Participation of children and youth with acquired brain injury

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Chapter 1
General Introduction

DEFINITION AND EPIDEMIOLOGY OF ACQUIRED BRAIN INJURY (ABI) IN CHILDREN AND YOUTH

Definitions of Acquired Brain Injury (ABI) and children and youth

ABI refers to any post-neonatal damage to the brain, due to an external cause (traumatic brain injury, TBI) or an internal cause (non-traumatic brain injury, NTBI).[1]

According to the World Health Organization[2] children are persons up to and including 14 years and youth persons up to and including 23 years. Within these age groups, preschool children (-5 years), adolescents (13-18 years) and young adults (19-23 years) can be distinguished.

Incidence of ABI

With respect to the incidence of TBI, epidemiological studies in children and youth have so far mainly focused on the age group up to 14 years. In this age group, the reported incidence rates for TBI vary from 70-798 per 100.000 persons per year.[3] Differences among reported rates may be due to differences in classification, inclusion criteria, hospital registrations or national health care systems. Reported rates are probably an underestimation, as it is suggested that mild TBI is unreported or unrecognized in up to half of the cases of head injuries.[4]

Data on the incidence of NTBI are variable as well, and are mainly available for specific causes, including brain tumours (3.5/100.000 in the age group up to 14 years)[5,6] and stroke (2-13/100.000 in the age group up to 14 years).[7]

Overall there is a trend towards an increasing incidence and prevalence of ABI in children and youth over the past decades.[3] This is probably in part related to better registration and also to improvements in medical care.

Causes of ABI

ABI in children and youth may result from events with an external cause (traumatic brain injury, TBI) such as accidents (in traffic, at home or during sports) and violence or from an internal cause (non-traumatic brain injury, NTBI), such as a brain tumour, stroke or infections such as meningitis or encephalitis.[1]

TBI has an acute onset, the onset of NTBI may also be acute (stroke) but is in some cases more gradual (tumour, infection). In the age group up to 4 years old NTBI is most often caused by meningitis; in the age groups from 5 up to 9 and 10 up to14 years old by brain tumours and in the group from 15 up to 19 years by toxic effects of substances.[8] The cause of TBI determines the type of lesion and damage of brain tissue, e.g. more focal or diffuse injuries. The consequences of NTBI can both be local (stroke, tumour), or more diffuse, affecting the entire brain (anoxia, hypoxia or infection).[9] Concerning the causes of TBI and NTBI in children and youth specifically in the Netherlands the information is sparse and incomplete.

Severity of ABI

The severity of ABI is classified as mild, moderate or severe in both TBI and NTBI, however the classification systems are different.[10,11]

Table 1 Classification of severity of injury

	Glasgow Coma Scale (GCS)	Post Traumatic Amnesia (PTA)	Loss Of Consciousness (LOC)
Mild	13-15	<1 day	0-30 minutes
Moderate	9-12	1 to 7 days	30 minutes to 24 hours
Severe	3-8	>7 days	>24 hours

From: Eastvold et al., 2013

In TBI, the classification is usually done during hospital admission, using The Glasgow Coma Scale (GCS)[10] (See Table 1) or the paediatric version of the GCS (PGCS)[11] in preverbal children up to 2 years old (See Table 2) as the gold standard combined with neurological and imaging measures.

Table 2 (Paediatric) Glasgow Coma Scale (GCS and PGCS)

Adult			**Pediatric**	
Spontaneously	4	Best Eye Opening	Spontaneously	4
To verbal stimuli	3		To verbal stimuli	3
To painful stimuli	2		To painful stimuli	2
No eye opening	1		No eye opening	1
Oriented	5	Best Verbal Response	Appropiate coo & cry	5
Confused	4		Irritable cry	4
Inappropriate words	3		Inconsolable crying	3
Incomprehensible	2		Grunts	2
No verbal response	1		No verbal response	1
Obeys commands	6	Best Motor Response	Normal spontaneous	6
Localizes pain	5		Withdraws to touch	5
Withdraws to pain	4		Withdraws to pain	4
Flexion to pain	3		Flexion to pain	3
Extension to pain	2		Extension to pain	2
No motor response	1		No motor response	1

From: Teasdale et al., 1974; Holmes et al., 2005

Moreover, the duration of Post Traumatic Amnesia (PTA) and of loss of consciousness (LOC) as well as other neurological signs are taken into account.[12,13]

In addition to the abovementioned instruments, the King's Outcome Scale for Childhood Head Injury (KOSCHI)[14] and the Glasgow Outcome Scale (GOS)[15] are developed and used to indicate the severity of injury and/or the prognosis in TBI.
Severity of NTBI (Table 3) is usually determined by means of the paediatric modified Rankin Scale (mRS),[16] despite a lack of formal validation in this group of children.

