Preterm birth, long-term outcome: how an early start affects school-aged children

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PART SEVEN

SUMMARY AND GENERAL DISCUSSION

Summary

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Nederlandse samenvatting

SUMMARY

Being born prematurely can lead to life-long neurodevelopmental challenges in multiple outcome domains [1, 2]. Therefore, children who are born very preterm (<32 weeks' gestation) are invited to outpatient departments on a regular basis to monitor their development and detect possible difficulties in everyday functioning at an early stage. However, patient follow-up often ends at two years of age, especially in research settings [3]. This is a concern, since children born very preterm are likely to grow into their deficits, the full extent of the consequences of preterm birth might not be seen until later childhood, adolescence or even adulthood.

The purpose of this thesis was to investigate a longitudinal cohort of children born before 32 weeks' gestation, and to study the associations between neonatal factors and outcomes at two and ten years of age. To contribute to the knowledge in this area, four topics were covered. First, we provided insight in the rates of impairment in multiple developmental domains at two and ten years of age, and investigated the individual trajectories between these two time-points. As it is important to have early prognostic markers that can help predict development, the second aim was to associate neonatal neuroimaging findings with both early and school-age outcome. Many studies use routine outcome measures to assess functioning, including intelligence quotients or standardized questionnaires; our goal was to increase understanding of other measures equally important when evaluating a child's daily functioning. Therefore, our third aim was to gain specific knowledge on classroom-evaluated school performance, since academic attainment depends on more than cognitive capabilities. For our fourth and final aim, we provided insight in day-to-day experiences of caregivers of preterm children over the years by asking them about their main concern and the child's best asset during two different life phases (toddlerhood and primary school). In this current chapter, the main findings of this thesis are discussed, leading to directions and opportunities for the future and future research.

Main findings

In **Chapter 1** we assessed the rate and stability of impairments in children born very preterm in the neurological, motor, cognitive and behavioral domain at two time-points (age two (corrected for prematurity) and ten). Each child was categorized as having no, mild or moderate-severe impairment for each of these domains. The individual outcomes at both timepoints were compared.

When all domains were taken together in a composite score, the number of children with a moderate-severe impairment increased almost threefold between two and ten years of age. In contrast, the number of children with a mild impairment decreased. However, when the domains were assessed separately, no differences were found in the distribution of normal, mild and moderate-severe impairment over time. So one could conclude that, on a group level, the outcome for children within the separate domains is relatively stable. But, as is reflected by the composite score, the individual trajectories revealed a considerable number of children showing changes in functioning (in the neurological, motor and cognitive, but not the behavioral domain). Within the motor and cognitive domain, all children with a moderate-severe outcome at age two still had a moderate-severe outcome at age ten. The individual shifts in functioning occurred mainly in children who had a normal or mildly abnormal early outcome, emphasizing that positive outcomes in toddlerhood should be interpreted with care and long-term follow-up is mandatory.

The considerable individual shifts in neurodevelopmental outcome as described in chapter 1, could indicate that the predictive value of neonatal prognostic parameters changes over time. Over the last decades, neonatal magnetic resonance imaging (MRI) has received increasing attention as a prognostic marker. Therefore, we investigated the associations between neonatal brain injury as shown on MRI and cognitive, motor and behavioral outcomes at both two and ten years of age in **Chapter 2**. All children within our cohort underwent an MRI scan around term equivalent age. Using the Kidokoro scoring system [4], neonatal brain injury and altered brain growth in white matter, cortical and deep gray matter and the cerebellum were assessed. Cognitive, motor, and behavioral outcomes were obtained during follow-up visits at both two (corrected) and ten years of age.

The global brain abnormality score, a general measure of neonatal brain injury, was associated with cognition, motor skills, and internalizing behavioral problems at two years of age. These associations remained after correction for perinatal factors and level of maternal education. However, at age ten, there was no longer an association with cognition (full-scale, verbal and performance IQ) and behavior. A large effect of the level of maternal education was found, affecting cognitive development at age 10. Both the average verbal and performance IQ of children of mothers with low levels of education were beneath the averages of children of highly-educated mothers (18 and 11 point respectively). The effect of maternal education on IQ was

most prominent in children with milder forms of brain injury; neonatal MRI remained an independent predictor of 10-year cognitive outcome for children with moderate-severe brain abnormality scores.

