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Results from the Tromsø Intervention Study on Preterms until children's age of nine.

The influence of structured early parental guidance on behavior-emotional development and well-being among children born preterm and parenting stress in their families.

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List of Papers

Paper I

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Paper II

Landsem IP, Handegård BH, Tunby J, Ulvund SE, Rønning JA. Early intervention program reduces stress in parents of preterms during childhood, a randomized controlled trial. *Trials* 2014; 15: 387.

Paper III

Landsem IP, Handegård BH, Ulvund SE, Kaaresen PI, Rønning PI. Early intervention influences positively Quality of Life as reported by prematurely born children at age nine and their parents; a randomized clinical trial. *Health and Quality of Life Outcomes* 2015; 13:25.

Summary in English

Three studies emanating from “The Tromsø Intervention Study on Preterms” (TISP) are summarized in the thesis. The main focus is whether an early structured intervention program, given to families with preterm infants in the newborn period may influence; children's socio-emotional behavioral development up to 9 years of age, mothers and fathers reports of parenting stress in the same period of time and children's quality of life by nine years.

TISP started in 1999 and the inclusion of children with families lasted until 2002. Infants born preterm from Troms or Finnmark (birth weight below 2000 gram) were recruited and randomized to a premature intervention group (PI = 72 children) and a premature control group (PC = 74 children). 75 healthy term newborns from the city of Tromsø were recruited to a form a term control group (TR). Children of mothers who did not speak Norwegian, which were triplets or was proven with severe neuro-developmental disorders were excluded from the study.

The intervention, a modified version of The Mother-Infant Transaction Program (MITP-M), included 8 hours of supervision for the mother (and father if present) last week of the child's stay in hospital and four home visits approximately 7, 14, 30 and 90 days after discharge. This was given to the PI group while parents in the PC- and the TR group received information according to the hospitals guidelines. The aim of MITP-M was to promote parents' enthusiasm for their children and help them recognize signs of children’s organization versus need for regulatory support. Furthermore, to show parents appropriate interactions with the child that would minimize child disturbance and increase interactional satisfaction for all partners.

All participating families are followed up through developmental tests of the children and data collections using questionnaires when the children were 6 months, 1, 2, 3, 5, 7, 9 years.
Dropout rates have been low. 129 preterm infants (88%) were still participating at children’s age of nine. The main focus was to analyze whether differences between the PI and the PC group emerged as a possible consequence of the intervention. The PI and the PC group were in addition compared with the results of the TR group.

Children's behavioral development is analyzed using mothers, fathers and teachers reports of behavioral problems at 2, 3, 5, 7 and 9 years of age. Teachers reported at 7 and 9 years. They had no information about children's group belonging. Longitudinal analyzes showed that the average prevalence of behavior problems varied according to the same pattern in the three groups from 2 to 9 years. PC mothers and PC fathers reported more behavior problems than PI parents at all follow-ups, but this constituted non-significant differences between PI and PC group with regard to internalizing and externalizing behavior from 2 to 9 years. No longitudinal differences were detected in longitudinal behavior development between the PI and the TR group but one was detected between the PC and the TR group. Fathers in PC group reported a steeper increase in symptoms of anxiety in children from their age of 5 until 9 years compared with fathers in the TR group.

Significant differences between the PI and the PC group became visible at children's age of 7 and 9 years. Both parents and teachers reported significantly less attentional problems and better social competence, adaptability and school-related performances in the PI group. PI children were in average not reported as different from the TR group at their age of nine, both what came to school adjustment, achievements and the occurrence of problems. Significant differences between the PC and the TR group persisted concerning the extent of behavior problems and competencies.

The second study reported mothers and fathers reports of child- and parent-related stress at all follow-ups from children's age of 6 months until 9 years. PI mothers reported significantly less stress than PC mothers at all times and the same was evident for fathers at children's age of 2, 3 and 5 years. PC mothers reported high and stable levels of child-related stress across pre-school years, especially related to statements concerning children's adaptability and mood. In contrast, PI- and TR-mothers reported decreasing levels of parenting stress from children's age of one. Differences between PI and PC group in terms of parents-related stress referred to less perception of parental attachment and competence in the PC group. The last study in this thesis analyzed children's and parent's reports of children's quality of life at their age of nine. Children in PI group reported higher physical wellbeing than the PC children while PI parents report higher emotional and school-related well-being than parents in PC group.

The research presented in this thesis indicate that the structured guidance given parents of preterms in the newborn period has promoted positive and long-lasting effects on the PI group as these children perform at similar level as their term born peers at 9 years of age.

Summary in Norwegian

Avhandlingen er en sammenfatning av tre studier som utgår fra The Tromsø Intervention Study on Preterms (TISP), tidligere omtalt som ”Tidlig Intervensjon 2000”. Hovedfokus i studiene er hvorvidt et tidlig strukturert veiledningsprogram, gitt til familier med prematurt fødte barn i nyfødtperioden kunne påvirke; barnas sosio-emosjonelle adferdsutvikling opp til 9 års alder, mødre og fedres rapport av foreldrestress i samme periode og barnas livskvalitet ved 9 år.

TISP startet i 1999 og inkluderingen av barn pågikk fram til 2002. Prematurt født barn fra Troms eller Finnmark, med fødselsvekt under 2000 gram ble rekruttert og randomisert til en prematur intervensjons gruppe (PI =72 barn) og en prematur kontroll gruppe (PC = 74 barn). I tillegg ble 75 friske, fullbårne nyfødte hjemmehørende i Tromsø rekruttert til en termin kontroll gruppe (TR). Barn av mødre som ikke snakket norsk, som var trillinger eller ble påvist med alvorlige nevro-utviklingsmessige tilstander ble utelukket fra studien.

Veiledningsprogrammet, en modifisert versjon av The Mother-Infant Transaction-Program (MITP-M), omfattet 8 veiledningstimer for mor (og far hvis til stede) siste uka av barnets opphold i sykehuset og fire hjemmebesøk ved cirka 7, 14, 30 og 90 dager etter utskrivelse. Dette ble gitt til PI gruppen mens barn og foreldre i PC og TR gruppene mottok informasjon i henhold til sykehusets retningslinjer. Siktemålet med MITP-M var å fremme foreldrenes begeistring for sitt barn og hjelpe dem å gjenkjenne barnets tegn på likevekt versus behov for reguleringsstøtte. Videre å lære dem hensiktsmessige måter å samhandle med barnet slik at barnet ble minst mulig forstyrret og samhandlingen mest mulig tilfredsstillende både for barn og foreldre.

Alle deltagende familier er fulgt opp med utviklingsmessige tester av barna og data innsamling ved hjelp av spørreskjema når barna var 6 mnd, 1, 2, 3, 5, 7, 9 år. Studien har hatt lite frafall av deltakere. Ved 9 år møtte 129 prematurt fødte barn (88 %). Hovedfokus var å analysere hvorvidt det framkom forskjeller mellom gruppene med prematurt fødte barn (PI & PC). I tillegg er PI og PC gruppene hver for seg sammenlignet med resultatene i termin kontrollgruppen.

Barnas adferdsutvikling er analysert ved hjelp av mødre-, fedre- og lærer rapporterte adferdsproblemer ved 2, 3, 5, 7 og 9 års alder. Lærere rapporterte ved 7 og 9 år. Disse hadde ikke informasjon om hvilken studiegruppe barnet tilhørte. Longitudinelle analyser viste at

gjennomsnittlig forekomst av adferdsproblemer varierte etter samme mønster i de tre gruppene fra 2 til 9 år. PC mødre og PC fedre rapporterte mer problemer enn PI foreldre på alle tidspunkt, men dette utgjorde ikke-signifikante forskjeller mellom PI og PC gruppen med hensyn til utagerende- og tilbaketrekkings adferd fra 2 til 9 år når. I sammenligninger med TR gruppen framkom ingen forskjeller mellom PI- og TR gruppen, mens en forskjell mellom PC- og TR gruppen var signifikant. Fedre i PC gruppen rapporterte en brattere økning av symptomer på engstelighet hos barna fra 5 år og opp til 9 års alder enn fedrene i TR gruppen.

Signifikante forskjeller mellom PI og PC gruppen ble synlig ved 7 og 9 år. Både PI foreldre og PI lærere rapporterte signifikant mindre oppmerksomhetsproblemer samt noe bedre sosiale ferdigheter, tilpasningsevne og skoleferdigheter blant barna enn rapportert i PC gruppen. Ved 9 år ble PI gruppen rapportert på samme nivå som TR gruppen både hva gjaldt skoletilpasning, prestasjoner og forekomst av problemer, mens signifikante forskjeller mellom PC- og TR gruppen vedvarte.

I den andre studien analyserte vi mødres og fedres rapport av barne- og foreldre relatert stress på alle oppfølgingstidspunkt fra barna var 6 måneder og opp til 9 år. PI-mødre rapporterte signifikant mindre stress enn PC-mødre på alle tidspunkt og det samme var tilfelle for PI- versus PC fedre ved 2, 3 og 5 år. PC- mødre rapporterte stabilt høyt barne-relatert stress opp til 5 års alder, spesielt relatert til utsagn som fokuserte på tilpasningsvansker og lunefullt humør hos barnet. PI- og TR-mødre rapporterte på sin side avtagende barne-relatert stress fra 1 års alder. Forskjellene mellom PI og PC gruppen hva gjaldt foreldre-relatert stress omhandlet spesielt rapport av mindre positive tilknytningsfølelser og foreldre kompetanse i PC gruppen.

Den siste studien i avhandlingen rapporterer noen forskjeller mellom prematurgruppene som berører barnas opplevde livskvalitet. Barn i PI gruppen rapporterer høyere kroppslig velvære ved 9 år enn PC barna mens PI foreldre rapporterer høyere følelsesmessig og skolerelatert velvære enn foreldre i PC gruppen.

Studiene i denne avhandlingen indikerer at veiledningsprogrammet som ble gitt PI gruppen har gitt langvarige, positive effekter i familiene og at PI barna fungerer på nivå med sine jevnaldrende født til termin ved 9 års alder.

Definitions and abbreviations

MITP	Mother Infant Transaction Program
MITP-M	Mother Infant Transaction Program, modified version in TISP
NBAS	Neonatal Behavior Assessment Scale
NICU	Neonatal Intensive Care Unit
PSE	Parenting Self-Efficacy
SES	Socio-Economic Status (parental years of education, employment, marital status, income, living conditions, among others)
TISP	Tromsø Intervention Study on Preterms

TISP, study groups:

PC	Preterm Control group
PI	Preterm Intervention group
TR	Term Control group

Birth & Medical terms

BW	Birth Weight

BW groups:

LBW	Low Birth Weight (BW < 2500 g)
VLBW	Very Low Birth Weight (BW < 1500 g)
ELBW	Extremely Low Birth Weight (BW < 1000 g)

BPD	Bronchopulmonary Dysplasia
CRIB	Clinical Risk Index for Babies (a tool for assessing initial neonatal medical risk)
GA	Gestation Age (the number of weeks that a baby has been in the uterus. Newborns delivered before 37 GA are considered premature)
KC	Kangaroo Care (the newborn is held with skin-to-skin contact with an adult)

Measurement & outcome subscales

ASEBA	The Achenbach System of Empirically Based Assessment

ASEBA Questionnaires:

CBCL	Child Behavior Checklist (questionnaire)
TRF	Teachers Report Form (questionnaire)

KINDL	The Kinder Lebensqualität Fragebogen (questionnaire)

PSI	Parenting Stress Index, full form:
PSI domains:	
CD	Child Domain
PD	Parent Domain
TS	Total Stress
PSI-sf	Parenting Stress Index, short form;
PSI-SF domains:	
DC	Difficult Child
PS	Parenting Stress
P-CDI	Parent-Child Difficult Interaction
QoL	Quality of life
SDQ	Strength and Difficulties Questionnaire

Statistical terms

ES	Effect Size
GLMM	Generalized Linear Mixed Models
ICC	Intraclass Correlation
LMM	Linear Mixed Models
OR	Odds Ratio

Introduction

1.1 Neonatal care in health care systems

The development of neonatal care over the last 60 years has been described as a movement from professional- and institution-based autocracy to a parent-professional partnership for the care of hospitalized children [1,2]. In the earliest years, preterm born children were still cared for as individuals and institutionalized independently of their parent's wishes. Bowlby had questioned the prevailing assumption that a child develops independently of the environment in 1952 [3]. Maternal roles were emphasized as important, and research documented the negative effects on child development of the practice of parent-child separation. [4-7]. The impact of parental involvement on the health and development of children has been noted [8]. This knowledge was gradually incorporated in the care of hospitalized children in general and for children born prematurely in particular [3,8-11].

The development of parental involvement has been described as a hierarchy, beginning with the access of parents to the hospital environment (1960s) and proceeding to participation (1980s), partnership and later family-centered care [12]. These processes involved considerable changes in parental roles and were requested by parents and dedicated health care providers and were also supported by changes in juridical laws and regulations [7,13,14].

Family-centered care aims to empower parents. In terms of care of families with prematurely born children, this implicates the transmission of interdisciplinary knowledge, confidence and self-efficacy [2,15-18]. Parents typically provide the first and most proximal environment in their children's life. For prematurely born infants, this natural protection is disturbed; both because parent-child skin-to-skin contact may be hindered by medical equipment/treatment, parents may have limited access to the neonatal intensive care unit (NICU) and the child may be cared for by many different people.

The multidisciplinary care of children born preterm has experienced significant improvements over the last few decades (antenatal steroids, postnatal surfactant therapy, specialized technology and equipment, specialized personnel and increased parental involvement)[1,19-21]. However, although

the survival rates for preterms have increased, morbidity has also risen [22,23]. In particular, the long-term outcomes related to socio-emotional, attentional and academic competencies among preterm born children continue to lag behind term-born peers [19,24,25].

1.2 Health and developmental risks of children born prematurely

The level of risk associated with preterm birth is inversely related to the length of the pregnancy [19,25-27]. In addition, the developmental impact of preterm birth cannot be described without relaying outcomes in different countries and areas with more or less developed health systems. Globally, the rates of preterm birth vary between 5 and 18%. Norway is positioned among the countries with the best outcomes because of the relatively low prevalence of preterm birth (4.9% in 2012) [28], high surveillance rates and relatively low morbidity in comparison to less developed countries. The differences between countries may be exemplified by reports from the World Health Organization (WHO) describing a 50% chance of surveillance at 24 gestational weeks (w of GA) with access to a NICU in a high income country, while a surveillance rate of 50% at 34 w of GA has been reported in several low and middle income countries [29]. Internationally, the prevalence of preterm birth has been reported to be increasing. A low birth weight (LBW) is reported in approximately 15.5% of newborns in developing countries, and in the USA, the occurrence of preterm birth has increased with 31% over the last 35 years [30]. However, the prevalence of LBW newborns (BW < 2500 grams) in Norway has stabilized over the last decade. Approximately 3000 newborns (4.9%) were born before 37 w of GA in 2012, 2% had a BW < 2000 grams and 287 had a BW < 1000 grams. [28].

Children born with the lowest birth weights (500 – 1500 grams) contribute greatly to the rates of perinatal mortality and morbidity despite accounting for less than 2% of all deliveries [19]. Several biological and environmental factors contribute to individual differences in the risk profiles of children. First, the severity of the neonatal course (need for treatment interventions, complications, experiences of pain, length of stay in hospital), followed by the quality of resources in the caring environment (e.g., socio-economic status, support, parental mental health) and, finally, the potential squeals they experience after preterm birth (e.g., lung disease, brain injury, neurological complications, hearing loss and blindness). The major handicaps mentioned above are reported in

5% of the general population and in 6-8% of low birth weight (LBW) children, 14-17% of very low birth weight (VLBW) children and 20-25% of extremely low birth weight (ELBW) children [19,25]. Moderate to late preterm children (32-36 $^{+5}$ w of GA) have been reported to have fewer major handicaps, but they may experience several problems during childhood. After controlling for confounders such as maternal race, prenatal steroids, infant gender and chorioamnionitis, a 23% decrease in adverse outcomes per week longer of pregnancy was reported for children who were born between 32 and 39 w of GA [30]. A high prevalence (50 – 70%) of dysfunction but with a low severity has been reported to occur in very low birth weight (VLBW) children. These problems are often identified as attention-related and/or social problems and, to some degree, to more internalizing behavior [24,26]. Children born preterm are often reported to exhibit under-achievement after entering primary school and more frequently require specialized school assistance [19,31]. Different features of these problems will be reviewed later in this thesis. A recurring problem is the absence of good predictors of the frequently reported, subtle problems that occur among children born preterm [15,19].

1.3 Development of behavioral problems in children born preterm

Unusual or abnormal behavior among children born preterm was reported long before neonatal intensive care medicine was defined. Prior to the Second World War, a syndrome characterized by behavioral difficulties (hyperactivity, susceptibility to distraction, unpredictability and shyness) was described [33]. In the 1970s, a description of transient dystonia was reported, and parents described problems such as irritability, crying and feeding difficulties [34]. The developmental outcomes of preterm children were subsequently extensively studied, but the behavior development of these children has been investigated very little compared with that of short and long-term cognitive growth [35]. Nevertheless, a greater number of behavioral problems and a higher incidence of psychological disorders have been reported in children born preterm compared with those born full-term [35]. A behavioral problem prevalence of 20% (twice the value determined for children with typical development) was reported in the Infant Health and Developmental Program (IHDP) for children aged 3, 5 and 8 years [35]. Similar results have been reported in other studies [26,27], while a Norwegian follow-up study reported that 40% of preterms (BW < 2000 grams) exhibited greater behavioral difficulties [36]. The IHDP study identified predictors of an increased risk of problems

such as maternal psychological stress at 40 w of GA, younger maternal age and maternal smoking. In addition, child- and birth related-factors such as gender, birth weight, gestational age and neonatal health were marginally predictive of behavioral problems [35]. Before specific areas of behavioral problems are described, some features of the children's general behavioral development, as expected across early and middle childhood, are mentioned.

The development of children comprises several dimensions and developmental milestones [37]. Developmental changes are described as normative, nonreversible, relatively stable, frequently sequential and, especially in children born preterm, associated with maturation [38]. The maturation and growth of children is especially apparent in the acquisition of new skills and the understanding and expression of language. Some milestones are included in regular health care assessments throughout childhood, e.g., motor and language achievements. Other milestones exist as more or less defined norms of the society impacting the developing child. To some degree, every child will be viewed in a mirror that is shaped by the expectations and pre-understanding of the norms that are integrated in others and in society. Five dimensions with developmental milestones concerning mental maturation and development have been described as important [37].

Social competence is mentioned first, and it may be defined as the effectiveness in developmentally appropriate social interactions. The main skills identifying such competence are cooperation, helpfulness and the ability to resolve conflicts [39]. During the newborn period, a type of social competence may be viewed as the ability of the child to elicit responses and positive responses from their caregivers [40,41]. The second dimension is attachment, which may be described as the deep, selective and enduring connection between a child and the caregiver that enables the child to form positive, close relationships with parents, peers and, later, partners. The third dimension, emotional competence may be defined as the multifaceted ability to be aware of one's own and other's emotions and to utilize this awareness in interpersonal interactions and in the regulation of emotional experiences. The fourth dimension is the multidimensional construct of self-perceived competence. This dimension considers the child's evaluation of his or her own abilities (cognitive, physical, social), especially in comparison to others. Finally, Denham [37] refers to a dimension called temperament and personality. These features are considered to be fundamental to how children function in social and familial relationships. Temperament is defined as an individual style

concerning reactivity and self-regulation in which emotional reactivity refers to the speed and intensity with which individuals respond to events.

Throughout childhood, all of these features that were briefly mentioned above develop within each individual child and are influenced by biological and environmental conditions [1]. The ease or success of these developments may be reflected in the behavior of the child, which is characterized either by successful adaptation and health or maladaptation and disorder [1]. The socio- emotional functioning of children during childhood is very important because it serves as a predictor and is associated with later behavioral problems, mental health and successful functioning in school [37,43].

Behavioral problems refer to dimensionally measured behavior, including both normal and atypical ranges of behavior [44]. Children born preterm display behavior that is similar to other developing children. Normative descriptions of expected problems in populations at different ages are relatively new, especially those described for children who have not yet reached middle childhood [43,45]. There is suggestive evidence concerning age-related changes in problem behavior, and differences between genders have been described [46]. Behavioral problems are frequently categorized according to a two-dimensional taxonomy that separates problems related to mood, anxiousness or depression as internalizing problems and out-acting/intrusive behaviors as externalizing problems [46-50]. In addition, problems related to the adaptation of children to their social surroundings have frequently been described as either attention-related or social-emotional problems [45,47]. Different types of problems are detailed in the following sections.

1.3.1 Internalizing problems

Internalizing problems are often described as mood and anxiety problems, including symptoms of depression, somatic complaints and withdrawal behavior [45-50]. Each feature may be related to different developmental difficulties at different ages and expressed in different ways across childhood [43], and a greater number of problems have a large influence on the social development of children [46]. In a large, longitudinal study of internalizing behavior in children aged two to eleven years old, different trajectories were described across childhood. Two-thirds of the children were reported to have few problems during childhood, while one-third exhibited problems with

decreasing, increasing or sustained elevated trajectories [43]. Interestingly, a greater number of maternal psychological symptoms during infancy predicted increasing, decreasing or elevated trajectories, while good maternal mental health predicted a stable, low trajectory. Toddler twin studies suggest that genetic factors account for 50% of the variance and a shared environment for 30% of the variance in internalizing symptoms [46]. Internalizing behavior has been less well studied and reported compared with externalizing behavior [46], and it is not as easy to observe in a child's behavior [45]. The detection and interpretation of internalizing problems are more dependent on the person reporting the problems (e.g., mother, father or teacher) and the age of the child [51]. In infancy, distress and fearful behavior related to separation from caregivers may be viewed as developmentally appropriate behavior, whereas it may be seen as separation anxiety in later childhood or a type of social phobia among adolescences [43,46]. Children born preterm have frequently been reported to have increased levels of internalizing behavior [24,51-56]. The etiology of this behavior pattern has been unclear and will be discussed later. In questionnaires that were answered by parents or teachers, this type of problem is typically expressed as the child as follows: acting too young, refusing to participate in activities, seems shy and with little expression in response to positive stimuli [48-50].

Agreement between different observers regarding this type of behavior is generally lower than that in reports on externalizing behavior [51,58-60]. In addition, internalizing behavior varies because many types of behavior differ between countries, especially with respect to socio-economic factors (SES) [61] and cultural differences [62]. A Norwegian population survey reported differences in parental reports of internalizing problems among 8-10-year-old children in Norway and Britain [62]. Norwegian parents seemed to under-report internalizing problems compared with British parents. This observation could depend on a higher "normalizing" view of emotional difficulties among Norwegian adults or, possibly, an under-detection of emotional difficulties in young children.

1.3.2 Externalizing problems

Externalizing behaviors are actions that are directed out towards others. According to the Achenbach System of Empirically Based Assessments (ASEBA), externalizing behavior consists of aggressive and delinquent behavior [47]. In questionnaires, aggressive or destructive behavior

among toddlers are described as, e.g., being jealous, screaming, destroying other things or eating non-food. Later in childhood, this behavior may be described as, e.g., screaming, fighting, teasing, bragging, talking too much or appearing irritable [49,50]. Signs of this type of behavior vary from typically non-appropriate and immature behavior to serious dysfunctional behavior. Thus, most children will to some degree display aggressive or oppositional behavior, especially during early childhood. Delinquent behavior is described as more serious, dysregulated and aversive behavior such as, e.g., stealing, running away from home, skipping school, and swearing [49,50]. Children who display elevated levels of externalizing behavior may be described as possessing underdeveloped self-regulatory abilities that may lead to uninhibited behavior and the expression of poor self-control [63]. Factors such as ethnicity [64,65], SES [64,66] and gender [64,66] are also associated with the amount of externalizing behavior [65]. A greater amount of externalizing behavior in toddlerhood has been reported to be a strong predictor of subsequent adaptation difficulties in early school years [67]; however, most children have decreasing trajectories of externalizing behavior after toddlerhood [67,68].

Normative trajectories of externalizing behavior have been described to decrease during childhood [45], and in contrast to internalizing behaviors, they are not described as elevated among children born preterm compared with full-terms [24]. An even earlier meta-analysis has described elevated levels of externalizing behavior in very preterm compared with full-term children [26]. The results of subsequent reports did not support this finding [24,56] even though a lower BW was found to be associated with more externalizing behavioral problems.

1.3.3. Attention problems

Attention is the ability of a child to orient to, shift between and focus on something in the external world [69]. Attention problems are often described as impulsivity, hyperactivity and inattention [48-50]. Questions concerning attention problems concern the ability of the child to act at an age-appropriate level, concentrate, and sit still and whether behavior as clumsiness and staring are observed [ibid]. While problems such as impulsivity and hyperactivity have been reported to decline during middle childhood, inattention appears to be more stable across the age groups [70]. Boys have been described to have more attention problems than girls [45,71]. Attentional

competence is a basic premise for interactions and contact with others, and it may be considered a potential mechanism for the development of later and/or other socio-emotional problems [69].

Children born preterm are more often identified with early attention problems than those born at term [72]. Teacher and parent ratings of problems have been reported with standard deviations (SDs) that are 0.43 and 0.59 higher than those reported for full-term peers [24]. A neuro-psychological model has been useful to briefly describe some of the elements of the highly complex processes involved in the development of attention [69,73]. Three networks in the brain have been described to be involved and interconnected:[1)] the orienting system, [2)] the arousal system and an [3)] executive attention system [73]. First, an orienting system is visible already in newborns and is fully functional during the first 6 months of life [74]. Newborns gradually become capable of orienting themselves to movements or objects and of disengaging or shifting their direction. The orientation qualities have been explored by assessing the duration of the gaze, changes in attentional focus and the ability of the infant to successfully disengage from stimuli. Second, the alerting or arousal system is related to the capacity of the child to maintain a state of alert arousal that enables him or her to successfully process information [69]. During infancy and early childhood, this development has been assessed by observing sequences of sustained (focused) attention in children during free play. Third, when infants reach toddlerhood, the executive control system matures. In this phase, attention becomes more related to planned and child-generated activities with objects. During further development, the attentional competence of children becomes more directly assessable by caretakers because the caretakers may observe the degree to which the child can pay attention to a task until it is successfully solved. A link between early focused attention and later cognitive outcomes has been suggested for children born preterm; attention at 7 months has been shown to be predictive of reported behavioral problems and cognitive abilities during the preschool years [75]. In their longitudinal study of normative behavior, Bongers et al. claimed that observable attention problems are especially apparent when children attend school [45].

Children born preterm have previously been reported to have greater problems in all attentional systems. [1)] They show less efficient orientating attention during the first 6 months of life [69,74], [2)] and they shift more frequently [76,77] [3)] and show a reduced ability to disengage from stimuli [74]. From the second half of the first year, some researchers have reported that preterm children exhibit shorter periods of focused attention, while others have not observed this difference [77]. At

the beginning of toddlerhood, when the executive system gains greater control of the arousal system, sustained attention becomes more apparent in preterm children.

Risk factors concerning the development of attention have been reviewed. A low BW negatively influences bio-neurological development, and there is a strong association between a lower BW and a greater number of attention problems [78]. A shorter gestational age predicts poorer attentional skills [31], and a higher medical risk seems to negatively influence attention. However, these observations have been difficult to assess due to the interference of other variables such as birth weight (BW) and GA [79]. In addition, male gender [71], decreased maternal psychological well-being and less successful parent-child interactions throughout childhood [80] have been identified as risk factors. Attention problems have been further reported to partially mediate the relationship between the birth condition (prematurity) and subsequent behavioral problems [81].

Some authors have concluded that children born preterm gradually develop more severe attention problems [ibid], which is consistent with the results of a large French study [82] reporting a greater number of attention problems at age five and of a Norwegian population-based study reporting a slower reaction time, reduced awareness and greater attention problems at age 11 in preterm children compared to term-born peers [83,84].

1.3.4 Social problems

Social problems are related to the adaptation of a child to his or her social surroundings. A tri-component model has been suggested as a conceptual framework to describe the features of social competencies and thereby of potential problems [85,86]. These interrelated components are described as follows: [1)] social skills (cognitive features such as theory of mind, compliance, attention and behavioral skills), [2)] social performance (the ability to use skills in appropriate ways in different contexts) and [3)] social adjustments, which include, e.g., the ability to form high-quality friendships, several friends, a high level of sociability and low levels of social withdrawal [86]. Importantly, each component level builds on the ability of the child to function at lower levels.

During the first years, it may be difficult to separate socio-emotional from attention problems and vice versa [69]. Parent-reported socio-emotional problems among two to three-year-old children have been estimated to occur 10 to 15% of children [87,88], and several reports have focused on the

problem of the under-detection of such problems in toddlerhood [43,87,89]. Social problems seem to be more easily perceived by caretakers when the child begins to function more independently. An immature or unsuccessful social adaptation may be highly influenced by less successful parent-child interactions [90]. The statements used to identify social problems in pre-school years may concern, e.g., clinging behavior, not going along with other kids, being teased, preferring younger playmates [48-50]. Social competence may be viewed as culturally appropriate manifestations of behavior at the opposite end of the problem behavior spectrum [87,91].

After the first year of life, poorly regulated behavior (frequently referred to as the “terrible twos”) can be identified as a precursor of social problems [44]. Social difficulties may first become visible as a lack of interest in social interactions during infancy, while an inability to manage peer interactions may characterize toddlerhood [37]. During the preschool years, peer interactions become more complex, and the ability of children to regulate arousal, cooperate and form friendships may be observed as more or less successful behaviors. If socio-emotional development decelerates, it will interfere with other features of development such as perception, learning, and achievement, and it will frequently become evident as dysregulated behavior [44].

Socio-emotional problems have been documented as highly stable [86,87]. Approximately 35% of children who were rated by their teachers as having elevated socio-emotional problems during the first year in elementary school had been identified with worrisome test-scores based on standardized measurements before age of three. 68% of those with parent-reported psychiatric disorders had been identified as having problems as early as during toddlerhood [44,88].

Very preterm children, especially those that are extremely preterm, have been reported to exhibit elevated social problems throughout childhood [92-94], and this tendency was confirmed in a recently published review [86]. Features of social adjustment in particular create a gap between VLBW children and full-term peers, while there is less consensus regarding features of social performance. However, VLBW children seem to catch up with their peers born full term in terms of the levels of prosocial behavior [ibid]. Those children who were reported to exhibit the greatest social difficulties across the studies had the lowest birth weights, were males and had reduced intellectual functional ability [66,86].

Children born preterm are at a high biological risk and have been described as being more dependent on maternal sensitivity to facilitate their social engagement [95,96]. Strong associations have been described between the biological regulation concerning the sleep/awake cycle and heart rate variability during the last trimester of pregnancy and later social rhythms/parent-infant interactions during infancy [41]. Parent-infant synchrony [40] and low levels of parental negativity [97] are also known to predict better infant self-regulation and socio-emotional adaptation.

1.3.5 Thought problems

Thought problems have a low prevalence [49,50]. These problems have been reported by parents and teachers as, e.g., fixed thinking about something, hearing things, repeating acts, seeing things, staring blankly, and expressing strange behavior or ideas. This subscale in the ASEBA's questionnaire is meant to intercept behavior associated with early psychopathology, e.g., schizophrenia [ibid].

1.3.6. Mental health among children born preterm

Two Norwegian population-based studies of low birth weight (LBW) children have reported impaired mental health outcomes during late childhood and as young adults compared to the sample born full-term [98,99]. Elgen et al. reported a three-fold increased risk of psychiatric disorders, and only 50% of the LBW young adults (age 19) reported good mental health throughout adolescence [ibid]. Affective, anxiety, and attention deficit hyperactivity (ADHD) disorders and antisocial personality disorders were the most common mental health problems, and 20% of the population had more than one diagnosis. The populations reported in the above-mentioned studies were born in the 1980s, and the results are consistent with previous reports from other countries [25,79,100,101].

1.4 Quality of life (QoL) of children born preterm

The QoL of former preterm children has been investigated extensively the last few decades, mainly by parental proxy reports on their children but also based on the self-reports of adolescents and young adults [102-104]. QoL is defined by the WHO as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [105]. The QoL concept is a highly multidimensional construct that attempts to measure subjective experiences. Decades ago, a Danish psychiatrist described QoL based on four classes of needs: biological needs, the need for warm human relationships, meaningful occupations and the need for diverse and exciting experiences [106,107]. Quality of life has also been separated into subjective and objective features in which the final description is based on societal standards, whereas the subjective part of QoL is based on individual life experiences and preferences [ibid]. An overview of the basic features of QoL in children and adolescents has also been described by Mattejat [108] and by Jozefiak [109] (Figure 1.).

Researchers investigating the QoL of children have used different conceptions or definitions of the concept (QoL, health-related QoL, well-being, among others) that are related in part to the type of study or measurement used [104]. Zwicker and Harris identified 6 studies that examined QoL in preschool-aged children who were born preterm [ibid]. Significantly poorer physical functioning was reported in four of these studies compared with the reports of children who were born at full term. Preterm children have also been reported to exhibit less competent social functioning and, in some studies, greater anxiety compared with children born at term [110]. ELBW children in particular have been reported to have a generally lower QoL than their peers born at full term [102,104,111]. Health-related QoL has also been reported by Norwegian parents for children aged 10 years who were born extremely preterm [112]. This Norwegian study indicated that learning and attention problems negatively influence the daily life of children and that boys in particular struggled more than their full-term counterparts.

Self-reporting has been used among preterm children who have reached adolescence, being approximately at 14 years of age [113]. Teenagers born preterm did not report such a large reduced QoL as their parents report compared with their full-term peers [104,114,115]. In a Norwegian study, VLBW teenagers with cognitive deficits had significantly lower global health and behavior, general health perception, self-esteem and family activities [99]. A review by Zwicker and Harris concluded

that the impact of prematurity is greatest during the younger years, and this condition to some degree even negatively influences life during adolescence and adulthood [104].

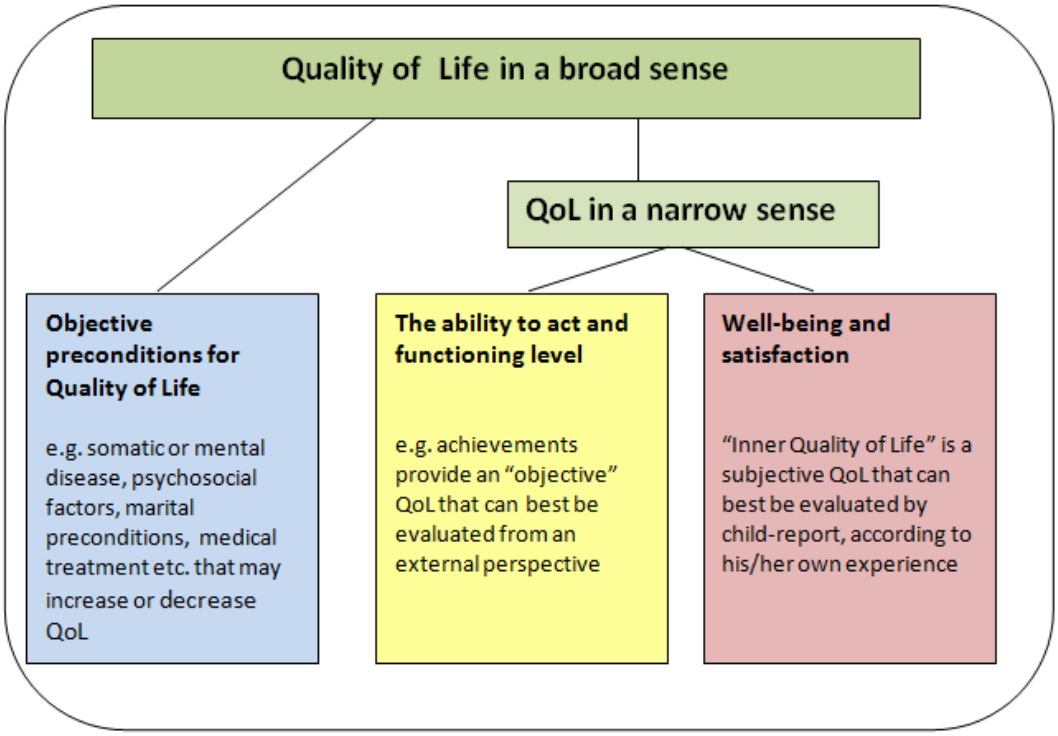


Figure 1. Basic features of Quality of Life

Figure originally published by T. Jozefiak [109], after Mattejat [108], and reprinted with permission.