Table 3 Modified Rankin Scale (mRS)

Score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead
TOTAL (0-6): _____	

From: Bonita & Beaglehole, 1988

Consequences of ABI in children and youth

With ABI, depending on its nature and severity, multiple neural systems may be involved, resulting in a large variety of potential consequences in body functions and structures. In addition the course of outcome after ABI is highly variable, ranging from a) full recovery, b) persisting and severe impairment, c) absence of impairment initially, with emerging problems over time to d) early slowed development, with catch-up over time.[17]
The complex and intertwined interaction between the health problem (ABI) and its consequences in various health-related domains (body functions and structures, activities and participation, personal and environmental factors) is represented in the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY) model (Figure 1).[18] Within this comprehensive framework 'Functioning' refers to abilities encompassing body functions (physiological functions of systems) and structures (anatomical parts), activities (execution of actions or tasks by an individual) and participation. Participation is the dynamic result of the complex interactions in the ICF-CY model, and defined as "the nature and extent of a person's involvement in meaningful life situations at home, school, work and community life".[18] Thereby, participation is vital for the development of physical, psychological and social emotional skills and competences, the shaping of identity, the achievement of physical and mental health and well-being.[19] It is conditional to fulfil one's

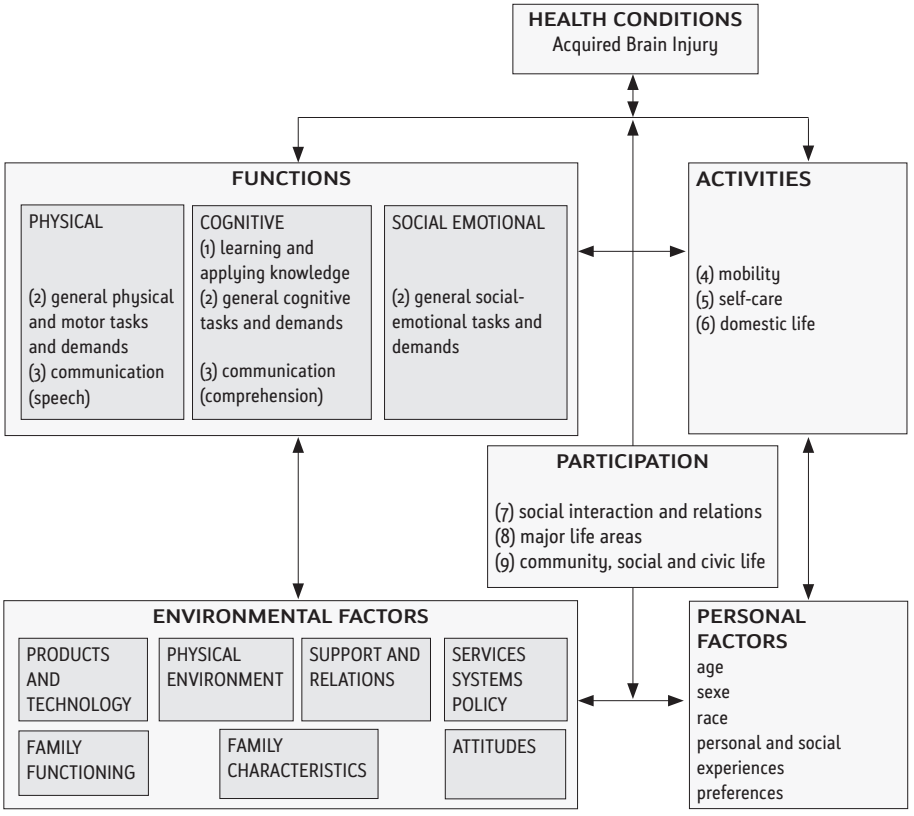
potential as an active participant at home and in the community and associated with positive outcomes in future life.[20]

In addition, the ICF-CY model underscores the influence of personal factors (individual background: e.g. gender, race) and environmental factors (physical, social and attitudinal environment) on body functions and structures and on activities and participation.

Furthermore, 'disability' is an umbrella concept, encompassing impairments of body functions and structures and limitations in activities and participation restrictions.[17,20]

Quality of life (QoL), with the ICF code nd-qol, refers to the general well-being of individuals, including mental, physical and social functioning, and is an important general outcome of ABI as health problem.[20] Overall it is found that consequences of paediatric ABI may reduce QoL, in particular after severe injuries.[21,22] In adolescent TBI survivors reduced QoL is seen in patients with all levels of severity.[23]

Figure 1 The model of the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY)



Based on: World Health Organization, 2007

Consequences of Traumatic Brain Injury (TBI)

TBI is the leading cause of death and permanent disability among children and youth worldwide.[1,3,4] Overall, the mortality rate in children with TBI is 1%.[4] In TBI the primary injury results immediately from the initial trauma. Complications (secondary injury) include e.g. cerebral hypoxia, hypotension or cerebral oedema. These may occur in the hours and days following the primary injury and cause additional damage.[2,4] Moreover, the physical consequences are associated with the presence or absence of injuries at other parts of the body.[13] Some consequences may be transient, such as those occurring in the post-acute phase (e.g. post traumatic amnesia) or the recovery phase (e.g. temporary post commotional symptoms as headaches, dizziness and irritability).[17] Some symptoms may recover quickly, whereas other problems such as limited energy or cognitive and behavioural consequences often persist at the long term and may impede participation.[25] A small number of children and youth are still in a vegetative or minimal conscious state 1 month after onset of a severe TBI. Worldwide, according to calculations, the actual prevalence was calculated as 49 per million people (PMP, exact numbers are unknown in the Netherlands.[26]

Consequences of paediatric TBI regarding functioning in ICF[2] terms are listed in Table 4.

