ORIGINAL ARTICLE

Development and evaluation of a follow up assessment of preterm infants at 5 years of age

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Background: Long term follow up shows a high frequency of developmental disturbances in preterm survivors of neonatal intensive care formerly considered non-disabled.
Aims: To develop and validate an assessment tool that can help paediatricians to identify before 6 years of age which survivors have developmental disturbances that may interfere with normal education and normal life.
Methods: A total of 431 very premature infants, mean gestational age 30.2 weeks, mean birth weight 1276 g, were studied at age 5 years. Children with severe handicaps were excluded. The percentage of children with a correctly identified developmental disturbance in the domains cognition, speech and language development, neuromotor development, and behaviour were determined.
Results: The follow up instrument classified 67% as optimal and 33% as at risk or abnormal. Of the children classified as at risk or abnormal, 60% had not been identified at earlier follow up assessments. The combined set of standardised tests identified a further 30% with mild motor, cognitive, or behavioural disturbances. The paediatrician's assessment had a specificity of 88% (95% CI 83–93%), a sensitivity of 48% (95% CI 42–58%), a positive predictive value of 85% (95% CI 78–91%), and a negative predictive value of 55% (95% CI 49–61%).
Conclusions: Even after standardised and thorough assessment, paediatricians may overlook impairments for cognitive, motor, and behavioural development. Long term follow up studies that do not include detailed standardised tests for multiple domains, especially fine motor domain, may underestimate developmental problems.

Survival of very preterm and very low birth weight (VLBW) live born infants has increased substantially in the 1980s and the 1990s, with some variation depending on the population investigated and mortality definition used.[1–6] Developmental outcome varies even more depending on the age of the child at assessment, the population studied, and the definition of handicap used. Follow up during the first two years of life shows the presence of chronic illnesses, especially chronic lung disease, and handicaps such as cerebral palsy and severe developmental delay in 10–20%.[7 8] Long term follow up to school age reveals an even higher frequency of developmental impairments. These include motor performance problems, visual and auditory impairments, problems in cognitive and behavioural development, and school failure.[9–14] In a nationwide follow up of VLBW infants in the Netherlands, the need for special education increased from 19% at age 9 to 28% at age 14 years.[11] Similar figures have been reported from Florida and Cleveland.[15 16]

At the moment of hospital discharge, the prediction of the long term outcome of individual infants is difficult and not accurate. By the age of 2 years major handicaps such as gross motor disturbances, severe mental retardation, and chronic illnesses will have become clear. Diagnosis of learning disabilities, problem behaviour, and mild motor problems, however, is often delayed until school age. Therefore, long term longitudinal follow up of these children is necessary. Such follow up programmes should aim at the early detection of any developmental disturbances that necessitates developmental intervention as well as at the evaluation of perinatal treatment. A third goal is to contribute to the scientific knowledge of pathways by which specific types of damage in the perinatal period lead to developmental problems in childhood or even in adulthood and to recognise, at an earlier age, factors that predict developmental problems at a later age.

In the Netherlands the majority of very preterm infants are treated in one of 10 perinatal intensive care centres. After treatment, survivors are referred to their local hospital for the remaining neonatal admission and post-discharge care. In the first years after birth they return a number of times to the centre of initial treatment for follow up assessments. Though treatment is similar in the 10 perinatal centres, the follow up programmes are not standardised and post-neonatal care may differ throughout the country. Furthermore, because of a shortage in perinatal care the developmental departments are constantly urged to restrict follow up programmes to the bare minimum. Therefore a national working party on neonatal follow up designed a standardised follow up programme that would offer post-neonatal care as well as standardised follow up figures for all very preterm infants in the Netherlands.

In this paper we present the development of a paediatrician's assessment for the most important developmental domains at 5 years of age and the validation of this assessment against a set of standardised tests. This assessment should help paediatricians to identify, before the age of 6 years, which survivors of neonatal intensive care have developmental disturbances that may interfere with normal education and normal life.

