefschrift 'On the road to optimize rehabilitation for young individuals with acquired brain injury', met prof. dr. Thea Vliet Vlieland als promotor en dr. Menno van der Holst en dr. Arend de Kloet als co-promotores.

Momenteel is Florian betrokken bij de vervolgprojecten 'Meedoen met Resultaat' en 'MOE: Meedoen, Opladen, Energie!' en bij het project Basalt in Beweging. Tevens is hij betrokken binnen de werkgroep 'Onderzoek en ontwikkeling' van Hersenletsel en Jeugd (HeJ) en werkt hij als freelance-docent aan de master Kinderfysiotherapie bij Hogeschool Avans+ te Breda.

Florian woont samen met Joyce Rikkers en geniet met haar van het bourgondische leven in Breda.

DANKWOORD

Zoals vaak gezegd wordt en ook echt zo is: ‘promoveren doe je niet alleen’. Daarom wil ik via deze weg iedereen bedanken die mij op welke manier dan ook heeft gesteund, in voor- en tegenspoed.

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Ik heb het geluk gehad om te kunnen werken met een fantastisch begeleidingsteam. Thea Vliet Vlieland (promotor), je was altijd de scherpe en kritische ‘wetenschappelijke toetssteen’ tijdens mijn leerproces, wat altijd heeft bijgedragen aan hoge kwaliteit van onderzoek en publicaties. Co-promotor Arend de Kloet, je stond altijd klaar met wijze raad en scherpe feedback, en ik ben dankbaar dat ik heb kunnen bijdragen aan de door jou zorgvuldig opgebouwde onderzoekslijnen. Menno van der Holst, naast de rol als co-promotor, dagelijkse begeleider, sparringpartner en luisterend oor, heb ik je ook altijd als mijn voorbeeld gezien in werk, wetenschap en soms ook persoonlijk vlak.

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(Christian Jumelet, Ben Willems, Mark van Wierst, Jarno Nelis, Frank Miltenburg, Leroy Spierings), de 'Bouldermaten' (Etienne van de Boel, Lotte van de Kamp, Jean-Baptist Vial, Joyce Martens en Jeroen Minten), de 'fieffies+aanhang' en de personal trainers van Helix SHC: ontzettend bedanken voor alle gezellige borrel-, eet-, wijn- spelletjesavonden en soms pittige sportsessies. Thomas de Rooij, hartelijk dank voor alle wijze kluslessen en barbecue-sessies. Bij jou en Nina voel ik me altijd thuis en ik waardeer het enorm dat je mijn paranimf wilt zijn. Camiel Naus, bedankt voor je gezelligheid en alle goede, soms filosofische, gesprekken. Ik ben ook dankbaar dat jij mijn paranimf wilt zijn.

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