Table 4 Consequences (limitations) of Traumatic Brain Injury in children and youth, in categories of the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY)[18]

	PHYSICAL	COGNITIVE	SOCIAL-EMOTIONAL
FUNCTIONS AND STRUCTURES	physical health, seizures taxability/fatigue [30,31] general motor functions, e.g. muscle tone, strength and endurance, coordination,[32] and balance[33] sensory functions[35]	general intellectual functioning,[35] cognitive/mental fatigue[31] memory, attention, speed of information processing, linguistic and praxis abilities[36], cognitive control (inhibition, working memory, flexibility of response)[37] central sensory processing[34] and sensory integration[38]	social cognition/information processing,[40] problem solving[41] specific behavioral / psychiatric disorders (e.g. impulsivity, disinhibition, temper control, mood swings, depression, loss of temper)[4,42]
ACTIVITIES	hip-extension strength, step length[33]; mobility, self care, daily routines[28]	learning and applying knowledge[32]	communicative competences[43] and pragmatic language skills[40]
PARTICIPATION	physical activity and sports[33]	lower school performance, educational attainment and work status[32,39]	social interpersonal interactions, relationships and activities,[4,44] diversity (preference) and intensity (frequency) in recreational activities[45] social competence,[46] social involvement during adolescence and young adulthood,[47,48] perceived quality of life[20,48,49] increased risk for alcohol and drug dependency[50]

Consequences of Non-Traumatic Brain Injury (NTBI)

In general, the death rate after paediatric NTBI is relatively high compared to TBI. In children and youth with stroke, a mortality rate of 16-42% is reported.[27] The occurrence of persisting problems after NTBI is relatively high as well. In children and youth with stroke, long-term consequences are seen in 50-75% of the patients.[27]

Although it is suggested that the consequences of NTBI are often similar to those of TBI,[28] due to differences in their causes and nature the outcome after a TBI cannot be extrapolated to the various aetiologies of NTBI.[29] Consequences of NTBI with respect to body structure and functions and activities and participation after paediatric NTBI are listed in Table 5.

Table 5 Specific consequences of Non-Traumatic Brain Injury in children and youth in categories of the International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY),[18] in addition to Table 4

		PHYSICAL	COGNITIVE	SOCIAL-EMOTIONAL
BODY FUNCTIONS AND STRUCTURES	Brain tumours	growth, puberty, hormone system, sexual functions[5] motor problems (e.g. ataxia , dysarthria, speech problems),[51] impaired sense of smell, impaired hearing, facial paralysis, dizziness, hypoesthesia[52] aphasia[52] visual (field) impairments, double vision, eye movements[5] neurotoxicity[29]	spatial orientation[52]	
	Stroke	hemiparesis[53] visual field impairments, speech[54]	learning difficulties - mental retardation,[59] poor attention[54]	behavioral problems[54]
	Meningitis/ encephalitis	motor deficits, including paralysis, ataxia and hemiparesis; loss of consciousness, seizures; visual and hearing difficulties[55-57]	decreased mental functioning[57,60]	behavioral problems [60,61]
	Anoxic/ hypoxic	poor motor outcome[9] risk of persistent vegetative state (hypoxic injury, e.g. after nearly drowning), seizures[58]	poor outcome, mental retardation (some types of epilepsy)[9]	
ACTIVITIES	Probably comparable with TBI in Table 4 No specific NTBI literature found			
PARTICIPATION		Probably comparable with TBI in Table 4 No specific NTBI literature found	Probably comparable with TBI in Table 4 No specific NTBI literature found	Socializing, wellbeing, quality of life[5,54]

This list is not complete since some conditions are relatively rare, and thus limited information on their consequences is available. An example of such a condition is ADEM (Acute Disseminated Encephalo Myelitis).

Regarding the consequences of paediatric TBI and NTBI it should first be noted that so far, the knowledge on the outcomes of paediatric NTBI is relatively sparse, as the focus of most research in paediatric ABI has been on TBI. Second, the literature on outcomes in children and youth with ABI shows inconsistent results. This variability is due to several reasons: a) studies lack well defined groups with respect to the type and severity of injury; b) there is variation regarding age at the time of injury; c) the number of time points and duration of follow-up is often limited; d) there is large variation in outcome measures; and e) studies usually have small sample sizes, resulting in limited statistical power, and have other methodological flaws.[42,62,63]

