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Favorable parental perception of behaviour at two years' corrected age in very preterm-born children

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ABSTRACT

Problems in behavioural and emotional outcome are amongst the long-term sequelae of preterm birth. The exact prevalence and associations with perinatal risk factors are unknown. Minimal research has been performed in pre-school aged children, compared to school age. The primary aim of this study was to determine the prevalence of parent-reported behavioural and emotional problems at the age of two in children born at less than 30 weeks' gestational age and/or birth weight less than 1000 g. The secondary aim was to determine whether perinatal factors were associated with the behavioural and emotional outcome.

Perinatal characteristics of 144 preterm-born children from the NeoLiFeS cohort were collected retrospectively. Of these children, 101 parents filled out a Childs Behaviour Checklist (CBCL) at the corrected age of two. The results of the CBCL tests were presented as *Z*-scores, a Z-score of 0 indicating the mean of behavioural scores in the norm population. A *Z*-score higher than zero indicates less behavioural problems than average, a negative Z-score indicates more problems. Associations between perinatal risk factors and CBCL-scores were analysed using linear regression analyses.

Prevalences of clinically relevant CBCL scores were low, 4%, 2% and 5% for total score, internalizing score or externalizing score, respectively. Being part of a twin was associated with higher internalizing *Z*-scores, indicating less problems in emotional behaviour. Bronchopulmonary dysplasia was associated with lower *Z*-scores in total and externalizing behaviour. In conclusion, in our cohort generally very few problems in behavioural and emotional outcome were reported at the age of two.

1. Introduction

Problems in behaviour are part of the long term sequalae of preterm-born children [1–8], these problems occur significantly more in preterm-born infants, compared with their term-born peers [2,3]. Problems in behaviour typically become more evident when children enter school, as tasks become increasingly demanding and complex [4]. A meta-analysis has shown that behavioural problems occur in both internalizing (within the self) and externalizing (conflicts with others) spectra [5]. These problems can be described as for instance withdrawn, shy, and inattentive behaviour and a lack of social skills [6].

The association between perinatal risk factors and adverse behavioural outcome is not clear yet. Lower gestational age, length of stay in the NICU, lower birth weight, prolonged ventilation, treatment with corticosteroids, and intraventriculair hemmorhage (IVH) are risk factors that have been associated with behavioural problems [9,10]. However, a meta-analysis including a risk-factor analysis reported inconclusive results, where socioeconomic deprivation and neurodevelopmental or cognitive delay were the only consistent predictors of behavioural problems. No clear evidence was found for the prognostic value of other risk factors [11].

Behavioural problems often proceed into later childhood [12,13]. Thus, early recognition and attention for these problems in the follow-up of preterm-born children is important. Several studies have focused on behavioural outcome at school age, but only few at preschool age. Therefore, research at preschool age is needed to try to prevent poor behavioural outcomes later in life [3,12]. Early screening and recognition could possibly lead to early interventions, supporting the child in its

Abbreviations: BPD, Bronchopulmonary Dysplasia; BW, Birth weight; CBCL, Child Behaviour Checklist; GA, Gestational age; IUGR, Intrauterine growth restriction; IVH, Intraventricular hemorrhage; NEC, Necrotizing enterocolitis; PVL, Periventricular leukomalacia; SES, Socio-economic status.

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development.

For the assessment of behaviour in pre-schoolers, The Child's Behaviour Checklist 1.5–5 years (CBCL) is mostly used. This parental questionnaire indicates problems in the child's behaviour in six areas: anxious/depressed behaviour, withdrawn behaviour, sleeping problems, somatic problems, aggressive behaviour and destructive behaviour [6,14,15]. Two main scales are discerned: the internalizing and externalizing scale. The internalizing scale particularly indicates problems within the self, such as, but not limited to anxiety, depression, withdrawal behaviour. The externalizing scale, on the contrary, represents conflicts with other people [15].