During follow-up assessment of preterm born children, standardized outcome measures are often used to assess a child's functioning. It is however debatable whether these outcomes truly reflect a child's day-to-day functioning. At school, for example, the demands on behavioral regulation become greater with increasing age to engage in learning activities and expend social skills. Studies including outcome related to school performance often use standardized tests to assess a child's reading, spelling or mathematical abilities. These are generally administered by a psychologist, in a clinically controlled environment with very little distractions. Since children born preterm are likely to experience cognitive difficulties and are more prone to behavioral problems [5], we investigated in **Chapter 3** how the children within our cohort performed at school, with all the distractions that are common in an elementary classroom.

First, data on special educational needs were compared to the Dutch national average; it was more common for children born preterm to have repeated a grade and/or be enrolled in special primary education. Despite these forms of additional educational support, children within our cohort more often obtained below average scores on reading comprehension, spelling, and especially mathematics at the end of third grade (age 8-9). This is a concern, as children born preterm are unlikely to catch up with their term-born peers later on when it comes to academic attainment [6]. Factors associated with lower scores were male sex, higher rates of white matter injury and lower levels of maternal education.

With the previous chapters showing that children born preterm often experience a wide range of impairments, we aimed to provide insight in the day-to-day experiences of their caregivers. In **Chapter 4,** both the quantitative outcomes of a behavioral questionnaire and the qualitative findings based on answers of parents and teachers on two open-ended questions relating to their main concern and most positive aspect about their child/pupil, were described.

Based on the behavioral questionnaires at the corrected age of two and age ten, filled in by parents, quantitative outcomes showed a large increase in children with clinical internalizing behavioral problems over time. For externalizing problems, the number

of children with normal, borderline clinical and clinical symptoms remained relatively stable over the years. Teachers reported less (borderline) behavioral problems in the clinical range, both internalizing as well as externalizing, compared to parents.

Qualitatively, main parental concerns in toddlerhood were reported across three clusters: *Developmental Milestones* (will my child be able to reach age-appropriate milestones?), *Development in Relation to the Self and Others* (mainly toddler behavior) and *Physical Development* (including their child's health). At ten years of age, the majority of parents reported concerns in the cluster *Development in Relation to the Self and Others*, capturing statements on emotional and social development, behavior, temperament, personality style, and mindset. Similar to parents, teachers mainly reported within the cluster *Development in Relation to Self and Others*, although the underlying themes differed. For example, teachers had more concerns related to their pupils social development, whereas parents worried more about their child's emotional development.

Considering the positive aspects about their child, parents made most statements within the cluster *Development in relation to the Self and Others* at both time-points. They often reported their child as being cheerful and happy at two years of age, while describing predominantly complex character traits later on, for example their child's perseverance, independence and curiosity. Teachers also mostly mentioned statements within this cluster, praising their pupils positive character traits.

GENERAL DISCUSSION

Follow-up should include more than intelligence quotients

The goal of follow-up assessment is to monitor the development of children born preterm over the years and assess their functioning at different time-points. This enables clinicians to inform caregivers about the child's strengths and weaknesses, making it possible to intervene and/or adapt the environment of the child accordingly. Data on long-term outcome provide meaningful insights in what might be expected for the future, informing the adequate counseling of parents of very preterm infants today.

One of the standardized outcome measures used during follow-up assessment is an intelligence test. However, it has been debated whether this is a reliable marker of a child's cognitive functioning [7]. Since children spend a considerable amount of time at school, evaluating outcomes like performance in the classroom can be a valuable way of monitoring a child's cognitive development in addition to standardized intelligence tests during follow-up visits. Within our cohort of children born very preterm, mean intelligence sores fell in the average range. However, preterm born children in our study had more difficulties with reading comprehension, spelling, and mathematics compared to their peers, indicating that intelligence alone is not predictive of a child's school functioning.