Consequences of paediatric ABI on the family

The impact of ABI in youth may also result in family adversity, with high levels of perceived burden, disrupted family systems and unmet support needs.[44] So far, studies on the consequences of family impact after ABI were mainly done in the United States and Australia, and were predominantly focused on TBI. It was found that although many families eventually adapt favourably to the often increased demands of the injury, still clinically significant stress was seen more than 12 months after the trauma in 40-45% of the families with a child with TBI.[64] This observation did not only apply to severe, but also to mild or moderate TBI. It has been suggested that in some cases family members may experience more problems than the child with an ABI.[64]

Due to the unexpected onset of an ABI, the unknown and often not visible consequences and uncertain prognosis, the impact on the family is often delayed until recovery has reached a stable phase and efforts at community reintegration have begun.[38]

Hawley[4] reported sibling stress in 56-33-13% and unmet information need in 83-79-71% of siblings, 2 years after the onset of severe-moderate-mild TBI, respectively. Brothers and sisters were found to suffer from mental stress (changes in mood, problems at school, feeling guilty, worries about recovery/future), changes in family functioning (roles, climate, activities), physical stress (extra tasks, sleeplessness) and chronically increased alertness and responsibility.[64,66] Moreover, it was found that only few families sought support.[67]

Notably, the instruments used to measure the impact of ABI on the family varied widely, again allowing no valid comparison between studies.

> *"Nearly loosing a child was a very traumatic experience as a parent. People telling us how lucky we are that our child is still alive is very depressing, in fact we are still mourning about loosing our child of before the ABI"*
>
> Quote of a parent of a child with ABI

In conclusion, studies on the impact of paediatric ABI on families has so far mainly focused on TBI, with a variety of instruments used to determine its occurrence and severity. The availability of an appropriate instrument for family impact after ABI is important, as it has been previously suggested that measuring and monitoring family impact and functioning should be promoted as long-term patients' outcome is related to family and environmental factors.[66,67]

Determinants of participation after ABI

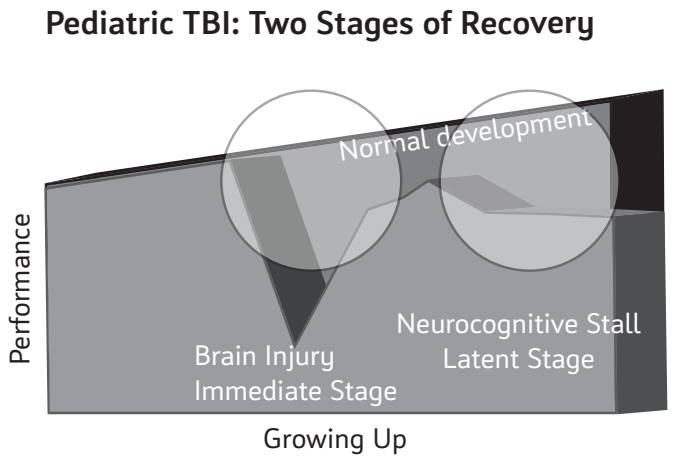
Research in paediatric ABI has long been mainly focussed on physical and cognitive outcomes (body functions and structure) and their determinants, only more recent studies focus on psychosocial outcome,[61] including participation. No systematic literature review study so far specifically addressed the determinants of participation outcomes in both TBI and NTBI. Only some narrative reviews on the outcome of ABI addressed the predictors of outcome.[62,63,68,69] Factors which were reported to be associated most consistently with participation following paediatric ABI included: health conditions (especially severity of injury, neurological complications), body functions and structure (especially movement functions, cognitive functioning, behavioural functioning, mood, mental fatigue), activities (especially communication, self-care), environmental factors (especially family functioning, family nurturing/parenting style, social economic status, acceptance in community, availability of special programs) and personal factors (especially pre-injury behavioural competences, pre-injury cognitive competences).[26,28,32,70] The studies included in these reviews were mainly focused on TBI and employed a large variety of measurement instruments for both predictors as well as outcomes of ABI. In addition, these studies varied with respect to the duration of follow-up.

Injury severity has been identified as an important predictor across all age groups, with more severe ABI being associated with greater problems with respect to motor, cognitive and behavioural functions than the mild group. The latter is consistent with a dose-response relationship between severity of injury and outcome.[32,35] However, several other pre-injury and current personal and environmental factors were found to be strongly associated with outcome as well.[70] It has been suggested that psychosocial outcomes do not always show the same relationship with severity of injury as physical and cognitive outcomes.[71,72]

Age at onset of ABI was found to be a major determinant for outcome of ABI in children and youth.[73] The long-held assumption that 'onset at earlier age means a better prognosis, due to relatively strong plasticity capabilities of the young brain' may have contributed to the general underestimation of the impact of ABI in children and youth.[74] Quite the opposite seems to be true, and this may be due to various reasons: a) brain maturation and development continue throughout childhood into early adulthood;[46] and b) the developmental stage of the brain

during the injury is crucial: growth, maturation and development of the brain interact with injury parameters and impact on acquisition and modification of knowledge, competences and skills and executive functions (e.g. in transitions to higher levels of education, work, social intimacy or living independently).[32,73] This cumulative phenomenon, the interaction between growth, maturation and ABI, is called 'growing into deficit'[46,74] after an immediate phase of recovery children and youth typically experience a decline in outcome that results in plateauing, as opposed to improving of outcome. The so-called "neurocognitive stall" (Figure 2) represents these developmental stage effects on recovery.[75]