1.5 Development of competencies up to middle childhood

The development of competencies is highly influenced by the ability of children to adapt to contexts and challenges [1,116]. Competencies may be difficult to discuss separately from behavior problems because they largely describe similar phenomena, which are described as resources or problems. Children born preterm have frequently been reported to possess impaired physical performance, reduced intellectual and social functioning and poorer school performance [19, 57,117,118]. Outcomes are mostly evaluated by comparing means at group levels. The complexity and nuances that could become visible at an individual level are not a focus.

While behavioral problems are evaluated by pre-defined statements, behavior as competencies in the ASEBA-system [47] are assessed by parent or teacher evaluations of the child *in comparison to children of the same age*. In terms of sports and activities, parents are asked to evaluate how much time the child participates in and to what degree he or she has been successful with the preferred activities. In relation to school performance, parents and teachers evaluate the competencies of children in subjects such as first language, math, history and other subjects [49,50].

A recent meta-analysis reported that VLBW children perform at the same level as full-terms in terms of language achievements across the pre-school years, while their performance in arithmetic was poorer [117]. It has been frequently stated that the burden of prematurity becomes apparent when these children are faced with greater demands from society (pre-school, school, among others). Similarly to the ability of attention and social problems to moderate QoL, it also affects the ability of children to manage new demands and expectations in a classroom setting. Children born preterm are often described as less ready for school and frequently have a delayed start in primary school [119]. LBW children have been reported to receive special educational services in primary school twice as frequently as the general population [83]. Similar results were reported in a sample of children who were born moderately to late preterm; 7.7% of the children received extra services in school versus 2.8% of the general population [57].

The behavior problems and development of competencies of children are associated with biological conditions as well as psycho-social factors such as parent-infant relationships and parental well-being [24, 117, 120-122]. Some authors have suggested that there is a differential impact of biological and psychosocial risk factors at different ages as the psychosocial risks increase in importance with age [123].

1.6 Parental adaptation to the caretaking of a child born preterm

1.6.1 Enjoyment of and attachment to the infant

Bromwich suggested that the behavioral establishment of an affective base can lay the foundation for parent-child attachment [124]. This attachment is frequently typed as *bonding*. Different interactional patterns have been described between mothers with children born preterm compared with mothers with full-term children as early as the 1980s [125]. At four months, preterm children were less responsive than their full-term peers despite the heightened levels of involvement of their mothers. At the age of two, mothers of preterm children performed less positive scaffolding and were less involved in interactions with their children compared with the mothers of full-term children. This finding may be considered to be an early observation of the *dependency of parents on children's responses* to their parenting efforts to enable them to continue good work. Parenting of children born preterm has been described to be associated with increased challenges because the children show fewer positive affects and smiles [126], more fuzziness and inattendance [6] and less stimulation of their mothers to perform spontaneous, intuitive maternal behaviors (so-called "motherese" characterized by kissing, snuggling, touching, child-directed talk and physical contact) [127]. Others have studied interactional patterns between mothers and 6-month-old infants and compared premature and full-term at children's age of 18 months on later outcomes [128]. A maternal "controlling pattern" was observed in almost 28% of the mother-preterm infant dyads compared with 12% of the full-term infant dyads. At 18 months, preterm infants in dyads with a controlling pattern had significantly fewer positive outcomes compared with preterms in cooperative pattern dyads and with full-term infants [128].

The impact of early impaired contact between children born preterm and their parents has been studied extensively during recent decades. Schmid et al. reported a long-term impact of maternal responsiveness and early interactions, and their results indicated that a less successful early interaction was associated with a higher risk of depression in offspring up to the age of 19 years [129]. The importance of responsiveness, sensitivity and synchrony will be described later in this thesis as possible mechanisms that play a role in the intervention.

1.6.2. Parenting stress and impact on parenting behavior

Parenting a child that is born preterm is associated with more long-term stress, even in families with a high level of socio-economic resources [130]. Consistent with the early theory of psychological stress is the concept of *parenting stress*, which has been described as a complex process consisting of four components: an *external event* met by a *cognitive appraisal* and followed by a *mobilization of individual coping mechanisms* and finally followed by a *stress reaction* in body and mind that is recognized as a parental behavior or affect [131,132]. Parenting stress is distinct from stress related to other life events and is described as a complex response to the demands of parenthood [ibid]. Parents with reported high levels of stress are more likely to have an authoritarian, harsh and negative parenting style, in which the parent is less involved with his or her children and foster children with a more unsecure attachment quality [132].

Abidin defined two dimensions of parenting stress [133]. They distinguish between features related to parental attributes (aspects of depression, attachment, competence, role restriction, isolation, spouse and health) and child attributes (aspects of adaptability, acceptability, demandingness, mood, distractibility/hyperactivity and ability to reinforce the parent [133,134]. The association between the main dimensions and sub-aspects are described in Abidin's model of parenting stress shown in Figure 2.

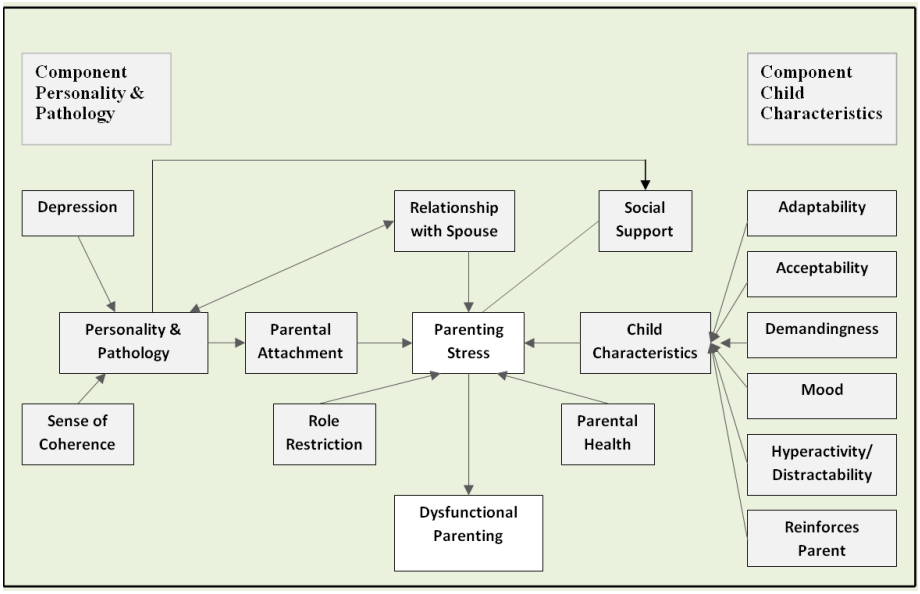


Figure 2. Theoretical Model for PSI
Reprinted with permission from the author (Abidin) [133].

Individual differences in parenting stress are stable over time, and they are associated with the quality of the parent-infant relationship and are essential to address its bidirectionality; parenting stress appears both as actions and as reactions [132].

Reducing parenting stress is considered to be important because it strengthens the mental health of the parent [132], may decrease the impact of maternal depression on parenting behavior [134] and improves the efficacy of interventions that target the sensitivity and responsiveness of the parents [135] and behavioral problems of the children [136]. This finding has been reported to be especially important among the parents of preterms because greater parenting stress has been reported repeatedly in such families [130,137], and parenting stress may have greater negative consequences on children born preterm than on children born full-term [138-140].

Maternal depression has been reported to have a universal negative effect on mother-child interactions across cultural and socio-economic differences [141], and maternal mental health problems have been reported to occur more frequently in families that have reared children born preterm [121] and also to have a significant impact on the outcomes of children born preterm [142,143]. However, paternal depression has also been reported to have a significant and deleterious effect on the parenting behavior of fathers [144]. Essex et al. reported that maternal depression and stress beginning in infancy are the most potent predictors of subsequent stress regulation and cortisol levels [145]. Preschoolers with the highest cortisol levels at the age of 4.5 years exhibited more severe mental health problems after enrollment in school [ibid]. This finding corresponds to the results of a Swedish study that reported a significant relationship between elevated parenting stress in children aged 1 and 8 years and the cortisol levels of children at 8 years of age [146]. Both studies indicated that long lasting levels of maternal stress during childhood may be more influential than an increase in maternal stress during only early or late childhood. Other groups have identified different trajectories of parenting stress during early childhood (stable high, decreasing or increasing stress) and both maternal, child and contextual factors accounting for stability and changes in trajectories [147]. Parenting stress has been effectively reduced by offering parenting education components [132,148], but other actions such as improving maternal-child attachment [149], mutuality [150] and responsiveness [151] have been suggested to be equally important.

The cognitive appraisal by a mother of an external event is one step in the generation of parenting stress [133], and Allen et al. reported that mothers who perceive their preterm children as very vulnerable at the time of hospital discharge tend to continue to have this perception [152]. This perception has been associated with less positive development over the first year of life of children born preterm [ibid]. A review of interventions that address the impact of parenting stress on the development of high-risk children highlighted the importance of the direct involvement of parents [132, 152]. Family-focused strategies have been reported to be more effective than interventions that mainly focus on the child, and a focus on the parent-child relationship appears to be more successful than focusing solely on the behavior of the parent [151].

1.6.3. Contribution of the children to the parent-child interactions

The contributions of infants to parent-infant interactions are important and have previously been summed up as three features of social competence: their predictability of behavior, social responsiveness and readability of cues [154]. While full-term infants are equipped to handle conditions of instability in the extrauterine environment, prematurely born infants are unable to readily adapt [155]. Immaturity, neonatal medical conditions and inappropriate environments continuously affect the physiology, behavior and integration between biology and the environment in these infants. When they interact with the environment, they may respond in either an organized or a disorganized way. The behavior of preterm infants is characterized by somewhat unpredictable fluctuations in autonomic, motor and state organizations, and they are less socially responsive than full-term infants and are less able to inform their caregivers in an understandable way about what they need [9,11]. Some responses may be appropriate according the level of maturity but are also frequently influenced by some level of disorganization. These deficits and lack of early social readability place them at risk for interactional difficulties [156].

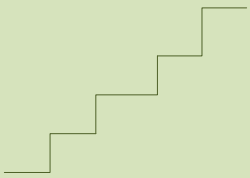
Early alterations caused by preterm birth may also influence later development. The period during which preterm birth takes place is considered to be a critical developmental window. It's described as a disruption of organizational events that causes the brain of the preterm baby to be organized in a different/immature manner compared with that of a full-term [19].

1.7 Early interventions addressing developmental difficulties

Forty years ago, Bromwich outlined three assumptions concerning how to enhance healthy development in infants and the development of supportive parent-child interactions [124]. The first assumption was that parent-infant interactions are *reciprocal processes* in which the behavior of each participant affects the responses of the other. The second assumption was that *mutual satisfying relationships* between the parent and child are an essential premise for the later successful development of the child. Finally, the third assumption was that parental *competencies grow concurrently* with increasing responses from the child, which provides positive feedback to the parent. These assumptions are in agreement with the descriptions of transactional relationships and mechanisms in human development, which will be presented later [157].

Bromwich described six stages of maternal behavior. The first, second and third stages describe the establishment of an affective base for later interactions. The next three steps describe how the parent becomes increasingly capable of initiating developmentally supportive activities with the child, thus generalizing the impact of new activities and further generating new and appropriate activities and experiences as the child achieves new developmental levels. In her view, a core rationale is that the *interventions should try to enhance the quality of mother-infant interactions* and not merely build on the instructions and teaching of the parents. The limited effects of instruction-based interventions are already described, and researchers have searched for alternative strategies [156].

Six stages of maternal behavioral progression:



1. Enjoyment of the baby
2. Sensitivity and responsiveness to infant cues
3. Mutually satisfying time together
4. Awareness of developmentally appropriate activities
5. Ability to generalize insights about activities and devise alternatives
6. Adaptation to achieved knowledge regarding new developmental levels during infant growth.

The early history of interventions with low birth-weight infants included a variety of direct and indirect preventive approaches. The theoretical perspectives included both the causes of parenting failures and the psychosocial and developmental maladjustments of the child [158]. Several areas,

which may disturb the early parent-child relationship, have at some point been identified as targets for intervention [153,159]:

- Early separation and failure of parental bonding [5,6,160],
- Stimulus deprivation programs [158],
- Deficits in infant capacities to elicit care [10,161,162],
- Parental emotional crisis related to preterm delivery [163],
- Pre-, peri- and postnatal medical complications [21,164] and
- Adverse childrearing environments [157,165].

The Mother-Infant Transaction Program (MITP), which was tested in a sample of prematurely born children in the present study, was designed in the late 1970s [166]. At that time, the parents were only short-term visitors in the NICU, and many parents had to resume their working duties while the child was hospitalized. A majority of the parents saw their child for only a limited number of hours before discharge. The formation of the MITP program was highly influenced by contributions from Bromwich based on her description of the maternal stages of behavior [124], as well as by Als & Brazelton based on their descriptions of the hierarchy of organizational levels that are critically important for the understanding of the behavior of preterm infants [9,10,11,168].

The conceptual framework described by Als was termed synactive because "*at each stage of development and each moment of functioning, the various subsystems of functioning exist side by side, are often truly interactive, but are also often in a holding pattern, as if providing a steady substratum for one of the system differentiation processes*" [168, p. 230]. This theory describes how one could observe the way an individual child handles the experiences of the world around him/her. The "observer-window" in this framework offers the interpretation of signs from the subsystems: autonomic system, motor system, state/organizational regulation, attention and interaction system and self-regulatory system [10,11]. A basic assumption was that the subsystems were continuously interacting with one another, like a child continuously interacting with his or her environment [10,11]. This observation is in accordance with the transactional understanding of development, which has informed the design of the MITP as well as this study [166,169].

1.8 A transactional model of development

The design of the Tromsø Intervention Study on Preterms (TISP) are consistent with the original MITP study [116,166,169], in which it was understood that nature (biology) and nurture (environment) had an equally important and interconnected impact on the development of children. This theoretical framework, a transactional understanding of development, is described in the studies conducted by Sameroff and colleagues [157,170]. In our study of the development of children born prematurely, this framework informs the following: [1)] both the child and its environment influence later development, [2)] the experiences of the child are a driving force of development together with all of the experiences facilitated by differences in the biological premises, intelligence, personality and perception of children, and [3)] the development of children is a product of the continuous, dynamic, bidirectional interactions between a child and the experiences provided by the social setting [170].

The differences between interactions and transactions can be explained by their effect on those involved. Interactions may be viewed as social exchanges informed by culturally appropriate responses that are consistent with the expectations of the recipients. However, transactional sequences require something new in the exchange between dialog partners because they must adapt to the responses from one another. "*Developmental changes are defined by changes in the way the child interacts with experience. They are driven by new complexities in either the individual or experience that require new adaptations in one or the other. In some areas the complexity already exists in the experience; in others it comes into play as the child reaches increasing levels of maturity*" [116, p.9]. At some age or level of development, most children show a greater continuity of behavior. This may be caused by some failure in either the child or the environment, or the adaptive process ends because the child has become an adult. Adulthood may be viewed as an equilibration in which individuals and environments are no longer in a state of adaptation. "*At this point, transactions become interactions*" [116, p.9].

Another central concept in the transactional framework is the issue of *regulation.* D'Apolito defines regulation as a state in which experiences are handled and regulation generates successful adaptation and possible development [155]. Self-regulation is defined as a cornerstone of early childhood development that cuts across all domains of behavior [1, p.26]. Others such as Feldman highlight two central features of regulation in the investigation of associations between early

neonatal biological regulation and later social regulation during the preschool years [41,171]; that is, the balance between mechanisms of excitation and inhibition and the ongoing interplay between environmental challenges and internal organization. Sameroff emphasizes the complex construct of regulation as a central phenomenon in modern developmental theory and exemplifies this balance. First, evolution is not restricted to biological change, and transactions resulting in or following regulation occurs in complex social settings. Second, the development of an individual child may be judged as a co-construction of the self-regulatory abilities and environmental "other-regulative" competencies of the child, which impede or facilitate development. Finally, Sameroff argues that some children may have severely compromised self-regulative capacities or their environments may be so chaotic that developmentally supportive transactions seem impossible [169]. Sameroff and Fiese emphasize that although the concept of self-regulation may provide an illusion that regulation is a property of the individual, it can only occur if there is a social surrounding exerting "other regulation".

1.9 Mechanisms involved in developmental change

The importance of parent-child attachment (bonding) and the historical roots of the concept have been mentioned previously [3, 4]. New research within that field has given increased attention to the concept of bio-behavioral synchrony between attachment partners [171,172], which is described as online physiological and behavioral co-regulation. Oxytocin hormone is known to play a central role in the establishment of breastfeeding, helping to let down the milk. There has been less focus on how the regulations of hormones interplay with the formation of affiliative bonds both in infancy and later in life. Oxytocin, the so-called "hormone of love", appears to be deeply grounded in human biology to support the formation of social bonds, care, security and healthy child development. Feldman defines affiliative bonds as "selective and enduring attachments that are formed on the basis of repeated exposure to coordination between physiological states and interactive behavior within each partner, between partners, and between the physiology of one and behavior of the other" [173,174].

This perspective, which appears to be embedded in transactions, may be of great importance for the early formation of parent-child relationships in families with children born preterm. Early

mother-infant synchrony is highly influenced by the successful maturation of internal hormonal regulation in the child [41]. From the beginning of the last trimester, both sleep-awake cycles and the regulation of arousal are undergoing important organizational development. The success of this maturational process seems to lay a foundation for the quality of mother–infant synchrony, which is described as a core activity in the social and emotional development of children [ibid].

Attachment difficulties have been described to occur frequently in preterm mother-child dyads [175,176], and gestational age has been reported as a moderate to strong predictor of maternal attachment difficulties [177]. The disturbance of early emotional bonds between parent and child may have long-lasting negative effects on the caretaking abilities of parents [177]. Interventional effects on attachment were not a focus of this study per se, but a disruption in parental attachment as a source of parent-related stress has been assessed [179]. The oxytocin regulative system is reciprocally engaged with the hypothalamic-pituitary-adrenalin axis (HPA) that mediates the stress response, and neuro-anatomical evidence suggests that there is a mutual regulation of the oxytocin and HPA systems [170,180].This finding has shed light on Abidin's detection and inclusion of an attachment-related subscale in the parenting stress questionnaire he designed more than thirty years ago [133]. The influence of both child- and parent-related parenting stress on child development has already been outlined and is also a source of transactional processes.

The bio-behavioral regulation that was briefly described above influences moment-to-moment interactions between parents and children. Synchrony is not only a matter of physiological and behavioral timing, but it also affects the interactional quality. It seems to influence parental sensitivity and responsiveness, which are core qualities in successful parent-child interactions [123,181].

During the last decade, the impact of early adverse experiences and neonatal stress on basic neurological structures has been described through collaborative research across biological, behavioral and social sciences, including knowledge of neuro-science [1,182,183]. Als et al. reported how developmentally appropriate care could protect the immature brain of the preterm baby against structural alterations caused by neonatal distress [184], while Milgrom et al. reported how

parental sensitivity training across the NICU stay were associated with improved white matter in the brain of the preterm child at 40 w of GA [185].

The above-mentioned studies confirm that early environments shape and calibrate the functioning of biological systems [186]. American Academy of Pediatrics (AAP) have designated this phenomenon as "toxic stress" and define it as stress that is extreme and frequent, extending activation of the stress response without the buffering presence of a supportive adult [ibid]. Current evidence suggests that the early experience of stress catalyzes a series of biological adaptations that change the way the brain, neuroendocrine stress response, and immune system function. Central to this idea is the biological regulation related to the hypothalamic-pituitary adrenal (HPA) axis. The HPA axis is involved in metabolic and cardiovascular responses to acute and chronic stress. The following is concluded: "*One of the primary consequences of early life toxic stress is HPA dysregulation, as the developing neuroendocrine system is chronically pressed into action*" [ibid, p.321, 187]. Preterm infants are highly vulnerable to exposure to stress [32,35, 140,188]. During the last trimester of pregnancy (30 to 40 w of GA), these infants may be exposed to adverse environments in a NICU while brain growth and maturation occurs at a high speed (myelination, migration, and synapse formation). The belief of an early critical period in child neuro-psychological development has been suggested for a long time [158] and was subsequently critically reviewed [1,42]. The importance of the experiences of the infant during the first months and years of life has been highlighted and expressed as "*not because this period of development provides an indelible blueprint for adult well-being, but because it sets either a sturdy or fragile stage for what follows*" [1,p.5]. In other words, this knowledge may shape bridges between the known neuroanatomic and neuro-developmental vulnerabilities in children born preterm and later developmental difficulties [19]. This concept was recently discussed by Feldman and colleagues, and the synchrony in coordination between biology and behavior during social contact has been suggested as a mechanism for early periods of sensitivity via effects on the social brain, regulation of oxytocin and adult sociality [173,174].

2. **Aims and questions**

To examine the long-term effects of an early intervention among children born prematurely with a birth weight < 2000 grams and the influence on their surroundings and parents.

1. **Behavioral-emotional development of the children up to nine years of age.**
    i. Does an early intervention influence long-term behavioral-emotional development, as reported by parents and teachers up to nine years of age?
    ii. Does an early intervention influence behavioral outcomes, social competence and adaptive behavior in school, as perceived by parents and teachers by seven and nine years of age?
    iii. Are specific birth weight groups or genders particularly affected by the interventions?
    iv. How does the behavioral development of preterms (with or without intervention) compare with the behavioral development of full-term children?

2. **Development of parenting stress until children's age of nine.**
    i. Has the early intervention influenced the longitudinal development of parenting stress as reported by mothers and fathers?
    ii. Are there cross-sectional differences between the preterm groups in the reports of mothers and fathers regarding parenting stress up to nine years of age?
    iii. How is the development of stress reported by parents in the two preterm groups compared with that reported by the parents of term controls?

3. **Child and parental proxy reports of quality of life (QoL) at nine years of age.**
    i. Did the early intervention influence the self-reported QoL and parental proxy reports of QoL of preterm children at nine years of age?
    ii. Did the intervention affect the level of agreement between the child and parental proxy-reported QoL in the two preterm groups?
    iii. Was QoL, as reported by children and parents in the two preterm groups, similar to that reported by children and parents in the term reference group?

3. Materials and methods

3.1 Participants

The studies presented and discussed are part of a larger, comprehensive study: the Tromsø Intervention Study on Preterms (TISP) [169]. TISP is a randomized controlled study of preterm infants with a BW < 2000 g who were born at the University Hospital of North Norway between March 1999 and September 2002 and a replication of a previous American study [166,167,189-191]. From the counties of Finnmark and Troms, 91% of all children born prematurely were recruited for the study. Children born without severe neurological or sensory impairments and with Norwegian speaking mothers were eligible for study inclusion. Twins were consequently recruited to the same group, while triplets were excluded from the study due to the character of the intervention. Decisions on sample size were based on the results of a previous study by Achenbach et al., and a difference of 7.5 points between groups in Bayley's MDI at age 2 (corresponding to a difference of 0.5 standard deviations) with 80% probability was calculated [169,192].

When eligible infants reached an age of 32 w of GA or more, the study coordinator informed their parents about the study and asked about participation. A total of 203 infants with a birth weight below 2000 g were recruited for the study. Thirty-five of these infants were lost to participation (14 died, 13 had non-Norwegian speaking parents, six were triplets, one was diagnosed with Down syndrome and one was not asked). The parents of 22 infants refused to participate in the study, while those of the remaining 146 preterm agreed to participate in the study. The coordinator collected written informed consent from all of the parents. The preterm infants were randomized in blocks of six using computer-generated numbers to form a preterm intervention group (PI, n = 72) and a preterm control group (PC, n = 74) and stratified according to a gestational age < 28 weeks and ≥ 28 weeks. Randomization was conducted by the research department of the hospitals, and the study results were available in numbered, sealed envelopes. Three children were excluded because of blindness during the two first years of the study. In addition, three children were excluded because of deafness; however, these children were again included in the study later in childhood after they regained their hearing with a cochlea implant. Children who were identified with disabilities at later follow-ups continued in the study if they were able to participate in the

age-appropriate assessments. The flow of the study from inclusion up to nine years of age is presented in Figure 3 [Appendix, part II].

Healthy newborn infants (GA ≥ 37 weeks and BW > 2800 grams) were recruited from the well-baby clinic at the same hospital to a term reference group (TR, n = 75). They were recruited by asking the parents of the first healthy newborn born after each preterm infant was recruited into the study. If the family refused to participate, subsequent families were asked sequentially. For practical reasons, all of the families recruited to the reference group lived in the area close to the city of Tromsø. Baseline information for each group is presented in Table 1 [Appendix, part I].

3.2 Study implementation

Eight experienced nurses performed the interventions. They received approximately one week of education before the pilot interventions and later implementation was started. The education included an introduction to developmental psychology and theory about state regulation, reflexes and how to initiate episodes of mutually responsive interactions with a newborn. In addition, four of the eight nurses were trained as NBAS examiners in the Neonatal Behavioral Assessment Scale (NBAS) during the study planning phase [191]. This extended knowledge throughout the entire intervention group because the development of the MITP intervention was highly inspired by the NBAS [10,193]. The initial educational introduction, training with video feedback and follow-up meetings across the 42-month inclusion period ensured a strong mutual understanding of the aims of the intervention that had been translated into Norwegian [194].

Families that were randomized to the intervention met the same intervention nurse during all of the sessions. This nurse may have met them earlier in the course of the NICU stay but was never one of the primary contacts of the family. The scheduling of intervention sessions was flexible because the nurses often postponed meetings if the child was in an inappropriate state (e.g., recently fell asleep during a session focusing on the capacity to focus alertness and social interactions). The majority of the pre-discharge sessions were performed during the final week in the hospital, but a few were conducted in the home of the family in situations with an accelerated discharge, or two sessions were given on the same day at the end of the hospital stay (e.g., morning and afternoon), which is consistent with the original study [166].

Families in the PC group were provided with the written guidelines of the NICU concerning treatment and information before discharge. This included a session with a demonstration and instructions regarding baby massage conducted by a child physiotherapist. Some parents became disappointed when their child was randomized to the preterm control group. In such cases, the parents were offered additional interactions about their baby if requested. The TR group was examined once by a pediatrician in the maternity ward and routinely on the third day of life.

3.3 The intervention program

The intervention program was a modified version of the Mother-Infant Transaction Program (hereafter referred to as MITP-M). MITP was designed by Rauh & colleagues in 1980 [166]. The modification introduced in the TISP study consisted of an initial session during which the parents of each child met their intervention nurse for a discussion in the absence of the infant present. This session provided a period to express feelings of grief and talk about experiences during pregnancy, delivery and the NICU stay. In addition, the parents were given the opportunity to become familiar and more relaxed with their intervention nurse. The mothers participated in all of the intervention sessions, and the fathers participated in 6 of the 12 sessions (54% of the intervention) with an inter-quartile range of 4 – 10 sessions.

The original MITP intervention consisted of seven one-hour sessions with the parents and their baby during the final week before discharge, and four home visits in the family's home at 1, 2, 4, and 12 weeks post-discharge. All of the hospital sessions were performed in a separate, quiet room with the baby, mother, father (when available) and intervention nurse. The interventions were adapted to the needs of each family and the natural speed with which the parents could learn and strictly follow the topics described in the MITP manual [166]. All of the sessions consisted of different agendas, and their main topics are briefly described in Figure 4.The contents of the MITP-M are provided in the Appendix, part III.

The finalization of the program at this age was justified by ending the original study [ibid] because it made up an intervention that could realistically be implemented with the financial and professional resources available. Unlike the original study, no logbooks were given to the families after the completion of the interventions. Completion of the intervention was monitored by a review of the

logbooks by the study director.

3.4 Measurements

The study focused on the number of reported behavioral problems. Behavioral development has been reported using standardized measurements that assess a broad range of competencies and areas of concern [49]. The analysis depends on reports of problems from parents and teachers and on measures of specific attainment of developmental milestones during childhood. Developmental goals can comprise specific motor, behavior or communicative skills, which have been reported previously [195].

When the socio-emotional and behavioral developments of children are analyzed through the lenses of reported behavioral difficulties, this phenomenon may be viewed as looking in a mirror. The extent of behavioral problems may indicate a greater or lesser struggle to comply with parental expectations, adapt to both one's own and environmental expectations and reach developmental milestones at age-appropriate stages.

Child Behavior Checklist **(CBCL/2-3 and CBCL/4-18)**

The behavioral problems of the children were reported by mothers and fathers on the CBCL/ 2-3 during toddlerhood and similarly on the CBCL/4-18 for children aged 5, 7 and 9 years [48,49]. Both questionnaires consist of statements (100 statements in the CBCL/2-3, and 113 in the CBCL/4-18). Each statement is transferred to a Likert scale of 0 to 2 (0 = not true, 1 = somewhat or sometimes true, 2 = very or often true). The parental reports are based on their perception of the child during the last 2 months across toddlerhood, while in the preschool/school years, it is extended to the perception of the behavior of the children during the last 6 months. Two broadband behavioral domains were calculated in both questionnaires (internalizing and externalizing behavior). These main dimensions are slightly different because questions about somatic complaints are based on internalizing behavior in childhood but not in toddlerhood, and the questionnaires has some different items related to behavior that are specific to the different ages. In the CBCL/2-3, two sub domains remain outside the broadband internalizing and externalizing syndromes (sleeping problems and somatic complaints), while CBCL/4-12 consists of three supplementary sub domains (social problems, thought problems and attention problems). In addition, CBCL/4-12 comprises

several questions that address the perceptions of parents regarding infant activities, social competence and competence in activities of daily living compared with their peers. The CBCL questionnaires were revised in 2001 and later modified in 2007 [47]. In the current study, the 1991 versions of the questionnaires were used across all follow-ups to facilitate the longitudinal analyses.

Teachers Report Form (TRF)

The TRF questionnaire is designed for teachers who have observed the behavior of a child over a period of at least two months [50]. Similarly to CBCL/4-18, the TRF consists of 113 statements and is scored on a Likert scale similar to CBCL. Approximately 15% of the statements are different due to differences in behavior that can be observed in a classroom/school setting compared with a home setting. Similarly to CBCL/4-18, the TRF provides standardized measurements of child and adolescent emotional/ behavioral problems and measures of competencies. Behavioral outcomes are summarized as total problems and scaled according to internalizing and externalizing dimensions. Internalizing behavior consists of the following subscales: withdrawn, anxious/depressed and somatic problems. In contrast, externalizing behavior consists of the following subscales: aggressive and delinquent problems (both in CBCL/4-18 and the TRF questionnaire). Behavioral problems are also rated on subscales related to thoughts, social life and attention.

Strengths and Difficulties Questionnaire (SDQ)

For children aged 5 and 9 years, mothers, fathers and teachers responded to selected statements and questions that were extracted from the SDQ [196]. In an attempt to avoid overlapping questions in different questionnaires, only 10 statements related to the social behavior of the children and some questions concerning the perception of parents and teachers of the difficulties of the children in everyday life were used. The statements were answered on a 3-point scale (agree, partly agree, do not agree), and the questions were answered by choosing one of four alternative answers [197]. The questionnaire is included in the Appendix, part IV.

Parenting stress index (PSI and PSI-sf)

The Parenting Stress Index-Full Form (PSI), 3rd. edition, was used for all assessments up to the age of seven years, while the Parenting Stress Index - Short Form (PSI-SF) was used for nine-year-old children [133]. The PSI consists of 120 questions covering three main dimensions of stress (child-, parent- and life-related stress). The PSI-SF consists of 36 questions that were extracted from the

parent- and child-related dimensions. Both questionnaires were translated and back-translated in cooperation with the creator (Abidin) [personal information, JAR, 2013]. A 5-point Likert scale ranging from “strongly agree” to “strongly disagree” made up the response alternatives on both questionnaires. The initial assessment of parenting stress among the mothers before randomization had limited success because many of the statements were left unanswered. A calculation of the responses on those scales sufficiently answered indicated that the initial level of parenting stress was similar in the two preterm groups. At six months, only one parent provided a report (mostly mothers), while both mothers and fathers provided separate reports on all subsequent occasions.

The PSI consists of two main dimensions that address child- and parent-related stress (covered by 101 statements/questions) and a life stress section (22 events or conditions that are often reported as stressful but may not be related to the current parenting challenges). The Child Domain contains 47 statements covering six subscales: Distractibility, Adaptability, Reinforces parent, Demandingness, Mood and Acceptability). The Parent Domain contains 54 statements covering seven subscales: Perceived competence, Isolation, Attachment, Health, Role restriction, Depression and Relation to Spouse. A total stress score was also computed based on all of the items excluding life stress questions. The theoretical model underlying the construct of the PSI is shown in Figure 2.

The PSI-SF is reported as a Total Stress score (TS) and based on three subscales, each of which consists of 12 items: Parental Distress (PD), Parent-Child Dysfunctional Interaction (P-CDI) and Difficult Child (DC). Some questions in both questionnaires are used to calculate a Defensive Responding score, which indicates the degree of potential inconsistent/denial reports by respondents.

Both the PSI-FF and PSI-SF are frequently used in research [198,199], and the correlation between TS for these two measures has been described as high (0.87) [133,200]. The PSI-SF, Difficult Child subscale consists solely of items from the Child Domain in PSI-FF, and Parental Distress subscale items are from the Parent Domain. The P-CDI subscale includes items from both the Child and Parent domains and focuses on parental perception of transactions with their child and their expectations about the behavior of the child [133]. The Norwegian versions of both PSI-FF and PSI-SF were translated by Rønning and Abidin and were used in this study with the permission of Abidin and Psychological Assessment Resources, Inc. (PAR) [201]. The questionnaires include some literal

differences such that questions in the PSI-SF may be perceived as more negative and definitive than those in the original full format of the PSI.

Kinder Lebensqualität Fragebogen (KINDL)

The Kinder Lebensqualität Fragebogen (KINDL) questionnaires have been translated and validated for use in Norwegian populations [202,203]. The translation was conducted by experienced Norwegian school teachers with university degrees in German [204].The questionnaires are short, generic and consist of a self-report questionnaire (Kid KINDL®) that is appropriate for children (7 to 13 years old), and a questionnaire for the parental proxy report (KINDL® for parents) [203]. The questionnaires consist of 24 corresponding items that are formed equally as either positive or negative statements about different facets of the child's life. Each statement addresses experiences over the past week and is rated on a five-point scale: 1) never, 2) seldom, 3) sometimes, 4) often and 5) always. The mean scores are calculated for each of the six subscales: physical well-being, emotional well-being, self-esteem, family, friends and school and for the total scale, and they were linearly transformed to a 0 to 100 scale, on which higher scores indicated a better QoL. All of the versions of the KINDL questionnaire were supplemented with a "disease module" consisting of a filtered question and six items about possible long-lasting illness or current hospital admission. The internal consistency and reliability were tested previously and compared with the original German version of the questionnaire [109]. The translated Norwegian version displayed better internal consistency (Cronbach's α) with an increasing age of the child. Among younger children (8-9 years old), Cronbach's α was low for the subscales of emotional well-being (0.52), friends (0.49) and school (0.47), while it varied between 0.62 to 0.68 on the other three subscales and was 0.83 on the total summary scale [109,202].

Seeking help

A simple report was designed for the present study to monitor parental use of seeking help on behalf of their children. The questions included the following: 1) type of contact (physiotherapy, child habilitation, child psychiatry services, special educational services and child welfare authorities), 2) the age of the children when the contact was initiated and 3) duration of contact. Parents provided response to this questionnaire when the children were nine years of age [Appendix, part V].

Birth, medical risk and family-related factors

Childbirth (weight, gestational age, sex, twin) and perinatal risk factors were collected before discharge. Risk factors included the clinical risk index for babies (CRIB), presence of bronchopulmonary dysplasia (BPD) and presence of several cerebral injuries [169,192]. Family-related variables were as follows: [1)] mother's age, [2)] mother's and father's years of education, [3)] mother's and father's annual income, [4)] number of siblings, [5)] parental marital status, [6)] housing conditions, [7)] occupational status, [8)] smoking habits and [9)] ethnicity. This information was reported in separate questionnaires before discharge from the hospital [Appendix, part VI].

Figure 5. Measurements in the thesis

Measurements	Pre-randomization	½ y	1 y	2 y	3 y	5 y	7 y	9 y
CBCL – behavior & emotional problems – parent report				x	x	x	x	x
TRF – behavior & emotional problems – teacher report							x	x
SDQ – prosocial behavior & peer problems – parent report						x		x
SDQ – preschool and school report						x		x
KINDLE - on quality of life								x
PSI – parenting stress	x	x	x	x	x	x	x	x
Socio-Economic Status	x		x	x	x	x	x	x
Help seeking								x

y = children's age in years.