Over the last decades, executive functioning received increasing attention for having an important role in a child's academic performance [8, 9]. It is an umbrella-term for a broad and complex system of neurocognitive functions, including working memory and inhibitory control [10]. Impairments in executive functioning are common in children born preterm [11], and can cause difficulties in meeting the general demands of the classroom and academic attainment. In specific school tasks, such as mathematics, children who are born preterm often struggle to combine several cognitive processes including visuospatial processing and working memory [12].

The use of standardized assessments makes it possible to monitor development over time and to compare outcomes, for example between different longitudinal cohorts. However, since the main goal of follow-up assessment is to adequately assess a child's functioning, we should be aware that outcome measures such as intelligence quotients may not be the most representative of a child's day-to-day functioning.

Therefore, examining executive functioning complementary to intelligence, and the inclusion of other outcomes such as classroom-evaluated school performance, should be considered in addition to the currently used intelligence tests.

The effect of early prognostic markers (such as neonatal MRI) should be interpreted with care considering the individual changes in outcome over time

Over the past decades, research studies shifted their focus from describing outcomes at a singular time-point to multiple moments in time [13]. This is important, since, as described in chapter 1, future functioning cannot be reliably predicted by developmental assessment in toddlerhood, especially for those children with early normal or mild abnormal outcome. Therefore, assessing development at multiple timepoints provides more reliable information on the number of children experiencing difficulties in everyday functioning. Considering the limited predictive value of early developmental outcome and the individual changes in functioning over time as described in chapter 1, the question is whether other prognostic factors are better in predicting who is at risk for an adverse development.

As seen in chapter 2, although neonatal MRI showed promising associations with short-term motor, cognitive, and behavioral outcomes, these associations did not last over time. Instead, there appeared to be a stronger association with environmental factors. Currently, neonatal MRI is not considered standard care for infants born preterm and it is debatable whether it should be [14, 15]. Taken the limited value of neonatal MRI for long-term functioning into account, it should be considered to only use MRI in those infants who are expected to have higher grades of brain injury, for example based on cranial ultrasound findings, instead of all preterm born infants.

The main factors in predicting classroom-evaluated school performance in chapter 3 were the child's sex, white matter injury and level of maternal education. For example, boys and children of mothers with low educational levels obtained lower scores on reading comprehension. This is not different from the general population, where sex differences favoring girls and a relation with maternal education are known as important factors influencing intelligence, executive functioning and, therefore, school performance [16].

Environmental factors should be taken into consideration

Since the level of maternal education was associated with school-performance and cognitive development in older children, it is important to take (multiple) environmental factors into account when trying to predict outcome. Studies have reported that, for example, sensitive parenting has a protective effect on neurodevelopment [17, 18]. This suggests that adapting early interventions for preterm born children, in terms of supporting their parents and enhancing early responsive care, will aid their development. However, the effectiveness of these intervention programs has been debated, since treatment effects that were observed on motor and cognitive outcomes in infancy and toddlerhood, did not last into school-age [19, 20].

The importance of qualitative research

Behavioral outcomes in children born preterm have been described for many years [1, 21, 22]. Most studies assess behavior through a questionnaire, and distinguish between internalizing and externalizing behavioral traits. Internalizing behavior is characterized by processes within the self, such as feelings of anxiety, depression and somatization, where externalizing behavior comprises actions that are primarily directed towards others and/or the environment [23]. In current literature, the behavior of children born preterm is classified as 'the preterm behavioral phenotype', comprising an unique co-occurrence of, often focused inwards, behavioral symptoms [24]. The risk of internalizing behavior is that these children often go unnoticed, since they do not draw (negative) attention to themselves. An additional difficulty is that, even though children born very preterm are more likely to be diagnosed with a psychiatric disorder such as Attention-Deficit/Hyperactivity Disorder and Autism Spectrum Disorder, there are many children who do not meet the requirements of an official classification but still experience great difficulties with their learning abilities and behavior [24, 25]. These children are, for example, more easily distracted, have difficulties to follow instructions and are disorganized when it comes to their schoolwork.