Abbreviations: CBCL, Child Behavior CheckList; DDST, Denver Development Screening Test; ENT, ear, nose, and throat; NICU, neonatal intensive care units; TOMI, test of motor impairment; VLBW, very low birth weight

POPULATION AND METHODS

Study population

The study population included 5 year old survivors born before 32 weeks of gestation or weighing less than 1500 g and treated in one of three Dutch neonatal intensive care units (NICUs). For logistic reasons the inclusion periods varied slightly: from 1 October 1992 to 15 June 1994 in the University Medical Centre Nijmegen (UMCN), from 15 November 1992 to 1 January 1994 in the Academic Medical Centre Amsterdam (AMC), and from 1 January 1993 to 1 January 1995 in the Máxima Medical Centre Veldhoven (MMC). During these time periods 764 infants were consecutively admitted to the three NICUs. One hundred and thirty one (17%) died before the age of 5 years; and 46 patients below 30 weeks gestation and treated in the AMC were excluded because they participated in another study.[17] Twenty one children with known severe cerebral palsy, blindness, severe mental retardation, chromosomal abnormalities, or inborn error of metabolism were excluded, because it was obvious that they would not be able to perform the tests. As a result, 566 children were eligible for the study. Perinatal data were prospectively collected during admission, stored in the NICU based databases, and retrospectively retrieved for data analysis.

Paediatrician's assessment

The paediatrician's assessment at 5 years consisted of a questionnaire sent to the parents and a structured assessment by a paediatrician, specially trained for this purpose.

The questionnaire addressed the following domains: social economic status, general health, visual and auditory function, motor development, cognitive development, language and behaviour. Social status of the child was assessed by questions about residence, upbringing, and number of siblings, and by questions about employment and education of both parents. General health was assessed by questions about medical consumption (visits to outpatient clinic, number of hospital admissions, number of operations, number of diagnostic tests), somatic symptoms of the ear, nose, and throat (ENT), respiratory, gastrointestinal, and central nervous systems, and the use of medicines. Visual and auditory functions were assessed by questions about hearing without or with hearing aids and vision without or with glasses. Cognitive development was assessed by questions about school performance, including learning problems and the need for remedial teaching or special school. Problem behaviour was addressed by a shortlist of those 15 problem items from the Child Behavior CheckList (CBCL), that discriminated most between normal children and children referred to mental health services in the general population.[18]

The paediatrician's assessment started with a check and further exploration of the data from the questionnaire, measurement of growth parameters, and blood pressure. This was followed by a formal physical examination.

Neurological function was assessed according to Touwen.[19] This assessment consists of 40 items that cover tone, reflexes, muscle power, involuntary movements, posture, balance, coordination, and gross motor skills. The children were assigned to the following categories: normal (no neurological abnormalities), minor neurological dysfunction (neurological abnormalities without influence on normal posture or movement), or cerebral palsy (neurological abnormalities with abnormal posture or movements).

The Denver Development Screening Test (DDST) was used to assess neuromotor and cognitive functioning.[20] The DDST consists of 105 test items, clustered into four groups: motor function, language, adaptation, and social behaviour. Each test item has a cut off point at an age that 90% of Dutch children are able to perform it.[20] A child was classified as abnormal when he scored two or more delays beyond the cut off point in each of two groups, or two delays in one group plus one delay in another group without compensation in the same group. He scored at risk when he scored two or more delays in one group or one delay in a group without compensation in the same group. In all other cases he scored normal.

Language was assessed by an age appropriate Dutch Language Screening Test, designed and validated by Gerritsen.[21] This test consists of 39 items covering the use of vocabulary, comprehension, memory and production of language, use of plurals and prepositions, and pronunciation. Normal score is equal or less than 17, at risk ranges from 18 to 25 and abnormal from 25 to the maximal score of 52.