3.5 Follow-up procedures

For the purpose of the study, all of the participating children received the same medical, developmental, and psycho-social assessments at corrected ages of 6 months and 1, 2, 3, 5, 7 and 9 years. All of the assessors outside the families were blinded to the group allocation of the children.

Questionnaires were sent to the families approximately fourteen days before the follow-up sessions and collected at the time of follow-up by the coordinator. Parents received written reports concerning the motor and cognitive development of the child after every follow-up. These included recommendations about referrals to other services if relevant that were signed by the study director. In addition, all of the parents were allowed to call to the study coordinator or director throughout the duration of the study and request advice if needed. All of the results are reported as intention to treat, and one family that was randomized to the intervention but that did not receive the intervention was included in the intervention group. The original study was planned to report the outcomes of the children at two years of age. Because the study was prolonged several times, it was approved on three occasions by the regional committee for medical ethics and the Norwegian Data Inspectorate (1999, 2005 and 2010).

3.6 Statistical analysis

The analysis of the results was dominated by group comparisons. TISP is a clinical trial, and intervention outcomes have been explored by comparisons between PI and PC outcomes and by comparing each of the preterm groups with the TR group. These analyses were generated using linear mixed models (SPSS statistics, version 20) because of repeated measures and the clustering effects of twin pairs.

In the longitudinal linear mixed-model analyses, time was treated as a continuous variable. Predicted mean group differences in each measurement occasion with 95% confidence intervals were also computed. This analysis was also based on a longitudinal model, but in the case of group comparisons, time was used as a categorical variable [205]. By changing the reference time point in the analysis, predicted group differences on each occasion could be estimated. Dichotomized variables were analyzed using generalized linear mixed models (GLMM), which generated odds ratios that were adjusted for the clustering effects of twin pairs.

Longitudinal analyses of behavioral outcomes included reports both on CBCL/2-3 and CBCL/4-18. The questionnaires contain some differences, making the use of raw scores inappropriate. Following a request to the owner of these questionnaires, we received a conversion table that made it possible to convert the existing raw scores from the CBCL/2-3 to T-scores [48].

Effect sizes were assessed in different ways in relation to the different types of statistical analyses. [1)] In the LMM models, they were computed as Pseudo R-square values and based on the square of the correlation between the observed and predicted values of the dependent variable [206]. After assessing the effect of the addition of variables in a linear mixed model analysis, the change in this pseudo R-square value was determined as an effect size measurement.

[2)] To analyze the effect sizes (ES) of treatment group comparisons, Hedges' g were computed [207]. Hedge' g is frequently recommended when sample sizes are small and is estimated by use of group-sizes, mean values and SD's to express an effect size. Higher values of Hedges' g indicate larger differences between groups. [3)] The levels of parental agreement were analyzed by intraclass correlations (ICCs). Differences between the two independent ICC coefficients for the PI and PC groups were tested as described by Alsawalmeh and Feldt [208]. This is a test of the equality of two reliability coefficients after adjustment for the unequal length of the instruments that were employed in the reliability analysis [ibid].

4. Summary of results

Paper I

Landsem IP, Handegård BH, Ulvund SE, Tunby J, Kaaresen PI, Rønning JA. Does an early intervention influence behavioral development until age nine in children born prematurely? *Child Development* 2015; 86(4):1063–1079

The longitudinal development of behavioral problems among PI and PC children followed similar trajectories across childhood from 2 until 9 years of age.

- In 23 of 24 reports on main behavioral dimensions (internalizing and externalizing), lower mean scores were reported for the PI children than for the PC children [non-significant difference].
- Slightly more PC children (18%) than PI children (11.8%) scored within a clinical range on reported problems (CBCL Total problems score > 35) [non-significant differences]. Boys were more frequent reported with high scores [non-significant difference].
- The mean T-scores on CBCL, Total problems were relatively low for all groups, ages and respondents compared to other reports.
- Across groups, mothers reported more Total Problems than fathers. [non-significant difference].

More attention problems and less successful adaptation to school were reported for PC children compared with PI children at 7 and 9 years of age.

- More attention problems were reported by mothers (ES = 0.48), fathers (ES = 0.48) and teachers (ES = 0.48) at age 7 years and by teachers (ES = 0.43) at age 9 years. Teachers reported significantly more inattention, hyper-impulsivity and somatic problems for the PC group at 9 years of age.
- More problems with thoughts were reported by PC fathers (ES = 0.52) and PC teachers (ES = 0.40) at age 9 compared with reports on PI children.
- Less successful adaptation to primary school demands were reported for PC children compared with PI children. Significant differences between preterm groups comprised measures of;
    - social competence and school performance at age 7 and the overall competence score at age 9 as reported by mothers.

- school performance at age 7 and activities and school performance at age 9 as reported by fathers.
- school achievements and perception at age 7 and competencies such as school performance, achievement, appropriate behavior and perception at age 9 as reported by teachers.

PI teachers perceived that PI children showed better adaptation to challenges in daily life compared with reports from PC teachers regarding PC children [blinded reports].

- PC children were reported to address definite or severe problems by teachers more than twice as often as PI children (OR = 2.9).
- Teacher's report of difficulties correlated significantly with parent's reports of referral to child psychiatric services, and PC children were referred to child psychiatric services more than twice as often as PI children.
- PC fathers reported problems in peer relationships were more frequently the cause of difficulties compared with PI fathers.

Some features of longitudinal development of behavioral problems on sub-domains differed significantly between the two preterm groups:

- Father's reported PC children with a BW > 1000 grams to exhibit more worrisome development in terms of externalizing problems across childhood compared with PI fathers for the similar group of PI children.
- Mothers reported that PC boys were more withdrawn during the preschool years than PI boys, but at nine years of age, they reported similar levels; an opposite tendency was reported for PI and PC girls.
- The fathers of PC boys reported a steeper increase in anxious behavior from age 5 to 9 years compared with the fathers of PI boys.

Preterm groups were compared separately with results of the TR group.

- The more worrisome development of anxious behavioral problems was reported for the PC compared with the TR group from 5 to 9 years of age by fathers.

- Significantly more behavior problems were reported in the PC compared with the TR group across all ages.
- Behavioral problems in the PI and TR groups developed with similar trajectories across childhood. At nine years of age, parents and teachers reported similar levels of behavioral problems and competencies for these groups.

Agreement between the parent's reports for internalizing and externalizing behavior differed between the two preterm groups on two occasions.

- At 2 years of age, PI parents showed greater agreement than PC parents concerning the internalizing behavior of infants.
- At 9 years of age, PC parents showed greater agreement than PI parents concerning the externalizing and total problems of children.

Differences in intervention participation influenced PI fathers reports at age 9 as fathers who had participated less reported more externalizing problems ($p = 0.001$) characterized by more aggressive behavior.

Paper II

Landsem IP, Handegård BH, Tunby J, Ulvund SE, Rønning JA. Early intervention program reduces stress in parents of preterms during childhood, a randomized controlled trial. *Trials,* 2014, 15: 387.

Mothers in the PC group reported increasing levels of child-related stress until 5 years of age that was particularly affected by limited adaptability and moodiness of the PC children. PI and TR mothers reported significantly different, declining levels across childhood compared to PC mothers.

- PC mothers reported more total and child-related stress compared with PI mothers at all follow-ups and more parent-related stress during the pre-school period.
- PC fathers reported more child-related stress at 2, 3 and 5 years of age and more total stress at 5 years of age.
- PI fathers who had participated less in the interventions reported more stress when children were 3, 5 and 9-year-old.

Mothers and fathers in the PI group reported higher correlations concerning parenting stress compared with the couples in the PC group.

Parenting stress was reported at similar levels in the PI and the TR families throughout childhood. PC group parents reported significantly more parenting stress than TR parents at all ages.

Across all of the groups, child and parent-related stress occurred at relatively low levels compared with the findings of American studies but were similar to the results of Scandinavian studies.

Paper III

Landsem IP, Handegård BH, Ulvund SE, Kaaresen PI, Rønning PI. Early intervention influences positively Quality of Life as reported by prematurely born children at age nine and their parents; a randomized clinical trial. *Health and Quality of Life Outcomes*, 2015; 13:25.

PI children reported improved physical well-being (ES = 0.57) compared with PC children at nine years of age.

- For all other features of well-being, both PI and PC children reported statistically similar results to the TR children.
- The BW and severe neonatal morbidity of the children were significant negatively correlated with reports of physical well-being.

PI parents reported better emotional well-being (ES = 0.34) and better well-being in school (ES = 0.54) than PC parents.

Agreement between children and parents was significantly lower in the PI group compared with the PC group. The pattern of agreement in the PI group was similar to that in the TR group.

PC parents reported significantly lower well-being among their children in all assessed features compared with TR parents. PI parents reported well-being at similar levels as TR parents in all assessed features except a lower score on the dimension of self-esteem.

5. Discussion

A core hypothesis of this study was that MITP-M would sensitize the parents to their infant's cues, which would lead to more adjusted and dynamic parent-infant interactions and thereby enhance the infant development. The main findings presented in this thesis support this hypothesis. The MITP-M intervention seems effective in; improving the long-term socio-emotional and behavioral development among preterm born children with BW < 2000g; reducing long-term parenting stress in parents of preterms and support self- and parent-reported QoL at children's age of nine.

Longitudinal behavior development was not affected by the intervention as the PI- and the PC children in broad outline with similar behaviorally trajectories across childhood. Even though, at seven and nine years of age the PI children were reported with less attentional problems, higher social competencies and better academic school performances than the PC children. Behavioral problems and competencies in the PI group were at similar levels as reported on the TR group from mothers, fathers and teachers at children's age of nine. The PC group continued to be reported with significantly more problems and less competencies than the TR group [paper I / 211].

PI mothers reported less child- and parent-related stress than PC mothers at all follow-ups across childhood and they reported a higher agreement with fathers than in the PC group. More child-related stress reported by the PC mothers made up a qualitatively different trajectory compared with the gradually decreasing trajectories reported from PI mothers and fathers in both groups. Both parents in the PI group reported parenting stress similar to the TR group at all follow-ups, whereas differences between the PC and the TR group increased with age throughout childhood [paper II / 179].

In the third study children and parents in the PI group reported better well-being on some measures of QoL at children's age of nine [paper III / 236].

In the following sections, the results are discussed in relation to possible influences of the MITP-M, relatedness to other results from TISP and recent research in the field of early child development and outcomes reported on preterm children.

5.1 Children's emotional behavior development

Behavioral problems of children have been reported repeatedly by TISP [209,210]. In the current study these reports were extended to include longitudinal analyses of behavior from children's age of 2 until 9 years and cross-sectional reports of problems and competencies at the ages seven and nine [211]. The trajectories reported were consistent with behavioral development that has been formerly reported for normative and at-risk samples. Even though, the overall level of problems reported were low compared to other studies [45,212]. Elgen et al. [36] reported a 40% increase in behavioral problems among children born preterm compared with full-terms at their age of eleven. Reports of behavioral problems on preterm children in TISP seem to be at a lower level. Non-significantly more PC- than PI children had high problem scores, 18% in the PC group versus 11.8% in the PI group.

Fewer problems in TISP compared to previous studies may be a positive effect of the follow-up program. Parents received written reports regarding their child's level of performance at every follow-up and could contact the study coordinator or director for talks whenever needed. This result address the importance of a well designed follow-up program for children born preterm.

Longitudinal behavior development in the PI and the PC group followed similar trajectories as in the TR group with one exception. PC fathers reported a more worrisome development of anxious behavior than TR children [211]. This corresponded with PC father's reports of a steeper increase of anxious behavior among PC boys than PI father's reports on PI boys from children's age of five until nine [ibid]. Very preterm children have previously been identified with increased risk of emotional problems in prepubescent years (6 to 13 years) and more emotional problems were especially reported on children born preterm, with male gender and those living with parents from low SES backgrounds [213]. A similar finding was reported from another large study were ELBW children were reported with a 4-fold increased odds of having emotional problems compared with term controls at six years of age [214].

This studies of emotional problems may sheds light on the different trajectories of anxious behavior reported by PC fathers compared to PI and TR fathers up to the age of nine years in TISP [209]. It is possible that the MITP-M have promoted a long-term protective effect against anxious problems in the PI group. Even though, significant differences were related to reports of more anxious problems

in relatively few PC boys in the current study and further sub-analysis could not be done because of lack of statistical power. PC parents reported that their child had been referred to specialized child-psychiatric services more than twice as often as PI parents on PI children. This information support the hypothesis that the MITP-M may have long-term protective effects concerning children's mental health.

Children in the PI- and the PC group develop similarly to the term control children in all other aspects of longitudinal behavior development reported from TISP. However, although they develop similarly to TR children, their development may be viewed as somewhat delayed and they may need more support from their family and the society as reported in previous studies [215-219]. The variation between individuals in TISP was reflected by high standard deviations in reports of behavioral problems throughout childhood. This result confirmed previous findings reported by Gilliom & Shaw that showed significant variability in individual-level trajectories of behavior [212]. Although PI children were reported to have more problems than term controls during earlier years, they seem to reach an age-appropriate/normative level of maturation, adaptability and competence at nine years of age.

It is very promising that the MITP-M seemed to support an accelerated developmental catch-up among PI children. In agreement with the transactional understanding underlying this study and previous publications, this finding may be partly due to a decrease in parental stress [133,145, 220,221], improved parent-child interactional relationship [220] and a reduced parental perception of the child's vulnerability [219,223]. This is supposed to influence the further development of the children up to puberty and adolescence via more positive transactions and effects on the child's own, parent's- and peer's perceptions.

Parent's reports of internalizing behavior

The extent of internalizing problems reported in TISP followed the tendency reported as normative trajectories of problems by Bongers et al. [45]. The number of problems increased slightly during childhood even though the reports from different respondents displayed slightly different patterns.

The trajectory of children's behavior in terms of internalizing problems throughout childhood is reported to be highly influenced by maternal psychopathology and stress [43]. Further investigations may uncover if similar associations appear in the present study and if the intervention may have reduced, not only parenting stress but also psychopathology in the PI group. The slightly larger amount of internalizing problems reported by PC mothers compared with other groups of respondents at two years may reflect a view of their children as more withdrawn (e.g., shy, fearful, sad), which coincides with them reporting more child-related stress, especially in relation to the adaptability and mood of the children [179]. Preterm children have been described to have a reduced capacity to express positive emotions (smiles, eye contact, vocalizations) [126,224] and more dysregulated behavior during toddlerhood [80, 225,226]. In addition, 21% of VLBW children were reported to have dysregulated behavior at 2 years of age in a recent Australian study [56], and VLBW children demonstrated significantly more internalizing problems and lower socio-emotional competence at 2 years of age compared with full-terms.

Deficits in the expressivity of children born preterm are thought to affect parent-child interactions [227,228]. Parents may feel less excited by their child, which may also affect their interpretation of the child's signs and needs. Earlier reports of more intrusive parental behavior in preterm parent-child dyads [138] may be interpreted as the attempts of parents to elicit smiles and responses when the child required less stimulation, resulting in more internalizing behavior. This highlights the importance of early parental sensitization to the expressions of every unique child [42,135,229].

Preterm infants have also been described to be more dependent on maternal scaffolding behavior to establish successful emotion-regulation compared with their peers [230]. PC parents may experience difficulties in detecting this prematurity-related behavior as early as PI parents who are supported by insights from the intervention and who as early as in two-year-old children reported non-significant less internalizing behavior compared with PC parents [211]. This finding may also correspond to reports of improved maternal adaptation to the temperamental style of the child at an age of one year, as reported by Olafsen et al. [232]. Later in childhood PC parent-child dyads

appear to be less disturbed by internalizing behavior. This may indicate an establishment of improved parent-child adaptation in children aged approximately three years for PC mothers and aged five years for PC fathers.

More anxious/depressed behavior and somatic complaints have repeatedly been reported in girls than boys from the age that they enter primary school [45]. In TISP, two features of internalizing behavior made up statistically different interactional trajectories from age 2 until 9 years. They were related to preterm groups and gender: a) potentially more anxious behavior in boys in the PC group compared with the PI group from the time of school entry, and b) a shift in withdrawal problems during the first years of school compared with the preschool years. According to withdrawal behavior, the PI and the PC boys increased in similarity with increasing age, while an opposite tendency was reported for girls up to the age of nine because PC girls were reported to be slightly more withdrawn than PI girls at age nine in comparison to previous years. The impact of these results is not clear because an increased number of problems were reported for relative few children. The differences may be transient or they may be precursors of a subsequent increased risk of psychopathology in the PC group similar to the results reported on VLBW children by Treyvaud et al. [79].

Teachers reported internalizing problems in the same order as parents, which were highest in the PC group and lowest in the TR group. The PI group placed itself in the middle of these two groups. Internalizing behavior may not be as visible for teachers as for parents, and it has been suggested previously that mothers are better observers of this type of behavior than teachers [65]. However, the teachers were blinded to children's group belonging, and therefore, their reports may be more trustworthy.

Figure 6. The mean reports of internalizing behavioral problems across childhood in all three study groups from all respondents.

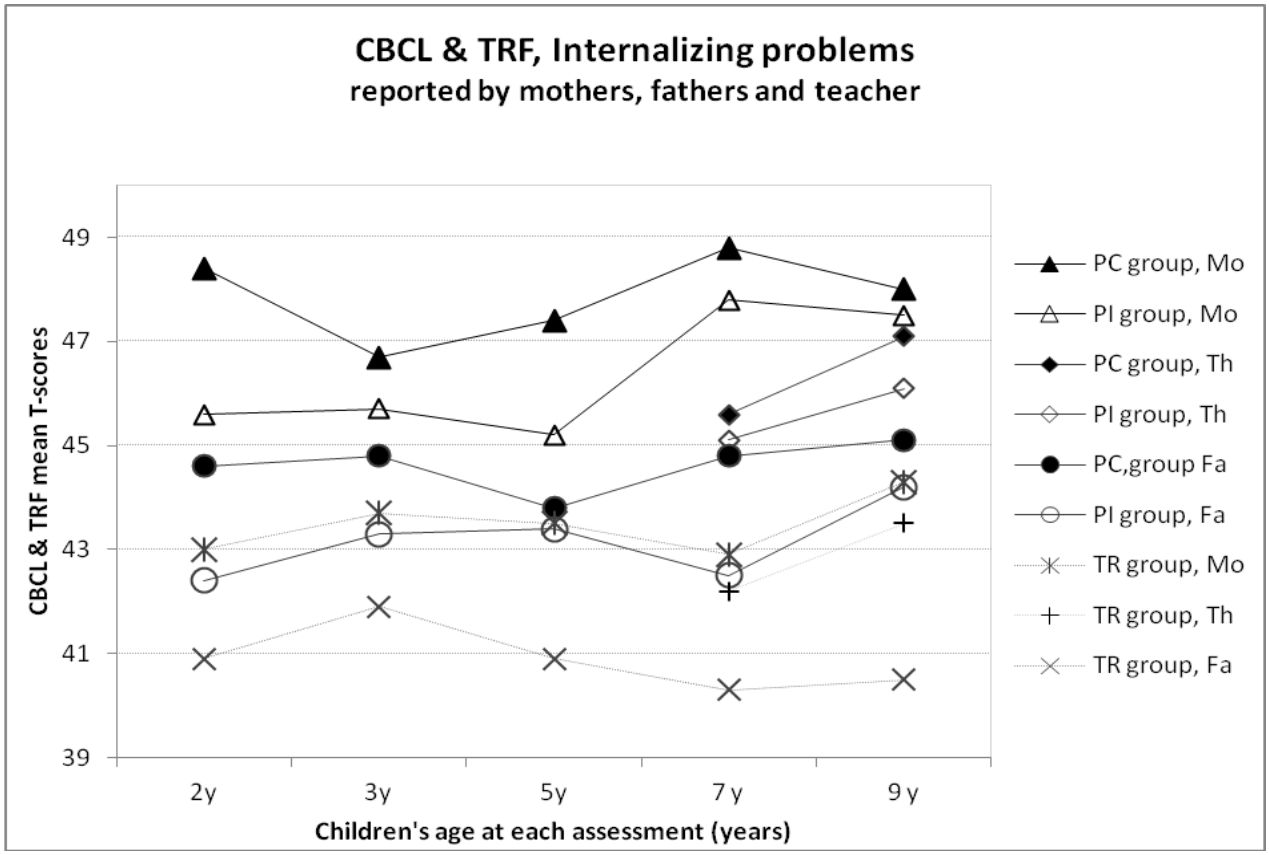


Figure 6. Mean T-scores for CBCL and TRF of internalizing problems reported by mothers, fathers and teachers in each study group at all follow-ups.

Parent's reports of externalizing behavior

Longitudinal investigations of externalizing behavior revealed similar patterns of decreasing problems in all groups, which is consistent with reports on normal populations [45,233]. The significant differences in behavioral outcomes reported by Nordhov [210] at age five years disappeared in our analysis when controlling for repeated measures. However, a similar pattern to that observed for internalizing behavioral problems was evident as the PI group was consistently reported with fewer externalizing problems than the PC group by mothers, fathers and teachers [211].

Externalizing behavior, as reported in all study groups and for all groups of respondents are presented in Figure 7. TR mothers reported decreasing problems in children as early as two years of

age. PI mothers reported a corresponding drop in the average number of problems after three years of age, while PC mothers reported a decreasing trajectory after five years of age. The delayed decrease in problems may first illustrate the parenting challenges that are faced by the mothers of preterm children compared with full-term mothers. Secondly may the intervention have expedited a more successful adaptation between the mothers and children in the PI group compared with the PC group.

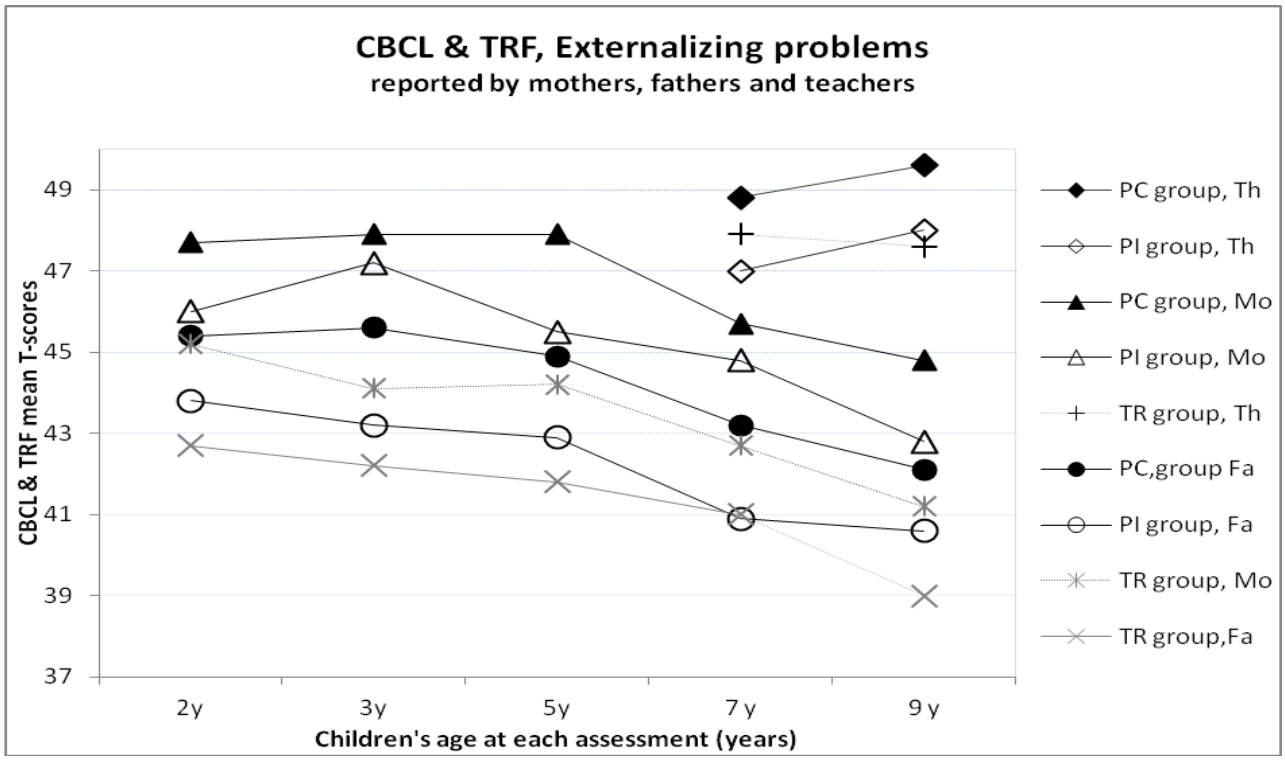


Figure 7. Mean T-scores for CBCL and TRF of externalizing problems reported by mothers, fathers and teachers in each study group at all follow-ups.

A surprising finding was the differences in the father's reports of externalizing behavior across childhood for the heavier group of preterm children. PC children with a BW > 1000 g had a significantly more worrisome trajectory concerning externalizing problems than the same sub-group in the PI group. Fathers of the heavier PC children reported externalizing behavior at stable and high levels from age 2 to 9 years while fathers of the same PI sub-group reported decreasing problems similar to normal populations from age five until 9 years.

This difference may be an effect of father's restricted access to the NICU in our hospital at the time when the study took place. Firstly, fathers of heavier children were generally less present in the hospital compared with fathers of smaller and medically sicker newborns. Fathers may thus have received less knowledge about how to interact with their infants in a developmentally supportive way. Secondly, mothers of heavier preterm children may have received less guidance regarding developmentally appropriate care compared with mothers of the smallest preterms. Mothers (and some fathers) with smaller preterms were hospitalized with their children for a longer period and had thus more possibilities to learn about their infant's signs, needs and behavior from professionals in the NICU irrespective of the intervention program. PI parents of the heavier preterm children may have established a similar enhanced understanding of their infant's expressions and needs during the MITP-m sessions while PC parents of the heavier preterm children may have been more dependent on their own personal resources.

This proposal of a possible reason of the significant differences in PI and PC father's reports of externalizing behavior corresponds with the research of Spinelli et al.[234]. They reported on parental stress trajectories in premature mother-infant dyads from the age of four months to three years. One of the groups of mothers who reported high levels of stress at 4 month of age consisted of mothers who had a short hospitalization with their preterm child [ibid].

5.2 Family climate and parental agreement

Parenting behavior or family functioning has not explicitly been studied in TISP. However, an understanding of the functioning of family systems has become possible; first, through reports of parent's perceptions of children's temperament during the first year [231,232], through reports on parent's attitudes toward child-rearing across toddlerhood [235] and lastly, through the reporting of several measures of parental agreement in the papers included in this thesis concerning behavioral problems, parenting stress and perceptions of children's quality of life at nine years of age [179,211, 236].

Harsh parenting involving higher parenting control has been, together with a demanding child temperament, interparental conflicts [237] and low paternal caregiving capacities [238], described as a precursor of externalizing behavior throughout childhood [233,239]. Several of these factors have been addressed in the studies mentioned above and are suggested to be associated with the reports of slightly more behavioral problems and challenged family climate in the PC group compared with the PI group. Although no differences were uncovered between the reactivity of PI and PC children during the first year, Olafsen et al. reported that PI mothers were more affected by their children's temperamental style at 6 months of age [231]. At an age of one year, this phenomenon had disappeared, which may have occurred because the PI mothers had adjusted their parenting behavior according to the characteristics of the children. However, a strong association between maternal stress and negative reactivity was reported by PC mothers at one year of age [232]. These early differences may be one underlying reason for the consistently small and non-significant differences in reported problems between the PI and PC groups at later follow-ups [211].

Nordhov et al. reported differences in child-rearing attitudes across toddlerhood between the PI and PC group [235]. Mothers who had received the intervention reported more nurturing child-rearing attitudes toward their children at one and two years of age, and the same tendency was detected at 3 years of age. The differences reported by mothers concerning the temperaments of their children and later child-rearing attitudes may reflect some differences in parent-child transactions and family climates between the PI and PC group.

These differences may also be discussed in relation to parental reports of children's behavior and parenting stress in the current thesis. PI parents reported a higher agreement than PC parents in their assessment of internalizing behavior at two years of age [211]. This observation may indicate that both mothers and fathers were able to recognize early signs of internalizing behavior among their children after the intervention, while PC parents obtained less agreement in the family at this early stage. PC parents may have lacked important insights and possibly misinterpreted behavior such as sadness, shyness, lack of affections, and avoidance of eye contact.

The interpretation of the results above may also be supported by higher parental agreement concerning child- and parent-related stress [179]. In children aged two years, differences in parental agreement covered both aspects of parenting stress, while at age three the difference was isolated to parent-related stress. PC fathers reported fewer behavioral problems at all ages and less parenting stress throughout childhood compared with PC mothers, which is with the pattern observed in the PI and TR group. However, the differences in parental agreement between the PC and PI group at age two and three years may indicate that PC fathers were less involved in the caretaking of their child, both before and after discharge from hospital, compared with the PI fathers. They may not have been aware of the challenges faced by the PC mothers regarding children younger than three years of age, during which PC parental agreement concerning child-related stress was equivalent to that in the PI group.

PI mothers and PI fathers may have been sensitized to their infant's behavior during infancy as a result of the intervention, and even though some fathers participated less in the intervention program, they may have been more easily inspired by the mothers and caught up with them more successfully compared with the PC fathers. Agreement between parents in the TR group has not been questioned, but TR fathers appeared to be generally less aware of behavioral problems of any type compared with their partners.

5.3 Socio-emotional problems, social competence and mental health

PI children were reported by their mothers to be more socially available at the age of one year [232] and with less social problems than PC children at five years of age [210]. This tendency continued in children aged 7 and 9 years, even significant differences reported by teachers at age nine disappeared when adjusting for the presence of twins in the sample. Similarly, PI mothers reported significantly fewer social problems at age nine years compared with PC mothers after the exclusion of one extreme outlier. In general, PC fathers did not report more social problems than PI fathers. However, among those fathers who reported that his child experienced difficulties in daily life, PC fathers identified this condition to be related more often to difficulties associated with peer relationships. Finally, PI mothers rated their children with higher social competence compared with PC mothers at seven years of age, and a similar non-significant difference was reported by both PI mothers and PI fathers at nine years of age.

Developmental goals concerning social functioning in early school years are described as the ability to form dyadic friendships with peers and the diminution of physical aggression [37], handling of frustration and self-regulating [242].The intervention may have strengthened the ability of the PI children to reach such goals at an age-appropriate time. This result makes sense because children born preterm have been reported to need a longer duration than full-terms to achieve similar levels of performance [215,242].

Socio-emotional problems are frequently identified as precursors of later complex school- or psycho-social problems. VLBW children without major handicaps were reported to display more socially inappropriate behavior from age 6 to 8 years compared to full-terms in a longitudinal study from the 1990s [66]. Recently, it was shown that 25% of a sample of ELBW children was identified with socio-emotional delays at two years of age [242]. Increased social problems among VLBW children have also been described to be predictive of later lower social competence and poorer school performance at eleven years of age [241]. In another study, 33% of the problems reported by teachers in elementary schools were presaged in parental reports for children aged 12 to 36 months [44]. Thus, socio-emotional problems may start early and be relatively stable throughout childhood.

Later studies continued to report a greater number of socio-emotional problems in preterm populations compared with full-terms [243]. They discovered socio-emotional problems at age five years to be predicted by emotional problems at two years of age [ibid]. Next, socio-emotional problems at five years of age and children with a higher social risk at seven years of age were more likely to meet the criteria for a psychiatric disorder at an age of 7 years [79]. Compared with terms, preterm children had a three times increased odds of meeting any psychiatric diagnosis at 7 years of age (24% of preterm children)[ibid]. The most common diagnoses were anxiety, attention deficit/ hyperactivity and autism spectrum disorders [244]. This finding is consistent with two Norwegian studies that investigated preterm populations. In a sample of VLBW children from the central region of Norway, 46% of children were found to have psychiatric problems at the age of 14 [245]. Among the children, 25% met the criteria for a psychiatric disorder [99], and the prevalence of psychiatric morbidity displayed a similar level at the age of 20 years [245]. In the western region of Norway, Elgen et al. reported that 27% of a VLBW sample exhibited a psychiatric disorder at the age of 11 years [36,98]. These results can be seen in relation to those of a Nordic study of impaired psycho-social functioning/problems that estimated the normative prevalence to be approximately 10% [246]. In TISP, parents reported children in the PC group as more than twice as often referred to specialized child-psychiatric services at children's age of nine compared to reports on PI children. This information was highly correlated with teachers reports of more difficulties in everyday life in the PC group compared with the PI group. The parental reports included not information about severity of symptoms or diagnosis but the findings above may be an indication of more severe socio-emotional problems in the PC group than the PI group in middle childhood.

How may the findings of higher social competencies among PI children compared with PC children be influenced by the early MITP-M intervention? One possible explanation addresses a more successful down-regulation of infant stress/distress from infancy and across preschool years in the PI group. PI parents may have learned how they can adjust their interactions and demands to the individual capacities of the child [80,239,247]. A reduction of stress might correspond to better cortisol regulation [146,220,248], higher performance in the anterior attentional system and improved control [249]. Another plausible explanation is the bidirectional relationship between the parent and child and the influence of less parenting stress in PI families [32,221,228]. Parenting stress

has been described to predict later child coping competence, and child coping competence predicted later parenting stress [222].

5.4 Attention problems and perceived academic performance

Preterm children aged seven and nine years exhibited two main differences; teachers and parents reported fewer attention-related problems and improved school achievement in PI compared with PC children [223]. PI children adapted more easily to school demands and new environments compared to PC children. A similar pattern was reflected by parental reports of stress at seven and nine years of age. PI parents reported less stress than PC parents, with significant differences observed between mothers of seven and nine-year-old children [ibid.].

There are several possible explanations why the intervention may have promoted better attentional capacities among preterm children in the PI group compared with the PC group. The maturation and development of children's attention throughout childhood may have been supported by a more successful down-regulation of initial neonatal distress and a subsequent consistent reduction of parenting stress in PI families [179]. In infancy, children may have greater incentives to impart robustness into the processing of the orienting system and subsequently the alerting system, positively impacting the ability of children to focus attention. Attention is a basic condition for the ability of a child to orient. Early orienting attentional capacity at 5 months of age has been described as a precursor, a "building block" for later attention that is needed for learning and performance until four years of age [250]. Finally, it is plausible to suggest that intervention-generated, well-tuned parent-child interactions in the PI group may have fostered more scaffolding behavior among PI parents. This could have supported the development of the effortful control system in children and more goal-directed attention in toddlerhood. During early childhood, executive functions are linked both with school readiness, academic performance and early-onset disorders (e.g., ADHD, inattention) [250,251].

The heightened risk for learning and attention problems among children born preterm has been well documented [83,84,117,252-254]. Groen-Blockhuis et al. reported strong evidence for a causal relationship between a lower BW and later attention problems [78]. Furthermore, children born preterm have been reported to have a more than doubled risk of developing ADHD disorders compared with full-term children and a 50% increased risk of requiring specialized pedagogical services [26]. In the study by Indredavik et al. [99], VLBW children reported attention problems that were similar to their full-term peers at 14 years of age, while both mothers and fathers of preterms,

on average, reported a three-fold increase in attention problems compared with parents of full-terms. As many as 25% of the VLBW children were identified with attention problems [ibid.]. This finding has later been associated with white matter abnormalities at an age of 15 years, and the authors suggested that a higher order of cognitive function, such as attention, depends on the intact communication between several cortical areas [256].

Attention is both a complex growing competency in the developing children and a prerequisite for developing other competencies such as social functioning and school achievements. However, the assessment of attention is poorly integrated in standardized cognitive measures. This finding may be a reason why the cognitive results reported in TISP at children's age of nine did not reveal any differences between the PI and PC group in contrast to the differences reported previously at children's five years of age [257,258]. Hauglann et al. reported similar intelligence coefficients (IQ) in the PI and PC group at the age of nine years and with marginal differences at seven years of age. They did not compare outcomes of IQ with the term control group. A Finnish follow-up study from the beginning of this millennium reported better cognitive development among VLBW children than reported in earlier publications but still they differed significantly from full-term controls already at the age of two [260]. It has also been noted that IQ scores did not represent a sufficient measure of the mental resources and capabilities of the children [259]. Aylward has stated that the sole use of IQ scores may mask the complex profiles of children with multiple areas of weakness that may negatively affect later functioning in school. This finding was supported by a study that identified problems in features such as attention, executive functioning and memory among preterm children who were assessed as normal in terms of IQ [25].