Even though behavioral questionnaires can provide insight in the areas children born preterm tend to struggle with, it does not take the day-to-day personal experiences of caregivers into account. Considering what parents mentioned to be their main concern, there was a clear shift in worrying about reaching age-related milestones and physical health in toddlerhood, to themes aligning with social and emotional

development at a later age. The importance of multiple informants when assessing behavioral difficulties was underlined by the observation that parents and teacher expressed their concerns in different themes, where teachers more often worried about their pupils social skills. It is possible that parents are less confronted with their child's interactions with other children.

In summary, the chapters in this thesis reinforce that children born preterm are at risk for long-term impairments. Being able to predict who is at risk, by neonatal neuroimaging or early assessment, remains difficult, especially in children who have milder forms of brain injury and/or experience milder difficulties at two years of age. Currently, most follow-up assessments use standardized outcome measures that might not show the full extent of a child's daily functioning. Additional measurements and/or the implementation of qualitative research can be of great additional value.

Study limitations

The original design of the PROUD-study was to investigate brain imaging findings in a prospective cohort of children born very preterm. Over time, follow-up outcomes at two and, later on, ten years of age were added. Because follow-up was not included in the original study design, there was no sample size or power analysis conducted to account for loss to follow-up at two and ten years of age during the recruitment of the cohort. Possibly due to the large interval, we had a fair percentage of loss to follow-up, as is the case with most longitudinal studies. We acknowledge that this may have influenced the generalizability of our findings.

Other factors possibly affecting the generalizability of our findings are the limited number of children with severe neonatal brain injury and the relatively high level of maternal education, with the majority of mothers attending higher vocational school or university. Studies focusing on more severely affected or extremely preterm born children and/or including different ratios in educational level might therefore find different outcomes.

Considering the assessment tools used, especially the Bayley Scale of Infant and Toddler Development, the 3rd edition seems to underestimate, especially mild, cognitive delays [26]. The use of a more sensitive tool might have a better predictive value for later functioning and improve the detection of impairments already at an early age.

The original study design did not include the purpose of qualitative research. Future studies investigating the perspective of caregivers should therefore be more extensive, by including for example a structured interview in a representative sample of parents and teachers. This generates opportunities to ask specific information in a wide range of topics, such as the impact of preterm birth on parents, not only right after birth, but also in the long-term.

Implications

In this section implications for policy, the educational system and future research will be further discussed.

Implications for policy

The current thesis shows that follow-up at two years of age on one hand is important to identify children who are already (severely) impaired in toddlerhood, since these children show little improvement in functioning over time. On the other hand, it is not a reliable assessment for later development in children who have a normal to mild abnormal outcome in toddlerhood. The rates of impairment start to rise during school-age, most likely due to the greater demands on abilities that are essential for learning at the start of primary school, such as attention regulation [27]. In the Netherlands, according to the guidelines of the national workgroup on neonatal follow-up (Landelijke Neonatale Follow-up; LNF) [28], follow-up assessments during primary school should be performed at age five and eight. However, in practice, this can unfortunately not always be achieved in all Dutch neonatal centers [29]. Currently, only children born below 30 weeks of gestation are included in long-term follow-up programs. In order to adequately monitor the development of all children affected by very preterm birth, investments should be made in for example staff trained to assess children born preterm, including pediatricians, neonatologist, physical therapists and child psychologists. This way, more preterm born children can be seen in outpatient departments by trained professionals, and hopefully, in the future, follow-up can be prolonged until at least adolescence. This will provide more information on long-term development of preterm born children.

