Summary
Preterm birth is a complication of pregnancy that is the leading cause of perinatal mortality and long-term morbidity. A child is born preterm if birth is before 37 weeks of gestation. Birth before 32 weeks of gestation, is defined as a very preterm birth. In the Netherlands, 1.5% of infants is born very preterm. Preterm birth rates are rising in the last decades. Due to improving neonatal care mortality has decreased in the last decades, however (long term) morbidity has not decreased. Therefore, neurodevelopmental follow-up studies of these preterm born babies have become increasingly important for the evaluation of neonatal care. Very preterm born children are at risk for a wide range of impairments. Outcome studies initially focused on major handicaps (such as blindness, hearing loss, cerebral palsy, and mental retardation) revealing in the first few years of life. Focus has by now shifted to a broader range of less severe outcomes that became apparent in longer term follow-up. Cerebral palsy occurs in approximately 5%, while milder neurological problems occur in as many as 45% of very preterm born children. Other domains on which disabilities occur more frequently are motor functioning, behaviour, intelligence and other aspects of neurocognitive functioning, such as executive functioning and attention.

Premature birth also has an impact on the parents. Premature birth and subsequent hospitalisation in the neonatal intensive care unit (NICU) are very stressful for parents and can be traumatic. Parents of preterm born children are at risk of persistently perceive their child as vulnerable as it grows up, which in turn is a risk factor for child behaviour problems. Maternal posttraumatic stress symptoms are also associated with subsequent mother-child interaction problems. According to Deater-Deckard and Bulkley, ‘the adaptation of a preterm born child is a product of complex transactions between biological and environmental risk and ameliorative factors that operate within powerful family and cultural contexts’. Environmental risks include factors that have been described earlier as consequences of preterm birth for parents (stress and perception of the child as vulnerable) and problems in parent-child interaction.

In this study, a model, based on the paper by Deater-Deckard and Bulkley is used to structure this thesis. The main aims of this thesis were to describe the development of very preterm born children at the age of 5 on multiple developmental domains in comparison with term born controls, and identify risk factors for developmental disabilities and for problems in the parental environment of very preterm born children at the age of 5. Describing the developmental problems of very preterm born children and identifying risk factors for developmental disabilities may contribute to the identification of children who are especially at risk, and the development of interventional programmes. It may contribute to the counselling of parents, both during and after the hospitalization in the NICU and to the discussion about NICU treatment decisions.

On the basis of these aims and the theoretical model, the following research questions were formulated: 1) What is the prevalence of disabilities on the areas of neurology, motor functioning,
behaviour, intelligence and broader neurocognitive functioning in very preterm born children in comparison with term born children?, 2) Which biological and environmental risk factors for disabilities in developmental functioning of very preterm born children at the age of 5 can be identified, and how do these risk factors interact?, and 3) How do the parental environment of very preterm born and term born children at the age of 5 compare and which risk factors for problems in the parental environment can be identified?

The following questions regarding the adjustment of clinical practices of follow-up and intervention on the basis of the results of this study were formed: 1) Which ages are optimal for follow-up assessment of very preterm children?, 2) Which developmental domains should be included in the follow-up of very preterm children?, and 3) What are possibilities for intervention aimed at improving developmental outcome in very preterm children?

This study is a single center cross-sectional (and partly prospective) cohort study as part of the follow-up program of the Emma’s Children’s Hospital/Academic Medical Centre, Amsterdam NICU. Two groups of 5 year old children participated in this study, the preterm study group, and a group of term born children served as controls. The very preterm group consisted of a consecutive sample of children born < 30 weeks of gestation and/or with birth weights < 1000 grams. The term control group consisted of children born > 37 weeks of gestation and/or birth weights > 2500 grams. Children came to the hospital for two visits, in which mother-child interaction, and intelligence and broader neurocognitive functioning were assessed by a developmental psychologist, and neurologic and motor functioning were assessed by a trained pediatrician or child physiotherapist. Parents completed questionnaires about the child’s behaviour, the child’s health, sociodemographic characteristics, their own psychological and parenting stress and perception of their child’s vulnerability.