As earlier stated, limited research has been performed on the prevalence of behavioural problems at pre-school age. Additionally, research on risk factors reported inconclusive results. Therefore, the aim of the study was to investigate the prevalence of parent-reported behavioural outcomes of preterm born pre-schoolers at 2 years old. In addition, we were interested if there were associations between specific perinatal risk factors and the presence of parent-reported behavioural problems at pre-school age. We hypothesized that the prevalence of behavioural problems would be increased compared with the norm population, and that perinatal factors that lead to a chronic disease contribute to these later behavioural problems.

2. Patients and methods

2.1. Study population

This study was performed at the outpatient clinic of the Beatrix Children's Hospital, University Medical Center Groningen (UMCG), the Netherlands. Infants were recruited from the NeolifeS cohort [16], a prospective observational study on infants born below 30 weeks of gestation and/or with a birth weight below 1000 g. The study was approved by the medical ethical committee of the UMCG (METC 2013-263), and written informed consent was provided by all parents. The recruited infants were born between May 2015 and June 2018. In this period, a total of 144 infants were recruited for the NeoLifes study. Of these children, 101 parents filled out a Childs Behaviour Checklist (CBCL) at the age of two, as is shown in Fig. 1. Children of parents not understanding Dutch were not able to fill in the list, and were therefore excluded from this study.

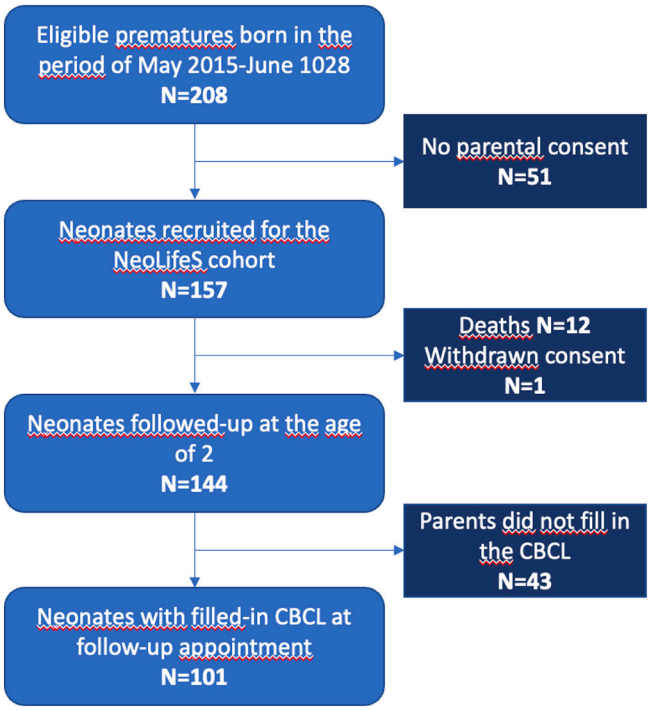

Fig. 1. Flowchart of the study population.

We obtained the infants' clinical information from their medical records. This included sex, gestational age, birth weight, small-for-gestational age (cut-off < p10, based on Niklasson et al. [17], twin pregnancy, Apgar score at 5 min, days of invasive ventilation, surgical/non-surgical necrotizing enterocolitis (NEC), IVH, periventricular leukomalacia (PVL), sepsis/infection, open ductus of Botalli, bronchopulmonary dysplasia (BPD) (defined as the need of supplementary oxygen at 36 weeks PMA), postnatal steroids use, retinopathy of prematurity, and socio-economic status (defined using the highest parental education).