Figure 2 The neurocognitive stall



From: Chapman, 2006

In conclusion, participation in children and youth with ABI is still an underrepresented area in the literature.[32,63] More insight into the association between functioning and participation after injury on the one hand and injury characteristics, pre-injury functioning and personal and environmental factors on the other hand is essential to enable the development of tailor-made interventions. For that purpose, more data on the nature of the injury, patterns of recovery and associated factors are needed. In addition, the literature concerning determinants of participation of children and youth has not been reviewed systematically.

Neurorehabilitation, ABI and serious gaming

Neurorehabilitation, i.e. rehabilitation programs for patients with ABI, is driven by plasticity of the brain: every stimulus results in changes in grey (cells) and white (connections) matter, independently of age.[76] Specific knowledge about the mechanisms of recovery of motor and cognitive functions after ABI, however is lacking.[77] Regarding the effectiveness

of neurorehabilitation in children and youth with ABI, systematic reviews[42,78] concluded that the evidence for the effectiveness of interventions to treat motor/neurocognitive/behavioural sequelae is sparse. Nevertheless, consensus statements about the principles of rehabilitation after ABI[79] include the recommendation that rehabilitation should: 1) start as early as possible,[71] (although the length of time since onset of the ABI should not be an exclusion criterion;[79] 2) be targeted, enjoyable, varied and tailor-made, with focus on the client's own real-world circumstances (e. g. daily living activities) to improve generalization, transfer and participation,[73] using and teaching of adaptive cognitive strategies;[79] 3) include interdisciplinary psycho-education, training and support in a systematic, structured and repetitive manner, with patients as active participants in goal setting and monitoring of progress[79] and be family-centered, by including and empowering parents and siblings.[80]
Neurorehabilitation, based on above-mentioned principles, can be enhanced by computer-based training. The latter is, in addition to conventional rehabilitation strategies, considered to be a promising tool. Some evidence for its effect has been demonstrated with gaming with commercial 'off the shelf' consoles'.[81] A systematic review of six high quality RCTs in adults after stroke provides evidence that computer-based cognitive rehabilitation is effective with respect to the improvement of overall cognitive functions, especially memory, thinking operations, executive functions and orientation were measured, after stroke.[82] Other recent studies showed effects of cognitive gaming on working memory in adults after stroke.[83]
A review of computer-based cognitive rehabilitation in children and youth has not been found. Overall, the authors of clinical studies on gaming, undertaken in children and youth with ABI, underscore the importance of more, large scale, methodical solid studies on the effect of neurocognitive outcome of gaming in rehabilitation after ABI in different age groups.[84]

The aim of this thesis

ABI in children and youth relatively often results in death or pervasive, lifelong problems in daily life at home, in school/work and community. Long-term consequences of ABI in children and youth on participation and family functioning and their determinants have been under researched. Current gaps concerning the knowledge on ABI in children and youth include:

- The incidence of ABI in children and youth in the Netherlands.
- The impact on participation and the family.
- Evaluation of effective rehabilitation strategies, in particular serious gaming.

This thesis therefore aims:

- To determine the occurrence and causes of ABI in children and youth in the Netherlands.
- To review the literature on participation of children and youth with ABI and on factors associated with participation.

- To translate, adapt and validate an instrument to measure and monitor participation after paediatric ABI into the Dutch language.
- To evaluate family impact in a cohort of children and youth with ABI and family.
- To evaluate the potential of gaming on improvement of physical, cognitive and social functioning of children and youth with ABI by means of a pilot study.

Outline of this thesis

- **Chapter 1** gives an overview of the literature on ABI in children and youth.
- **Chapters 2 and 3** describe a multicentre, retrospective cohort study on the incidence and causes of paediatric ABI in the Netherlands.
- **Chapter 4** presents the results of a systematic review on determinants of participation of children and youth with ABI.
- **Chapter 5** describes the translation and cross-cultural adaptation and validation of the Child and Family Functioning Survey (CFFS), an instrument to measure and monitor participation after ABI, into the Dutch language.
- The impact of ABI on the family is the focus of **Chapter 6**.
- **Chapter 7** describes a pilot study on the effect of gaming to improve functioning in children and youth with ABI.
- **In Chapter 8** the findings of the studies presented in this thesis are summarized and discussed.