When we aim to assess a child's day-to-day functioning, it should be considered to conduct a more extensive follow-up assessment during these time-points and

include, aside from parental questionnaires, for example outcome measures regarding executive functioning (including working memory and cognitive flexibility) or school performance outcomes obtained in regular classrooms. Qualitative research highlights the importance of looking beyond the outcomes of behavioral questionnaires, since individual stories are unique and are hard to capture in quantitative research. So when truly grasping the influence of preterm birth on caregivers, asking them about their day-to-day experiences is important, in addition to standardized questionnaires classifying problem behavior.

The rate of impairment increased within our cohort from two to ten years of age, past the endpoint of the Dutch regular follow-up program. However, development continues and it is known that children born preterm are likely to experience difficulties in a range of areas during adolescence and adulthood, such as professional careers and forming romantic relationships [30].It should therefore be reconsidered to prolong follow-up into at least adolescence, since the quality of life can be greatly affected by difficulties within these areas. When it is not possible to include all preterm born children in the outpatient facilities of Dutch neonatal centers, investments should be made in facilities where parents can ask their questions to specialized professionals when they encounter difficulties. Knowledge on the functioning of preterm born children in this phase of life also creates possibilities for the development of targeted interventions, for example the enhancing of social skills or the support of a job coach.

Implications for the educational system

With the incidence of very preterm birth in the Netherlands affecting approximately 2500 infants each year, it is very likely for an elementary school teacher to have a preterm born child in the classroom. Teachers will not always be aware of their pupils' prematurity; parents may choose not to tell school to avoid stereotyping, or don't feel the need to inform their child's teacher. Knowing most impairments develop or become more visible during school age, it is important for school teachers to be familiar with the possible consequences of preterm birth and the effects on development and learning. For example, many children born preterm struggle with their working memory [31]. It might appear as though they are not paying attention, while in reality, their working memory is insufficient to cope with the demands of the task. Therefore, these children can be supported by allowing them to work in a quiet place or to give visual instruction in addition to verbal instructions.

A recent study showed that knowledge on long-term outcomes of premature birth is limited amongst teachers [27]. Information regarding preterm birth and how to support preterm born children should be accessible during their training. For teachers who already work at schools, additional trainings such as online modules (for example the in English available Preterm Birth Information for Educational Professionals [32]) can be provided. Primary school builds the foundation for future learning. Being able to attend and participate in primary school is therefore essential. Since the 1990s, there has been a political trend towards inclusive education in the Netherlands, indicating that children with special educational needs are included in mainstream primary schools with additional support [33]. Besides teachers, the support staff of mainstream primary schools should therefore also be taken into account when it comes to education on the effects of preterm birth, since they will most likely be the ones working with the children who are in need of additional support.

Implications for future research

The level of maternal education is an important predictor of functioning during school-age. A high level of maternal education is a protective factor in children with milder forms of brain injury, indicating that children of mothers with a low level of education are especially at risk. Future research should focus on the complex intertwine of multiple factors, including genes, perinatal, postnatal and sociodemographic factors, such as socioeconomic status and parenting style to understand the pathways of how parental education influences functioning. This may also provide guidance towards targeted interventions for specific groups of preterm born infants and their families.

Most of the children within our cohort had relatively mild forms of neonatal brain injury. It would be of interest to see whether the predictive value of neonatal MRI on long-term functioning differs in cohorts with extremely preterm born children (gestational age below 28 weeks) and in children with higher brain abnormality scores, since other studies suggest that moderate-severe brain injury is predictive of cognitive development and motor skills in toddlers and school-aged children [34, 35], whereas the predictive value seems limited in cohorts with less apparent brain injury [36].

Currently, neonatal MRI is not part of routine clinical care for preterm infants. With the results of this thesis in mind it is the question whether it should be, considering it

is only beneficial for a select group of children. However, within a research setting, it might be useful to assess the effect of medical interventions and new daily practices at the NICU on brain development and brain injury to see whether the incidence of brain abnormalities changes over time in consecutive cohorts of preterm infants. Since long-term outcome can be very different compared to short-term outcome, it is important to consider outcome at multiple timepoints in order to adequately assess the effectiveness of, for example, neonatal interventions. Furthermore, additional, quantitative, MR imaging techniques (for example based on volumetric MRI and Diffusion Tensor Imaging) may be able to better predict future functioning, but currently these techniques are not commonly used in clinical practice.