Proximal environmental factors, such as difficult parent-child interactions, and distal environmental factors, such as reduced social-economic status (SES), in families are supposed to influence the school performance of children [61,165,259]. This is reflected in the results of the current study, the intervention may to some degree have made the PI families more resilient. Still, at children's age of nine, a greater amount of stress related to difficult interactions with children was reported by PC parents compared with PI and TR parents [179]. We suppose that the patterns of interactions within each family may have been well consoled after all those years. Both parents and children may have formed fixed pictures regarding whom and how the other is concerned. Thus, more stress in the PC

families may be viewed as a hidden disturbance, a proximal and relational environmental factor that influences the overall performance of these children.

PI children were viewed as comparable with full-term peers by their teachers in terms of school and academic performance. However, a more intense use of pedagogical specialized services may have been necessary to reach this level. A total of 34% of the PC children, 28% of the PI children and only 3% of the TR children had received additional school services during the preschool/school years, according to parent's reports at nine years of age.

A slight increase in parenting stress among PI mothers and fathers of children aged seven years may be a sign of the elevated parental support and involvement needed in this group compared with the TR group. The catch-up within the PI group may have been supported by both additional school services and an increase in parental investments.

5.5 Parenting stress and possible influences on children's behavioral problems

Long-lasting stress that is present early in development has been described with detrimental effects on the well-being of parents, children and the relationship between them [199]. In line with previous reports from TISP [192, 209], more parenting stress were reported in the PC group compared with the PI group at all follow-ups until children's age of nine [paper II]. Reports of stress have been analyzed longitudinally from infancy up to the age of nine years and especially PC mothers seem affected by increasingly more child related stress across childhood. The same aspects of parenting stress created the biggest differences between the preterm groups throughout childhood. This was primarily reports of more distractibility, more moodiness and maternal perception of less competence and attachment.

The sub-dimensions mentioned above cover aspects of parenting stress associated with difficulties in parent-infant interactions [133] which continued to be reported as significantly more frequent by PC mothers compared with PI mothers at children's age of nine [paper II]. This corresponds with the study by Gray et al. where the largest difference in parenting stress between a preterm- and a term group was related to difficulties in parent-child interactions [139]. They did not discover differences between groups in early infancy (4 months) [261], while significantly more maternal stress was reported in the preterm group at age one [139]. In that study, symptoms of maternal depression and infant temperament were detected as independent risk factors at both follow-ups (4 & 12 months) [139,261]. Stress related to dysfunctional parent-child interactions has also been reported to show specificity to child internalizing problems in a study of referred children between the ages of 5 and 17 years [262]. The association was independent of psychopathology among the parents. Mechanisms of causality have not yet been investigated in TISP. It seem very important to continue the investigations and explore to what degree differences in child outcomes between preterm groups are caused by enhanced parent-child interactional relationships from infancy until middle school age.

Child-related stress

PC mothers reported more child-related stress across childhood compared with PI mothers, and this made up a different trajectory in children up to the age of seven years compared with reports from other groups and PC fathers [179]. Child-related stress is thought to reflect how parents perceive the attributes of their child [133] and how much they struggle with their care-taking responsibilities in light of the child's illness, behavioral problems or emotional disturbances [132]. As we all become stressed when faced with big challenges in life (e.g. feeling our life is threatened, our children are in danger), child-related stress may be perceived as an answer to a challenging situation, and it is a rational response to a demanding situation [132,133].

PC mothers reported also the most internalizing, externalizing, attention and social behavioral problems among all of the respondents across all of the assessments [223]. Together with their reports of the most parenting stress among all of the respondents, these results is consistent with the findings of a Canadian study in which parenting stress caused by high levels of distractibility in the preschool years predicted behavioral problems at seven years of age in a sample of full-term and moderately preterm children [32].

The areas that created differences in child-related stress between PC and PI mothers have been previously reported as challenging for children born preterm; these children are less likely than full-terms to instigate interactions, are less attentive, show less positive emotions and are sometimes regarded as less attractive social partners [154,263]. These features were addressed in MITP-M in which the parents were supported to detect the social identity of their child and to be emotionally affected by the early signs of responsivity in the behavior of their infant [264]. This may have promoted feelings of love, acceptance and positive attitudes in the PI parents.

In addition, MITP-M provided information regarding how parents could effectively co-regulate their infant and modify their actions to facilitate a more effective adaption of the child to life in the home environment. Preterm children experience high levels of stress during their stay in the NICU [265-267]. Their altered behavior and reactions to stimuli may be viewed as consequences of their adaptation to non-appropriate environments. Parents of preterms must help their infants re-adapt to more nurturing environments and thus help them to become less distressed. This phenomenon has been confirmed in recent research showing that positive parenting behavior and reduced parenting stress appear to ameliorate the negative effects of early pain among very preterm

children [188]. These parental factors have also been associated with less internalizing behavior in children aged 18 months [53]. Another study described associations between neonatal pain and stress and an altered HPA axis functionality up to 7 years of age in children who were born very preterm [267]. These studies underscore that children born preterm require successful parental co-regulation throughout childhood.

Parent-related stress

MITP-M seems to have subdued the pressure of parent-related stress on children's mothers. PI mothers reported significantly less parent-related stress from infancy until 5 years of age and again borderline less stress compared to PC mothers at nine years. In contrast to child-related stress, parent-related stress may be more subtle because it reflects the perception of the parents regarding their own parenting capabilities and the resources available to meet these demands [132]. Differences between the preterm groups were most pronounced in the subscales Attachment and Competence and to some degree in the scale focusing on marital satisfaction (PSI-Spouse).

The PSI subscale of Attachment focuses on parent's perception of emotional closeness to their child, which is an important factor in the fostering of their intrinsic motivation of being parents [133]. The disruptive experience of becoming parents weeks and month before planning, the limited possibilities to stay intimately close (skin to skin), the unfamiliar environments in the NICU and the continuous presence of strangers are all risk factors of elevated attachment-related stress among these parents [5,40,227]. In one study, only 20% of mothers of preterm children were described as having a secure attachment to their children at 6 months of age compared with 53% of mothers of full-terms [227]. However, a relatively recent Finnish study did not report greater attachment difficulties in preterm mother-child dyads compared with dyads of full-term newborns [268]. Attachment difficulties may also be difficult to observe. Bienfait et al. observed low correlations between the reports of mothers and NICU nurses regarding mother-child bonding difficulties after two days in the NICU [269]. She concluded that mothers must have the possibility of expressing their feelings because their need for help may not be easy to observe by others. In TISP, this need was especially addressed by the first session added to the original MITP [169].

The powerful experience of being emotionally touched by the meeting with one's own newborn baby is an important story - rewritten in prose literature, in philosophy and in writings about becoming a parent [132,270,271]. These sometimes overwhelming passionate feelings may be viewed as a nature-given gift to new parents, supported by a biological-endocrine system to insure the caretaking of newborn infants [171-174]. The bio-behavioral synchrony between attachment partners, who describe connections between behavior and physiological systems, represents a powerful new knowledge that has not yet been fully investigated [173]. Nevertheless, this understanding has partly grown from studies of preterm infants for whom the quality of synchrony

may be reduced due to both early separation and difficult interpretation of the behavior of the child. Strong associations have been reported between physiological stability (heart rate variability and sleep-awake organization) in the third trimester [41], parent-child interactive synchrony later in infancy [40] and the ability of the child to self-regulate him or herself during the preschool years [41,80].

In some way, the MITP-M intervention may have restored or strengthened parental attachment perceptions and thereby created significantly fewer attachment-related stresses in the PI group compared with the PC group. After the interventions, the PI parents may have been able to "re-interpret" the behavior of the infant so that expressions of emotional instability became a "call for support" or a changeable mood of the infant "a call for paucity" in interactions and activities.

Perceptions of competence were the second parent-related dimension of stress making up differences between the PI and PC group throughout childhood. The MITP-M is described as a sensitizing intervention, but many teaching elements are included in this intervention. Parents must be aware of and recognize the type of signs, behavior, and expressions that may guide the daily caretaking of their child. Parenting Self-Efficacy (PSE) is thought to be a central element in the beliefs and expectation of parents regarding their ability to parent successfully [272,273]. Parenting stress is strongly associated with PSE [274], and PSE may be viewed as an important coping mechanism in the process characterizing the development of stress [276,276]. PSE is commonly viewed as a strengthening factor in parenting competence, but studies of preterm children have revealed that high levels of PSE without knowledge of child development were inversely associated with outcomes. The mothers with high PSE but little developmental knowledge were the least sensitive in interactions with their children [277]. Thus, a naive sense of self-efficacy may be potentially negative if parents are responsible for a preterm born child who displays unusual reactions to overstimulation or inappropriate handling. Low levels of self-efficacy may not be more common among parents of very preterm infants compared with parents of more mature children [278]. However, these researchers found that PSE regarding parenting tasks mediated the relationship between psychological symptoms and self-perceived parental competence. In TISP, there is limited information about the self-efficacy of the parents, but it seems relevant to mention these relationships as one possible mechanism underlying the differences reported for parent-related stress (paper II).

5.6 Influences on children's quality of life

In children aged nine years, TISP generated the first result in which children themselves reported outcomes independently of their parents [236]. Both PI children and their parents reported a somewhat higher quality of life, on average, than the PC families, and we suggest that the MITP-M can have long-lasting positive effects on well-being in families rearing preterm born children. Group differences became evident in different aspects of QoL in the children's and parent's reports, namely as bodily sensations in children and as a perception of emotional well-being and well-being in school among parents.

The results have already been discussed thoroughly in relation to comparable research [279-285] as well as previous and current reports from TISP in paper III [236]. Thus, a brief summary of the main finding will be presented herein. The PI children reported a higher level of bodily well-being than the PC group, and they also rated their bodily well-being as non-significantly higher than that of the TR children. Although a low BW and neonatal illness were negatively associated with QoL, neither these nor other birth, medical or socio-demographic factors explained the significant difference between the PI and PC group. It may be questioned whether the improved bodily well-being in the PI group was caused by better, early parent-child emotional co-regulation as reported by Treyvaud et al. [244] and as such created a more nourishing family climate with less stress in the PI families [179]. This finding may correspond with the strong associations detected between children's report of bodily wellbeing at nine years of age, and mother's, father's and teacher's reports of behavioral problems at seven years of age [236].

PI parents perceived their children to have a higher QoL than the PC group in the dimensions of emotional well-being and the ability of the child to thrive in school. Corresponding with other studies [283,286], a strong association was found between parents' proxy reports of emotional well-being and maternal reports of stress. Associations were evident at all ages, and the strongest association was observed between parental reports of emotional well-being and maternal stress reported at seven years of age.

PI parents also rated their children as enjoying a significantly higher school-related QoL, in line with the CBCL and TRF results [paper I & III]. This difference seemed to mostly affect boys but was highly related to attention problems reported by teachers at nine years of age [236]. The congruence

between reports of attention problems and QoL is not surprising. Being able to stay focused and assimilate messages are essential skills for all children, enabling them to experience well-being, social belonging and learning in school.

Figure 8 shows the means for different subscales and respondents.

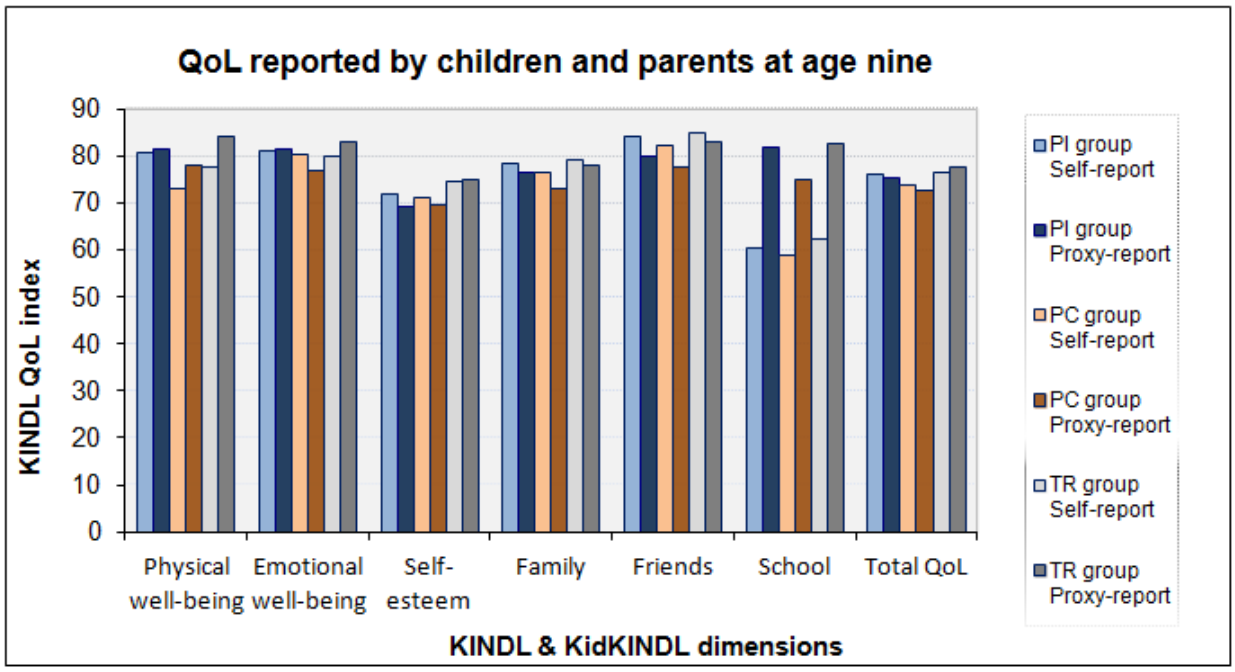


Figure 8. Mean total and dimensionally separated QoL reported by children and parents in each study group at nine years of age.

In general, both children and parents rated QoL in the children as relatively high. PC children reported lower bodily well-being than PI children but the same level as TR children across all dimensions.

However, PC parents rated their children as having a lower QoL in all dimensions compared with TR parents, while PI parents reported a QoL similar to the reports provided by parents of full-terms on all scales, excluding slightly lower self-esteem. As repeatedly stated, minor difficulties related to prematurity may first became visible when children enter the school system [57,83]. Parents in both preterm groups may face greater challenges in this phase, as reflected by reports of somewhat greater parenting stress [paper II] and withdrawn behavior of the child [paper I]. This may also affect the parent's experience of their children's self-esteem.

6. Strengths and limitations

TISP has been acknowledged for its strong design [287] and repeated continuation of the study, permitting long-term follow up into middle childhood. Although many of the reported outcomes are influenced by several mapped and unmapped factors, the randomization process revealed a high level of equality between the PI and PC group.

Next, the high participation and low drop-out rates of the families in all three study groups has been a success factor. This may be a result of the participating families, [a)] a loyalty and idealistic belief in the value of the study, [b)] perceived personal benefits of the follow-up program, [c)] reports about one's own child development and, especially, [d)] easy available communication with and advice from the study coordinator, who met them at all sessions from the time of study recruitment until the children were nine years of age. Another strength that must be mentioned is the use of multiple informants which is especially recommended when assessing children's affective symptomatology [288].

Subsequently, the collection, punching and scientific processing of the data were conducted by the same small team (study coordinator and statistician) across all years to form a qualitative guarantee of the data material.

However, some weaknesses must be mentioned. Research reported in this thesis was solely based on data from questionnaires. Information about children's behavior, QoL or parenting stress was not assessed more directly. A main aim of the study was to compare outcomes between groups, for which the use of validated and well-designed questionnaires seemed appropriate.

In most studies that continue for more than a decade, such as TISP, new knowledge may inform the research field about factors that should be monitored because they may influence children in each group differently. In TISP it had been beneficial if exposure to painful events and the use of skin-to-skin contact (e.g. kangaroo care) with parents had been registered for all study participants during the NICU stay. This information is not available. The final years demonstrated that exposure to neonatal pain has a substantial negative impact on the cortisol regulation and behavior at school of children [289], while skin-to-skin contact with parents has been reported to support long-term developmental outcomes [267,290].

7. Clinical implications/ implications for later research

In the last 9 years, TISP has reported promising results for children born preterm as well as their families [192,209,210,234,258,229,230,257,291,292]. Although the MITP is more than 30 years old, the modified version tested in TISP (MITP-M) verified that children born preterm may catch-up with their peers born full-term in the middle of childhood. This was provided by parents who obtained the appropriate support in a phase that was important for the parent-child relationships. These results are consistent with the latest theories introduced by Feldman who suggested that early periods of sensitivity can be determined for the development of children and introduced as parent-child synchrony as a core mechanism for the early regulation and coordination of biology and behavior during social contact [173].

Although several possible reasons for the effects of the MITP-M are mentioned in this thesis, they must be tested scientifically. It will be important to investigate whether parenting stress is a precursor of behavioral problems in children or whether the behavior of children is a more primary trigger of a relationship between stress and behavior, which has been suggested to be influenced bi-directionally [1,68,122,234,294]. We have not yet analyzed to what degree early externalizing behavior is followed by later internalizing behavior in our sample, but this is a relevant topic because previous research has suggested that disruptive young children are likely to experience coexisting internalizing difficulties or difficulties that appear during later childhood [212].

The success and quality of parental bonding to the newborn child lays a foundation for the attachment quality of the child [294-296]. All children develop close emotional bonds to those who take care of them, but not all bonds (attachments) provide equal amounts of security [1,297,298]. Sherman et al. did not find associations between negative reactivity and attachment classifications in children aged 5 months, but at the age of one year, those children identified with an insecure and ambivalent attachment style were most reactive [299]. The attachment security of children was not exclusively investigated in the present study, but higher levels of maternal and paternal attachment-related stress were reported in the PC group from the age of 6 months and throughout childhood. This finding may indicate that the intervention strengthened parental attachment and subsequently the attachment quality of the children in the PI group. Fearon & Belsky found significant associations between early attachment quality and externalizing behavioral problems in

middle childhood, especially among children living with additional environmental risk and in boys [300]. Attachment quality may be enhanced by the MITP-M, and this hypothesis should be further investigated.

Modifying the MITP-M for the future

The MITP-M intervention is designed as a pre- and post-discharge intervention and was started the last week of the child's hospitalization [166,194]. During the last 15 years, the progress observed in TISP in terms of new knowledge has challenged Norwegian NICU's to facilitate higher degrees of parental presence and participation across the period of hospitalization of preterm infants. These changes have been inspired by knowledge concerning developmental care (especially Newborn Individualized Development Care and Assessment Program, NIDCAP) [301-307], previous reports and presentations from TISP and studies focusing on developmental benefits for the preterm child provided with intimate and sustained skin-to-skin contact with primary adults (mother/father) [301,305].

Similar processes have been documented in many countries, and the importance of guiding the parents of preterms throughout the entire NICU stay has been frequently underlined [38,308]. Key elements in such interventions are described as [a)] including parents in caregiving activities, [b)] introducing and maintaining shared attention of the child's development, [c)] shape-structured settings for learning, [d)] building bridges between familiar and new knowledge, and gradually transferring responsibility to parents in terms of suggesting problem solutions and next performing activities [308]. This is also in line with recommendations from Fegran after her study in a Norwegian NICU [2,7] and in line with the "old" recommendations by Bromwich [124].

Research supporting this statement may be exemplified by an Australian study [309]. In that study, they modified the MITP to an intervention with 9 parental-guiding sessions that were delivered across the NICU stay followed by one single home visit [309]. This intervention is known as the "Premie Start Program" and was implemented by a team of psychologists that had worked extensively with preterm populations. They reported positive interventional effects as less distressed preterm children at a term-equivalent age (40 weeks GA) [ibid.], enhanced mother-infant interactions, more social and self-regulative behavior among the children and less stressed mothers

at 3 months of age [310] and improved social behavior competencies among the children at 6 months of age [309,310].

A review of interventions aimed at enhancing the mother-child interactional relationship detected eight different interventions that exhibited some efficacy [227,311]. Interventions that promote "cue-based care", defined as maternal care given to the infant in response to the infant's behavioral cues, in combination with sensitive responsive mothering, appeared to be the most effective. The early introduction of interventional support has also focused as children becoming less responsive to interventions as they grow older [15]. Others have recently reviewed the use of home-visiting programs for high-risk populations and documented them as positively associated with enhanced parent-child interactions [312].

The MITP-M has given TISP outstanding results with respect to long-lasting positive effects, both related to the development of children, parental well-being and parent-child interactions. The features mentioned above have been largely incorporated into the MITP-M. Further modifications should focus on how parts of the intervention could be administered earlier than the final week before discharge and next on how the sessions after discharge could be administered in a collaboration between the family, MITP-M interventionists in the NICU and community health care providers.

The Norwegian national guidelines, which include a description of the recommended follow-ups of children born prematurely, were published in 2007 [164], which is one year after a summary of knowledge regarding possible effective interventions in the follow-ups of children born preterm [312]. Even the guidelines were influenced by early results from TISP and other national/ international research investigations the conclusions and recommendations in the guidelines do not include a systematic pre- and post-discharge intervention such as the MITP-M [164]. This may be because the most promising results from TISP have been published over the last five years. Several elements from the MITP-M intervention were even incorporated into the general recommendations. To date, no research can confirm the sufficiency of these recommendations or to what degree they are followed across the country.

Four home visits during the first 3 month were included in the MITP-M intervention. In regular early follow-up in all municipalities, home visits are performed by public health nurses. The forwarding of

knowledge, reliance and family-nurse relationships of the NICU professionals to primary health care professionals may vary due to routines, work load and attitudes concerning cooperation across health-care levels. Some studies have reported a lack of knowledge regarding the development of children born preterm among public health nurses [314,315]. In particular, in areas with one or two nurses working alone this is frequently mentioned as a factor for concern.

An early follow-up program should be based on an approach in which families in need of different types of support (above standard discharge information) can be ensured in a systematic but also flexible and multiprofessional way. This would imply structured cooperation between professionals and the families and between health care actors at different health care levels. This cooperation should take into account how much knowledge and experience may be available at each family's home. At present, most families want to leave the NICU and hospital as soon the child is sufficiently physiologically regulated, and the nutrition may be given safely at home. Many children leave the hospital more than one month before they reach full-term according to the corrected age (40 w of GA). This observation implies great responsibilities on the parents of children during the transition to the home environments, and a lack of well-experienced support during the first weeks and months may heighten the risk of interactional problems and subsequent developmental risks [311].

As stated by Watson [38], "Leaving the NICU is only the first step". Preemies show additional problems as the complexity of the tasks increase, and many problems do not become apparent until later in childhood. Some parents may find it difficult to build parental competencies that allow them to reach the 2-3 highest steps of the staircase described by Bromwich [124,156]. As concluded by several reports, a longer follow-up is highly important for many children born preterm, providing them with the possibility of developing into the best possible version of themselves [316,317].

Long-term follow-up

Some developmental difficulties and the need for specialized treatment/education were detected at all of the follow-ups in TISP and in all of the study groups. Those children/families who asked for it were supported by the study coordinator or director to contact specialized services. In general, this phenomenon may have generated a child-family supportive effect; families did not need to waste time and energy in the search for adequate help when needed. Parents from families in all groups repeatedly mentioned the usefulness of and their thankfulness for the follow-up program in TISP. The gap between the TISP follow-up program and regular services in the Norwegian health-care system concerning children born preterm is wide, and in the future follow-up must be more defined and revised.

In the previously mentioned guidelines [164], recommendations for follow-up routines for children born prematurely are separated between the specialized health care system and the primary health care system. Children with an extremely low birth weight, below 28 w of GA, or children with medical complications are defined as in need of specialized health care follow-up, whereas others are recommended to receive follow-up in the regular primary health care system [ibid]. Recently, The Norwegian Knowledge Centre for the Health Services (Kunnskapssenteret) was asked to summarize prognostic studies of ELBW infants who received acute lifesaving treatment [318]. No Norwegian studies focusing on the evaluation of post-discharge follow-up programs have been found, and thus attention is needed in this area of study.

The results reported in TISP demonstrates the absence of a precise association between birth conditions, neonatal risk conditions and later socio-emotional developmental outcomes, despite the high importance of bio-medical factors. Other factors such as the distress of the children, parental bonding, the mental health conditions and self-efficacy of the parents, access to social support and several other socio-economic factors may greatly influence the developmental outcomes of the children. Research has confirmed that children born preterm (BW < 2000 grams) must be followed up throughout childhood [316,317]. Both proximal and distal environmental factors should be measured in the follow-up after preterm delivery because birth and medical information only predict some of the problems that may be experienced by these children throughout childhood [259].

8. Conclusions

The MITP-M intervention supported a process of gradual normalization of the behavioral-emotional development of children born preterm from birth until the age of nine years.

On average, the children born preterm (BW < 2000 g) in families who received the intervention reported more problems than their healthy, full-term peers throughout childhood. However, at nine years, their teachers and parents rated them as having similar social and academic competencies compared with children who were born full-term and to have similar levels of socio-emotional behavioral problems.
On the other hand, children born preterm (BW < 2000g) in families who received standard information and guidance before and after discharge from the hospital continued to be reported with more problems and less competencies than the two other groups of children.

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Paper I

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Does An Early Intervention Influence Behavioral Development Until Age 9 in Children Born Prematurely?

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This study examined whether the Mother–Infant Transaction Program prevents behavioral problems among preterm children (birth weight < 2000 g) until age 9. The program was administered to 72 preterms, while 74 preterms and 75 full-terms formed control groups (N = 221). Behavior was reported by parents (Child Behavior Checklist) and teachers (Teachers Report Form) and by all on selected Strengths and Difficulties Questionnaire (SDQ) questions. Long-term behavioral development appeared to be qualitatively unaffected by the intervention. At ages 7 and 9, fewer attention problems and better adaptation to school were reported from parents and teachers of the intervention group compared to preterm controls. At age 9, teachers reported fewer difficulties in the intervention group and better academic performance. In these areas they were reported as being at the statistically same level as term controls.

Children born preterm are at increased risk of developmental problems (Shonkoff & Phillips, 2000). Prematurity is correlated with behavioral difficulties and a higher incidence of problems in everyday life that persists throughout primary school (Bhutta, Cleves, Casey, Cradock, & Anand, 2002). A higher incidence of attentional deficits is found to be the most obvious problem, but internalizing problems as reported by parents and externalizing behavior as reported by teachers also occur (Aarnoudse-Moens, Weisglas-Kuperus, van Goudoever, & Oosterlaan, 2009). Problems are related to deficits in several cognitive functions and increases in learning problems, especially in disciplines such as mathematics, reading, and spelling (Aarnoudse-Moens et al., 2009). Problems are discovered to be inversely related to birth weight (BW) and probably more frequent among male born children. Between 50% and 60% of premature born children are reported to require special learning assistance (Aylward, 2005; Bhutta et al., 2002). The prevalence of behavioral problems at 8 years is reported to be about 20%, which is twice the reported rate in the general population (Bongers, Koot, van der Ende, & Verhulst, 2003; Gray, Indurkhya, & McCormick, 2004). A Norwegian study found that 40% of preterm born children displayed abnormal behavior at age 11 (Elgen, Holsten, & Odberg, 2012; Elgen, Sommerfelt, & Markestad, 2002). They were also 3 times as likely to receive a diagnosis of psychiatric disorder as their term peers, in accordance with other studies (Johnson, 2007).

Several interventions have been tested in attempts to prevent the development of problem behavior (Glazebrook et al., 2007; McAnulty et al.,

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2010; McCarton et al., 1997; Meijssen et al., 2010; Newnham, Milgrom, & Skouteris, 2009), documenting some immediate effects. However, long-term follow-ups are few (Guralnick, 2012). Only one small study has reported successful intervention effects on preterms that persisted until 9 years of age (Achenbach, Howell, Aoki, & Rauh, 1993) and the current study is a modified replication of their design.

The theoretical foundation of these studies is a transactional understanding of child development (Sameroff & Fiese, 2000). The developing child is an active participant in the creation of his or her interhuman environments. This is formed by the contextual interplay between individual biological conditions (child) and the child's interactions with the environment (family, school). As stated by Hauser-Cram et al. (2001), "Development occurs within multiple hierarchical contexts that are reciprocally related" (p. 21). When children are born prematurely, the natural transactions are easily interrupted because of these infants' immature expressions and limited capacity to self-regulate and emit recognizable alertness responses (Feldman, 2006). This limits the possibilities of caregivers to establish development-supportive caretaking (Nugent, Keefer, Minear, Johnson, & Blanchard, 2007).

The emotional crisis affecting many parents of preterms is also known to influence development (Abidin, 1995; Nurcombe et al., 1984). This study included an initial session when parents could vent feelings such as grief, anger, or frustration related to the preterm delivery, the hospital stay, and how this condition had affected their lives. The reinforcement of parental self-esteem and confidence was another aim of the program as parental experiences and discoveries of each child's developmental expression were highly acknowledged throughout the sessions. The parental guidance was given in steps as the systems of newborn behavior (physiological, motor, state, and emotional regulation) were explored one at the time and progressively put together.

Parents of preterms may also find it difficult to emotionally attach to their newborn. Interactions between parent and child may suffer because of lack of feedback from the child and experiential avoidance is described as a significant predictor of weakened maternal involvement and responsiveness (Evans, Whittingham, & Boyd, 2012). This was taken into account already in the first session, which was dedicated to enhancing the parent–child relationship by waiting for a moment where the child was able to enter a quite alert state and supported to display the best alertness possible. In the following sessions, parents were helped to understand how early biological regulation continuously interacts with the child's availability and self-regulation. Homeostatic stability, sleep–waking cyclic patterns, and the maturity of state regulation are closely associated with the infant's later patterns of interaction (Feldman, 2006). The child's regulatory competence was explored by helping parents recognize signs of well-organized systems versus arousal and signs of stress. At the same time they were helped to make adequate adjustments to these signs and to discover changes as the child matured.

Several mechanisms are likely to be involved in behavior regulation throughout childhood. In infancy, a more flexible maturation from biological rhythms to early social rhythms strengthens the parent–child synchrony (Feldman, 2006) and makes more finely tuned face-to-face interactions possible. This has been shown to strengthen the child's self-regulatory competence (Feldman, Greenbaum, & Yirmiya, 1999; Olafsen et al., 2006; Olafsen et al., 2012). Improved self-regulation is a predictor of fewer behavioral problems in preschool children (Feldman, 2009), and the beneficial effect was assumed to continue into middle childhood years, as has been documented for children diagnosed with disabilities (Hauser-Cram et al., 2001). This study hypothesized that the early intervention would improve long-term behavioral and socioemotional development in premature children. This hypothesis was supported by intervention effects already published: less parenting stress reported until age 2, improved regulatory competence in infancy and significantly improved cognitive, and behavioral outcomes at age 5 (Kaaresen, Rønning, Ulvund, & Dahl, 2006; Nordhov et al., 2010; Nordhov, Rønning, Ulvund, Dahl, & Kaaresen, 2012; Olafsen et al., 2008; Olafsen et al., 2012). In the Vermont study, Rauh, Achenbach, Nurcombe, Howell, and Teti (1988) suggested that the intervention had fostered transactional patterns that began to interact with the children's development after infancy, characterized as a possible "sleeper effect" in a later study (Achenbach et al., 1993). We lean upon later research showing how the development of regulative behavior seems to be crucial in overall child development (Feldman, 2006, 2009).

This study investigated the long-term intervention effects on behavioral development of preterm children until age 9. Both longitudinal and cross-sectional investigations were incorporated in the

analysis. The following questions were asked: (a) Does an early intervention influence longitudinal behavioral-emotional development, as reported by parents and teachers until age 9? (b) Does an early intervention influence behavioral outcomes, social competence, and adaptive behavior in school as perceived by parents and teachers at ages 7 and 9? (c) Are specific BW groups or genders particularly affected by the intervention? (d) How does the behavioral development of preterms (with and without intervention) compare to the behavioral development of full-term children?

Method

Participants

The Tromsø Intervention Study on Preterms (TISP) is a randomized, controlled study of preterm infants with BW < 2000 g, born at the University Hospital of North Norway between March 1999 and September 2002 (Rønning, Dahl, Ulvund, Kaaresen, 1999). Decisions on sample size were based on the results of a previous study by Achenbach et al. (1993) and were calculated to detect a group difference in Bayley's Mental Developmental Index (MDI; Bayley, 1993) at age 2 of 7.5 points (corresponding to a 0.5 *SD* difference) with 80% probability (Kaaresen et al., 2006). Preterm infants were randomized in blocks of six to form a preterm intervention group (PI; $n = 72$) and a preterm control group (PC; $n = 74$), stratified within gestational age (GA) < 28 weeks. Infants of non-Norwegian-speaking parents and infants diagnosed with severe neurological or sensory impairments were excluded (Figure 1). Children identified with disabilities at later follow-ups continued in the study if able to participate in the age-appropriate assessments. Subanalyses, with children nearly reaching this criterion, were included and will be reported. Healthy newborn infants (GA ≥ 37 weeks) were recruited from the maternity ward at the same hospital as a term reference group (TR; $n = 75$). The PC group followed the Neonatal Intensive Care Unit (NICU) guidelines for discharge of preterm infants. The TR group was examined once by a pediatrician, routinely on the 3rd day of life. Baseline data for each group (Table 1) have previously been described in detail (Kaaresen et al., 2006).

Intervention

The intervention program was a modified version of the Mother–Infant Transaction Program (MITP; Rauh, Nurcombe, Achenbach, & Howell, 1990). Each intervention consisted of seven 1-hr sessions with parents and their baby during the last week before discharge, and four home visits 1, 2, 4, and 12 weeks postdischarge. All sessions were performed in a separate, quiet room with the baby, mother, father (when available), and the intervention nurse. One exception was the initial session where parents met the nurse without the baby present. The interventions were adapted to each family's needs, but strictly followed the topics as described in the MITP manual (Rauh et al., 1990). The seven sessions in the hospital had different agendas, which can briefly be listed as: (a) an exploration of the infant's regulation and social competencies; (b) signs of stress and stability in the homeostatic system and (c) the motoric system, with focus on tone, posture, and movements; (d) the infant's regulation of states and transition's between these; (e) how parents could help the infant become alert and available for interactions; and (f) how to use this knowledge in daily caretaking such as bathing. In the last hospital session all topics were discussed, the parents asked questions, and elements were repeated if asked for.

The first home visit dealt with the families' adaptation to the new environment and how they made adjustments with the infants' needs in mind. In the next visit, parent–child social interactions were addressed and parents' stories about new activities were applauded. The third visit, 1 month after discharge, focused on parents' observations of their infant's behavioral style and on how they could adapt to the rhythms and capacities of their infant. In the last visit at 3 months postdischarge, the program was summed up and changes that had appeared were reviewed with the parents. At this time most of the families expressed that they had identified some useful rhythms and routines in their daily life.