References

1. Greenwald BD, Burnett DM, Miller MA. Congenital and acquired brain injury. Brain injury: Epidemiology and pathophysiology. Archives of Physical Medicine and Rehabilitation 2003; 84:S3-7.
2. World Health Organization (WHO) 2013. http://search.who.int/search. Date accessed 08-01-2014.
3. Schneier AJ, Shields BJ, Hostetler SG, et al. Incidence of pediatric traumatic brain injury and associated hospital resource utilization in the united states. Pediatrics 2006;118:483-492.
4. Hawley CA. Behaviour and school performance after brain injury. Brain Injury 2004;18:645-659.
5. Aarsen FK, Paquier PF, Reddingius RE, et al. Functional outcome after low-grade astrocytoma treatment in childhood. Cancer 2006;106:396-402.
6. Cancerresearchuk.orgbrain/cancerstats/types/incidence.nl; 06-08-2013. Ref Type: Electronic citation.
7. Chung CY, Wong V. Pediatric stroke among Hong Kong Chinese subjects. Pediatrics 2004:114:e206-12.
8. Zeigler D, Wang C, Yoast R, et al. The neurocognitive effects of alcohol on adolescents and college students. Preventive Medicine. 2005;40:23-32.
9. Smania N, Avesani R, Roncari L, et al. Factors predicting functional and cognitive recovery following severe traumatic, anoxic, and cerebrovascular brain damage. Journal of Head Trauma Rehabilitation 2013;28:131-140.
10. Teasdale G, Jennett B. Assessment of coma and impaired consciousness: a practical scale. Lancet 1974;13:81-84.
11. Holmes JF, Palchak MJ, MacFarlane T, et al. Performance of the pediatric glasgow coma scale in children with blunt head trauma. Academic Emergency Medicine 2005;12:814-9.
12. Eastvold AD, Walker WC, Curtiss G, et al. The differential contributions of posttraumatic amnesia duration and time since injury in prediction of functional outcomes following moderate-to-severe traumatic brain injury. Journal of Head Trauma Rehabilitation 2013;28:48-58.
13. Kuks JBM, Snoek JW, Oosterhuis HJGH. Schedelhersentrauma. In: Kuks JBM, Snoek JW, Oosterhuis HJGH, redacteuren. Klinische neurologie. 15e druk. Houten: Bohn Stafleu Van Loghum. 2003;75-89.
14. Crouchman M, Rossiter L, Colaco T, et al. A practical outcome scale for paediatric head injury. Archives of Disease in Childhood 2001;84:120-124.
15. Wilson JT, Pettigrew LEL, Teasdale GM. Structured interviews for the Glasgow Outcome Scale and the extended Glasgow Outcome Scale: Guidelines for their use. Journal of Neurotrauma. 1998;15:573-585.
16. Bonita R, Beaglehole R. Recovery of motor function after stroke. Stroke 1988;19:1497-1500.
17. Anderson V, Brown S, Newitt H, et al. Long-term outcome from childhood traumatic brain injury: Intellectual ability, personality, and quality of life. Neuropsychology 2011;25:176-184.
18. World Health Organization: International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY). Geneva: World Health Organization;2007.
19. Limond J, Dorris L, McMillan T. Quality of life in children with acquired brain injury: Parent perspectives 1-5 years after injury. Brain Injury 2009;23:617-622.
20. Horneman G, Folkesson P, Sintonen H, et al. Health-related quality of life of adolescents and young adults 10 years after serious traumatic brain injury. International Journal of Rehabilitation Research 2005;28:245-249.
21. Neuner B, von Mackensen S, Krümpel A, et al. Health-related Quality of Life in Children and Adolescents with Stroke, Self-Reports, and Parent/Proxies Reports: Cross-Sectional Investigation. Annals of Neurology 2011;70:70-78.
22. Di Battista A, Soo C, Catroppa C, et al. Quality of life in children and adolescents post-TBI: A systematic review and meta-analysis. Journal of Neurotrauma 2012;29:1717-1727.
23. Green L, Godfrey C, Soo S, et al. A preliminary investigation into psychosocial outcome and quality-of-life in adolescents following childhood traumatic brain injury. Brain Injury 2013;7-8:872-877.
24. Porth, C. Essentials of Pathophysiology: Concepts of Altered Health States. Lippincott Williams & Wilkins, Hagerstown, MD:2007.
25. Galvin J, Froude EH, McAleer J. Children's participation in home, school and community life after acquired brain injury. Australian Occupational Therapy Journal. 2010;57:118-126.
26. Eilander HJ, Wijnen VJM, Scheirs JGM, et al. Children and young adults in a prolonged unconscious state due to severe brain injury: Outcome after an early intensive neurorehabilitation programme. Brain Injury 2005;19:425-436.
27. Delsing BJ, Catsman-Berrevoets CE, Appel IM. Early prognostic indicators of outcome in ischemic childhood stroke. Pediatric Neurology 2001;24:283-289.
28. Bedell GM, Dumas HM. Social participation of children and youth with acquired brain injuries discharged from inpatient rehabilitation: a follow-up study. Brain Injury 2004;18:65-82.
29. Johnson AR, DeMatt E, Salorio CF. Predictors of outcome following acquired brain injury in children. Developmental Disabilities Research Reviews 2009;15:124-132.
30. Skandsen T, Ivar LT, Fredriksli O, et al. Global outcome, productivity and epilepsy 3-8 years after severe head injury. The impact of injury severity. Clinical Rehabilitation 2008;22:653-62.