References

1. Aarnoudse-Moens, C.S.H., et al., *Meta-Analysis of Neurobehavioral Outcomes in Very Preterm and/or Very Low Birth Weight Children.* Pediatrics, 2009. **124**(2): p. 717-728.
2. Johnson, S. and N. Marlow, *Early and long-term outcome of infants born extremely preterm.* Archives of Disease in Childhood, 2017. **102**(1): p. 97-102.
3. Synnes, A. and M. Hicks, *Neurodevelopmental Outcomes of Preterm Children at School Age and Beyond.* Clinics in Perinatology, 2018. **45**(3): p. 393-408.
4. Kidokoro, H., J.J. Neil, and T.E. Inder, *New MR Imaging Assessment Tool to Define Brain Abnormalities in Very Preterm Infants at Term. Am J Neuroradiol*, 2013. **34**(11): p. 2208-2214.
5. Burnett, A.C., et al., *Exploring the "Preterm Behavioral Phenotype" in Children Born Extremely Preterm.* Journal of Developmental and Behavioral Pediatrics, 2019. **40**(3): p. 200-207.
6. Twilhaar, E.S., et al., *Academic trajectories of very preterm born children at school age.* Archives of Disease in Childhood-Fetal and Neonatal Edition, 2019. **104**(4): p. F419-F423.
7. Aylward, G.P., *Cognitive and neuropsychological outcomes: More than IQ scores.* Mental Retardation and Developmental Disabilities Research Reviews, 2002. **8**(4): p. 234-240.
8. Samuels, W.E., et al., *Executive functioning predicts academic achievement in middle school: A four-year longitudinal study.* Journal of Educational Research, 2016. **109**(5): p. 478-490.
9. Gerst, E.H., et al., *Cognitive and behavioral rating measures of executive function as predictors of academic outcomes in children.* Child Neuropsychology, 2017. **23**(4): p. 381-407.
10. Burnett, A.C., et al., *Executive Function in Adolescents Born < 1000 g or < 28 Weeks: A Prospective Cohort Study.* Pediatrics, 2015. **135**(4): p. E826-E834.
11. Anderson, P.J., *Neuropsychological outcomes of children born very preterm.* Seminars in Fetal & Neonatal Medicine, 2014. **19**(2): p. 90-96.
12. Simms, V., et al., *Mathematics difficulties in children born very preterm: current research and future directions.* Archives of Disease in Childhood-Fetal and Neonatal Edition, 2013. **98**(5): p. F457-F463.
13. Roberts, G., et al., *The stability of the diagnosis of developmental disability between ages 2 and 8 in a geographic cohort of very preterm children born in 1997. Arch Dis Child*, 2010. **95**(**10**): p. 786-790.
14. Pearce, R. and J. Baardsnes, *Term MRI for small preterm babies: do parents really want to know and why has nobody asked them?* Acta Paediatrica, 2012. **101**(10): p. 1013-1015.
15. Edwards, A.D., et al., *Effect of MRI on preterm infants and their families: a randomised trial with nested diagnostic and economic evaluation.* Archives of Disease in Childhood-Fetal and Neonatal Edition, 2018. **103**(1): p. F15-F21.
16. Ardila, A., et al., *The influence of the parents' educational level on the development of executive functions.* Developmental Neuropsychology, 2005. **28**(1): p. 539-560.
17. Doyle, L.W., et al., *Biological and Social Influences on Outcomes of Extreme-Preterm/Low-Birth Weight Adolescents.* Pediatr, 2015. **136**(6): p. E1513-E1520.
18. Zohsel, K., et al., *Long-Term Consequences of Preterm Birth on Cognitive Development and Academic Achievement: Is There a Protective Effect of Maternal Responsiveness?* Kindheit Und Entwicklung, 2017. **26**(4): p. 221-229.