2.2. Outcome

All infants born below 30 weeks of gestation and/or a birth weight below a 1000 g are routinely seen for long-term follow-up at a corrected age of 24 months. Assessment of behaviour is part of our follow-up program at a corrected age of 24 months. For this purpose, parents fill out the CBCL. The CBCL is a well validated questionnaire about the children's behaviour [15,18]. On this questionnaire, (one of) the parent (s) fill out questions about behavioural, emotional and social aspects of their child's life. The list consists of 100 questions, which parents can answer in 3 different ways:'1. Not true, 2. Somewhat/sometimes true and 3. Very/often true.' Using this list, health care workers obtain information on seven so-called 'problem' scales: 'emotional reactivity, anxious/depressed, somatic complaints, withdrawn, sleep, attention and aggression'. These various problem scales can be added up to form three summary scales:

1. Internalizing CBCL score: scores on problem scales 'emotional reactivity, anxious/depressed, somatic complaints and withdrawn behaviour' are added up.
2. Externalizing CBCL score: Scores on problem scales 'attention problems and aggressive behaviour' are added up.
3. Total CBCL score: scores on problem scales 'sleep problems and other problems' are added up.

These scores can be transformed into T-scores. Higher T-scores on the CBCL indicate more behavioural problems. For these three scales, scores of 60 through 63 (approximately 83th–90th percentiles) are so-called borderline scores and scores of ≥64 (>90th percentile) are considered as clinically significant [15,19]. The T-scores have a mean of 50 and an SD of 10. We transformed these CBCL T-scores into *Z*-scores. A T-score of 50 is transformed into Z-score of 0, a T-score of 60 into Z-score of −1 and a T-score of 40 into Z-score of +1. In this way, positive Z-scores indicate less behavioural problems than average, and negative scores indicate more behavioural problems.

2.3. Statistical analysis

The statistical program IBM SPSS Statistics 23.0 was used for the statistical analyses. A database was created with perinatal factors, perinatal complications and CBCL scores.

Univariable linear regression analyses were performed to find associations between perinatal risk factors and the behavioural and emotional outcome. Associations were considered as statistically significant with a p-value <0.05.

3. Results

In the cohort of 144 children, 101 CBCL lists were filled out. Twenty-seven children were lost to follow up and for 16 children lists were not filled out, or filled out incompletely.

Table 1
Characteristics of the children with and without filled-in CBCL list, presented as n (%) or median (p25–p75).

Characteristic/group	With CBCL (n = 101)	Without CBCL (n = 43)	P-value*
GA (weeks)	27.9 (26.5–28.9)	28.3 (26.9–29.6)	0.024
BW (grams)	1045 (825–1195)	1175 (875–1400)	0.239
BW (SD for GA)	−0.01 (−0.77–0.52)	−0.05 (−0.69–0.75)	0.763
Sex: male	62 (61%)	26 (60%)	0.917
Apgar score	8 (7–8)	8 (6–8.25) (N = 42)	0.731
Twin	25 (25%)	12 (28%)	0.692
SES		–	n.a.
Low	3 (3%)		
Middle	29 (29%)		
High	36 (36%)		
Missing	33 (32%)		
NEC or SIP	No: 86 (86%)	No: 41 (95%)	0.378
	NEC stadium 2A: 6 (6%)	NEC 2A: none	
	SIP or NEC ≥ stadium 2B: 9 (9%)	SIP or NEC ≥ stadium 2B: 2(5%)	
IVH			0.932
Grade 1	25 (25%)	10 (23%)	
Grade 2	6 (6%)	3 (7%)	
Grade 3	2 (2%)	2 (5%)	
Grade 4	3 (3%)	1 (2%)	
PVL			0.381
No	43 (43%)	16 (38%)	
Grade 1	57 (56%)	26 (60%)	
Grade 2	1 (1%)	1 (2%)	
Persistent ductus	Clinical: 14 (14%)	Clinical: 10 (24%)	0.206
	Ibuprofen: 37 (37%)	Ibuprofen: 11 (26%)	
	Clipped: 8 (8%)	Clipped: 1 (2%)	
Sepsis (positive blood culture)	36 (36%)	14 (33%)	0.396
Days of ventilation	3 (0.5–12)	4 (0−11)	0.760
BPD	32 (32%)	14 (33%)	0.918
Postnatal steroids	13 (13%)	5 (12%)	0.836

GA = gestational age, BW = birthweight, SES = socio-economic status, NEC = necrotizing enterocolitis, SIP = single intestinal perforation, IVH = intraventricular hemorrhage, PVL = periventricular leukomalacia, BPD = bronchopulmonary dysplasia. n.a. = not applicable.
* p-values derived from Mann–Whitney U tests, or Chi-square, where appropriate.