31. Lerdal A, Bakken LN, Kouwenhoven SE, et al. Poststroke fatigue-a review. Journal of Pain and Symptom Management 2009;38:928-949.
32. Anderson V, Brown S, Newitt H, et al. Educational, vocational, psychosocial, and quality-of-life outcomes for adult survivors of childhood traumatic brain injury. Journal of Head Trauma Rehabilitation 2009;24:303-312.
33. Katz-Leurer M, Rotem H, Keren O, et al. Recreational physical activities among children with a history of severe traumatic brain injury. Brain Injury 2010;24:1561-1567.
34. Flood G, Dumas H, Haley S. Central auditory processing and social functioning following brain injury in children. Brain Injury 2005;19:1019-1026.
35. Ewing-Cobbs L, Prasad MR, Kramer L, et al. Late intellectual and academic outcomes following traumatic brain injury sustained during early childhood. Journal of Neurosurgury 2006;105:287-296.
36. Catroppa C, Anderson VA, Morse SA, et al. Outcome and predictors of functional recovery 5 years following pediatric traumatic brain injury. Journal of Pediatric Psychology 2008;33:707-718.
37. Levin HS, Hanten G, Li X. The relation of cognitive control to social outcome after paediatric TBI: Implications for intervention. Developmental Neurorehabilitation 2009;12:320-329.
38. Jaffe KM, Polissar NL, Fay GC, et al. Recovery trends over three years following pediatric traumatic brain injury. Archives of Physical Medicine and Rehabilitation 1995;76:17-26.
39. Nybo T, Koskiniemi M. Cognitive indicators of vocational outcome after severe traumatic brain injury (TBI) in childhood. Brain Injury 1999;10:759-766.
40. Yeates KO, Swift E, Taylor G, et al. Short- and long-term social outcomes following pediatric traumatic brain injury. Journal of the International Neuropsychological Society 2004;10:412-426.
41. Janusz JA, Kirkwood MW, Yeates KO, et al. Social problem-solving skills in children with traumatic brain injury: long term outcomes and prediction of social competence. Child Neuropsychology 2002;8:179-194.
42. Babikian T, Asarnow R. Neurocognitive Outcomes and Recovery After Pediatric TBI:Meta-Analytic Review of the Literature. Neuropsychology 2009; 3:283-296.
43. Hanten G, Wilde EA, Menefee DS, et al. Correlates of social problem solving during the first year after traumatic brain injury in children. Neuropsychology 2008;22: 357-370.
44. Prigatano GP, Gray JA. Parental concerns and distress after paediatric traumatic brain injury: A qualitative study. Brain Injury 2007;21:721-729.
45. Law M, Anaby D, DeMatteo C, et al. Participation patterns of children with acquired brain injury. Brain Injury 2011;25:587-595.
46. Donders J, Warschausky S. Neurobehavioural outcomes after early versus late childhood traumatic brain injury. Journal of Head Trauma Rehabilitation 2007;22:296-302. worden.
47. Brown M, Gordon WA. Impact of impairment on activity patterns of children. Archives of Physical Medicine and Rehabilitation 1987;68:828-832.
48. Cattelani R, Lombardi F, Briant R, et al. Traumatic brain injury in childhood: intellectual, behavioural and social outcome into adulthood. Brain Injury 1998;4:283-296.
49. Rosema S, Crowe L, Anderson V. Social Function in Children and Adolescents after Traumatic Brain Injury: A Systematic Review 1989-2011. Journal of Neurotrauma 2012;29:1277-1291.
50. Ponsford J, Whelan R, Bahar-Fuchs A. Alcohol and drug use following traumatic brain injury: A prospective study. Brain Injury. 2007;21:1385-1392.
51. van Calenbergh F, Demaerel P, Sciot R, et al. Long-term survival in a child with a brain stem dermoid cyst. Surgical Neurology 2005; 63:261-263.
52. Lannering B, Marky I, Lundberg A, et al. Long-term sequelae after pediatric brain tumors: their effect on disability and quality of life. Medical and Pediatric Oncology 1990;18:304-310.
53. Friedman N. Pediatric Stroke: Past, Present and Future. Advances in Pediatrics 2009;56: 271-299.
54. Sofronas M, Ichord RN, Fullerton HJ, et al. Pediatric Stroke Initiatives and Preliminary Studies: What Is Known and What is Needed? Pediatric Neurology 2006;34:442-448.
55. Baraff LJ, Lee SI, Schriger DL. Outcomes of bacterial meningitis in children: a meta analysis. Pediatric Infectious Disease Journal 1993;12:389-394.
56. Fritsch P, Gruber-Sedlmayr U, Pansi H, et al. Tick-borne encephalitis in Styrian children from 1981 to 2005: a retrospective study and a review of the literature. Acta Paediatrica 2008;97:535-538.
57. Bingen E, Levy C, de La Rocque F, et al. Bacterial Meningitis in Children: A French Prospective Study. Clinical Infectious Diseases 2005;41:1059-1063.
58. Kriel RL, Krach LE, Luxenberg MG, et al. Outcome of severe anoxic/ischemic brain injury in children. Pediatric Neurology 1994;10:207-212.
59. Ganesan V, Prengler M, Wade A, et al. Clinical and radiological recurrence after childhood arterial ischemic stroke. Circulation 2006;114:2170-2177.
60. Carter JA, Neville BG, Newton CR. Neuro-cognitive impairment following acquired central nervous system infections in childhood: a systematic review. Brain Research Reviews. 2003;43:57-69.
61. Halket S, de Louvois J, Holt DE, et al. Long term follow up after meningitis in infancy: behaviour of teenagers. Archives of Disease in Childhood 2003;88:395-398.
62. Trenchard SO, Rust S, Bunton P. A systematic review of psychosocial outcomes within 2 years of paediatric traumatic brain injury in a school-aged population. Brain Injury 2013;27:1217-1237.
63. Van Tol E, Gorter JW, DeMatteo C, et al. Participation outcomes for children with acquired brain injury: A narrative review. Brain Injury 2011;25:1279-1287.