In Chapter 2, the prevalence and co-occurrence of disabilities on the domains of neurology, motor functioning, intelligence and behaviour in both groups was described. Furthermore, the association between disabilities and parental education was studied. In this chapter, 104 very preterm and 95 term born children participated. For the assessments, an intelligence test (the third version of the Wechsler Preschool and Primary Scale of Intelligence [WPPSI-III-NL], measuring full scale, verbal and performance intelligence and processing speed), behavior questionnaires for parents and teachers (Strengths and Difficulties Questionnaires [SDQ]), motor (Movement Assessment Battery for Children Second Edition [M-ABC-2]) and neurological tests (Touwen neurological examination) were used. A child was considered to have a disability if the score on at least one of the tests was abnormal. Of the preterm children, 75% had at least one disability and 50% had more than one, compared to 27% and 8% respectively of term controls (p < .01). The preterm-term difference
in full scale IQ increased from 5 IQ-points if parental education was high to 14 IQ-points if it was low, favoring the term children in both groups. A similar pattern was found for behavior, but not for motor and neurological outcome. We concluded that disabilities occur frequently after very preterm birth, and tend to aggregate. Neurological and motor outcomes are mostly influenced by biological risk, while in cognitive and behavioral outcome social risk also plays a strong role.

In Chapter 3, very preterm and term born children were compared on a broad array of neurocognitive functions (intelligence, processing speed, working memory, inhibition, focused attention, sustained attention, visual-motor coordination, face- and emotion recognition). We also investigated whether medical risk factors can be identified for neurocognitive dysfunctions, after taking into account socioeconomic status and child characteristics at birth. In this chapter, 102 very preterm and 95 term born children participated. The following tests were used: the WPPSI-III-NL (intelligence), Digit Span of the third edition of the Wechsler Intelligence Scale for Children (working memory), the preschool version of the Stop Signal Task (inhibition and sustained attention), and Baseline Speed, Focused Attention Objects, Tracking, Pursuit, Face Recognition and Identification of Facial Expressions of the Amsterdam Neuropsychological Test battery (processing speed, focused attention, visual-motor coordination, face- and emotion recognition). Very preterm children scored worse than controls on all domains, except on inhibition and sustained attention, for which results were inconclusive. Principal component isolated four factors: visual-motor coordination, face and emotion recognition, reaction time/attention and accuracy/attention. Disabilities on these factors were present more often in very preterm children. When child characteristics at birth and parental education were accounted for, bronchopulmonary dysplasia, a respiratory complication due to preterm birth, was significantly negatively associated to all four factors. We concluded that very preterm children are at risk for problems on a broad array of neurocognitive functions. Bronchopulmonary dysplasia is an independent risk factor for impaired neurocognitive functioning.

In Chapter 4, we investigated the prediction of cognitive abilities at age 5 (full scale, verbal and performance intelligence and processing speed) by cognitive development at the ages of both 2 and 3, in very preterm born children. We also studied whether domains other than cognition (psychomotor, neurological and behaviour) at the age of 2 and 3 would improve the prediction of cognitive development at age 5. Finally, we explored whether perinatal and sociodemographic characteristics improved the prediction of cognitive outcomes at 5 years when development at age 2 or 3 was already accounted for. In this chapter, 102 very preterm children were assessed at age 2 and 3 using the second version of the Bayley Scales of Infant Development, Child Behavior Checklist and Touwen neurological examination, and at age 5 using the WPPSI-III-NL. Cognitive development at age 2 and 3 explained 44% and 57% respectively of full scale intelligence
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at age five. Adding psychomotor, neurological and behavioural outcomes and perinatal and sociodemographic characteristics to the regression model increased explained variance to 57% and 64% respectively. These percentages were comparable for verbal intelligence. Processing speed quotient and especially performance intelligence were predicted less accurately. Our most important conclusions were that not all aspects of intelligence are predicted sufficiently by cognitive development at age 2 and 3. Follow-up of very preterm children until at least age 5 is needed to distinguish between different aspects of cognitive development.