3.1. Patient characteristics

Patient characteristics are shown in Table 1. No differences for the presence of perinatal risk factors in children with and without CBCL-score were found.

3.2. Behavioural outcome at the age of two

The median total, internal and external CBCL T-scores were 45 (54–40), 45 (53–37) and 48 (57–43), respectively. These scores were translated into median Z-scores and were respectively +0.50 (−0.4–1.0), +0.50 (−0.3–1.3) and + 0.20 (−0.7–0.7). At 2 years four children (4%) scored a clinically relevant (≥64) CBCL total problem score, two children (2%) scored a clinically relevant internalizing problem score and five (5%) a clinically relevant CBCL externalizing problem score. Borderline scores (T-scores between 60 and 63) on total, internalizing and externalizing areas were obtained in four (4%), nine (9%), and nine (9%) children, respectively. In Table 2 these results are presented. There were no significant differences between boys and girls in T-scores for all three scores.

3.3. Perinatal risk factors and behavioural outcome

Most of the perinatal risk factors were not significantly associated with behavioural scores. However, the presence of bronchopulmonary dysplasia was associated with lower total and internalizing Z-scores in the univariable analyses, and with lower total and externalizing Z-scores in the multivariable analyses, adjusting for gestational age, SD for birth weight according to gestational age, and treatment with postnatal steroids. This means that infants with BPD have more problems in behaviour with a magnitude of 0.4 to 0.5 SD, compared with infants without BPD. Being a part of a twin is associated with better CBCL internalizing

Table 2
Z-scores of total, internalizing and externalizing behaviour, and distribution of normal, borderline and clinical problems regarding behavioural/emotional outcomes, both for the total cohort, and separately for boys and girls, at the corrected age of two.

Median Z-scores (p25; p75)	Normal N (%)	Borderline	Clinical	
Male + Female sex (N = 101)				
CBCL Tot.	0.50 (−0.40; 1.00)	93 (92%)	4 (4%)	4 (4%)
CBCL Int.	0.50 (−0.30; 1.30)	90 (89%)	9 (9%)	2 (2%)
CBCL Ext.	0.20 (−0.70; 0.70)	87 (86%)	9 (9%)	5 (5%)
Female sex (N = 39)				
CBCL Tot.	0.30 (−0.60; 0.70)	36 (92%)	2 (5%)	1 (3%)
CBCL Int.	0.10 (−0.50; 0.90)	35 (90%)	3 (8%)	1 (3%)
CBCL Ext.	0.20 (−0.50; 0.60)	34 (87%)	3 (8%)	2 (5%)
Male sex (N = 62)				
CBCL Tot.	0.5 (−0.40; 1.20)	57 (92%)	2 (3%)	3 (5%)
CBCL Int.	0.70 (−0.15; 1.70)	55 (88%)	6 (10%)	1 (2%)
CBCL Ext.	0.30 (−0.80; 0.80)	53 (85%)	6 (10%)	3 (5%)

CBCL = Child behaviour Checklist, tot. = total, int. = internalizing, ext. = externalizing.

Table 3
The relation between various perinatal risk factors and CBCL z-scores, using univariate linear regression analyses. B (95% CI) signifies the change in Z-score of the CBCL category, per unit change of each perinatal or demographic characteristic.