Finalizing the program at this age was justified by the ending of the original study and because it made up an intervention that could realistically be implemented with the financial and professional resources available. Mothers participated in all sessions, while fathers participated on average in 6 of the 12 sessions (interquartile range = 4–10 sessions). Eight nurses were trained to perform the interventions, and each family was followed by the same nurse throughout all the sessions with no additional contact afterward. Unlike the original study, no logbooks were given to the families after the interventions were finished. Completion of the intervention

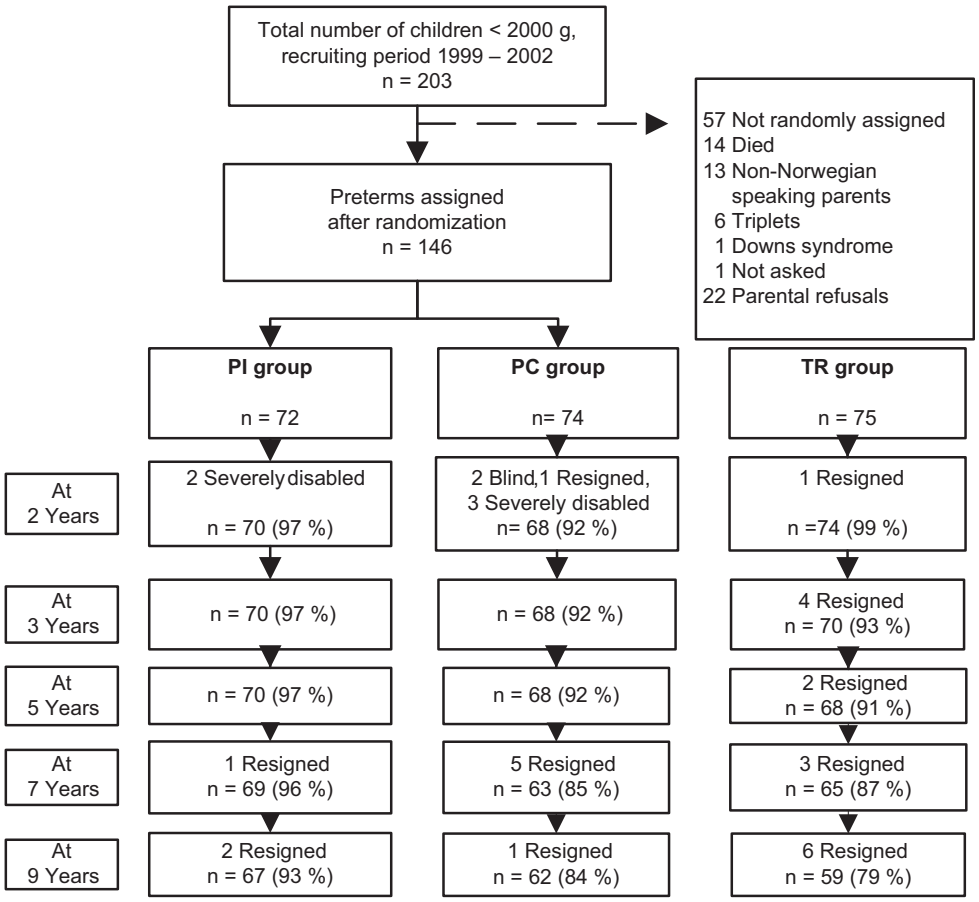

Figure 1. Study flow diagram from ages 2 to 9. PI = preterm intervention; PC = preterm control; TR = term reference.

was ensured by review of logbooks by the study director (J. A. Rønning).

Instruments

Mothers and fathers reported independently on their children's behavioral problems by completing the Child Behavioral Check List (CBCL/2–3 and CBCL/4–18) at ages 2, 3, 5, 7, and 9 years, (Achenbach, 1991a, 1992). Teachers, who were blind to the children's group affiliations, reported on the Teachers Report Form (TRF) at the ages of 7 and 9 years, (Achenbach, 1991b). Both CBCL and TRF provide standardized measures of child and adolescent emotional/behavioral problems and social competences. Behavioral outcomes are summarized as total problems and broadly scaled on Internalizing and Externalizing dimensions. *Internalizing behavior* consists of the subscales withdrawn, anxious/depressed, and somatic problems, whereas *externalizing behavior* consists of the subscales aggressive and delinquent problems in the CBCL/4–18 and the TRF questionnaires. Behavioral problems were also rated on subscales related to thoughts, social life and attention. Differences between the outcomes of CBCL and TRF take the different environments in which child behavior is observed into account (Achenbach, 1991b, 1992). Parents and teachers also answered questions related to peer problems, prosocial behavior, and the impact supplement extracted from the Strengths and Difficulties Questionnaire (SDQ) at age 9 (Goodman & Scott, 1999). Childbirth and perinatal risk factors were collected before discharge as Clinical Risk Index for Babies (CRIB), existence of bronchopulmonary dysplasia, and existence of several cerebral injuries (Table 1). Parents reported their use of help seeking on behalf of their children at every follow-up. These included type of contact (physiotherapy, child habilitation, child psychiatry services, special educational services, and child welfare authorities), children's age when the contact was initiated, and duration of contact. Social variables (mother's age, years of education, annual income, number of sib-

Table 1
Birth, Medical, and Demographic Characteristics of Infants and Parents

	PI group (n = 72)	PC group (n = 74)	TR group (n = 75)
Infant characteristics			
BW (g), $M \pm SD$	1,396 ± 429	1,381 ± 436	3,619 ± 490
400–1,000 g, n (%)	20 (28)	20 (27)	
1,001–1,500 g, n (%)	15 (21)	20 (27)	
1,501–2,000 g, n (%)	37 (51)	34 (46)	
GA (week), $M \pm SD$	30.2 ± 3.1	29.9 ± 3.5	39.3 ± 1.3
< 28 weeks, n (%)	17 (24)	19 (27)	
28–32 weeks, n (%)	36 (50)	37 (50)	
≥ 33 weeks, n (%)	19 (26)	18 (24)	
Boy, n (%)	38 (53)	39 (53)	40 (54)
Twin, n (%)	16 (22)	14 (19)	0
Parental steroid use, n (%)	53 (74)	57 (77)	
SNAP II, $M \pm SD$	8.3 ± 10.9	10.4 ± 11.3	
CRIB score (N = 85), $M \pm SD$	3.2 ± 2.8	2.7 ± 2.9	
Received ventilation, n (%)	29 (40)	37 (50)	
Duration of ventilation, n (%)	7.0 ± 18.6	7.1 ± 17.3	
Postnatal steroid use, n (%)	9 (13)	10 (14)	
Oxygen therapy at 38 weeks GA, n (%)	11 (15)	14 (19)	
Abnormal cerebral ultrasound, n (%)			
IVH Grade 1 or 2	7 (10)	8 (11)	
IVH Grade 3 or 4	3 (4)	5 (7)	
Periventricular leukomalacia	4 (6)	8 (11)	
Maternal and social characteristics			
Mother's age (years), $M \pm SD$	30.8 ± 6.1	29.1 ± 6.4	29.7 ± 6.1
Firstborn child, n (%)	40 (56)	37 (54)	27 (37)
Mother's education[a] $M \pm SD$	14.6 ± 2.8	13.5 ± 3.2	14.9 ± 2.8
Father's education[a] $M \pm SD$	13.8 ± 3.1	13.5 ± 3.2	14.4 ± 3.2
Mother's monthly income[b]	15.8 ± 7.7	14.6 ± 6.7	15.9 ± 8.0
Father's monthly income[b]	21.1 ± 8.7	19.9 ± 8.1	21.9 ± 9.8

Note. BW = birth weight; CRIB = Clinical Risk Index for Babies; GA = gestational age; IVH = intraventricular hemorrhage; PC = preterm control; PI = preterm intervention; *SD* = standard deviation; SNAP II = Score of Acute Neonatal Physiology II; TR = term reference.
[a]Education in years. [b]In Norwegian 1,000 kroner, calculated for 131 families due to 15 twins.

lings, etc.) were reported by parents on separate questionnaires before discharge from hospital.

Follow-Up Procedures

For the purpose of the study, all participating children received the same medical, developmental, and psychosocial assessments at corrected ages of 6 months and 1, 2, 3, 5, 7, and 9 years. All assessors were blind to the children's group allocation. Questionnaires were collected and families were followed up by a study coordinator at each follow-up session. Parents received written reports about the child's motor and cognitive development after every follow-up. These included recommendations about referrals to other services if relevant, signed by the study director. All results are reported as intention to treat, and the study was approved on three occasions by the regional committee for medical ethics and the Norwegian Data Inspectorate (1999, 2005, and 2010). The study is registered in the ClinicalTrials.gov, NCT00222456.

Analysis

Calculated t scores based on normative samples were used in longitudinal analyses across CBCL/2–3 and CBCL/4–18 as the questionnaires have some different items and different numbers of items. Mean raw scores were used in cross-sectional and descriptive statistics as recommended by Achenbach (1991a, 1991b, 1992). In the longitudinal linear mixed-model analyses, time was treated as a continuous variable. Predicted mean group differences

on each measurement occasion with 95% confidence intervals were also computed. This analysis was still based on a longitudinal model, but in this case time was treated as a categorical variable (Twisk, 2006). By changing the reference time point in the analysis, predicted group differences on each occasion could be estimated. Because of repeated measures and the clustering effects of twin pairs, all the analyses were generated with linear mixed models (LMMs; SPSS statistics, version 20), generating adjusted mean scores for each follow-up age. On Level 1 (within measurements) the covariance structure is the one implied by the standard multilevel model (Singer & Willett, 2003). On Level 2 (within family), a variance components structure was used since the correlation between the slope and the intercept was generally low. Dichotomized variables were analyzed by generalized LMMs, which generated odds ratios adjusted for clustering effects of twin pairs. Effect sizes (ESs) in LMMs were mostly computed as pseudo R^2 and based on the square of the correlation between observed and predicted values of the dependent variable (Singer & Willett, 2003). When assessing the effect of adding variables in a LMM analysis, the change in this pseudo R^2 value is given as an ES measure. For analysis of treatment group comparisons an ES as Hedges' g was computed (Hedges & Olkin, 1985).

Parental agreement was analyzed by intraclass correlations (ICCS) and the difference between the two independent ICC coefficients for the PI and PC groups was tested as described by Alsawalmeh and Feldt (1992).

Results

Participant randomization resulted in well-balanced preterm groups, except for a difference of 1 year in maternal education in favor of the intervention group (Table 1). Thus, maternal education is controlled for in all analyses. In the PI group, fathers with fewer years of education participated in fewer interventional sessions than fathers with more years of education ($F = 4.8$, $p = .03$). Other variables had no significant impact on fathers' participation. Possible implications related to inclusion criteria, outliers, fathers' participation, and parental agreement in the preterm groups will be reported in a final separate paragraph.

The dropout rates were low in all groups throughout the study (Figure 1 and Table 2), and 129 preterms (88%) were still attending the follow-up session at 9 years of age.

Evaluation of Longitudinal Behavioral Development

In responses to the first question, parents did not report different developmental patterns between preterm groups on any of the CBCL problem scales from the age of 2 until 9, nor did teachers report any interactions between groups and age on TRF dimensions from 7 to 9 years. Nonsignificant differences in favor of the PI group were reported (Table 3). The number of problems reported remained at a relatively low level compared to those reported by Achenbach (1991a, 1991b; Figures 2 and 3).

Different patterns were displayed in parents' and teachers' evaluations of internalizing versus externalizing behavior in the preterm groups (Figures 2 and 3). Across groups, all informants reported increased internalizing behavior with age. Teachers also reported increased externalizing behavior, whereas parents reported diminishing levels of problems of externalization. There was considerable variation in parents' and teachers' assessments of the children, as indicated by the high standard deviations in both preterm groups (Table 3).

Table 2
Frequencies of Parents' and Teachers' Reports on Child Behavioral Problems and Competencies

Respondent	PI group (n = 72), n (%)[a]	PC group (n = 74), n (%)[a]	TR group (n = 75), n (%)[a]
2 years			
Mother (CBCL)	62 (86)	59 (80)	63 (84)
Father (CBCL)	57 (79)	49 (66)	59 (79)
3 years			
Mother (CBCL)	69 (96)	66 (89)	67 (89)
Father (CBCL)	60 (83)	53 (72)	58 (77)
5 years			
Mother (CBCL, SDQ[b])	68 (94)	63 (85)	65 (87)
Father (CBCL, SDQ[b])	62 (84)	52 (70)	58 (77)
Preschool teacher (SDQ[b])	60 (83)	54 (73)	59 (79)
7 years			
Mother (CBCL)	68 (94)	64 (87)	63 (84)
Father (CBCL)	56 (78)	53 (72)	55 (73)
Teacher (TRF)	58 (81)	55 (74)	56 (75)
9 years			
Mother (CBCL, SDQ[b])	66 (95)	61 (82)	61 (81)
Father (CBCL, SDQ[b])	55 (76)	50 (68)	53 (71)
Teacher (TRF, SDQ[b])	58 (81)	55 (74)	57 (76)

Note. CBCL = Child Behavior Checklist; PC = preterm control; PI = preterm intervention; SDQ = Strengths and Difficulties Questionnaire; TR = term reference; TRF = Teachers Report Form.
[a]Number of reports and percentage of the original number of participants in the group. [b]Questions extracted from the SDQ.

Table 3
Differences Between the PI and PC Groups as Reported by Mothers and Fathers at 2, 3, 5, 7, and 9 Years of Age on CBCL Main Behavioral Domains

Mean score (*SD*) Adjusted difference, 95% CI[a]	2 years		3 years		5 years		7 years		9 years	
	PC	PI	PC	PI	PC	PI	PC	PI	PC	PI
Total problems										
Mother	31.2 (16.8)	27.4 (15.3)	31.0 (20.1)	28.9 (16.8)	21.6 (16.0)	17.2 (12.6)	22.0 (18.7)	17.6 (16.0)	20.3 (21.2)	17.0 (19.8)
	3.8 [−2.6, 10.2]		1.2 [−4.9, 7.4]		4.2 [−2.0, 10.4]		3.5 [−2.7, 9.7]		2.9 [−3.2, 9.1]	
Father	24.3 (12.2)	22.6 (15.4)	24.8 (13.6)	21.1 (14.6)	17.4 (15.9)	12.5 (8.3)	16.7 (13.4)	10.8 (13.9)	16.8 (25.3)	10.8 (11.2)
	2.9 [−2.9, 8.7]		4.9 [−0.8, 10.6]		5.0 [−0.6, 10.7]		5.4 [−0.3, 11.1]		5.4 [−0.3, 11.2]	
Internalizing										
Mother	7.1 (4.8)	6.2 (4.3)	6.8 (5.1)	5.9 (4.5)	4.5 (4.4)	3.6 (3.5)	5.3 (5.1)	4.6 (4.2)	5.0 (5.4)	4.7 (5.8)
	1.1 [−0.7, 2.8]		0.8 [−0.9, 2.4]		1.0 [−0.6, 2.9]		0.5 [−1.2, 2.1]		0.3 [−1.4, 2.0]	
Father	5.3 (3.4)	4.5 (3.7)	5.4 (4.0)	4.6 (4.1)	2.9 (3.1)	2.9 (2.6)	3.4 (3.7)	2.4 (3.6)	4.1 (7.5)	3.0 (4.0)
	1.0 [−0.6, 2.5]		1.1 [−0.4, 2.7]		0.4 [−1.2, 1.9]		1.0 [−0.5, 2.6]		1.1 [−0.5, 2.7]	
Externalizing										
Mother	10.8 (7.4)	9.3 (5.9)	11.2 (8.2)	10.3 (6.1)	7.9 (6.6)	6.1 (5.4)	7.1 (7.5)	6.0 (6.9)	6.6 (7.8)	5.2 (7.9)
	1.4 [−1.1, 4.0]		0.3 [−2.2, 2.8]		1.3 [−1.2, 3.8]		0.5 [−1.9, 3.0]		0.9 [−1.6, 3.4]	
Father	8.9 (5.5)	7.6 (5.6)	8.9 (5.7)	6.8 (5.1)	6.3 (7.2)	4.4 (3.5)	5.5 (6.2)	3.8 (5.9)	5.2 (9.2)	3.1 (4.0)
	1.6 [−0.7, 3.9]		2.4 [−0.2, 4.6]		1.8 [−0.4, 4.0]		1.3 [−0.9, 3.5]		1.7 [−0.6, 3.9]	

Note. CBCL = Child Behavior Checklist; PC = preterm control; PI = preterm intervention.
[a]Adjusted difference for repeated measures and clustering effects of twin pairs by use of linear mixed models.

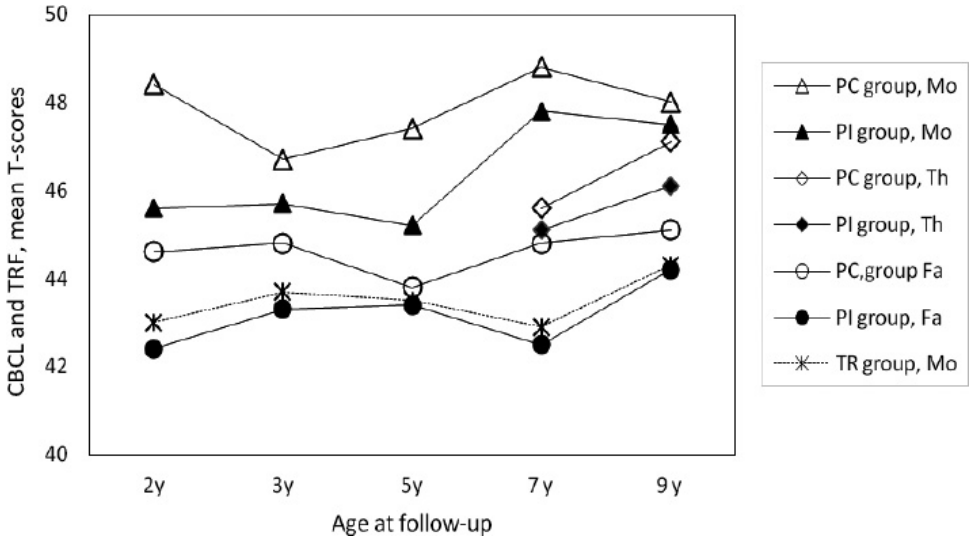

Figure 2. Parents and teachers report on CBCL/TRF, internalizing problems in the PI and PC groups from ages 2 to 9. Because mothers and fathers reported on different questionnaires through childhood (CBCL/2–3 and CBCL/4–18); CBCL = Child *t* scores and not mean scores are presented. A *t* score = 50 represents raw scores at the 50th percentile in a normative American sample (Achenbach, 1991a, 1991b, 1992). PC = preterm control; PI = preterm intervention; TR = term reference; CBCL = Child Behavior Checklist; TRF = Teachers Report Form; Mo = mothers; Fa = Fathers; Th = Teachers.

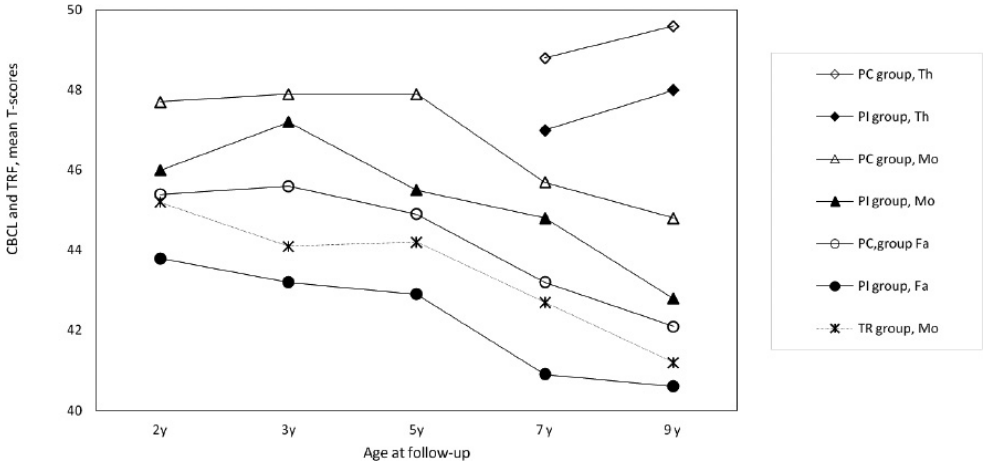

Figure 3. Parents and teachers report on CBCL/TRF, externalizing problems in the PI and PC groups from ages 2 to 9. Because mothers and fathers reported on different questionnaires through childhood (CBCL/2–3 and CBCL/4-18); *t*-scores rather than mean scores are presented. A *t*-score = 50 represents raw scores at the 50th percentile in a normative American sample (Achenbach, 1991a 1991b, 1992). PC = preterm control; PI = preterm intervention; TR = term reference; CBCL = Child Behavior Checklist; TRF = Teachers Report Form; Mo = mothers; Fa = Fathers; Th = Teachers.

Cross-Sectional Differences Between Preterm Groups at Ages 7 and 9

The responses to the second question will be presented in two sections as behavioral problems are reported first and subsequently reports about perceived competencies.

Behavioral Problems

Fewer attention problems in the PI group were reported by mothers, $F(1, 118) = 6.3$, $p = .01$, ES = 0.48; fathers, $F(1, 95) = 4.8$, $p = .03$, ES = 0.48; and teachers, $F(1, 102) = 6.6$, $p = .01$, ES = 0.48, at age 7. Teachers also reported a significant difference

on attention problems at age 9 (see Table 4). At 9 years, both fathers, $F(1, 92) = 8.6$, $p = .004$, ES = 0.52, and teachers (see Table 4) reported lower scores on thought problems in the PI group than in the PC group.

At age 9, teachers perceived fewer difficulties in the PI group than in the PC group, $F(1, 97) = 5.5$, $p = .02$, ES = 0.48. The SDQ question: "Does the child have difficulties?" was subsequently recoded as two categories: (a) absent/minor or (b) definite/severe problems. The PC group had odds that were almost 3 times as high of being perceived as having definite or severe difficulties by teachers at age 9, $t(212) = 2.2$, $p = .03$, OR = 2.9, 95% CI [1.1, 7.6]. Parental evaluations of difficulties corresponded with those of teachers, close to significance for mothers, $F(1, 112) = 3.7$, $p = .058$, ES = 0.39. Fathers in the PI group, who initially had reported their child to have difficulties, perceived more seldom these difficulties as affecting peer relationships compared to fathers in the PC group, $F(1, 31) = 5.5$, $p = .02$, ES = 0.79. A significant correlation between teachers' reports of difficulties and parent's reports regarding referrals to specialized child and adolescent psychiatric services was uncovered, $F(1, 110) = 38.1$, $p < .001$, $r = .57$. Children in the PC group were more than twice as frequently referred as children in the PI group.

Perceived Competences

Generally speaking, in accordance with teachers (Table 4) mothers and fathers perceived a better adaptation to school in the PI group at the ages of 7 and 9 than in the PC group, as reported on the CBCL, total competence scale. At age 9 this generated moderate ESs: mothers, $F(1, 108) = 5.4$, $p = .02$, ES = 0.50, and fathers, $F(1, 84) = 8.6$, $p = .004$, ES = 0.62). A new variable named "school problems" was defined as a score below the 10th percentile for term children of the same sex and age on the variable TRF, academic performance. The PC group experienced significantly more school problems than the PI group at the age of 9, $t(109) = 2.7$, $p = .009$, OR = 3.7, 95% CI [1.4, 9.7].

Outcomes Related to Interactions With Children's BW and Gender

Responses to the third question revealed 1 three-way interaction with group, age, and BW, and 2 three-way interactions with group, age, and gender.

Three-Way Interaction Between Preterm Groups, Age, and BW Groups

Preterm groups were split into subgroups according to whether BW was more or less than

Table 4
Teachers' Reports on Children's Behavioral Problems and Perceived Competences at Age 9 as Reported on TRF

	PI group (n = 55)	PC group (n = 58)	Adjusted mean differences [95% CI]	p	ES[a]	TR group (n = 57)
Reported problems						
Total, *M* (*SD*)	12.4 (13.9)	18.5 (18.5)	−6.1 [−12.2, 0.0]	.06*	0.45	10.4 (16.9)
Internalizing	3.3 (4.5)	3.7 (4.6)	−0.4 [−2.1, 1.2]	.61	0.08	2.1 (3.2)
Externalizing	3.6 (5.5)	5.0 (6.6)	−1.4 [−3.7, 0.8]	.20	0.23	4.3 (7.5)
Social	0.9 (1.7)	1.7 (2.4)	−0.8 [−1.6, −0.1]	.09*	0.38	0.9 (1.9)
Thought	0.2 (0.5)	0.6 (1.3)	−0.4 [−0.7, 0.0]	.05	0.40	0.1 (0.5)
Attention	4.7 (5.4)	7.8 (8.4)	−3.1 [−5.7, −0.5]	.02	0.43	3.1 (5.1)
Aggressiveness	3.1 (4.9)	4.4 (5.9)	−1.3 [−3.3, 0.7]	.20	0.24	3.8 (6.6)
Hyper impulsiveness	2.7 (3.0)	4.3 (4.8)	−1.6 [−3.1, −0.1]	.04	0.39	1.9 (3.4)
Inattention	3.5 (4.2)	5.8 (6.4)	−2.3 [−4.3, −0.3]	.04	0.42	2.2 (3.5)
Perceived competencies						
Academic performance	3.1 (0.5)	2.8 (0.8)	0.3 [0.1, 0.6]	.009	0.45	3.2 (0.5)
Working hard	4.4 (1.3)	3.7 (1.3)	0.7 [0.2, 1.2]	.01	0.54	4.6 (1.2)
Behaving appropriately	4.7 (1.2)	4.1 (1.3)	0.6 [0.2, 1.1]	.01	0.48	4.4 (1.2)
Learning	4.3 (1.3)	3.6 (1.4)	0.7 [0.2, 1.2]	.01	0.52	4.6 (1.1)
Happy	4.4 (1.0)	4.2 (0.8)	0.2 [−0.1, 0.6]	.3	0.22	4.4 (1.0)
Sum of competence items	17.9 (4.0)	15.6 (3.7)	2.3 [0.8, 3.7]	.004	0.60	18.1 (3.6)

Note PC = preterm control; PI = preterm intervention; TR = term reference; TRF = Teachers Report Form.
[a]Effect size (EF) = Hedges' *g*.
*Before adjusting for twin pairs the differences between preterm groups were significant at the .05 level.

1,000 g. A significant three-way interaction between preterm groups, age, and BW on externalizing problems was reported by fathers, $F(1, 417) = 4.5$, $p = .03$. The three-way interaction increased the pseudo R^2 by .029 units. Throughout childhood, fathers reported the heaviest children in the PC group as having more externalizing problems than the other three subgroups (Figure 4).

Three-Way Interaction Between Preterm Groups, Age, and Gender

Mothers reported a three-way interaction between group, age and gender on problems of withdrawal from age 2 until 9, $F(1, 484) = 4.3$, $p = .04$. The three-way interaction increased the pseudo R^2 by .012 units. Mothers of the PC group reported boys as being at a higher level through all preschool ages. However, by age 9 this had fallen to a score close to that of the PI boys. On the other hand, girls were reported to be on the same level in both groups until the age of 7 (within a range of one *t*-score unit). At age 9 the difference between PI and PC girls had increased, as the PI girls were reported to have fewer withdrawn problems than the PC girls.

The second interaction involving group, age, and gender was found in fathers' reports on CBCL anxious/depressed problems from age of 2 until 9, $F(1, 439) = 6.5$, $p = .01$, increased pseudo R^2 by .018. PI and PC fathers reported fewer problems from toddlerhood until age 5 on both boys and girls. From 5 until 9 years of age, the mean score increased for boys in the PC group, while the mean score continued almost unchanged among boys in the PI group. A large part of the increase among the PC boys was due to two persons, which limits the generalizability of this result. Girls in both groups were reported as relatively unchanged from age 5 until 9.

Behavioral Development in Comparison to Term References

No Group × Age interactions between the PI and TR groups were found on any dimensions of behavioral problems. However, one Group × Age interaction was found between the PC and TR group on CBCL, anxious/depressed problems, $F(1, 441) = 9.2$, $p = .003$, increased pseudo R^2 by .013 units, as reported by fathers. The PC and TR groups were scored at similar levels until age 5, but gradually increasing problems were reported at ages 7 and 9 in the PC group.

In cross-sectional analyses significant differences were found on most CBCL behavior dimensions between the PC and TR groups at all follow-ups until age 9. Few significant differences were revealed between the PI and TR groups. At 9 years, no significant differences were reported between the PI and TR groups by mothers, fathers, or teachers.

Results Related to Inclusion Criteria, Outliers, and Respondents

Analyses Related to Inclusion Criteria and Deviant Variable Values

When behavior problems reported on children with disabilities (two in the PI group) were

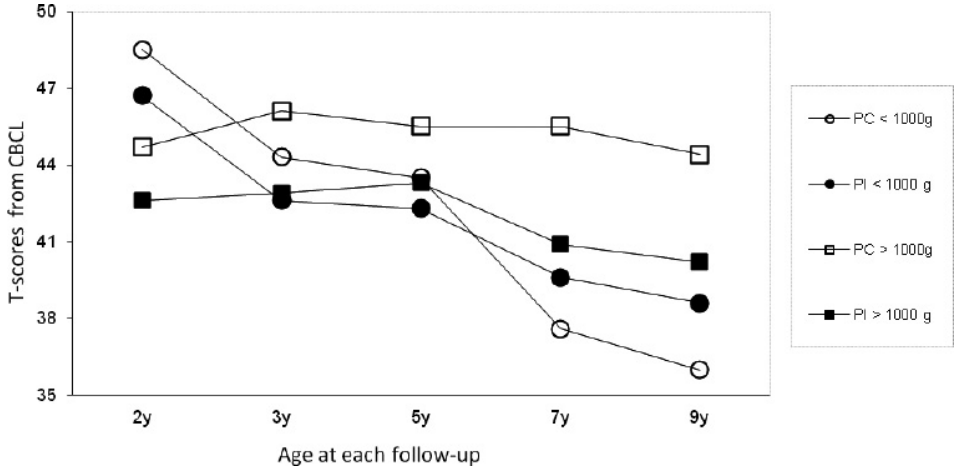

Figure 4. Three-way interaction between group, age, BW, and externalizing problems from age 2 until 9. PC = preterm control; PI = preterm intervention; BW = birth weight; CBCL = Child Behavior Checklist.

included in the analyses, fewer differences between preterm groups remained significant. They were unable to carry out the age-appropriate assessment but the families found it valuable to continue to participate in the study. Teachers' reports of more difficulties in everyday life in the PC group were still evident ($p = .03$).

Data were methodically controlled for potentially disruptive effects of outliers. The consistency was found to be high, with one exception (one child). When these scores were excluded at age 9, several significant differences in favor of the PI group became evident (fewer attention problems and difficulties as reported by mothers, and fewer total and social problems as reported by teachers).

Outcome Variations in the PI Group Related to Fathers' Participation

Fathers participated on average in 6 of 12 sessions (interquartile range = 4–10 sessions). Differences in participation did not influence fathers' reports at age 7. At age 9 fathers who had participated less reported more externalizing problems, $F(1, 98) = 7.5$, $p = .01$, characterized by more aggressive behavior, $F(1, 98) = 6.9$, $p = .01$. These differences were explained by father's length of education, as fathers with relatively less education reported more problems.

Parental Agreement in Ratings of Behavioral Problems

On CBCL main dimensions, the level of agreements between parents in the PC and PI groups changed across childhood. The agreement was higher in the PI group on internalizing scores at age 2 ($ICC_{PC} = 0.26$, $ICC_{PI} = 0.57$, $p = .03$; Alsawalmeh & Feldt, 1992). At age 9 contrary differences were uncovered as agreement between PC parents was higher in reports of externalizing behavior ($ICC_{PC} = 0.76$, $ICC_{PI} = 0.53$, $p = .01$) and total problems ($ICC_{PC} = 0.79$, $ICC_{PI} = 0.63$, $p = .03$).

Discussion

The basic hypothesis in this study was that the intervention could make the immature expressions characterizing preterm infants interpretable for parents and thereby enhance the formation of positive transactions and foster longlasting developmental benefits. Main findings are that the longitudinal trajectory of behavior development, reported on preterm groups until age 9, was not affected by the early intervention even though the intervention may have promoted some protective effects regarding anxious behavior in the PI group. At ages 7 and 9 fewer attentional problems and a better adaptation to school were reported by mothers, fathers, and teachers in the PI group, and similarly, teachers reported a lower incidence of experiencing definite or severe difficulties in everyday life in the PI group. Both preterm groups followed the same trajectory as the TR group, except for a greater likelihood of anxious/depressed behavior in the PC group. Interestingly, at age 9 there were no statistical differences between the PI and the TR group regarding problems or competencies. These findings are consistent with those of the original MITP study (Achenbach et al., 1993). Thus, the basic hypothesis was largely confirmed.

First, similar trajectories of behavior development were reported in the PI and PC groups. From 3 years of age externalizing behavior decreased in both groups while slightly growing internalizing behavior was reported until age 9. Both patterns were consistent with main behavioral dimensions reported in the TR group and normative patterns reported by Bongers et al. (2003). In addition, relatively low levels of problems were reported in TISP, compared to nonintervention studies (Achenbach, 1991a, 1991b; Bongers et al., 2003; Elgen et al., 2002; Hall & Wolke, 2012; Taylor, Klein, Minich, & Hack, 2000). Few children were reported to have more than minor problems in any of the groups. This is consistent with the pattern reported by Hall and Wolke (2012), who found a 75% rate of low emotional problems in a cohort of premature children. As in Elgen et al. (2003), abnormal problems were defined as CBCL, total problems reported above the 90th percentile for the same gender in the term control group. The prevalence of abnormal problems was reported at 15% (mothers and fathers) in the PI group and correspondingly 16% (fathers) and 26% (mothers) in the PC group. Analogous reports from teachers were 11% in the PI group and 20% in the PC group. Elgen et al. (2002) reported abnormal behavioral problems in 40% of their sample and a rate of psychiatric diagnoses at 27% among preterms at 11 years of age (BW < 2,000 g). Comparisons are nevertheless uncertain. We suggest that the low level of problems identified could also be the result of a general strengthening effect caused by the follow-ups, as parents repeatedly received feedback on their child's development.

Internalizing behavior was reported to increase with age across all groups, but parents of preterms generally reported at levels higher than those reported for. This corresponds to reports of more

frequent internalizing and socioemotional problems among preterms than term peers throughout childhood (Aarnoudse-Moens et al., 2009; Loe, Lee, Luna, & Feldman, 2011). On the other hand, gradually diminishing levels of externalizing problems were reported by parents, while teachers reported externalizing problems to rise until age 9. Differences between parents, and teachers, reports may be due to unequal child–adult relationships, environments, and activities where children were observed (Grietens et al., 2004). Bongers et al. (2003) reported that boys displayed more externalizing behavior than girls and a similar tendency was evident across ages in this study, although not statistically significant. In 81% of the studies reviewed by Bhutta et al. (2002), preterm born children were identified as at risk of more externalizing problems than were terms. Other studies have confirmed the falling trend in our data (Aarnoudse-Moens et al., 2009).

Agreement between parents' reports was higher in the PI group compared to the PC group at age 2 (internalizing dimension) but at similar levels across groups from ages 3 to 7. However, at age 9 higher agreements were reported from PC parents (externalizing and total problems) compared to PI parents. Higher agreement is supposed to indicate more shared views (Buehler et al., 1997). In toddlerhood (age 2) the knowledge offered by the intervention may have raised PI parents' sensitivity and endeavoring to interpret children's behavior and feelings, while these challenges may have been more concealed for PC parents. In contrast, at age 9 PC parents reported more challenges among their children and this may have increased their unanimity.

Several cross-sectional differences were identified between the preterm groups at ages 7 and 9. The most pronounced was that the early intervention seems to have strengthened the children's attention. Aarnoudse-Moens et al. (2009) reported increased attentional problems to be a lasting challenge for premature children, ~0.5 *SD* higher than their term peers. Others have confirmed this, showing the connection between prematurity and attentional problems to be mediated by slow responses and deficits in visuospatial working memory (de Kievet, van Elburg, Lafeber, & Oosterlaan, 2012) and impaired cognitive outcomes (Loe et al., 2011). Attentional problems are also thought to be a strong predictor of adaptive problems and academic underachievement (Mulder, Pitchford, Hagger, & Marlow, 2009), and this relates to the next important finding: Both parents and teachers reported the PI group to perform significantly better in school than the PC group. It is promising that the PI group seems to have improved their ability to adapt to school, which is a frequently described major challenge for preterm born children (Aylward, 2005; Bhutta et al., 2002). Significantly more school problems were revealed in the PC group compared to the PI group at age 9. Despite this, at age 9 PC and PI group parents reported similar frequencies of contact with pedagogical psychological services (34% and 28%, respectively). The prevalence is 10 times as high as among the term controls (3%), but moderate compared to about 50% reported by Aylward (2005). The discrepancies between these two findings (similar use of special services but differences in perceived academic performance) may be due to a proactive approach being taken by parents in the PI group, for example, by asking at an early stage for help.

Blind to children's group allocation, teachers of PC children reported more perceived difficulties than the teachers of the PI group at age 9. This result was significantly associated with parents' reports regarding referrals to specialized child and adolescent psychiatric services. Perceived difficulties were reported on the single SDQ question: "Does your child have difficulties?" which has been described as having a strong predictive value for the child's later mental health (Goodman, 1999; Goodman & Goodman, 2011). Children in the PC group were more than twice as often referred as the PI group. This finding may indicate a preventive intervention effect regarding children's mental health problems. The risk of psychiatric disorders among children has been investigated by comparing high scores on parents' ratings of problems. In a study screening for child psychiatric disorders, CBCL total problem scores ≥ 35 were regarded as an appropriate cutoff point and a prevalence of 10.1% among 8- to 9-year-old schoolchildren were reported (Bilenberg, Petersen, Hoerder, & Gillberg, 2005). With a similar cutoff, 18% of the PC group scored in the clinical area while 11.8% in the PI group met this criterion (nonsignificant difference).