64. Wade S, Taylor HG, Drotar D, et al. Childhood traumatic brain injury: initial impact on the family. Journal of Learning Disabilities 1996;29:652-66.
65. Hawley CA, Ward AB, Long J, et al. Prevalence of traumatic brain injury amongst children admitted to hospital in one health district: a population-based study. Injury 2003;34:256-260.
66. Gan C, Campbell KA, Gemeinhardt M, et al. Predictors of family system functioning after brain injury. Brain Injury 2006;20:587-600.
67. Micklewright JL, King TZ, O'Toole K, et al. Parental Distress, Parenting Practices, and Child Adaptive Outcomes Following Traumatic Brain Injury. Journal of the International Neuropsychological Society 2012;18:343-350.
68. Agnihotri S, Keightley ML, Colantonio A, et al. Community Integration interventions for youth with Acquired Brain Injuries: a review. Developmental Neurorehabilitation 2010;13:369-382.
69. Chevignard MP, Truelle JL. Community integration following severe childhood traumatic brain injury. Current Opinion in Neurology 2010;23:695-700.
70. Anaby D, Law M, Hanna S, et al. Predictors of change in participation rates following acquired brain injury: results of a longitudinal study. Developmental Medicine and Child Neurology 2012;54:339-346.
71. Anderson V, Catroppa C. Advances in postacute rehabilitation after childhood acquired brain injury. A focus on cognitive, social and behavioural domains. American of Journal Physical Medicine and Rehabilitation 2006;85:767-778.
72. Anderson V, Catroppa C. Recovery of executive skills following paediatric traumatic brain injury (TBI): a 2 year follow-up. Brain Injury 2005;19:459-470.
73. Anderson V, Moore C. Age at injury as a predictor of outcome following pediatric head injury. Child Neuropsychology 1995;1:187-202.
74. Dennis M. Margaret Kennard (1899-1975): not a 'principle' of brain plasticity but a founding mother of developmental neuropsychology. Cortex 2010;46:1043-1059.
75. Chapman SB. Neurocognitive stall: A paradox in long term recovery from pediatric brain injury. Brain Injury Professional 2006;3:10-13.
76. Buch ER, Johnen VM, Nelissen N, et al Noninvasive associative plasticity induction in a corticocortical pathway of the human brain. Journal of Neurosciences 2011;31:17669-17679.
77. Ribbers GM. Oratie, 2013. https://www.rijndam.nl/onderzoek/neurorevalidatie; accessed 25 November 2013.
78. Laatsch L, Harrington D, Hotz G, et al. An evidence-based review of cognitive and behavioral rehabilitation treatment studies in children with acquired brain injury. Journal of Head Trauma Rehabilitation 2007;22:248-256.
79. Headway Review of Guidelines and Evidence: Rehabilitation following Acquired Brain Injury. http://www.headway.ie/download/pdf/rehabilitation_review.pdf; accessed 25 November 2013.
80. Bedell GM, Khetani MA, Cousins M, et al. Parent perspectives to inform development of measures of children's participation and environment. Archives of Physical Medicine and Rehabilitation 2011;92:765-773.
81. Yong Joo L, Soon Yin T, et al. A feasibility study using interactive commercial off-the-shelf computer gaming in upper limb rehabilitation in patients after stroke. Journal of Rehabilitation Medicine 2010;42:437-441.
82. Chaa Y, Kima H. Effect of computer-based cognitive rehabilitation (CBCR) for people with stroke: A systematic review and meta-analysis. NeuroRehabilitation 2013;32:359-368.
83. Lundqvist A, Grundström K, Samuelsson K, et al. Computerized training of working memory in a group of patients suffering from acquired brain injury. Brain Injury 2010;24:1173-1183.
84. Jaeggi SM, Buschkuehl M, Jonides J, et al. Short- and long-term benefits of cognitive training. Proceedings of the National Academy of Sciences of the United States of America 2011;108:10081-10086.