Characteristic	CBCL total				CBCL internalizing				CBCL externalizing			
	Univariable		Multivariable[#]		Univariable		Multivariable[#]		Univariable		Multivariable[#]	
	B (95% CI)	P-value	B (95% CI)	P-value	B (95% CI)	P-value	B (95% CI)	P-value	B (95% CI)	*P*-value	B (95% CI)	P-value
GA (per week higher)	−0.1 (−0.2; 0.1)	0.311	−0.1 (−0.2; 0.01)	0.080	−0.1 (−0.2; 0.1)	0.442	−0.1 (−0.3; 0.01)	0.070	−0.05 (−0.2; 0.1)	0.414	−0.1 (−0.2; 0.2)	0.363
BW (per SD for GA)	0.04 (−0.2; 0.2)	0.683	0.03 (−0.2; 0.01)	0.977	0.1 (−0.1; 0.4)	0.199	0.1 (−0.1; 0.3)	0.306	0.03 (−0.2; 0.2)	0.777	−0.01 (−0.2; 0.2)	0.895
Sex (female versus male)	−0.3 (−0.6; 0.1)	0.179			−0.3 (−0.7; 0.1)	0.177			−0.1 (−0.5; 0.3)	0.526		
Apgar score (per point lower)	0.1 (−0.1; 0.2)	0.258			0.1 (−0.1; 0.2)	0.320			0.04 (−0.1; 0.2)	0.583		
Twin (versus singleton)	0.3 (−0.1; 0.7)	0.121			0.6 (0.1; 1.0)	0.012*			0.2 (−0.2; 0.6)	0.363		
SES (high vs middle vs low)	−0.2 (−0.6; 0.2)	0.322			−0.1 (−0.5; 0.3)	0.622			−0.2 (−0.6; 0.2)	0.325		
SIP or NEC ≥ stadium 2B versus no or < 2B	−0.3 (−0.9; 0.5)	0.326			0.4 (−1.2; 0.3)	0.238			−0.48 (−1.1; 0.1)	0.131		
IVH	−0.1 (−0.2; 0.1)	0.477			−0.1 (−0.3; 0.1)	0.264			−0.03 (−0.2; 0.1)	0.747		
PVL	0.1 (−0.4; 0.3)	0.707			0.0 (−0.4; 0.4)	0.891			0.02 (−0.3; 0.4)	0.921		
Persistent ductus arteriosus	0.03 (−0.2; 0.1)	0.695			−0.1 (−0.3; 0.1)	0.156			0.003 (−0.2; 0.2)	0.973		
Sepsis	−0.1 (−0.3; 0.1)	0.484			−0.1 (−0.3; 0.1)	0.294			−0.1 (−0.3; 0.1)	0.528		
BPD	−0.4 (−0.8; −0.02)	0.038*	−0.5 (−0.9; −0.1)	0.026*	−0.4 (−0.9; −0.02)	0.040*	−0.4 (−0.9; 0.06)	0.085	−0.3 (−0.7; 0.1)	0.140	−0.4 (−0.9; −0.01)	0.046*
Postnatal steroids	−0.1 (−0.7; 0.4)	0.589	−0.1 (−0.7; 0.5)	0.739	−0.4 (−1.0; 0.2)	0.239	−0.4 (−1.0; 0.3)	0.272	0.2 (−0.3; 0.7)	0.772	0.3 (−0.3; 0.9)	0.287

GA = gestational age, BW = birthweight, SD score = standard deviation score, SES = socio-economic status, NEC = necrotizing enterocolitis, IVH = intraventricular hemorrhage, PVL = periventricular leukomalacia, BPD = bronchopulmonary dysplasia.

* Statistically significant (p-value < 0.05).

Included in the multivariable model BPD, GA, BW (SD for GA) and postnatal steroids.

scores. These results are shown in Table 3 and in Fig. 2.

4. Discussion

Our study indicated that the prevalence of parent-reported behavioural problems was low in this cohort of very preterm born children at the age of two. Only one to 4% of the children scored a clinically relevant T-score on the total, internalizing or externalizing problem scale at the corrected age of 2 years. The validated norm T-score in the CBCL questionnaire was 50, the corresponding *Z*-score 0. Our hypothesis that the prevalence of behavioural problems would be higher than that in the norm population was not confirmed. Instead, the reported behaviour in this cohort of preterm born children was above average, as the median CBCL total, internalizing and externalizing Z-scores in this cohort were up to half a standard deviation better than the norm. Of all perinatal risk factors associated with a chronic disease later on only BPD was associated with behavioural problems. We found a negative association between the presence of BPD and the reported total and externalizing CBCL scores, regardless of postnatal steroids. Finally, our results indicate that twins had less emotional problems than singletons, since twins scored better Z-scores in comparison to singletons.