Our third question returned to the longitudinal investigation. Analyses revealed two outcomes of behavior where the group allocation may have affected preterm girls and boys differently and one variable where behavior development varied related to the degree of prematurity. First, PC mothers reported their sons closer to PI boys with increasing age with respect to withdrawn behavior, whereas daughters in the PC group were reported

with higher levels of withdrawn behavior at ages 7 and 9 than PI daughters. Second, fathers reported that PC boys displayed more anxious/depressed behavior than PI boys from age 5 to 9, whereas girls were reported at quite similar levels throughout childhood. These two interactions address aspects of internalizing behavior and are of particular interest as higher incidences of anxious and depressed behaviors have repeatedly been reported among premature born children (Johnson & Marlow, 2011; Loe et al., 2011). However, the ESs are small and these interactions may have appeared by chance.

Third, we uncovered different trajectories in fathers' reports of externalizing behavior. Preterms with BW > 1,000 g in the PC group were reported to display more externalizing problems from ages 5 to 9, compared to children with BW > 1,000 g in the PI group and children with BW < 1,000 g in both groups. Previously, less favorable developmental outcomes have been reported among preterms with the lowest weights or GAs (Litt, Taylor, Klein, & Hack, 2005; Saigal et al., 2003). One conceivable reason for the contrasting result may be related to differences in the caretaking offered for fathers in the newborn period. Heavier and medically stable infants stayed in the hospital for shorter periods and their fathers were given limited opportunities to be present and participate in the daily care of their infants (before they were randomized to either the PI or the PC group). Compared to fathers of the most immature children in both groups (with prolonged hospital stay) and PI fathers who participated in the interventions, they received less information and practical guidance on how to understand their baby's cues and expressions. At children's age of 2 the same subgroup of PC fathers reported more child-related stress than the other subgroups and this may have been an early indicator of the same phenomena (Kaaresen et al., 2008). Parenting stress is a strong predictor of both present and later child behavior problems (Gray et al., 2004). At least this result emphasizes the need to ensure that fathers of preterm infants receive adequate amounts of training in seeing, interpreting, and reacting to their infants' cues and expressions.

Finally, we compared behavioral problems reported by PI and PC parents with those reported by parents of term controls. One significant difference in longitudinal development of anxious and depressed behavior was uncovered as fathers reported a more worrisome trajectory of behavior on children in the PC group compared to the TR group. Higher prevalence of internalizing behavior has previously been reported in populations of preterms (Aarnoudse-Moens et al., 2009) and we speculate that the intervention may have offered protective effects as a similar difference not was detected between the PI and TR groups. In addition, significantly more problems were reported in the PC group than in the TR group at all follow-ups. This confirmed the pattern previously described that preterm born children face more problems across childhood compared to term peers (Aarnoudse-Moens et al., 2009; Bhutta et al., 2002). The finding of no cross-sectional differences between the PI and TR groups at age 9 is promising and may indicate that the intervention has contributed to a large degree of normalization related to preterm born children's behavioral development.

Several mechanisms, activated from early childhood, may have contributed to the positive intervention effects found in the PI group at age 9. Olafsen and colleagues (Olafsen et al., 2006; Olafsen et al., 2012) reported that infants in the PI group initiated more social communication at age 1, and in particular enhanced capacity to initiate joint attention was observed among poorly regulated children. Those findings may support the findings of Lawson and Ruff (2004) and Feldman (2009), that a capacity for early focused attention can predict behavioral regulation at age 5. In the first months of life, a period characterized by rapid developmental transitions (Nugent et al., 2007), the infant is completing the change from intrauterine to extrauterine regulation. Schmid et al. (2011) concluded that the amount of maternally initiated contact behavior at a very early developmental stage (assessed at 3 months) may be crucial for children's mental health later in life. An important early regulation of attention and emotion is also taking place (Lavelli & Fogel, 2005). The general focus of the MITP program as designed in the 1980s was to help parents to facilitate and appreciate moments of joint attention with their baby, and thus be able to adjust their own actions so that basic biological rhythms in the child were minimally disturbed (Feldman, 2006). Responsiveness and the quality of face-to-face reciprocity have been described as important contributors to the development of child self-regulation competences, especially in premature children (Evans et al., 2012; Feldman et al., 1999).

Although significant improvements in neonatal care treatments have been introduced since then, similar effects on behavior at age 9 were confirmed in this study. The intervention seems to have had

some unique effects beyond this, due to: (a) the clear structure of parental guidance, (b) introduction of important concepts and understandings about the regulation difficulties of preterms, (c) the enhancement of parental empowerment, and (d) the importance of supporting early social communication between parents and the child. The study by Milgrom et al. (2013) confirms this, as the authors report several positive intervention effects of the MITP as early as at 6 months.

Another important result is the conceit of active involvement and support of fathers. PI fathers, who had participated in relatively few intervention sessions, were less educated and tended to report more externalizing and aggressive behavior at age 9 than those who participated in more interventions. A similar result has been reported by Herbert, Harvey, Lugo-Candelas, and Breaux (2013) as both low paternal socioeconomic status and more paternal depressive symptoms predicted impaired outcomes on a wide range of children's outcomes across early childhood. This highlights the importance of early paternal involvement, especially in less educated families.

Strengths and Limitations

The high participation rate throughout childhood is a major strength of this study. Parents evidently judged the value of the study to be high, and the repeated follow-ups have been a lasting motivational factor. Indeed, the follow-up regime itself could have enhanced parental security. These may have biased our study groups in the direction of lower rates of problems relative to Norwegian general populations of terms and preterms (Jozefiak, Larsson, Wichstrom, & Rimehaug, 2012). Another strength is the study design, whereby preterms were stratified within groups and randomized to intervention or control. The sample size was defined by the aim of finding significant differences between preterm groups at the age of 2 (Kaaresen et al., 2006). The participation rates at 9 years were close to 90%, but the clustering effect of twin pairs in the preterm groups made the sample size somewhat limited. This made analyses of subgroups underpowered and the clinical relevance of results more difficult to interpret.

Other possible limitations of the study are the collection of information about the children's behavior. Parental reports may be highly influenced by their engagement in and knowledge of the study, and these should therefore be treated as subjective information. On the other hand, teachers' reporting on TRF is regarded as being more objective, as teachers were blinded to the children's group affiliation. It should be mentioned that the TR group may not be representative for all terms. However, this group did serve as an important reference.

Further research is needed, as the predischarge part of this early intervention was carried out in the course of each child's last week in the neonatal unit. Similar guidance and parental sensitization begins much earlier in today's clinical NICU practice in many countries. This may affect how the intervention should be designed and implemented, and therefore needs to be investigated. Different versions of the intervention need to be tested following adjustment to the parental presence and family-centered care that is now typical to ensure that the positive intervention effects reported last.

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Paper II

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TRIALS

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Early intervention program reduces stress in parents of preterms during childhood, a randomized controlled trial

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Abstract

Background: It is well documented that heightened levels of parenting stress have a negative influence on children's socio-emotional and behavioral development. Parenting stress may therefore be regarded as an outcome variable in its own right. This study investigated whether a sensitizing intervention influences stress reported by parents of prematurely born children until the children were age nine.

Methods: Preterm infants (N =146, birth weight <2,000 g) were randomized to intervention (N =72) with the Mother-Infant Transaction Program (MITP) or a preterm control group (N =74) that received standard hospital care. A term reference group comprised 75 healthy, full-term neonates. Parents reported on the Parenting Stress Index (PSI) when the children were 6 months, 1, 2, 3, 5, 7 years old and on the PSI-Short Form (PSI-SF) at age 9. Main outcomes were the mother's and father's reports of total, child and parent-related stress. Cross-sectional and longitudinal analyses were performed using linear mixed models (LMM), taking dependency in the data caused by twin pairs and repeated measures into account. Response rates were high across all follow-ups, and still reached 85% from mothers and 72% from fathers at 9 years.

Results: Mothers in the intervention group reported better longitudinal development of child-related stress than mothers of preterm controls, as they perceived their children as being more adaptable and less moody throughout childhood until the age of seven. Less stress in the intervention group was revealed by cross-sectional analysis of maternal reports at all ages, while fathers reported similar differences at ages three and five. Parents in the intervention group reported stronger agreement on several stress scores on several occasions. Fathers with high interventional participation (mean 54%) reported significantly less stress at age nine than those who participated less. Both parents in the intervention group reported levels of stress similar to those experienced by the term reference group at all follow-ups, while differences between the preterm control and term reference groups increased.

Conclusions: This early intervention reduces stress among parents of prematurely born children to a level reported by parents of term-born children and enhances agreement between parents.

Trial registration: Clinical Trials Gov identifier NCT00222456, 05.09.2005.

Keywords: Early intervention, Preterm, Parenting stress, Longitudinal study, Long-term follow-up

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Background

High levels of parental stress have frequently been reported when children are born preterm [1,2]. Prematurely born children are at increased risk of behavioral problems compared to term-born infants [3,4]. Reducing the levels of stress is important not only for improving parental psychological health but also because it may improve the efficacy of interventions that target these children's behavioral problems [5]. These interventions thus justify the assessment of parenting stress as an important outcome in the evaluation of an early intervention program [4,5].

Parenting stress has been defined as a mismatch between perceived resources, expectations and actual caregiving demands [5], and covers stress from different origins that places the parent-child relationship under lasting pressure [6,7]. Schappin *et al*. [8] concluded that stress experienced by parents of preterm infants has gradually decreased over the last thirty years, probably due to increased quality of care for preterm infants. On the other hand, Treyvaud *et al*. [9] recently reported that parents of very preterm children continue to report more child- and parent-related stress lasting until children's age of (hereinafter 'age') seven. This may indicate that parents of prematurely born children find it just as difficult to interpret and adapt to the immature expressions of a preterm-born infant today as they did 30 years ago, irrespective of their child's medical condition. The gap between normal parental expectations and infant expressive capacity needs to be reduced following the birth of a preterm child.

Abidin has described stress as a multidimensional concept; cumulative, highly influenced by the environment, and a result of transactions between parent and child that promote negative feelings in the parent [6]. Based on this model, the Parenting Stress Index-Full Form (PSI-FF) was created to capture (a) stress related to the parent's personality and vulnerability; (b) child characteristics as perceived by the adult; (c) life events and; (d) the extent of supportive environment that parents experience. The PSI-FF distinguishes between different aspects of perceived stress in child and parental dimensions, and the Child Domain in particular reveals parental perceptions of stress related to children's individual characteristics.

Several studies have reported that high levels of parenting stress may disrupt parental sensitivity and responsiveness and lead to ineffective, dysfunctional parenting with possible negative impacts on child development [5,9-11]. A meta-analysis concluded that significantly more child-related stress was reported by parents of prematurely-born children than those of term-born, in areas such as distractibility/hyperactivity, demandingness and acceptability among children at ages between 1 month and 12 years [8]. These results are in accordance with studies that have reported prematurely-born children to be more demanding than term-born because of immature expression; poor self-regulation and restricted capacity to interact socially in environments that are noisy, bright or are generally characterized by non-optimal stimuli [12].

A premature birth may also disturb the maturation of parental attachment bonds, which are regarded as an essential part of the parental behavioral system, preparing adults for caregiving [13-15]. Parental bonding is supposed to have a special impact on parents' capacities to cope with stress, as significant associations have been reported between low levels of stress and parental reports of a preferred parental bonding type (high level of care and low level of control) at age seven [16]. Parental attachment bonds may be regarded as complementary to the infants' care-seeking attachment and deal with emotional ties that involve the development of feelings of love [15]. Parental attachment is in line with Abidin's construction of an Attachment subscale in the PSI-FF, which is loaded with questions that address parents' perceived difficulties in establishing an emotional closeness to the infant [6,15]. Prematurity has been found to be a strong predictor of diminished caregiving quality, while research has reported a weak impact of prematurity on the development of child attachment [13,17]. All aspects mentioned above underline the importance of strengthening parents' ability to cope with the delivery of a preterm child and to manage this stressful situation.

Several interventions that aim to ameliorate these problems have been investigated. Key components of interventions, all of which involve efforts to improve parental outcomes and subsequently child outcomes, have been described as psychosocial support, parent education and therapeutic developmental interventions targeting the infant [18]. The meta-analysis by Bakermans-Kranenburg, van Ijzendoorn *et al*. concluded that interventions that were able to enhance parental sensitivity were the most effective [19]. This study evaluates whether a modified version of the Mother-Infant Transaction Program (MITP) [4] could strengthen parents' perceptions of their preterm child and prevent the increased levels of parenting stress that have repeatedly been reported [20,21]. The MITP was designed to facilitate social availability and interactions with the newborn infant and thereby strengthen parental enthusiasm, pleasure and empowerment [4]. Our group has previously reported lower levels of parenting stress in the intervention group until age two [22,23]. Moreover, the intervention appears to improve the children's socio-emotional and behavioral development [24,25]. On the basis of these findings, we hypothesized that preterm intervention (PI) parents would continue to report less stress throughout childhood, as stability in parents' perception of parenting stress is well documented [20,21]. The following questions were addressed: 1) has the early intervention influenced the longitudinal development of

parenting stress as reported by mothers and fathers? 2) are there cross-sectional differences between the preterm groups in mothers' and fathers' reports of parenting stress at any age until nine, when controlled for repeated measures? 3) how is the development of stress reported by parents in the two preterm groups compared with that reported by parents of term controls?

Methods

Participants

This study is a part of the Tromsø Intervention Study on Preterms (TISP); a randomized, controlled study of preterm infants with birth weight (BW) <2000 g, recruited between March 1999 and September 2002 (Rønning, Ulvund, Dahl & Kaaresen, 1998, unpublished research protocol). Preterm infants were randomized into blocks of six by using computer-generated numbers, to form an intervention group (PI, N =72) and a preterm control group (PC, N =74), and stratified according to gestational age (GA) <28 and GA ≥28 weeks. Healthy newborns (GA ≥37 weeks) were also recruited from the neonatal nursery to form a term reference group (TR, N =75). Written, informed consent was received from all participants before inclusion. Preterm controls (PC) followed the neonatal intensive care unit (NICU) guidelines for discharge of preterm infants, while term controls (TR) were routinely examined once by a pediatrician on their third day of life. Baseline data for each study group have previously been described in detail elsewhere [22,23], and are shown in Table 1.

Table 1 Birth, medical and demographic information

	PI group	PC group	TR group
	N =72	N =74	N =75
Infant characteristics	1,396 ± 429	1,381 ± 436	3,619 ± 490
BW, mean ± SD, g	20 (28)	20 (27)	
400 to 1000 g, n (%)	15 (21)	20 (27)	
1001 to 1500 g, n (%)	37 (51)	34 (46)	
1501 to 2000 g, n (%)	30.2 ± 3.1	29.9 ± 3.5	39.3 ± 1.3
GA, mean ± SD, week	17 (24)	19 (27)	
<28 week, n (%)	36 (50)	19 (27)	
28 to 32 week, n (%)	38 (53)	37 (50)	
≥33 week, n (%)	16 (22)	18 (24)	
Boy, n (%)	38 (53)	39 (53)	40 (54)
Twin, n (%)	16 (22)	14 (19)	0
Prenatal steroid use, n (%)	53 (74)	57 (77)	
SNAP II, mean ± SD	8.3 ± 10.9	10.4 ± 11.3	
CRIB score, mean ± SD, N =85	3.2 ± 2.8	2.7 ± 2.9	
Received ventilation, n (%)	29 (40)	37 (50)	
Duration of ventilation, n (%)	7.0 ± 18.6	7.1 ± 17.3	
Postnatal steroid use, n (%)	9 (13)	10 (14)	
Oxygen therapy at 38 week GA, n (%)	11 (15)	14 (19)	
Abnormal cerebral ultrasound, n (%)			
IVH grade 1 or 2	7 (10)	8 (11)	
IVH grade 3 or 4	3 (4)	5 (7)	
Periventricular leukomalacia	4 (6)	8 (11)	
Maternal and social characteristics			
Mother's age, mean ± SD, years	30.8 ± 6.1	29.1 ± 6.4	29.7 ± 6.1
First-born child, n (%)	40 (56)	37 (54)	27 (37)
Mother's education, mean ± SD, years, N =131	14.6 ± 2.8	13.5 ± 3.2	14.9 ± 2.8
Father's education, mean ± SD, years, N =131	13.8 ± 3.1	13.5 ± 3.2	14.4 ± 3.2
Mother's monthly income, mean ± SD, 1,000 Norwegian kroner, N =131	15.8 ± 7.7	14.6 ± 6.7	15.9 ± 8.0
Father's monthly income, mean ± SD, 1,000 Norwegian kroner, N =131	21.1 ± 8.7	19.9 ± 8.1	21.9 ± 9.8

Abbreviations: BW birth weight, *CRIB* Clinical Risk Index for Babies, *GA* gestational age, *IVH* intraventricular hemorrhage, *PC* preterm control group, *PI* preterm intervention group, *SNAP* Score for Neonatal Acute Physiology, *TR* term reference group.

Intervention

The intervention program was a modified version of the MITP [4] aimed at 1) enhancing parents' understanding of their child's expressions, and 2) promoting a sensitive, positive and practical transaction between parents and child. Eight nurses were trained to perform the intervention and each family was guided by the same nurse during all the sessions. Each intervention consisted of 7 hour-long sessions with parents and their baby during the last week before discharge, and 4 home visits at 1, 2, 4, and 12 weeks post-discharge [4]. The modification of the MITP included an initial session during which parents could vent their feelings about their preterm child. Mothers participated in all sessions while the fathers' mean participation rate was 6.5 sessions (SD =3.4), which constituted 54% of the intervention program. In the first session the parents and the intervention nurse investigated the child's capacities, focusing on the baby's readiness and social communication abilities. During the following sessions, the parents were helped to recognize and be sensitive to behavioral cues, signs of disturbed regulation and stress in the child's physiological, motor and state organization. The guidance was given while they observed the infant together, and all comments, questions and suggestions from the parents were appreciated. Finally, this understanding was applied to daily care by helping parents to make adjustments to their child's strengths and vulnerabilities, in order to reduce stress levels and maximize the parents' social engagement with their babies. During the four home visits, these topics were revisited and fine-tuned to individual needs, especially in connection with the child's temperament, which was one of the main topics of the third home visit. The

families had no other contact with the intervention nurses. All sessions were documented by logbooks written by the interventionists, and implementation according to the intervention manual [4] was ensured by logbook reviews carried out by the study director (JAR).

Measures

At the ages of 6 months, 1, 2, 3, 5 and 7 years, parents completed the Parenting Stress Index-Full Form (PSI-FF, third edition) while the Parenting Stress Index-Short Form (PSI-SF) was used when the children were 9 years old [6]. The PSI-FF consists of 120 questions covering three main dimensions of stress (child, parent and life stress) while the PSI-SF consists of 36 questions extracted from the parent- and child-related dimensions. A five-point Likert scale ranging from 'strongly agree' to 'strongly disagree' made up the response alternatives on both questionnaires. At 6 months, only one parent reported (mostly mothers) while mothers and fathers reported separately on all the subsequent occasions.

The PSI-FF consists of two main dimensions: Child Domain (47 items covering the subscales: Distractibility, Adaptability, Reinforces Parent, Demandingness, Mood and Acceptability), and Parent Domain (54 items covering the subscales: Perceived Competence, Isolation, Attachment, Health, Role Restriction, Depression and Relation to Spouse). A Total Stress (TS) score was also computed on the basis of all items except the life-stress questions. The PSI-SF is reported as a Total Stress score and by three subscales, each of which consists of 12 items: Parental Distress (PD), Parent-Child Dysfunctional Interaction (P-CDI) and Difficult Child (DC). Some questions in both questionnaires are used to calculate a Defensive Responding score, which indicates the degree of possible inconsistent/denial reporting from respondents.

Both PSI-FF and PSI-SF are frequently used in research [26,27], and the correlation between Total Stress scores on these two measures is described as high (0.87) [6,28]. The PSI-SF, DC subscale consists solely of items from the Child Domain in PSI-FF, and the Parental Distress subscale items from the Parent Domain. The P-CDI subscale includes items from both the Child and Parent Domains and focuses on the parental perception of transactions with their child and their expectations about the child's behavior [6]. The Norwegian versions of both PSI-FF and PSI-SF were translated by Rønning and Abidin, and were used in this study with the permission of Abidin and Psychological Assessment Resources, Inc. (PAR). The questionnaires have some literal differences, in that questions in the PSI-SF may be perceived as more negative and definitive than those in the original PSI-FF format. The Life Stress (LS) questionnaire is part of the PSI-FF and was also used at age nine. The LS questionnaire consists of 22 items covering major life events in the family that are assumed to be challenging, even though they not are directly associated with child or parental challenges.

Follow-up procedures

All the participating children received the same medical, developmental, and psychosocial assessments with recommendations about contacting other services if needed (age 6 months, 1, 2, 3, 5, 7, 9 years). Questionnaires were sent to the families approximately two weeks before each assessment. TISP was approved by the Regional Committee for Medical Ethics (2010/2153/REK nord) and the Norwegian Data Inspectorate on three occasions (in 1999, 2005, and 2010).

Analysis

Because of repeated measures and the clustering effects of twin pairs, all longitudinal and cross-sectional analyses were performed by multilevel modeling (linear mixed models (LMM), SPSS statistics, version 20, SPSS Inc., Chicago, IL, USA). In the longitudinal analysis, time was treated as a continuous variable. In the cross-sectional analysis, predicted mean group differences with 95% confidence intervals (CI) were calculated. These analyses were also based on a longitudinal model, but in these cases time was treated as a categorical variable [29]. By varying the reference time point in the analysis, predicted group differences could be calculated. To assess agreement between parents, intraclass correlations (ICC) were computed, and the difference between the two independent intraclass correlation coefficients for the PI and the PC groups was tested as described by Alsawalmeh and Feldt [30]. The impact of variable intervention participation by fathers was analyzed by LMM and adjusted to take into account the clustering effects of twin pairs, and effect sizes in this case was given by Pearson correlations. Effect sizes (ES) created by the use of Hedges' g are reported on predicted cross-sectional differences in mean scores between the PI and PC groups [31]. A P-value < .05 was considered significant. Randomization and inclusion criteria resulted in well-balanced study groups with one exception. Mothers in the PI group had an average of one more year of education at inclusion time (Table 1). The response rates were good throughout the study, still reaching 85% among mothers and 72% among fathers across all groups at age 9 (Figure 1).

Results

Longitudinal development of parenting stress in the PI and PC groups

No group by age interactions were uncovered on PSI, TS as reported by mothers or fathers from age 6 months until 7 years (Figure 2). Mean scores in all three groups were low compared to the American normative mean score (222 points) reported by Abidin [6].

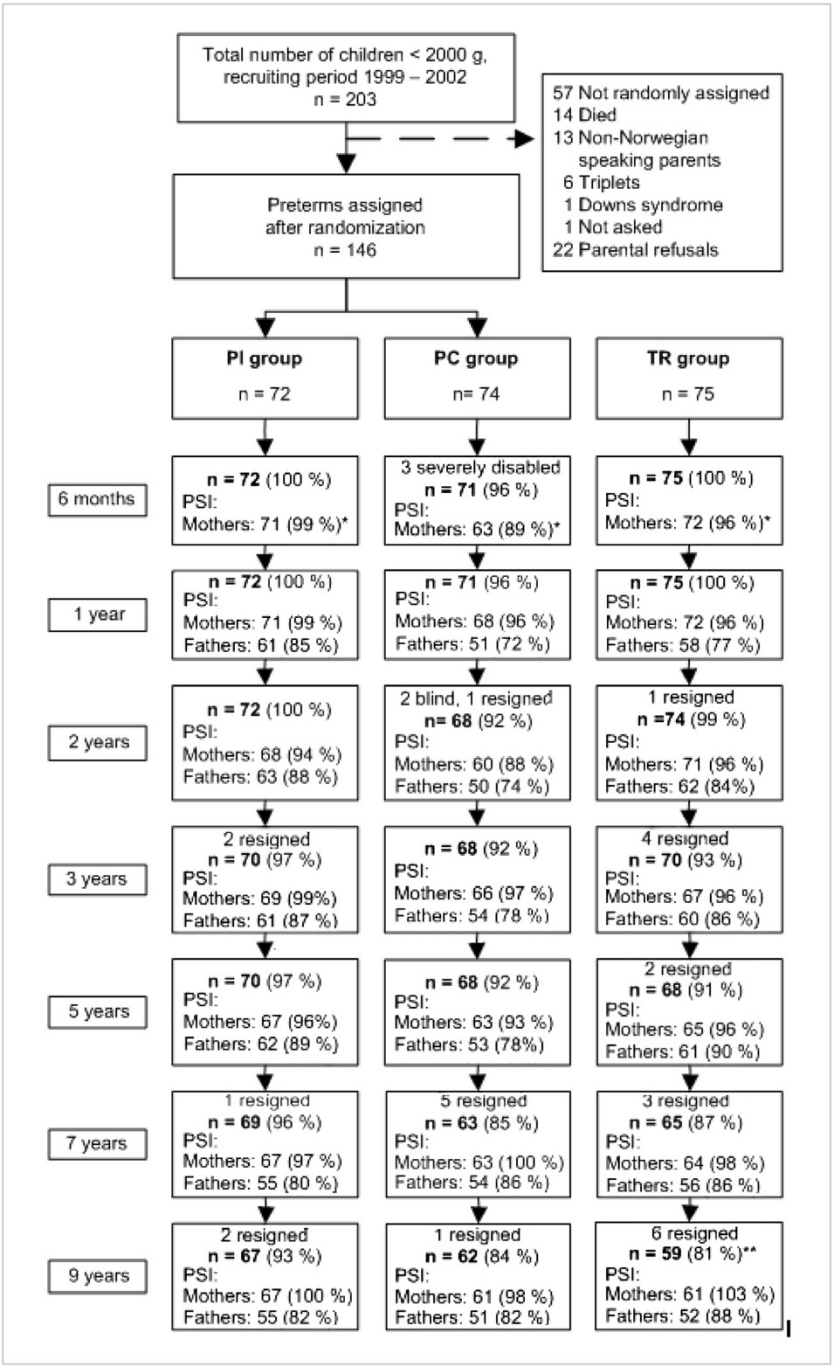

Figure 1 Study flow and parents' reports on Parenting Stress Index (PSI) from 6 months to 9 years of age. At age 9, two mothers in the TR group reported on PSI but their child did not attend the follow-up session.

In PSI-Child Domain a group by age interaction was reported by mothers from age 6 months until 7 years ($F(5,642) = 2.7$, $P = .02$). While PI mothers reported child-related stress as being at its highest at 6 months and decreasing until age 7, PC mothers reported increasing levels from age one until 5 years (Figure 3).

The interaction concerning child-related stress in maternal reports may primarily be a result of two similar interactions in the subscales Adaptability ($F(5,654) = 3.3$, $P = .006$) and Mood ($F(5,663) = 3.2$, $P = .007$). All group by age interactions continued to be significant when controlled for maternal education (Table 1). No group

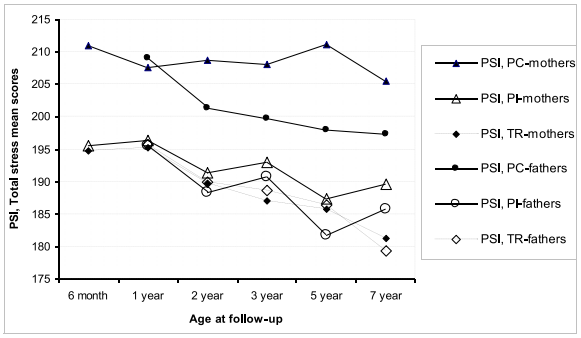

Figure 2 Parenting Stress Index (PSI), Total Stress reported by mothers and fathers in the preterm intervention (PI), preterm control (PC) and term control (TR) groups from 6 months until 7 years.

by age interactions were reported either by mothers in PSI-Parent Domain or by fathers in either child- or parent-related stress.

Parenting stress in the PI and PC groups at different ages

Cross-sectional differences (at age 6 months, 1, 2, 3, 5, 7 and 9 years) in parental reports of child- and parent-related stress are reported first (stress reported at age 6 months, 1 and 2 years has been reported earlier [22,23], but now predictions are based on a longitudinal model). Next, significant differences in different aspects of parenting stress (PSI, subscales) are reported. Lastly, agreement between parents in the PI and the PC group are compared.

Mother's reports of child, parent and total stress are displayed in Table 2. Differences between preterm groups were mostly around 0.5 SD, and ESs were at their highest at 5 years in CD (ES =0.62). Mothers in the PI group reported less total stress than mothers in the PC group at every follow-up from age one until nine. Similarly, they reported significantly less child-related stress from age two until nine and less parent-related stress at ages two, three and five.

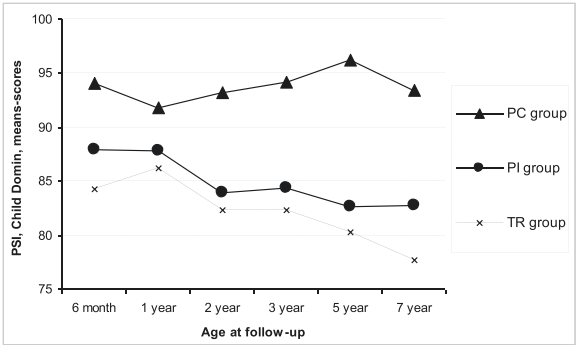

Figure 3 Mothers' reports on Parenting Stress Index (PSI)-Child Domain from age 6 months until 7 years.

Fathers in the PI group reported significantly less child-related stress (PSI, CD) than fathers in the PC group at 2, 3 and 5 years and less total stress at age 5 (Table 3). Significant correlations were uncovered between reported stress and the number of interventions in which PI fathers had participated. Fathers who had participated less reported more stress at age 3 in: Total Stress (t(57) =2.2, $P = .03$, r = −0.32) and child-related stress (t(58) =3.0, $P = .004$, r = −0.37). A similar result was found at age 9; Total Stress (t(58) =2.5, $P = .02$, r = −0.33); Parent-Child Difficult Interaction (P-CDI) (t(52) =3.0, $P = .01$, r = −0.38) and DC (t(50) =2.44, $P = .02$, r = −0.32).

Group differences in sub-dimensions of stress

The subscales of child- and parent-related stress, in which significant differences between the PI and the PC group emerged, are displayed in Table 4. For all differences (whether significant or not) less stress was reported in the PI group. At 6 months, outcomes on one single subscale (Attachment) showed a significant difference between the preterm groups (t(278) =2.9, $P = .004$, ES =0.56). Fathers reported a similar difference on this subscale at age 1 (t(256) =2.8, $P = .006$, ES =0.55). More positive feelings were reported by the PI group at age 1 on the PSI subscale 'Reinforces parent' by both mothers (t(405) =2.3, $P = .02$, ES =0.46) and fathers (t(328) =2.0, $P = .05$, ES =0.44). Mothers in the PC group reported more stress related to lack of competence at age 1 (t(220) =2.3, $P = .02$, ES =0.47) and this difference between preterm groups persisted until age 7, with the largest effect reported at age 5 (ES =0.67).

A pattern of PI parents perceiving their child as being happier than did PC parents emerged in fathers' reports at age 1 (t(364) =2.2, $P = .03$, ES =0.45) and in mothers' reports at age 2 (t(443) =2.6, $P = .01$, ES =0.51). This difference continued to be reported by fathers until age 5 and by mothers from age 2 until 7 with increasing ES, reaching 0.60 at age 7. Mothers in the PI group also reported less distractibility/hyperactivity, better adaptability to everyday challenges and a higher acceptability, indicating that infants in the PI group matched their parents' expectations in a more appropriate way than those in the PC group. At age 5, both parents reported these differences (Table 4). Lastly, a significant difference in the subscale Spouse (t(235) =2.0, $P = .05$, ES =0.37), as reported by fathers, emerged at age 5 between the preterm groups. Analyses of the questions in this subscale indicated that fathers in the PC group spent less time with their partners than those in the PI group.

Parental agreement concerning stress in the two preterm groups

The level of agreement between mothers and fathers were computed separately for the PI and the PC groups.

Table 2 Mean scores and predicted mean differences in Parenting Stress Index (PSI) main dimensions as reported by mothers in the preterm intervention (PI) and preterm control (PC) groups

		N[a] PC, PI	PC group mean (SD)	PI group mean (SD	Predicted mean difference, (95% CI)[c]	P	ES[b]	TR group mean (SD)
6 months	Child Domain	68,72	94.3 (15.4)	88.1 (14.6)	5.1 (−1.0,11..2)	.1	0.34	84.3 (13.3)
	Parent Domain		116.9 (20.8)	108.9 (19.3)	5.3 (−2.2,12.7)	.2	0.26	110.4 (20.3)
	Total Stress		211.6 (34.3)	195.8 (30.2)	9.6 (−2.9,22.1)	.1	0.30	194.8 (30.6)
1 year	Child Domain	68,71	92.3 (14.6)	87.6 (17.8)	4.3 (−1.8,10.4)	.2	0.26	86.2 (15.4)
	Parent Domain		116.7 (20.3)	107.9 (20.6)	7.9 (0.5,15.3)	.04	0.39	110.1 (20.5)
	Total Stress		208.9 (32.6)	195.5 (35.5)	12.9 (0.5,25.2)	.04	0.39	195.3 (33.0)
2 years	Child Domain	60,68	93.5 (16.3)	84.2 (16.1)	9.8 (3.5,16.0)	.002	0.60	82.3 (15.2)
	Parent Domain		116.2 (18.9)	107.1 (19.6)	9.1 (1.6,16.6)	.04	0.47	107.2 (21.7)
	Total Stress		210.0 (30.8)	191.6 (33.1)	19.1 (6.5,31.6)	.003	0.60	189.7 (34.8)
3 years	Child Domain	66,69	95.3 (19.7)	84.2 (16.3)	10.5 (4.4,16.7)	.001	0.58	82.3 (14.9)
	Parent Domain		115.3 (21.4)	107.2 (20.6)	8.1 (0.6,15.6)	.04	0.39	105.0 (18.0)
	Total Stress		210.6 (37.8)	191.7 (33.6)	18.4 (6.0,30.7)	.004	0.52	187.1 (31.1)
5 years	Child Domain	63,67	97.1 (22.1)	82.3 (19.2)	12.9 (6.8,19.1)	< .0005	0.62	80.3 (15.1)
	Parent Domain		115.9 (23.4)	104.8 (21.8)	8.4 (0.9,15.9)	.03	0.37	105.9 (21.7)
	Total Stress		213.0 (39.9)	186.8 (37.9)	21.8 (9.5,34.2)	.001	0.56	185.8 (33.8)
7 years	Child Domain	63,67	94.0 (21.0)	82.7 (19.1)	9.7 (3.6,15.9)	.002	0.48	77.7 (15.2)
	Parent Domain		113.9 (23.2)	105.8 (22.8)	5.7 (−1.9,13.3)	.1	0.25	103.7 (24.3)
	Total Stress		207.9 (39.8)	188.8 (38.6)	15.8 (3.4,28.2)	.01	0.40	181.2 (37.5)
9 years	Difficult Child	61,67	25.4 (9.1)	21.3 (8.9)	3.9 (1.6,6.1)	.001	0.43	19.1 (5.4)
	Parental Stress		21.4 (7.1)	19.0 (6.0)	2.1 (−0.1,4.3)	.06	0.32	19.1 (6.5)
	Parent-Child Difficult Interaction		20.3 (5.7)	17.6 (5.6)	2.4 (0.6,4.3)	.01	0.42	16.4 (4.4)
	Total Stress		67.0 (19.6)	57.9 (17.9)	8.3 (3.0,13.6)	.002	0.44	54.7 (14.9)

[a]Number of reports from mothers in the PC and PI groups.
[b]Effect size, Hedges' g, based on predicted mean differences.
[c]Analyzed with linear mixed models (LMM), adjusted for repeated measures and clustering effects of twin pairs.
ES, effect size.