In Chapter 5, we investigated whether maternal and paternal perception of child vulnerability is an independent risk factor for behaviour problems in very preterm and term born children, when other risk factors for behaviour problems (perinatal risks, true child vulnerability, sociodemographic characteristics, parental psychological distress) are taken into account. In this chapter, 104 very preterm and 95 term born children participated. Behaviour, parental perception of child vulnerability and parental stress were measured using the SDQ for parents and teachers, the Child Vulnerability Scale, the short form of the Profile of Mood States, and the Dutch Parenting Stress Index – short form, respectively. Low/middle parental education, preterm birth, very small for gestational age-status at birth, maternal and paternal stress and maternal perception of child vulnerability all appeared to be independent risk factors for parent-rated behaviour problems. Maternal perception of child vulnerability was a risk factor for behaviour problems specifically in preterm born children (both with and without true vulnerabilities). Risk factors for teacher-rated behaviour problems were low/middle parental education, foreign parental country of birth, very small for gestational age-status at birth and true child vulnerabilities. We concluded that only in parent-rated behaviour, maternal perception of child vulnerability is a risk factor for behaviour problems in preterm children. Therefore, preventing maternal perception of child vulnerability may help to reduce behaviour problems in preterm born children.

In Chapter 6, we compared quality of mother-child interaction between preterm and term born children at age five, and studied the association of mother-child interaction with sociodemographic characteristics and child disabilities. In this chapter, 94 very preterm and 85 term born children participated. Quality of mother-child interaction was assessed using the Three Boxes observation procedure and observation-videos were scored using the NICHD Early Child Care Research Network coding system. Disabilities were assessed using an intelligence test (WPPSI-III-NL), behaviour questionnaires for parents and teachers (SDQ), motor (M-ABC-2) and neurological (Touwen) examinations. Mothers of preterm born children were less supportive of and more interfering with their children’s autonomy than mothers of term born children. This difference was only partly explained by sociodemographic factors. Dyads showed a lower quality of mother-child interaction if children had a severe disability, especially when mothers had a lower level of education. We
concluded that five years after birth, mother-child interaction of very premature children and their mothers compared unfavourably to term children and their mothers. Mothers with a lower level of education, raising a preterm child with severe disabilities, struggle most with giving adequate sensitive support for the autonomy development of their child. Focused specialised support for these at risk groups is warranted.

CONCLUSIONS

Regarding the first research question (concerning the occurrence of disabilities in preterm born children), it was concluded that seventy-five percent of preterm born children have one or more disabilities in the area of neurological functioning, motor development, behaviour or intelligence. Preterm born children also more often have disabilities on the neurocognitive domains of attention, visual-motor coordination and emotion- and face recognition. Regarding the second research question (biological and environmental risk factors for disabilities in very preterm born children), it was concluded that certain developmental domains, namely neurologic and motor development and some aspects of neurocognitive development (attention, visual-motor coordination and face- and emotion recognition) are predominantly biologically determined. Other domains, namely behaviour and intelligence, are associated with a combination of biological and environmental factors. Environmental risk seems to modify biological risk, or more specifically, environmental risk seems to have more impact when the biological risk of preterm birth is present. Specific biological risk factors are neonatal infections and bronchopulmonary disease for neurocognitive functioning and very small for gestational age-status at birth for behaviour problems. Specific environmental risk factors were socioeconomic status (parental education) for behaviour and intelligence and parental stress and maternal perception of child vulnerability for behaviour. Regarding the third research question (concerning the parental environment of very preterm and term born children), it was concluded that perception of child vulnerability was higher in parents of preterm born children as compared to parents of term born children. Another conclusion was that very preterm children (especially those with severe disabilities) received less respect for their autonomy from their mothers (particularly when they had a low level of education) than term children.

The following clinical implications of our results were formulated. Concerning optimal timing of follow-up assessments, it was concluded that follow-up at the age of 5 should be added minimally to early follow-up at the age of 2. Concerning the developmental domains that should be included in follow-up assessments, it was concluded that follow-up of child development should ideally encompass assessments on the domains of neurological, motor, behavioural, and broad neurocognitive development. Assessment of the parental environment via questionnaires should also be a recurring part of follow-up. A more intensive assessment of mother-child
interaction should be added in case of a combination of risk factors (low socioeconomic status and child disability). Concerning possibilities for interventions, it was concluded that a preventive intervention program, focused on child development and parent-child interaction is indicated for all very preterm children. Intensive preventive intervention is most important and can be expected to be most effective for children with a combination of high biological and environmental risk. Referral for specific interventions should be made if developmental disabilities and/or problems in the parental environment are found in long term follow-up assessments.