Our results are not in agreement with existing literature on very preterm infants, where more emotional and behavioural problems were reported than in our cohort [5–7,12,20,21]. We cannot fully explain these discrepancies, but have thought about possible explanations.

First, the CBCL questionnaire is a parental report, which is a subjective instrument. Parents fill out the CBCL with the history of their child in mind. So, even if the child had behavioural problems, his or her parents may consider it as 'normal', just fitting into what they would expect of a preterm-born child. Or, sometimes the filled-out CBCL-lists were not in accordance with behaviour that children themselves showed during the follow-up visit, observed by doctors and healthcare workers. As mentioned before, parents mostly fill in the CBCL questionnaire solely, so, for a more objective measurement the use of multiple and more objective assessors might be better. When looking closely into the filled-out lists, it was clear that the lists were filled in very differently between parents. Some parents had filled out the lists very considerate, but others just circled 'not at all' (0) in one stroke on almost every question there is. Even term-born children will not score a 0 on every item on the list. One can think of several reasons for filling out the list

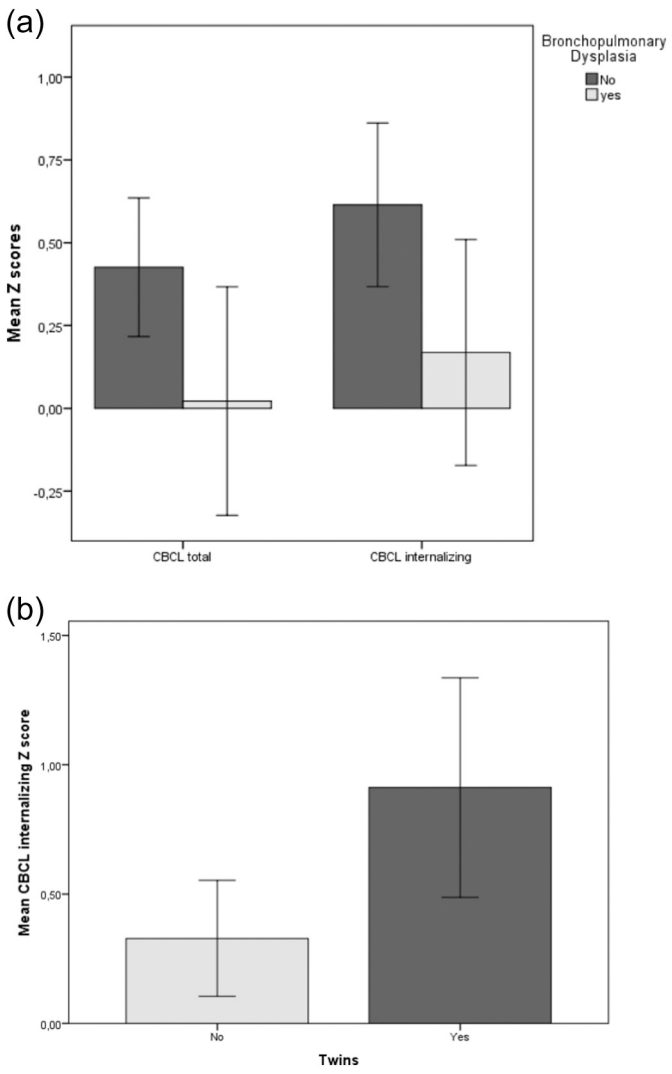

Fig. 2. a. Differences between children with and without BPD in CBCL total and internalizing *Z*-scores b. Differences in CBCL internalizing Z-scores between twins and individuals.