Where significant differences in agreement between groups occurred, intraclass correlations in the PC and PI groups are reported and supplemented with *P*-values [29]. At age 2: Child Domain (ICC_{PC} =0.25; ICC_{PI} =0.69; $P < .001$), Parent Domain (ICC_{PC} =0.31; ICC_{PI} =0.64; $P = .01$), Total Stress (ICC_{PC} =0.24; ICC_{PI} =0.71; $P < .001$); age 3: Parent Domain (ICC_{PC} =0.26; ICC_{PI} =0.59; $P = .01$); age 7: Total Stress (ICC_{PC} =0.43; ICC_{PC} =0.65; $P = .05$) and age 9: DC (ICC_{PC} =0.36; ICC_{PI} =0.61; $P = .04$), Parent-Child Difficult Interaction (ICC_{PC} =0.20; ICC_{PI} =0.65; $P < .001$). Similar tendencies were reported on all other main outcomes except Child Domain at ages three and five, where agreement was at the same level.

Did parents of preterm infants report more stress than parents of terms?

Stress reported by the PI and PC groups was compared with reports from the TR group in separate longitudinal and cross-sectional analyses (Figure 2).

The PC and the TR groups compared

Group by age interactions were found in total and child-related stress as reported by mothers and in child-related stress as reported by fathers (Table 5). These three interactions are characterized by similar trajectories, as the TR group reported decreasing levels of stress from age one whereas the PC group reported stress at a higher and stable level across pre-school ages. Similar differences were found in several sub-dimensions (Table 5).

Cross-sectional comparisons between the PC and the TR groups revealed significant differences in all main stress domains from age two until nine as reported by mothers. PC fathers reported more child-related stress than TR fathers at all follow-ups from age of one until seven and more Total Stress at age seven and nine. Both mothers and fathers in the PC group reported more Parent-Child Dysfunctional Interactions at age 9 than the TR group ($P < .01$).

Table 3 Mean scores and adjusted mean differences on Parenting Stress Index (PSI), main dimensions as reported by fathers in the preterm intervention (PI) and preterm control (PC) group

	Fathers reports	N[a] PC, PI	PC group mean (SD)	PI group mean (SD	Predicted mean difference, (95% CI)[c]	P	ES[b]	TR group mean (SD)
1 year	Child Domain	51,61	96.0 (13.9)	89.3 (15.8)	4.5 (−1.8,10.8)	.2	0.30	89.3 (12.2)
	Parent Domain		113.5 (21.2)	105.3 (19.6)	6.6 (−1.4,14.6)	.1	0.33	106.3 (15.3)
	Total Stress		209.4 (32.7)	194.6 (33.9)	10.3 (−3.1,23.6)	.1	0.31	195.7 (24.9)
2 years	Child Domain	50,63	92.6 (13.1)	86.2 (16.9)	6.6 (0.4,12.9)	.04	0.43	85.8 (11.3)
	Parent Domain		108.4 (17.8)	103.3 (24.6)	5.6 (−2.3,13.6)	.2	0.26	103.8 (16.9)
	Total Stress		200.4 (27.2)	189.4 (40.3)	11.7 (−1.6,25.2)	.08	0.33	190.0 (24.9)
3 years	Child Domain	54,61	93.8 (14.8)	86.2 (16.6)	7.6 (1.3,13.8)	.02	0.48	85.9 (12.7)
	Parent Domain		105.4 (18.2)	103.7 (23.8)	3.0 (−4.9,11.0)	.5	0.14	102.6 (17.0)
	Total Stress		199.9 (31.0)	189.3 (37.5)	10.4 (−3.0,23.7)	.7	0.30	188.7 (27.4)
5 years	Child Domain	53,62	93.9 (20.2)	82.1 (15.6)	9.8 (3.6,16.1)	.002	0.55	85.1 (15.5)
	Parent Domain		105.2 (20.7)	98.1 (21.8)	5.3 (−2.7,13.3)	.2	0.25	101.4 (18.8)
	Total Stress		199.7 (37.3)	180.4 (34.9)	14.6 (1.3,28.0)	.03	0.41	186.4 (32.1)
7 years	Child Domain	54,55	92.4 (19.9)	87.2 (19.3)	4.7 (−1.6,11.0)	.1	0.24	80.8 (16.2)
	Parent Domain		105.2 (21.9)	100.2 (24.6)	4.2 (−3.8,12.2)	.3	0.18	98.7 (18.5)
	Total Stress		197.6 (38.5)	186.4 (40.5)	9.0 (−4.4,22.4)	.2	0.23	179.4 (32.6)
9 years	Difficult Child	51,55	21.6 (7.9)	21.3 (8.7)	0.6 (−1.6,2.7)	.6	0.07	18.8 (5.9)
	Parental Stress		19.5 (6.4)	20.5 (8.6)	−0.1 (−2.5,2.3)	.9	0.01	18.3 (5.6)
	Parent -Child Difficult Interaction		19.0 (5.6)	18.6 (6.0)	0.5 (−1.5,2.5)	.6	0.09	16.4 (4.5)
	Total Stress		60.1 (17.6)	60.3 (21.3)	1.0 (−4.7,6.7)	.7	0.05	53.5 (14.9)

[a]Number of reports from mothers in the PC and PI group.
[b]Effect size, Hedges' g, based on predicted mean differences.
[c]Analyzed with linear mixed models (LMM), adjusted for repeated measures and clustering effects of twin pairs.
ES, effect size; TR, term control group.

The PI and TR groups compared

No differences were found in the longitudinal report of total, child- or parent-related stress. In the distractibility/hyperactivity and mood sub-scales, PI fathers reported lower means before school-age and higher means at age 7 compared with TR fathers (Table 5). No significant cross-sectional differences between the PI and the TR groups emerged in reports of parenting stress from age 6 months until 9 years.

Discussion

This study evaluated whether a sensitizing, early intervention affected the development of parenting stress among mothers and fathers of prematurely born children until age nine. The overall results indicated that the intervention reduced maternal stress, but to a lesser degree affected paternal stress in the intervention group. Different longitudinal patterns between the preterm groups were reported by PI and PC mothers on dimensions addressing child characteristics. PI mothers perceived their children as displaying higher adaptability and happiness throughout childhood than did PC group mothers. In addition, stress in the PI and PC groups was reported at quantitatively different levels at different follow-ups. PI mothers reported less total and child-related stress at all ages while PI fathers reported a similar difference from PC fathers at age five. The intervention may also have heightened the parental agreement within families as a stronger association between mothers and fathers responses was repeatedly found in the PI group compared with the PC group. Finally, parents in the PI group reported similar levels of parenting stress to those of terms at all follow-ups, while longitudinal and cross-sectional differences between the PC and TR groups increased with age. Thus, our main hypothesis was supported, as parents in the PI group reported stress below the levels of the PC group throughout childhood, and in fact was comparable to parents of term-born children.

In answer to the first question, a stress-subduing effect was found in the PI group concerning maternal perception of child-related stress in such aspects as adaptability and mood. More stress reported in these aspects of parenting stress has in particular been associated with difficulties in the parent-child relationship [5,6]. The intervention had a sustained focus on support of early parent-child relationships. Parents were asked to initiate and facilitate social interactions whenever the child seemed to be 'available' but also to be sensitive to the child's signs of distress and

Table 4 Significant differences between the preterm control (PC) and preterm intervention (PI) groups on Parenting Stress Index (PSI), subscales

	Mothers report		Fathers report	
	Subdomains of child-related stress	Subdomains of parent-related stress	Subdomains of child-related stress	Subdomains of parent-related stress
6 months		Attachment[b]		
1 year	Reinforces parent[a]	Competence[a]	Reinforces parent[a]	Attachment[b]
		Attachment[a]	Mood[a]	
2 years	Distractibility[a]	Competence[b]	Distractibility[a]	
	Adaptability[a]	Attachment[a]	Mood[a]	
	Demandingness[b]	Spouse[a]		
	Mood[b]			
	Acceptability[b]			
3 years	Distractibility[a]	Competence[c]	Distractibility[b]	
	Adaptability[c]	Attachment[a]	Mood[a]	
	Demandingness[a]			
	Mood[b]			
	Acceptability[a]			
5 years	Distractibility[c]	Competence[c]	Distractibility[c]	Spouse[a]
	Adaptability[c]	Attachment[b]	Adaptability[a]	
	Demandingness[b]		Reinforces parent[a]	
	Mood[c]		Demandingness[a]	
	Acceptability[b]		Mood[b]	
7 years	Distractibility[b]	Competence[b]		
	Adaptability[a]			
	Demandingness[a]			
	Mood[b]			
	Acceptability[b]			

All analyses generated with liners mixed models (LMM), adjusted for repeated measures and the clustering effect of twin pairs. a = P <0.05, b = P <0.01, c = P <0.001.

Table 5 Significant interactions with age between the term reference (TR) group and the preterm groups

Group by age interactions:	PSI dimension (mother or father)	F (df1, df2)	P
TR - and the PC group	Total Stress (Mo)	8.0 (1,641)	.005
	Child Domain (Mo)	12.5 (1,650)	< .0005
	Child Domain (Fa)	4.3 (1, 443)	.038
	Distractibility/Hyperactivity (Mo)	9.7 (1,660)	.002
	Distractibility/Hyperactivity (Fa)	4.6 (1,446)	.033
	Adaptability (Mo)	11.1 (1,659)	.001
	Demandingness (Mo)	7.7 (1,658)	.006
	Mood (Mo)	5.8 (1,670)	.016
	Competence (Mo)	5.6 (1,663)	.019
	Acceptability (Fa)	4.0 (1, 453)	.045
TR - and the PI group	Distract/Hyperactivity (Fa)	7.3 (1,473)	.007
	Mood (Fa)	5.4 (1,489)	.020

Fa, reported by fathers; Mo, reported by mothers.

need for 'time-out'. This may have initiated better-timed transactional patterns between PI mothers and their infants compared to the PC group. At the first follow-up (6 months) mothers in the PC group more often reported their children as fussy and in a bad mood when they woke up than the PI mothers did. This difference had disappeared by age one. However, from age two onwards, mothers in the PC group reported increased stress related to their children's mood and adaptability, while the PI group mothers reported diminishing levels of stress until age seven. These results were dependent on the mothers' answers to several PSI questions, but were strongly influenced by one item throughout childhood: 'I feel that my child is very moody and easily upset'. Accordingly, reports from mothers at age one and later show that the PC mothers perceive less happiness, fewer smiles and fewer emotional responses from their children than the PI mothers. It has already been shown that premature babies may be less successful in showing strong positive arousal responses (for example, smiles) than full-term infants [32]. This suggests that the intervention had an influence on maternal stress, in terms of how mothers perceive their child and on their emotional relationship. The following paragraphs briefly discuss possible underlying mechanisms.

Heightened levels of stress are supposed to negatively affect maternal responsiveness [33]. Laucht, Esser *et al.* [34] studied the impact of maternal responsiveness on behavioral development in premature children. They found that problems such as anxiety and depressive mood decreased with age in children with highly responsive mothers, but increased where less sensitive mothering behavior was observed. We might speculate whether the intervention enhanced the ability of PI mothers to acquire realistic expectations and a deeper understanding about their children's cues and need for support. Olafsen *et al.* [35] found that mothers who had participated in the intervention reported a strong association between stress and their children's regulatory competence at 6 months. This may be an early indication of a more sensitive and synchronous interactional parent-child style. They may have been better able to read their child's cues and 'do what it takes' to help their child in its immature regulation efforts. Another interventional aspect which may have decreased parenting stress in the PI group is the incorporation of the initial ventilation session, which may have strengthened the parents' feelings of security and helped to improve their self-confidence [18,34]. The session may also have influenced these parents' establishment of a more robust parental attachment, which has been described as a powerful antecedent of the quality of mothers' sensitive behavior [14,19,34]. The importance of maternal attachment has been documented by Coppola, Cassibba *et al.* [36] in connection with mother's sensitivity at age 3 months. This was particularly powerful in mother-infant dyads with prematurely born children.

Even though maternal perceptions of child-related stress throughout childhood created the most significant differences between the preterm groups, the first reported difference appeared in parent-related stress, on the subscale Attachment at 6 months. Giving birth to a preterm child has been described as having a negative impact on maternal attachment [17,33,37]. The prolonged stay in the hospital and the NICU environments disrupts the natural physiological contact between mother and child. Borghini *et al.* [38] found that only 20% of mothers of preterm infants had a secure attachment representation at children's age of 6 months compared to 53% of mothers of terms. According to Abidin, the PSI subscale Attachment was designed to assess the intrinsic motivation of parents in their roles as mothers or fathers [6], and this concept appears to be closely related to the development of a caregiving system as described by Walsh [15]. PC mothers reported significantly higher stress scores than PI mothers on several questions at 6 months, for example, 'it takes a long time for parents to develop close, warm feelings for their children' and 'sometimes my child does things that bother me just to be mean'. These statements illustrate that a difference in experienced closeness and understanding of the child may have emerged between the PI and the PC mothers as early as 6 months post-discharge, with an impact on parental perception of stress.

Evans *et al.* [33] found that experiential avoidance and prenatal expectations were important predictors of maternal attachment and responsiveness styles. They suggested that avoidance could be used as a coping mechanism among mothers who struggled to deal with the new situation, but also as a predictor of weaker maternal attachment and responsiveness. As already mentioned, premature children may more often be characterized by a more serious expression than full-term children [32]. This may be associated with reports of emotional instability, observed for example as changeable moods, as have been more frequently reported among preschool preterms children than terms [39]. We therefore think that both maternal attachment and the infants' expressions of emotionality might have been positively altered by the intervention. The toddlers may have regulated their mother's feelings by their degree of susceptibility. When mothers in the PI group, guided by their new understanding of their individual child, were able to initiate interactions and elicit positive emotional expressions from their child, it may have become easier for them to establish an emotional closeness to the child and reduce their experiences of stress.

Deater-Deckard [5] emphasized that parenting stress is experienced as negative feelings toward both oneself and the child. More PC mothers expressed such negative

feelings in terms of fewer smiles and lack of positive responses from their infants at age one than PI mothers. This produced a significant difference on the subscale 'Reinforces parents'. This may be due to different expectations between these groups of mothers, but could also be a sign of subdued expressions of happiness among infants in the PC group, possibly influenced by a weaker emotional closeness to their mothers in these early months of life.

The early differences between the preterm groups included a difference in maternal experience of competence at age one, and subsequently significant differences in both competence and all child-related dimensions from age two until seven. Parental education has been found to be one of several key components in early interventions for preterm infants [18] and the MITP offered PI parents plenty of practical information and insights. We wonder whether the gradually increasing differences in maternal reports of stress between preterm groups, and a perception of poorer mother-infant adjustment among PC mothers, could be related to transactional mechanisms affecting the establishment of early parent-child synchrony and parental support of their child's regulation [40]. Feldman *et al*. [41] found that better synchrony in early parent-child interactions at age 3 months predicted higher self-regulation skills among the children at age two. This was particularly important for children who were perceived by their parents as being difficult to manage [41]. This makes sense, as the difference between groups in stress concerning adaptability, distractibility, demandingness and acceptability were most evident at ages three, five and seven. Hauser-Cram *et al.* [42] reported similar increases in child-related stress among parents of children identified with disabilities. They identified variations in children's self-regulation skills and mother-infant interactional skills as critical components.

PI fathers' reports of stress seemed to be less affected by the intervention than those of PI mothers. The fewer significant differences between PI and PC fathers may also be influenced by great variability in father's interventional participation. Negative correlations between paternal stress and PI father's participation rates were evident on several measurement occasions. At age nine, correlations between stress and participation were significant in paternal perception of the child, father-child interactions, and their overall reports of stress. Similar correlations between paternal stress and the intervention participation have previously been reported by Kaaresen *et al.* at age one [22]. This may indicate that the associations are effects of intervention, but they may also be influenced by other factors such as differences in fathers' motivation, knowledge, and so on. Interestingly, the highest negative correlation between reported stress and fathers' participation were related to participation in the four home visits ($r = -0.34$). If this is a unique intervention effect it highlights the importance of including home visits in early intervention programs, in line with a recently published review [43]. The inclusion of fathers may also have promoted a higher degree of shared perception of stress between PI parents compared with PC parents. Morgan *et al.* [7] argues that better agreement regarding roles and challenges would be likely to produce more similar levels of parenting stress within families. A stronger agreement in the PI group was evident, especially at ages two and nine. A further interpretation of these results is difficult, since until recently, fathers have not been taken into account as independent informants in studies of parenting stress and child developmental outcomes [7].

Finally, we compared parenting stress between the preterm groups and the term reference group. Parents in the PI group reported child- and parent-related stress similar as TR parents, while both longitudinal and cross-sectional differences between the PC and the TR group throughout childhood did emerge. Even though the meta-analysis by Schappin *et al*. suggested that parents of preterm children have become less exposed to increased parenting stress during the past few decades [2,8], our findings cannot confirm that conclusion. On the other hand, the occurrence of increased parenting stress frequently reported by parents of prematurely born children seemed to be eliminated by this intervention.

Strengths and limitations

A major strength of this study is the high participation rates that were maintained throughout the study period, reaching 85% among mothers and 72% among fathers across groups even at age nine. Although randomization generated a high degree of equality between preterm groups in aspects of birth, medical and socio-economic variables, PI mothers did have an average of one year more education than the PC mothers. Maternal education has previously been reported to be negatively correlated with parenting stress [44] but in the latest meta-analysis by Schappin *et al.* [8] maternal educational levels were not found to influence any aspect of parental stress. Nevertheless, all our analyses controlled for the difference of one year in mean maternal education. A limitation related to the construction of the study lies in the nature of self-reported questionnaires. Data collected by the PSI questionnaire are a result of parents' subjective perception of stress on a specific day. An inclusion of biological parameters, such as the measurement of cortisol, may have safeguarded against faulty conclusions. Data may also be influenced by the way questions are asked in the two questionnaires. In the PSI-SF, questions are expressed more directly (more directly problem-orientated formulations), which may have amplified differences between respondents in their perceptions of greater or less stress.

Clinical implications

We have previously reported interventional influences on the longitudinal trajectories and cross-sectional differences on children's behavioral outcomes [25]. Parenting stress is known to be closely correlated with children's behavioral development [45] and relationships between parenting stress and child behavior outcomes will be reported in papers to follow. This study demonstrates how an early child-centered and family-focused intervention may reduce parenting stress across childhood. This is a finding, not only concerning families taking care of prematurely born children but possibly also for other children and families at risk.

Conclusions

As hypothesized, we conclude that this sensitizing intervention reduced maternal parenting stress and positively influenced mothers' perceptions of their children's adaptability and happiness. Different longitudinal patterns in child-related stress were reported by PI mothers than by PC mothers throughout childhood. In all PSI main dimensions, significantly higher levels were reported by PC mothers and fathers at every age until the age of five. Stronger correlations were found in parenting stress reported by parents in the PI group than the PC group, indicating more shared perceptions of their children after intervention.

Finally, both parents in the PI group reported parenting stress similar to the term reference group at all follow-ups, whereas differences between the PC and TR group increased with age throughout childhood.

Abbreviations

CI: confidence interval; CRIB: Clinical Risk Index for Babies; ES: effect size; GA: gestational age; ICC: intraclass correlation; LMM: linear mixed models; LS: Life Stress; MITP: Mother-Infant Transaction Program; NICU: neonatal intensive care unit; PC group: preterm control group; PD: Parental Distress; PI group: preterm intervention group; PSI: Parenting Stress Index; PSI: DC, subscale in PSI-SF named Difficult Child; PSI-FF: Parenting Stress Index-Full Form; PSI: P-CDI, subscale in PSI-SF named Parent-Child Dysfunctional Interaction; PSI: PD, subscale in PSI-SF named Parental Distress; PSI-SF: Parenting Stress Index-Short Form; SNAP: Score for Neonatal Acute Physiology; TISP: Tromsø Intervention Study on Preterms; TR group: term control group; TSS: Total Stress Score.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

IPL carried out the statistical analyses, interpretation of the data and drafted the paper. BHH critically revised the statistical analyses, interpretation of data and the article for intellectual content. JT coordinated the implementation of the study and critically revised the interpretation of data and the article for intellectual content. SEU contributed to the conception and design of the study and critically revised the paper for intellectual content. JAR contributed to the conception, design and implementation of the study and critically revised the interpretation of data and the article of intellectual content. All authors have read and approved the final manuscript.

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Paper III

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HEALTH AND QUALITY OF LIFE OUTCOMES

RESEARCH Open Access

Early intervention influences positively quality of life as reported by prematurely born children at age nine and their parents; a randomized clinical trial

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Abstract

Background: The Tromsø Intervention Study on Preterms evaluates an early, sensitizing intervention given to parents of prematurely born children (birth-weight < 2000 g). The current study investigated the potential influence of the intervention on children's self-reported and parental proxy-reported quality of life (QoL) at children's age of nine.

Methods: Participants were randomized to either intervention (PI, n = 72) or preterm control (PC, n = 74) in the neonatal care unit, while healthy term-born infants were recruited to a term reference group (TR, n = 75). The intervention was a modified version of the Mother-Infant Transaction Program, and comprised eight one-hour sessions during the last week before discharge and four home visits at 1, 2, 4 and 12 weeks post-discharge. The two control groups received care in accordance with written guidelines drawn up at the hospital. Participants and parents reported QoL independently on the Kinder Lebensqualität Fragebogen (KINDL) questionnaire. Differences between groups were analyzed by SPSS; Linear Mixed Models and parent–child agreement were analyzed and compared by intra-class correlations within each group.

Results: On average, children in all groups reported high levels of well-being. The PI children reported better physical well-being than the PC children ($p = 0.002$). In all other aspects of QoL both the PI and the PC children reported at similar levels as the term reference group. PI parents reported better emotional wellbeing ($p = 0.05$) and a higher level of contentment in school ($p = 0.003$) compared with PC parents. Parent–child agreement was significantly weaker in the PI group than in the PC group on dimensions such as emotional well-being and relationships with friends ($p < 0.05$). PI parents reported QoL similar to parents of terms on all aspects except the subscale self-esteem, while PC parents generally reported moderately lower QoL than TR parents.

Conclusions: This early intervention appears to have generated long-lasting positive effects, improving perceived physical well-being among prematurely born children and parent's perception of these children's QoL in middle childhood.

Trial registration: Clinical Trials Gov NCT00222456.

Keywords: Preterm children, Early intervention, Quality of Life, Long-term follow-up

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Background

It is important to include measurement of health status and QoL in neonatal long-term follow-up studies, because interventions in the neonatal period may have effects that only become evident after a period of latency in toddlerhood [1]. Until recently, long-term developmental outcomes on prematurely born children have been dominated by reports of functional ability and the presence or absence of physical sequelae [1-5]. Perceived health and quality of life and physical and cognitive functioning are related but not identical concepts [1,6]. It has been shown that quality of life can be improved beyond symptom levels, thus psychopathology does not have a simple linear relationship to well-being [7]. Mental and social well-being is fundamentally important as reflected in the saying; "it is not how life is, but how the individual can deal with it that matters".

The World Health Organization has defined Quality of life (QoL) as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [8]. QoL is a holistic concept of well-being, even though the concept may be interpreted and described differently [6]. Descriptions of QoL frequently cover factors such as; a subjective phenomenon, a multidimensional construct and an aspect which is related to physical, psychological and social dimensions that includes both positive and negative facets of life [6,9,10]. Thus, it is not possible to directly observe QoL and no universal definition is available [9].

Studies reporting global or health-related aspects of QoL among preterm children are few. They consist mainly of parents' proxy reports on pre-school children or self-reported QoL by adolescents or young adults [6,11]. These studies confirm that prematurity often implies a heavier developmental burden related to morbidity, use of extra health-care services, having fewer friendships, and lower level of education [11-13]. Although several studies have reported that the differences between preterm and term born children diminish with time [12-14], others conclude that being born with a low birth weight has long-lasting negative implications for mental health and quality of life as perceived by the individual concerned [15]. One single, small study has reported self-rated QoL among preterm children at middle school-age [16]. These children scored their health-related QoL significantly lower than term peers at age 9 to 10 years, in line with studies that reported parental proxy QoL in preterm children at this age [12,17].

The need for interventions which could strengthen the QoL of preterm children has been pointed out [15,18] but as far as we know, no results have yet been published. This study looked at whether early sensitization of parents of preterms (birth weight < 2000 g) could positively influence children's and parent's proxy perception of QoL in middle school-age. The sensitizing intervention program took place in the newborn period, and its primary focus was to reinforce the parent–child relationship [19]. Parents were introduced to their infant's social availability; they were taught to identify their child's signs of stress and how they could adjust their own activities and interactions to suit their child as well as possible [19,20]. This was intended to improve both parental confidence and parent–child co-regulation, offering more possibilities for mutual joyful and successful interactions.

In accordance with a transactional understanding of development, better co-regulation in these families was expected to enable them to adapt to new developmental challenges as the child grew [21]. Better co-regulation would confirm parental perception of their own role as good caregivers for their child and probably contribute to a more relaxed family climate. On the other hand, increased parenting stress has frequently been associated with less successful co-regulation [22,23] and has been described as influencing children's quality of life from the earliest years [24,25]. Tu *et al.* [23] reported that maternal stress had an important modulating functioning for the preterm infant's capacity to recover from early pain-related distress in infancy. They reported high levels of cortisol to be strongly associated with the preterm's infant's capacity to focus attention at eight months when exposed to high levels of maternal parenting stress. Lee *et al.* [25] described how QoL, as perceived by the primary caregivers, was directly related to parenting stress, which in turn was directly related to children's proxy reported QoL at preschool age. A persistent reduction in parenting stress has already been reported in our study by mothers in the intervention group, compared to mothers of preterm controls [26,27]. These results are thought to influence children's and parents' reports of QoL at age nine and will be incorporated in the analyses. QoL has also been described as being powerfully influenced by emotional and behavioral problems, and prematurely born children have repeatedly been reported as having higher levels of attentional, social and internalizing difficulties than term born children [5]. In our study, better cognition and fewer behavioral problems were reported in the intervention group at pre-school ages [28,29]. These tendencies seem to persist throughout childhood as fewer attentional problems and better adaptation to school have been reported on the PI group until age nine [30].

On the basis of previous findings we hypothesized that children and parents in the intervention group would report better quality of life than the preterm control group. A definition by Jozefiak of an "inner QoL", which addresses solely the subjective experiences of QoL, was

modified to this study; "QoL is the subjective reported well-being in regard to the child's physical and mental health, self-esteem, perceived relationship to friends and families as well as to school" [10,31]. An additional question raised in this study pays attention to the level of intra-familiar child and parental-proxy agreement. A previous review of QoL studies focusing on young children with various health-conditions reported this level of agreement to be affected by children's age and health but also with great variability between studies [32]. The need of more studies was highlighted. Jozefiak et al. [10] reported significant but low correlations between parents and children's reports in their school selected sample. Positive maternal perceptions of children's emotional well-being have previous been reported to be negatively and significantly related to maternal involvement [33]. We wonder if the intervention may have changed the parent–child agreement concerning measures of QoL. We have already reported a more successful adaptation to school requirements among the PI children which may indicate that these children evaluate their quality of life more independently from their parents than the preterm controls [30]. This study asks three questions: Did the early intervention influence preterm children's self-reported QoL and the parental proxy reports of QoL at age nine? Secondly, did the intervention affect the level of agreement between child and parental proxy reported QoL in the two preterm groups? Thirdly, was QoL reported by children and parents in each of the two preterm groups at similar levels as QoL reported by children and parents in the term reference group?

Methods

Participants

This study is part of a comprehensive clinical trial; the Tromsø Intervention Study on Preterms (TISP) which recruited infants with BW < 2000 g between March 1999 and September 2002 (Rønning JA, Ulvund SE, Dahl LB, Kaaresen PI: Study-protocol, 1998, unpublished). Computer-generated random numbers were use to allocate preterm infants to an intervention group (PI, n = 72) or a control group (PC, n = 74). The randomization was performed in blocks of 4 to 6 and was stratified according to gestational age (GA) < 28 and GA ≥ 28 weeks. Healthy newborns (GA ≥ 37 weeks and BW > 2800 g) were also recruited from the well-infant nursery to form a term reference group (TR, n = 75). Parents of the first baby born after a preterm infant allocated to the preterm intervention group were asked to participate in the study. If they declined the next family was asked. Study design and calculation of sample size have been described in detail in previous publications [26]. Written informed consent was received from all adult participants before inclusion. Preterm controls (PC) followed the NICU's guidelines for discharge of preterm infants, while term references (TR) were routinely examined once by a pediatrician on their third day of life. Demographical baseline data for each study group have previously been described in detail [26], and are summarized in Table 1.

Intervention

The intervention program was a modified version of the Mother-Infant Transaction Program (MITP), a further

Table 1 Birth, medical and demographic characteristics at randomization

	PI Group N = 72	PC Group N = 74	TR Group N = 75
Infant characteristics			
BW, mean ± SD, g	1396 ± 429	1381 ± 436	3619 ± 490
400 - 1000 g, *n* (%)	20 (28)	20 (27)	
1001 - 1500 g, *n* (%)	15 (21)	20 (27)	
1501 - 2000 g, *n* (%)	37 (51)	34 (46)	
GA, mean ± SD, wk	30.2 ± 3.1	29.9 ± 3.5	39.3 ± 1.3
< 28 wk, *n* (%)	17 (24)	19 (27)	
28 - 32 wk, *n* (%)	36 (50)	37 (50)	
≥33 wk, *n* (%)	19 (26)	18 (24)	
Boy, *n* (%)	38 (53)	39 (53)	40 (54)
Twin, *n* (%)	16 (22)	14 (19)	0
SGA	11 (14)	10 (13)	
Prenatal steroid use, *n* (%)	53 (74)	57 (77)	
SNAP II, mean ± SD	8.3 ± 10.9	10.4 ± 11.3	
CRIB score, mean ± SD, *N* = 85	3.2 ± 2.8	2.7 ± 2.9	
Received ventilation, *n* (%)	29 (40)	37 (50)	
Duration of ventilation, *n* (%)	7.0 ± 18.6	7.1 ± 17.3	
Postnatal steroid use, *n* (%)	9 (13)	10 (14)	
Oxygen therapy at 36 wk GA, n (%)	11 (15)	14 (19)	
Abnormal cerebral ultrasound, *n* (%)			
IVH grade 1 or 2	7 (10)	8 (11)	
IVH grade 3 or 4	3 (4)	5 (7)	
Periventricular leukomalacia	4 (6)	8 (11)	
Maternal and social characteristics			
Mother's age, mean ± SD, y	30.8 ± 6.1	29.1 ± 6.4	29.7 ± 6.1
Firstborn child, *n* (%)	40 (56)	37 (54)	27 (37)
Mother's education, mean ± SD,[a)]	14.6 ± 2.8	13.5 ± 3.2	14.9 ± 2.8
Father's education, mean ± SD,[a)]	13.8 ± 3.1	13.5 ± 3.2	14.4 ± 3.2
Mother's monthly income,[b)]	15.8 ± 7.7	14.6 ± 6.7	15.9 ± 8.0
Father's monthly income,[b)]	21.1 ± 8.7	19.9 ± 8.1	21.9 ± 9.8

[a)] = education in years.
[b)] = in Norwegian 1000 kroner, calculated for 131 families due to 15 twins.
CRIB = Clinical Risk Index for Babies.
IVH = Intraventricular Hemorrhage.
SGA = defined as BW > 2SD below the mean for GA.
SNAP II = Score of Acute Neonatal Physiology II.

development of the Neonatal Behavioral and Assessment Scale (NBAS) [18,34]. MITP is designed as a stepwise parental guidance process, with gradually increasing complexity in the knowledge offered to parents [19]. Each family received eight one-hour sessions during the final week before discharge from hospital, and four home visits at 1, 2, 4, and 12 weeks post-discharge [19]. The modification of the MITP included an initial session during which parents could vent feelings such as grief, anger or frustration related to the preterm delivery, the hospital stay and how those conditions had affected their life (Study-protocol, unpublished). The MITP aimed to 1) enhance parents' understanding of their child's expressions, and 2) promote sensitive, positive and practical transactions between parents and child. Eight nurses were trained to perform the intervention and each family was guided by the same nurse during all the sessions.

All of the mothers participated in all the sessions, while the fathers' mean participation rate was 6.5 sessions (SD = 3.4), which constituted 54% of the intervention program. At first, the parents and the interventionist investigated the child's capacities, focusing on the baby's readiness and social communication abilities. During the following sessions, the parents were helped to recognize and be sensitive to behavioral cues, signs of disturbed regulation, and stress in the child's physiological, motor and state organization. In the last two sessions before discharge this knowledge was combined with daily caring activities such as bathing, feeding and preparation for sleep. Parents were helped to make adjustments to their child's strengths and vulnerabilities, resulting in reduced levels of stress and maximizing their social engagement with their babies. During the four home visits, these topics were revisited and fine-tuned to individual needs, especially in connection with the child's temperament, which was one of the main topics of the third home visit. The families had no further contact with the interventionists and in contrast to the original MITP study, parents did not receive a logbook of the interventions [19]. Consistent implementation of the intervention was ensured by a review of logbooks carried out by the study director (JAR).

Follow-up procedures

All participants received the same medical, developmental, and psycho-social assessments on all follow-ups. Recommendations about contacting other services (physiotherapy, pedagogical-psychological services, child habilitation, specialized child psychiatric services and child welfare authorities) were given if needed throughout childhood (age 6 months, 1, 2, 3, 5, 7, 9 years). TISP was approved by the Regional Committee for Medical Ethics and the Norwegian Data Inspectorate on three occasions (in 1999, 2005 and 2010).

Data collection

Approximately 14 days before the nine-year follow-up session questionnaires were sent to the families [31]. Parents and children were requested to report QoL independently.

Measures

Child and parent-reported quality of life

The KINDL-questionnaires consist of a self-report questionnaire (Kid KINDL®) appropriate for children (7 to 13 years), and a questionnaire for parental proxy report (KINDL® for parents) [31,35]. These questionnaires are short, generic and have been translated for use in Norwegian populations [9,31]. Each comprises 24 corresponding items that are equally formed as either positive or negative statements about different facets of the child's life. Each item addresses experiences over the past week and is rated on a five-point scale; [1)]never, [2)]seldom, [3)]sometimes, [4)]often and [5)]always. Outcomes consist of a global QoL sum-score and six subscales; physical well-being, emotional well-being, self-esteem, family, friends and school. Mean scores are calculated for each of the subscales and total score and linearly transformed to a 0 to 100 scale, on which higher scores indicate better QoL. The questionnaire was validated by Jozefiak et al. [9]. Relatively low internal consistency (Cronbachs alpha) were reported by the 4th grade students (9 – 10 years) on the subscales; emotional well-being (0.52); friends (0.49) and school (0.47) but fairly acceptable reliability on the others; (total scale (0.83); physical well-being (0.66); family (0.62) and self-esteem (0.68). All versions of the KINDL questionnaire are supplemented with a "disease-module" consisting of a filter question and six items about possible long-lasting illness or current hospital admission.

Parenting stress index

Mothers and fathers reported via the Parenting Stress Index (PSI) full version on all follow-ups until seven years of age and correspondingly on the PSI short version (PSI-SF) at age nine [27].

Children's behavior

Children's behavior problems were reported on the Child Behavior Checklist (CBCL) [30] at ages 2, 3, 5, 7 and 9. At ages 7 and 9 teachers reported on Teacher Report Form (TRF) [30].

Demographic, birth and medical factors

Birth and medical information was collected from medical records at inclusion time. Socio-demographic variables were reported by parents before discharge from the hospital (Table 1.).

Analysis

Previous studies have shown that the intervention has an effect on child and parent-related stress and child behavior [26-30]. At nine years, stress and behavior are correlated with QoL variables and therefore used as covariates in analyses that tested group differences on QoL measures. Because of the clustering effects of twin pairs, groups were compared by means of multilevel modeling (Linear mixed models (LMM), SPSS statistics, version 20) [36]. Analyses were controlled for birth and medical factors and those that influenced outcome measures were included in the analyses to increase the validity of group comparisons. Agreement between parent's and children's scores in the different study groups was analyzed by intraclass correlations (ICC), and the difference between the two independent intraclass correlation coefficients for the PI and the PC groups was tested as described by Alsawalmeh & Feldt [37]. Effect sizes (ES) created by the use of Hedges' g are reported on predicted differences in mean scores between groups [38]. An effect size below 0.40 is usually regarded as small, a value between 0.40 and 0.60 as moderate and finally viewed as strong if ES exceeds 0.60. A p-value < 0.05 was considered significant.