19. Spittle, A., et al., *Early developmental intervention programmes provided post hospital discharge to prevent motor and cognitive impairment in preterm infants.* Cochrane Database of Systematic Reviews, 2015(11).

20. Vanderveen, J.A., et al., *Early interventions involving parents to improve neurodevelopmental outcomes of premature infants: a meta-analysis.* Journal of Perinatology, 2009. **29**(5): p. 343-351.

21. Allotey, J., et al., *Cognitive, motor, behavioural and academic performances of children born preterm: a meta-analysis and systematic review involving 64 061 children.* BJOG, 2018. **125**(1): p. 16-25.

22. Bhutta, A.T., et al., *Cognitive and behavioral outcomes of school-aged children who were born preterm - A meta-analysis.* Jama-Journal of the American Medical Association, 2002. **288**(6): p. 728-737.

23. Verhulst, F.C., Van der Ende, J., *Handleiding ASEBA-Vragenlijsten voor leeftijden 6 t/m 18 jaar: CBCL/6-18, YSR en TRF.* Rotterdam: ASEBA Nederland, 2013.

24. Johnson, S. and N. Marlow, *Preterm Birth and Childhood Psychiatric Disorders.* Pediatric Research, 2011. **69**(5): p. 11R-18R.

25. Johnson, S., et al., *Psychiatric Disorders in Extremely Preterm Children: Longitudinal Finding at Age 11 Years in the EPICure Study.* Journal of the American Academy of Child and Adolescent Psychiatry, 2010. **49**(5): p. 453-463.

26. Anderson, P.J., et al., *Underestimation of Developmental Delay by the New Bayley-III Scale. Arch Pediatr Adolesc Med*, 2010. **164**(4): p. 352-356.

27. Elvert, C., S. Johnson, and J. Jaekel, *Teachers' knowledge and approaches to supporting preterm children in the classroom.* Early Human Development, 2021. **159**.

28. follow-up, W.L.N. *Aanbeveling Landelijke Neonatale Follow-Up - NICU follow-up*. 2015 January 18th, 2022]; Available from: https://landelijkeneonatalefollowup.nl/index-6.html.

29. Erasmus MC, S.K. *Polikliniek Neonatologie. Follow-up spreekuur*. 2022 [cited 2022 June 16th]; Available from: https://patientenfolders.erasmusmc.nl/folders/polikliniek_neonatologie_follow-up_spreekuur.

30. Bruin, K.M.V., et al., *Profiling the preterm or VLBW born adolescent; implications of the Dutch POPS cohort follow-up studies.* Early Human Development, 2015. **91**(2): p. 97-102.

31. Farooqi, A., B. Hagglof, and F. Serenius, *Behaviours related to executive functions and learning skills at 11years of age after extremely preterm birth: a Swedish national prospective follow-up study.* Acta Paediatrica, 2013. **102**(6): p. 625-634.

32. Johnson, S., Clayton, S., Cragg, L., Gilmore, C., Griffiths, R., Marlow, N., Simms, V., Wharrad, H. *Preterm Birth Information for Education Professionals*. [cited 2022 June 22nd]; Available from: www.pretermbirth.info.

33. Ruijs, N.M., I. Van der Veen, and T.T.D. Peetsma, *Inclusive education and students without special educational needs.* Educational Research, 2010. **52**(4): p. 351-390.

34. Anderson, P.J., et al., *Associations of Newborn Brain Magnetic Resonance Imaging with Long-Term Neurodevelopmental Impairments in Very Preterm Children.* J Pediatr, 2017. **187**: p. 58-+.

35. Kidokoro, H., et al., *Brain Injury and Altered Brain Growth in Preterm Infants: Predictors and Prognosis.* Pediatr, 2014. **134**(2): p. E444-E453.

36. Brouwer, M.J., et al., *Preterm brain injury on term-equivalent age MRI in relation to perinatal factors and neurodevelopmental outcome at two years.* Plos One, 2017. **12**(5).