this way. Parents have been through a difficult time with their child, since it was born preterm. For this reason, it could be difficult to realize that their child's behaviour does not fall within the normal range. It is known that parents experience high levels of stress during the NICU stay. Preterm birth is often unexpected and the contact with their child is interrupted [22]. This often results in emotional and physiological problems, such as, but not limited to: anxiety, depression, fatigue and sleep depression [22,23]. This could possibly lead to a different interpretation of the questions in the CBCL-questionnaire, and/or it is imaginable that parents cannot face the fact that there are problems in behaviour, after going through this difficult start with their child. Another explanation might a protective attitude of parents after their long history with the child in the hospital. If they report normal behaviour, it will save their child from more hospital appointments and concerns.

Second, the age at follow-up in our cohort was younger (pre-school age) than the age in most of the existing literature. Although the CBCL-questionnaire was validated for this age, it is more difficult to notice behavioural and emotional problems, since the children do not attend school yet and have fewer social events than later in life. Thus, the age of 2 years might not be adequate to detect problems in behaviour and emotion.

Literature about the association between perinatal risk factors and adverse behavioural and emotional outcome is inconclusive [11]. Some studies have reported that a lower gestational age is associated with poorer behavioural outcome, but others did not find any association [9]. The length of stay in the NICU, lower birth weight, gender, the need of prolonged ventilation, treatment with corticosteroids and IVH are perinatal factors which may increase the risk of behavioural problems [9,10]. Treatment with dexamethasone could influence behaviour as well [24]. A lower SES is also strongly associated with behavioural outcome [10]. In our study all children had fairly complete medical records, in which perinatal factors were described. BPD was the only perinatal risk factor, independent from postnatal corticosteroid treatment, that we found to be negatively associated with behavioural and emotional outcome. This is in line with studies in very preterm infants with follow-up at school-age up to the age of 15, in which BPD was a negative predictor for educational outcome [25–28]. Studies in younger aged children were inconclusive [11]. A recent study in extremely preterm infants, however, also reported more behavioural problems at the age of 2 in case of BPD [29]. In contrast with our findings, they reported particularly more internalizing and less externalizing problems, whereas we, after adjustment, found more externalizing problems. Even so, the associations found at the age of 2 in both studies may predict problems later in life. We did not find any other associations, probably due to the low incidence of behavioural problems in our cohort.

We found a positive association with the reported emotional outcome when being part of a twin. Data on the differences in emotional and behavioural outcome between twins and singletons is limited. Moilanen et al. (1999) found that twin girls had less frequent psychiatric symptoms than singleton girls, but this did not apply to boys [30].

We recognize some limitations of our study. The first limitation is the loss to follow-up rate of 30%. The perinatal risk factors were, however, comparable with the included children and also not different from prevalences in other NICUs reported in literature. Therefore, we think that the present data are representative for preterm infants born in the mid-2010s.

We do realize that the SES data is missing in the lost to follow-up group, so that we could not compare the groups based on SES. We cannot rule out, however, that the presence of emotional or behavioural problems was the reason for not filling out the CBCL-lists. The second limitation is the fact that parental-reports were used to study the behavioural outcome, which is a subjective method.

In conclusion, our study indicated that parental-reported behavioural and emotional outcome of very-preterm children born in the mid-2010s is generally well. Furthermore, we found a negative association between the presence of BPD and the reported behavioural and emotional outcome and a positive association between the reported emotional outcome and being part of a twin. Further research is needed, not only to investigate more objective tools to study the behavioural and emotional outcome at this young age, but also to determine the behavioural outcome of this cohort later in childhood.

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CRediT authorship contribution statement

I declare that I participated in the design, execution, and analysis of the paper by T Bosch and colleagues entitled ‘Behavioural and emotional outcome at the age of two in preterm born children’, that I have seen and approved the final version and that it has neither been published nor submitted elsewhere. I also declare that I have no conflict of interest, other than any noted in the covering letter to the editor.

Declaration of competing interest

None declared.

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