Results

Participation and comparisons of background variables

Randomization resulted in well-balanced preterm groups with one exception. There was a significant difference between the preterm groups in terms of maternal education, as the PI mothers had an average of one year more of education than the PC group at the time of inclusion in the study (Table 1). However, maternal education had no influence on group comparisons in this study. Participation rates remained very high throughout the study. At nine years, the response rates on QoL across groups were 83% on children's self-reports and 85% on parental proxy reports (Figure 1). Fewer children were lost to follow-up in the PI group compared to the PC- and TR group. PC children, who did not respond to the Kindl questionnaire tended to be reported with more neonatal morbidity (SNAP II and Oxygen at 36 weeks GA) compared to PI children who dropped out, even though no statistical differences appeared. Mothers were the main informant of QoL proxy reports in all groups (PC: 84%, PI: 74%, TR: 92%).

Self-reported QoL in the PI and the PC group

PI children reported significantly higher QoL than PC children on the subscale "physical well-being" (F (1, 103) = 10.2, $p = 0.002$, ES = 0.57) controlling for birth-weight (BW) and neonatal illness severity (SNAP II). Physical well-being reported by children was influenced by BW (F (1, 118) = 6.5, $p = 0.012$) and SNAP II (F (1, 118) = 6.1, $p = 0.015$), indicating that children with lower BW or more severe neonatal illness tend to report physical well-being somewhat lower in both preterm groups. Children's physical well-being at age 9 was not influenced by children's gender but significantly associated with maternal (F (1, 118) = 7.6, p = 0.007), paternal (F (1, 97) = 5.7, p = 0.018) and teacher (F (1, 104) = 8.6, p = 0.004) report of total behavior problems at age 7. Finally, parents' proxy reports of physical well-being were strongly associated with children's reports (F (1, 108) = 36.0, $p < 0.0005$) but in that case the impact of BW and SNAP became non-significant, while the difference between the PI and the PC group endured (F (1, 104) = 8.4, $p = 0.005$). No significant differences between the PI and the PC group were found in self-reported quality of life on global QoL or the other subscales.

Parental proxy reported QoL in the PI and the PC group

PI parents reported significantly higher QoL than PC parents on two KINDL subscales. The first difference appeared in the subscale "emotional well-being" (F (1, 112) = 3.9, $p = 0.05$, ES = 0.34) when BW, SGA and SNAP II were controlled for; all of these were significantly associated with this outcome. Parental reports of emotional well-being were strongly associated with maternal report of child-related stress at age 7 (F (1,116) = 56.1, p < 0.0005). Similar associations were revealed between stress reported at age 2, 3 and 5 and emotional well-being, all of which made the impact of group allocation non-significant. Next, PI parents reported higher QoL on the subscale "school" (F (1, 116) = 9.2, $p = 0.003$, ES = 0.54) than PC parents after controlling for BW, SGA and SNAP II. Male gender was associated with lowered QoL in the school dimension (F (1, 115) = 8.1, $p = 0.005$) but this association disappeared when the significant association with teacher's report of attentional problems at 9 years had been controlled for (F (1, 99) = 32.7, $p < 0.0005$). A trend towards a difference between the PI and the PC group was found on parental reports of Total QoL before controlling for birth and medical factors (F (1, 113) = 4.0, $p = 0.054$, ES = 0.32).

Means of all QoL outcomes as reported by children and parents are presented in Figure 2. The strength of group comparisons are reported Table 2.

Agreement between children's and proxy-reported QoL

Intraclass correlations between children's and parent's reports of QoL varied between the KINDL-subscales and to some degree between groups (Table 3).

Significant differences between the PI and the PC group were detected in the subscales "emotional well-being" and "friends". In both cases the agreement between parents and children in the PI were low compared to the PC group. A similar difference between the PC and the TR group was

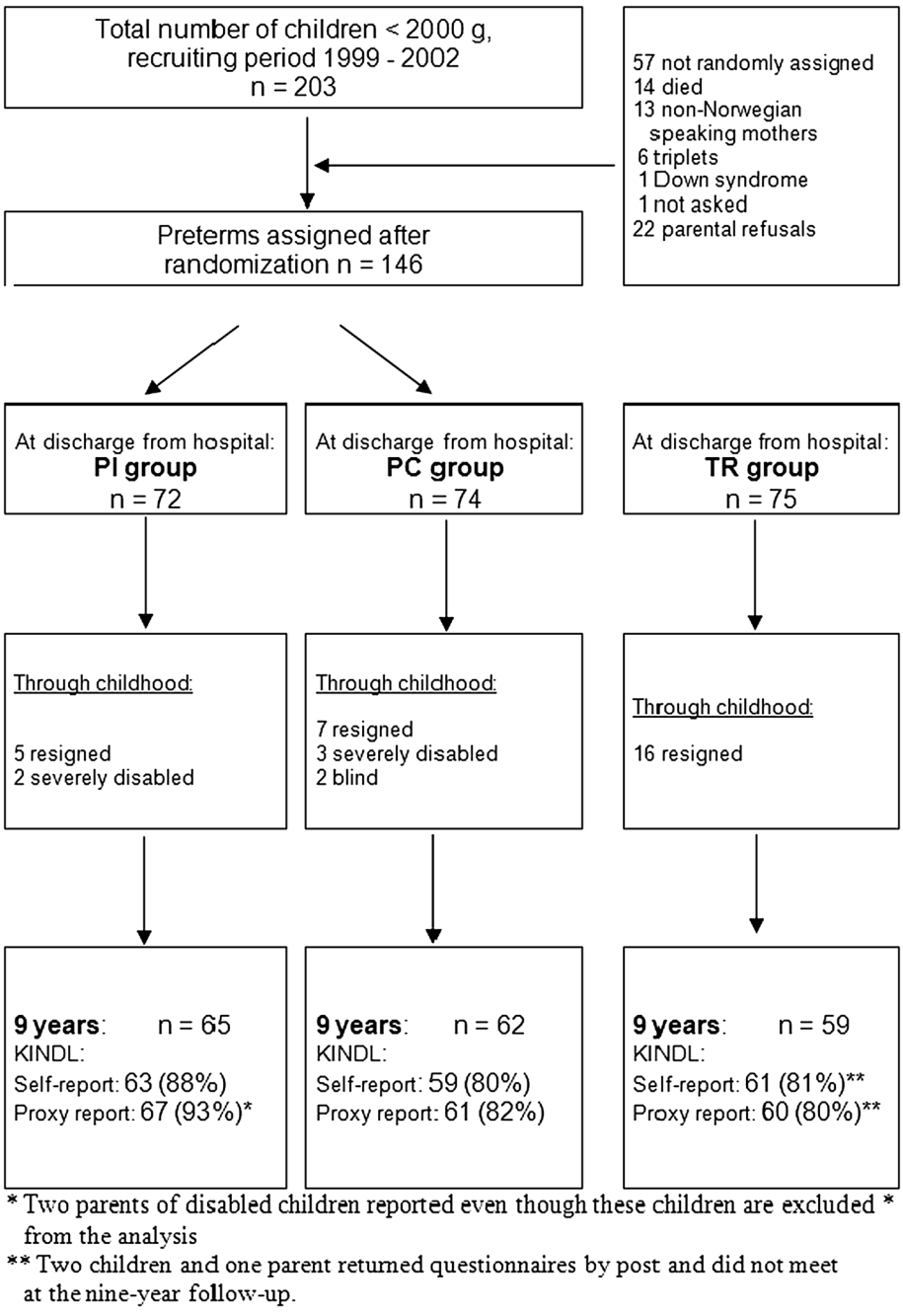

Figure 1 Study flow.

detected on the subscale "friends", while no significant differences were revealed between the PI and the TR groups.

Reports of QoL in the PI and the PC groups compared with the term reference group

The PC group compared with the TR group

Children in the PC group reported QoL at the statistically same level as term references, even though they tended to report lower QoL, especially on the subscale "school" (F (1, 119) = 3.2, p = 0.08, ES = 0.32) (Figure 2). On the other hand, parents in the PC group reported consistently lower QoL compared to TR parents on all subscales which constituted a five-point difference in mean Total QoL (F (1, 114) = 11.7, $p = 0.001$, ES = 0.65) Table 2.

The PI group compared with the TR group

Children in the PI group reported QoL similar to the TR group on all outcomes. The same pattern emerged in

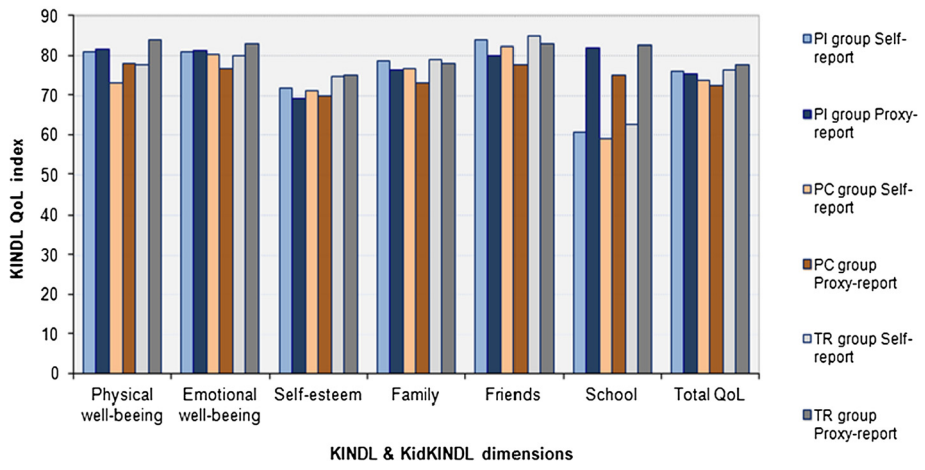

Figure 2 Mean QoL reported at 9 years by children and parents in the PI-, PC- and TR group.

the parental proxy reports, with one exception. PI parents perceived their children as having less self-esteem than did parents in the TR group (F (1, 119) = 6.5, p = 0.012, ES = 0.37). This difference disappeared when controlling for children's birth weight and paternal income at inclusion time, as lowered self-esteem was related to lower birth-weights and lower paternal income.

Discussion

This is the first paper from TISP in which the children themselves have reported outcomes independently of their parents. Previous reports of behavioral, motor and cognitive outcomes throughout childhood have indicated several positive effects of the intervention program [26-30,39-42]. This is now supplemented by reports of QoL, and the PI children differ from the PC children, as they experienced significantly higher physical well-being (subsequently named bodily well-being) at age nine, while PI parents perceived significantly higher emotional well-being and a better school-related life among their children compared to parents of preterm controls. Our hypothesis is supported as the intervention may generate a better quality of life among preterm born children and we suggest that the early intervention can have long-lasting positive effects on well-being in families rearing prematurely born children.

In general, QoL was reported at relatively high levels across all groups. Mean scores were mostly above 75 on total QoL and subscales (except school-related QoL) and were comparable to the general population of Norwegian children aged 8 to 16 years reported by Jozefiak [9,10]. Studies reporting QoL among preterm children of middle school-age are few, and those published have employed different definitions and measurements [6,16,17]. Self-reported QoL by preterm children at this age seems to have been only reported once [16], and to the best of our knowledge, this is the first report on QoL as an outcome in a RCT of an early intervention program in preterm children. Comparisons of results with other studies of QoL are therefore limited.

The PI children reported a higher level of bodily well-being than the PC group. Even though low BW and

Table 2 Strength of significant differences between study-groups (ES)

	PI scores > PC		TR scores > PC		TR scores > PI	
	Children	Parents	Children	Parents	Children	Parents
Physical well-being	0.57**	-	-	0.44*	-	-
Emotional well-being	-	0.34*	-	0.52**	-	-
Self-esteem	-	-	-	0.46*	-	0.37*
Family	-	-	-	0.46*	-	-
Friends	-	-	-	0.46*	-	-
School	-	0.54**	0.32 (*)	0.55**	-	-
Total QoL	-	0.34(*)	-	0.65***	-	-

Effect size (ES) = Hedges' g.
Level of significance: (*) = p <0.08; * = p < 0.05; ** = p < 0.01; *** = p < 0.001.

Table 3 Parent–child agreement in the three study groups and across all groups

KINDL®	PI group	PC group	TR-group	Across groups
	(n) ICC	(n) ICC	(n) ICC	(n) ICC
Physical well-being	(62) 0.57	(59) 0.48	(60) 0.46	(181) 0.50
Emotional well-being*	(63) 0.19	(59) 0.50	(60) 0.41	(182) 0.36
Self esteem	(63) 0.34	(58) 0.49	(60) 0.42	(181) 0.43
Family	(63) 0.53	(59) 0.37	(60) 0.53	(182) 0.49
Friends*,**	(63) 0.31	(59) 0.60	(60) 0.38	(182) 0.46
School	(61) 0.22	(58) 0.21	(60) 0.04	(179) 0.17
Total QoL	(63) 0.67	(59) 0.57	(60) 0.51	(182) 0.60

ICC: Intraclass-correlation.
n: number of parent–child pairs.
*Significant difference in parent–child agreement between the PI and the PC group ($p < 0.05$).
**Significant difference in parent–child agreement between the PC and the TR group ($p < 0.05$).

neonatal illness were negatively associated with QoL neither these nor other birth, medical or socio-demographic factors explained the group difference.

The difference was revealed by four questions that asked about children's feelings of being strong and full of energy, tired or worn-out or suffering from illness, and headache or stomach-ache [31]. We assume these questions reflect an inner quality of life experience which may be subtle and not readily observable by parents. Both PI and PC parents reported their children as being at similar levels, and neither group reported differences in the disease dimension of the KINDL questionnaire. This fairly robust difference between the PI and the PC children may be an effect of the intervention. Olafsen *et al.* [40] reported a possible positive effect of the intervention on infant-parent co-regulation. They suggested that the intervention improved the PI mothers' sensitization to their children's regulatory competence across the first year because mother-infant dyads in the PI group had established a kind of co-regulation at age one, while a strong correlation between parental stress and children's negative reactivity continued to be evident in the PC group. PI children were also reported by their parents to be more socially available at age one [41]. The development of infant self-regulation is a main developmental task in toddlerhood and preterms are particularly dependent on their parent's ability to support their early immature regulatory efforts [43]. Feldman has described noteworthy coherence in regulatory patterns across early childhood, including the physiological regulation of cardiac vagal tone and sleep-awake cyclicity (becoming measurable in the last trimester of the pregnancy) and regulation of emotional, attentional and behavioral development until age five [44-46]. Early emotional regulation, and especially negative emotionality, was similarly found to predict several psychosomatic problems in middle childhood in a Swedish longitudinal study from age 11 months until 9 years [47]. The main associations were found in symptoms of headache and stomach ache both of which were also influenced by parental perception of parental control. In another Swedish study of 10-year-old school children [48], Svedberg *et al.* reported that 27% to 50% of the variance in QoL could be explained by psychosomatic symptoms. Problems frequently reported were sleeping problems, depression, problems of concentration and stomach-aches. These studies refer to aspects of child well-being that are closely related to the questions asked and findings reported above. We wonder if better bodily well-being in the PI group is caused by better, early parent–child emotional co-regulation and as such creates a more nourishing family climate with less stress, as has previously been reported [27].

On the other hand, PI parents perceived their children to have a higher QoL than the PC group in the dimensions emotional well-being and the child's thriving in school. These analysis draw attention to the parental reports of stress, because parental proxy reports of emotional well-being were highly associated with maternal reports of child-related stress throughout childhood. The difference in emotional well-being between preterm groups seems to be fully explained by differences in maternal reports of stress. We have recently reported that PI mothers experienced less child- and parent related stress than PC mothers at all follow-ups until age nine. This consisted of statistically different patterns were PI children's adaptability increased and moodiness decreased with age while PC children were reported at less preferable levels throughout childhood. Furthermore, PC mothers reported significantly more stress related to mother-child interactions at age nine [27]. The impact of parenting stress on children's quality of life seems to largely agree with Lee *et al.* [25], who found that parenting stress was directly related to children's QoL in both term and preterm populations. It is also in accordance with the findings of Østberg and Hagekull, who reported general parenting stress to be the primary predictor of maternal ratings of children's adjustments [49]. Like Renk [33], these authors emphasize the importance of interventions that are able to change parental perception of children's adjustments in a positive, accepting direction.

The second difference appeared in parental ratings of children's well-being in school, where PI parents rated their children as enjoying a significantly higher QoL. Fewer attentional problems and more competencies in several aspects have previously been reported by parents and teachers in the PI group than the PC group [30]. It is not surprising that the same differences appear in parents' reports of school-related QoL. Being able to stay focused and take in messages are essential skills for all

children, enabling them to experience well-being, social belonging, and learning in school.

Preterm children in both groups rated their school-related QoL much lower than their parents did, a pattern similar to that previously described in population studies [9]. Children compare themselves with classmates every day and thus have more information about their strengths and weaknesses than their parents have. They may also be less aware of the period of time on which they were to report (only the previous week).

Concerning the second question asked, some differences in parent–child agreement did become visible. PI parents answered less similarly than their children (lower ICC) compared with the PC parents on the subscales "emotional well-being" and "friends". (A similar difference was detected between the PC and the TR group on the subscale "friends", with lower ICC in the term reference group). Less agreement between the parent–child reports may be perceived as less parental involvement in the children's inner life. In the study of relationships between maternal perceptions and young children's behavioral problems, Renk [33] showed that positive maternal perception correlated negatively and significantly with their involvement with their children, while the opposite pattern was described for negative maternal perception. Marques *et al.* [50] reported a higher QoL agreement between children diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) and their parents than in typically developing children, which may support the view described above. On the other hand, QoL agreement between children and their parents was recently reviewed by Jardine *et al*. [32], and several factors appear to influence the levels of agreement (type of measurement, children's age, parenting stress and the statistics employed). While higher inter-parental agreement concerning child and parent-related stress is supposed to indicate a well-functioning home environment [51] an opposite function may be related to the QoL agreement between parent and child, all of which makes the interpretation of results more difficult. Nevertheless, we suggest that the poorer agreement in the PI group is a sign of less involvement, due to less parental concern regarding the children.

A secondary finding was that both term and preterm children reported that their QoL was at a similar or lower level than their parents did. In a comparative study of QoL, Jozefiak *et al.* found that within the school sample, parents tended to rate their children's QoL higher than the children did, while the opposite divergence of views was identified in the referred sample of children [52]. This was only assessed at a group mean level, but the overall impression is that both preterm groups largely show a similar pattern to that of the school sample referred to above.

No differences in self-reported QoL were evident between the preterm groups and the full-term references. The PC group tended to score below the level of the PI and the TR group on several scales. Because the focus of the KINDL questionnaire differs in several respects from other studies that report QoL in middle childhood [16], comparisons with other studies are uncertain.

The burden of prematurity became more visible in parental reports. PC parents consistently reported their children's QoL as being lower on all subscales than did parents of terms. This is in agreement with previous reports [17], but somewhat surprising in view of the extensive follow-up program that offered continued opportunities to ask for help. Previous studies have identified parents of preterms as frequently experiencing a lack of professional support throughout childhood [17,53], and have suggested that this influences parents' reports of QoL. Even though all families in the current study could potentially have benefitted equally from the follow-up program, and enjoyed equality of support in their search for other services (psychological, pedagogical, physiotherapy) [30], significant differences persisted.

On the other hand, PI parents reported QoL similar to the reports by parents of terms on all scales, except for slightly lower self-esteem. This is promising, as it suggests that the intervention had long lasting effects that almost normalized PI parents' perceptions of their children in middle childhood. The KINDL self-esteem dimension includes statements such as; feeling proud of and pleased with oneself; having lots of ideas and being "on the top of the world" [10,31]. Preterm children have repeatedly been described as being more withdrawn and reticent than their full-term peers [2,5]. Such behavioral styles may have influenced parental proxy reports of self-esteem, as they may be perceived as signs of lowered self-esteem. Both groups of preterm children reported self-esteem at a similar level as term peers.

Strengths and limitations

A major strength in this study is the RCT design and the high participation rate throughout the study. 83% of the children and 85% of parents reported on KINDL at nine years. However, several limitations need to be mentioned. First, a limitation is inherent in the nature of the self-reported questionnaires, in that parents and their child may have influenced each other's reports. Families were requested to respond independently, but this could not be controlled as the questionnaires were completed before the follow-up session. On the other hand, the combination of self- and proxy reports is a strength as the two cover different aspects of children's life [54]. Secondly, we need to address the limitations of self-reporting by nine-year-old children. The KINDL questionnaires were validated in a Norwegian cross-sectional

survey [10]. Psychometric properties varied due to the children's age, and internal consistency was lower than in the original German version of KINDL among the youngest children (age 8 to 10 years), especially on the subscales "friends", "school" and "emotional well-being" [9,31]. On the other hand, Varni *et al.* concluded that self-reported health-related QoL may be reported by children as young as five [54]. Thirdly, comparisons with other studies are limited: [1)]Different questionnaires cover different aspects of QoL making comparisons irrelevant, [2)]Previous studies have reported on relatively old samples from the 1970s and 1980s and [3)]most studies have tended to focus on extremely preterm children, who may have experienced more difficulties overall than our sample.

Conclusions

This early intervention appears to have a long lasting influence on parental perceptions of their preterm child. First, PI parents reported that their children had significantly better "inner-QoL" on aspects of emotional well-being and contentment in school than parents in the PC group. Secondly, they reported a lower degree of parent–child agreement, which may indicate fewer parental concerns related to emotional and social functioning in the PI group. PI children reported better bodily well-being than the PC children. On all aspects of QoL except self-esteem, they are regarded by their parents as being similar to term peers. On the other hand, the parents of the preterm controls reported their children as having lower QoL in all areas (physical well-being, emotional well-being, self-esteem, family, friends and school) than did parents of terms at age nine.

Abbreviations

BW: Birth weight; CBCL: Child behavior checklist; CI: Confidence interval; ES: Effect size; ICC: Intraclass correlation; KINDL: Kinder Lebensqualität Fragebogen; LMM: Linear mixed model; MITP: Mother-Infant Transaction Program; NBAS: Neonatal behavioral and assessment scale; NICU: Neonatal intensive care unit; PC group: Preterm control group; PI group: Preterm intervention group; PSI: Parenting stress index, full version; PSI-SF: Parenting stress index, short form; QoL: Quality of life; SGA: Small for gestational age; SNAP-II: Score for neonatal acute physiology; TISP: Tromsø intervention study on preterms; TR group: Term reference group; TRF: Teacher report form.

Competing interests

The authors declared that they have no competing interests.

Authors' contributions

IPL carried out the statistical analyses, interpretation of the data and drafted the paper. BHH critically revised the statistical analyses, interpretation of data and the article for intellectual content. SEU contributed to the conception and design of the study and critically revised the paper for intellectual content. PIK contributed to the conception and design of the study and critically revised the paper for intellectual content. JAR contributed to the conception, design and implementation of the study and critically revised the interpretation of data and the article of intellectual content. All authors read and approved the final manuscript.

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APPENDIX

Appendix, part 1.

Table 1. Birth, medical and demographic characteristics of infants and parents

	PI Group N = 72	PC Group N = 74	TR Group N = 75
Infant characteristics			
BW, mean ± SD, g	1396 ± 429	1381 ± 436	3619 ± 490
400 - 1000 g, *n* (%)	20 (28)	20 (27)	
1001 - 1500 g, *n* (%)	15 (21)	20 (27)	
1501 - 2000 g, *n* (%)	37 (51)	34 (46)	
GA, mean ± SD, wk	30.2 ± 3.1	29.9 ± 3.5	39.3 ± 1.3
< 28 wk, *n* (%)	17 (24)	19 (27)	
28 - 32 wk, *n* (%)	36 (50)	37 (50)	
≥ 33 wk, *n* (%)	19 (26)	18 (24)	
Boy, *n* (%)	38 (53)	39 (53)	40 (54)
Twin, *n* (%)	16 (22)	14 (19)	0
Prenatal steroid use, *n* (%)	53 (74)	57 (77)	
SNAP II, mean ± SD	8.3 ± 10.9	10.4 ± 11.3	
CRIB score, mean ± SD, *N* = 85	3.2 ± 2.8	2.7 ± 2.9	
Received ventilation, *n* (%)	29 (40)	37 (50)	
Duration of ventilation, *n* (%)	7.0 ± 18.6	7.1 ± 17.3	
Postnatal steroid use, *n* (%)	9 (13)	10 (14)	
Oxygen therapy at 38 wk GA, n (%)	11 (15)	14 (19)	
Abnormal cerebral ultrasound, *n* (%)			
IVH grade 1 or 2	7 (10)	8 (11)	
IVH grade 3 or 4	3 (4)	5 (7)	
Perventricular leukomalacia	4 (6)	8 (11)	
Maternal and social characteristics			
Mother's age, mean ± SD, y	30.8 ± 6.1	29.1 ± 6.4	29.7 ± 6.1
Firstborn child, *n* (%)	40 (56)	37 (54)	27 (37)
Mother's education, mean ± SD,[a)]	14.6 ± 2.8	13.5 ± 3.2	14.9 ± 2.8
Father's education, mean ± SD,[a)]	13.8 ± 3.1	13.5 ± 3.2	14.4 ± 3.2
Mother's monthly income,[b)]	15.8 ± 7.7	14.6 ± 6.7	15.9 ± 8.0
Father's monthly income,[b)]	21.1 ± 8.7	19.9 ±8.1	21.9 ± 9.8

[a)] = education in years

[b)] = in Norwegian 1000 kroner, calculated for 131 families due to 15 twins

CRIB = Clinical Risk Index for Babies

SNAP II = Score of Acute Neonatal Physiology II

IVH = Intraventricular Hemorrhage

Appendix, part II

Figure 3. Study Flow from randomization up to nine years of age

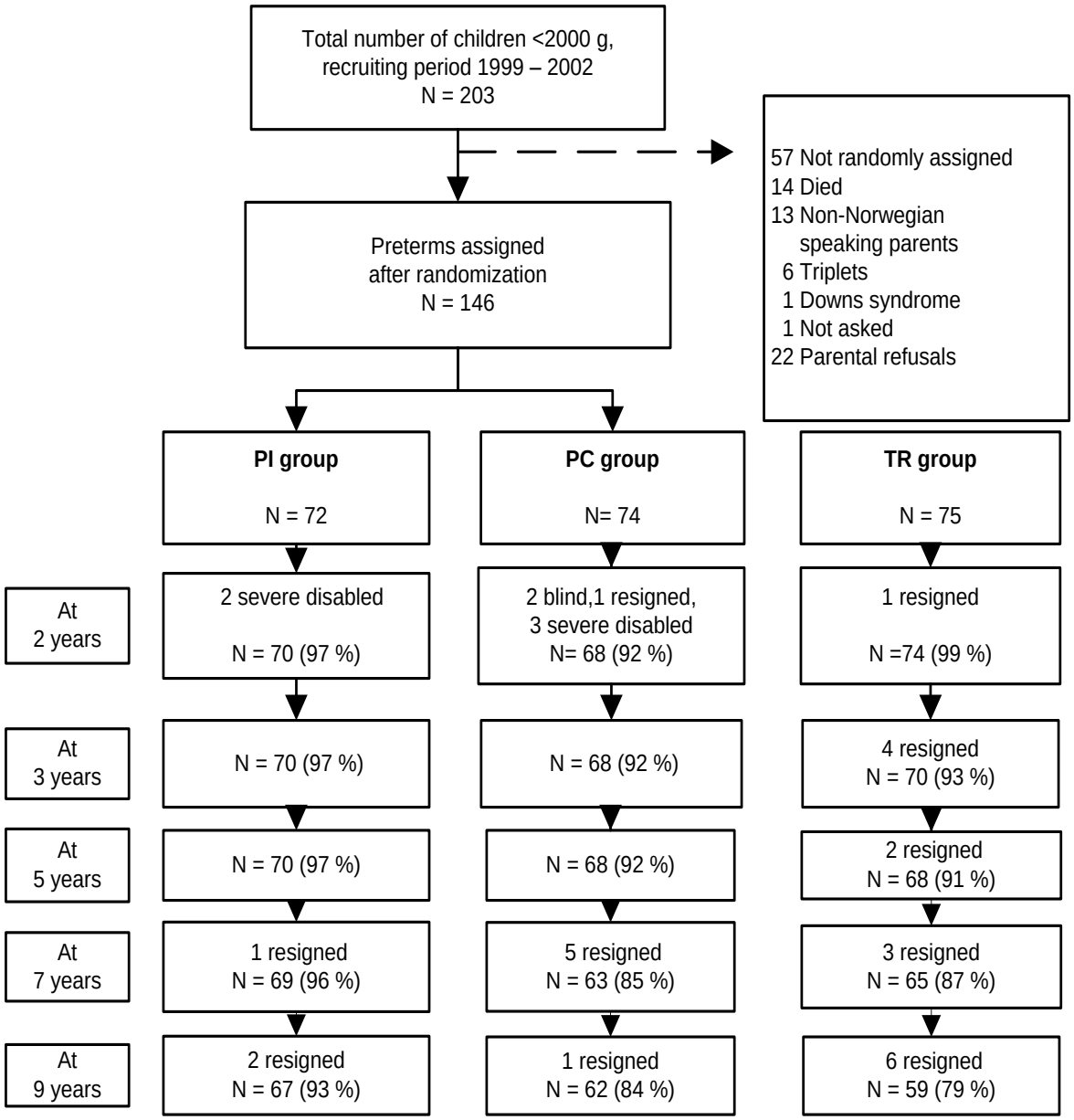

Figure 4. Contents of the modified Mother-Infant Transaction Program (MITP-M)

1. Ventilation session.
A talk about parent's experiences, feelings and thoughts related to the pregnancy, delivery and stay in the neonatal care unit while the child has been hospitalized.

2. Helping parents to know their baby.
The first session is dedicated to elicit the best alertness possible from the baby. Parents receive a demonstration of how their child may be, at least briefly, responsive to faces, voices and objects and interested in social interactions. Using elements from a NBAS assessment, parents are invited to look, ask and become attached to and proud of their baby's individuality.

3. How does the infant's body inform us about levels of arousal or balance?
This session focus on the expressions of the child's homeostatic reflexive system and how signs of stress or stability become visible in the skin, breathing patterns, automatic movements and visceral system. Parents are taught to understand how they can adapt to this language by adjusting their actions.

4. How do the infant's body movements inform us about levels of arousal or balance?
This session focuses on the infant's movements, tone and posture. Parents are instructed in how these expressions contribute information about the infant's level of organization/distress.

5. Understanding the infant's expression of and transitions between sleep and awake states.
The parents are introduced to their infant's unique expression of states and how states define the infant's availability and capacities.

6. How parents can help the infant become alert and available for interactions
This session builds upon the previous ones by incorporating knowledge about physiological and motor signs of stability or distress during the exploration of infant alertness.

7. How can parents use this knowledge in daily caretaking
Through activities such as waking, diaper changing, feeding and bathing, parents are guided to use knowledge from the previous sessions to provide care with minimal stress and disturbance regarding the infant's organization.

8. An overview of the first six sessions, preparing for discharge
In the last hospital session, all of the topics are discussed, the parents asks questions and elements are repeated if requested.

9. Home visit 1: Adaptation to the new environment at home
How the family may have made adjustments with the infant's needs in mind

10. Home visit 2: Expanding the family repertoire concerning play and mutual engagement
Parent-child social interactions are addressed, and parents' stories about new activities are applauded.

11. Home visit 3: Recognizing the behavioral style of the infant
The third visit, one month after discharge, focuses on parents' observations of their infant's behavioral style and on how they can adapt to the rhythms and capacities of their infant.

12. Home visit 4: Summarizing the program and recognizing developmental change
The program is summarized, and changes that have appeared are reviewed with the parents. The program is terminated, and the relationship between the family and the interventionist is closed in a solemn way.

Appendix, part VI

Questionnaire with extracted elements from SDQ

For administrasjon
ID-nr : 7 år ☐ 9 år ☐
☐☐☐

Sterke og svake sider (SDQ-Nor) utvalgte spørsmål

Vennligst kryss av for hvert utsagn: Stemmer ikke, Stemmer delvis eller Stemmer helt. Prøv å svare på alt selv om du ikke er helt sikker eller synes utsagnet virker rart. Svar på grunnlag av barnets oppførsel de siste 6 månedene.

Barnets fornavn ..... Gutt/Jente

Besvares av: ☐ Mor ☐ Far ☐ Lærer

	Stemmer ikke	Stemmer delvis	Stemmer helt
1. Omtenksom, tar hensyn til andre menneskers følelser	☐	☐	☐
4. Deler gjerne med andre barn (godter, leker, andre ting)	☐	☐	☐
6. Ganske ensom, leker ofte alene	☐	☐	☐
9. Hjelpsom hvis noen er såret, lei seg eller føler seg dårlig	☐	☐	☐
11. Har minst en god venn	☐	☐	☐
14. Vanligvis likt av andre barn	☐	☐	☐
17. Snill mot yngre barn	☐	☐	☐
19. Plaget eller mobbet av andre barn	☐	☐	☐
20. Tilbyr seg ofte å hjelpe andre (foreldre, lærere, andre barn)	☐	☐	☐
23. Kommer bedre overens med voksne enn med barn	☐	☐	☐

Har du andre kommentarer eller bekymringer?

Vær så snill å snu arket - det er noen få spørsmål til på den andre siden

Samlet, synes du at barnet ditt har vansker på ett eller flere av følgende områder: med følelser, konsentrasjon, oppførsel eller med å komme overens med andre mennesker?

Nei	Ja- små vansker	Ja – tydelige vansker	Ja – alvorlige vansker
☐	☐	☐	☐

Hvis du har svart "Ja", vennligst svar på følgende spørsmål:

· Hvor lenge har disse vanskene vært tilstede?

Mindre enn en måned	1-5 måneder	6-12 måneder	Mer enn ett år
☐	☐	☐	☐

· Blir barnet selv forstyrret eller plaget av vanskene?

Ikke i det hele tatt	Bare litt	En god del	Mye
☐	☐	☐	☐

· Påvirker vanskene barnets dagligliv på noen av de følgende områder?

	Ikke i det hele tatt	Bare litt	En god del	Mye
Forhold til jevnaldrende	☐	☐	☐	☐
Læring av ferdigheter/ leker etc.	☐	☐	☐	☐

· Er vanskene en belastning for deg eller familien som helhet?

Ikke i det hele tatt	Bare litt	En god del	Mye
☐	☐	☐	☐

Underskrift ..... Dato .....

Mor / Far / Andre (vennligst beskriv):

Tusen takk for hjelpen

Appendix, part V

Help-seeking Questionnaire

For administrasjon
ID-nr : 9 år

"Prosjekt tidlig intervensjon 2000"

Har barnet hatt behov for hjelp/veiledning fra instansene nederst på arket?

Ja ☐ Nei ☐

Hvis svaret er ja; sett en strek for når kontakten startet og når den opphørte.

Eks: 1 4
Fysioterapi |----------|

ÅR	1	2	3	4	5		7		9
Fysioterapi									
PPT									
Habilitering									
Barnevern									
BUP									

Appendix, part VI

Parents report of family and socio-economic factor prior to discharge from the hospital

Tidlig intervensjon 2000

Spedbarn, Barneavdelingen
RiTØ

Deltager nr……..

***Mors navn*……*Født*……..**

***Barnets navn*……*Født*……**

SOSIALE OG ØKONOMISKE FAKTORER

Sivil status

Gift ☐
Samboende ☐
Enslig ☐
Annet ☐

Mors utdannelse

Totalt antall års skolegang
(inklusiv grunnskole) ☐☐

Gått på høyskole/Universitet

☐ Nei
☐ Ja
Hvis ja, antall år……

Mors yrke (før svangerskapspermisjon)

Hjemmeværende ☐
Trygdet ☐
Arbeidsledig ☐
Student/skole-elev ☐
Deltidsarbeid ☐
I så fall, antall timer pr. uke ……
Fulltids yrkesaktiv ☐

Yrke ……

Fars utdannelse

Totalt antall års skolegang
(inklusiv grunnskole) ☐☐

Gått på høyskole/Universitet

☐ Nei
☐ Ja
Hvis ja, antall år……

Fars yrke

Hjemmeværende ☐
Trygdet ☐
Arbeidsledig ☐
Student/skole-elev ☐
Deltidsarbeid ☐
I så fall, antall timer pr. uke ……
Fulltids yrkesaktiv ☐

Yrke ……

SNU ARKET !

Bolig

Enebolig/rekkehus.....☐

Leilighet .....☐

Annet: .....

☐ Selveid

☐ Leier

Ca m^2 .....

Økonomi

Mors inntekt siste måned (før svangerskapspermisjon). Inkludert evt. trygdeytelser .....

Fars inntekt siste måned (inkludert evt. trygdeytelser).....