The results were summarised into five domains: cognitive development, neuromotor development, language development, behaviour and general health, and a final conclusion: (1) all domains normal, "optimal"; (2) further examination necessary, "at risk"; or (3) treatment necessary or already treated in one or more domains, "abnormal".

Validation instruments

The combined results of the paediatrician's assessment were validated against a combined set of standardised tests for cognitive, motor, and language development. This set consisted of the revised Amsterdam child intelligence test (IQ test),[22] the Movement Assessment Battery for Children (movement ABC),[23] and the full Child Behavior CheckList (CBCL).[24 25] Trained child psychologists and child physiotherapists performed these tests. They were blinded to the findings of the paediatrician's assessment. The IQ test took one hour, the movement ABC, 45 minutes.

The revised Amsterdam child intelligence test has been normalised for Dutch children between 4 and 7 years of age. Children with a score between −2 and −1 standard deviations were considered at risk, those below 2 standard deviations were abnormal.

The movement ABC indicates motor functioning in daily life.[23] Normative data have been collected in the USA, UK, and the Netherlands and yielded similar cut off points for normal American and Dutch children.[23 26] Total scores below or equal to 10.5 (15th centile) were considered normal, from 11.0 to 17.0 (5th centile) at risk, and above 17.0 abnormal.

The CBCL is a standardised measure of child behaviour, developed by Achenbach and normalised for Dutch children by Verhulst.[25 27] Total scores up to and including 59 are considered normal, from 60 up to and including 63 intermediate, and from 64 upwards "clinically important" disturbance of behaviour.

When all tests gave a normal result the final conclusion was "optimal"; when the results of one or more of the three tests was "at risk" or "abnormal", the final conclusion was "at risk" or "abnormal" respectively.

Statistical analysis

Differences of continuous perinatal risk factors between groups were compared with the Student's t test, and differences between dichotomous risk factor with the χ^2 test; p values <0.05 were considered statistically significant. Comparison of the paediatrician's assessment with the formal assessments was expressed as sensitivity, specificity, and percentage correctly classified. Since no arbitrary cut off points were involved and classification into normal or abnormal was fixed by the test definition, ROC curves did not apply. Positive and negative predicted values, likelihood ratios, and post-test probabilities estimated the performance of the test in practice.

RESULTS

Of the 566 eligible children, 135 (23.9%) were not assessed for various reasons (table 1), but language problems played an important role. Non-response rate was 65% (36/55) in children of non-Dutch and 19% (99/511) of Dutch speaking families ($p = 0.000$). Of the 431 tested children, 395

Table 1 Eligible and assessed patients

	n	%	n	%
Cohort 1992–94	764	100		
Died	131	17.2		
Excluded because of participation in another study	46	6.0		
Excluded because of severe handicap	21	2.8		
Eligible	566	74	566	100
Not assessed				
Address unknown			30	5.3
Moved outside the country			7	1.2
Impossibility to make a convenient appointment			52	9.2
Refusal by the parents			46	8.1
Assessed			431	76.2

Table 2 Risk factors in the study group and the non-response group

	Assessed (n=431)	Not assessed (n=135)	p value
Male	55%	49%	
Multiple births	36%	21%	0.001
Congenital malformations	10%	7%	
Gestational age, weeks (SD)	30.2 (2.0)	30.1 (1.9)	
Birth weight, g (SD)	1276 (332)	1327 (321)	
Caesarean section	48%	47%	
Apgar score at 5′ <7 (n=565)	17%	14%	
Resuscitation including endotracheal ventilation	24%	28%	
Positive pressure ventilation	49%	49%	
Surfactant administration	19%	18%	
Bronchopulmonary dysplasia	14%	17%	
Intraventricular haemorrhage, grade 1–4	19%	26%	
Days in NICU (SD)	32 (31)	32 (28)	

Table 3 Results of the separate tests

	Paediatrician's assessment	Movement ABC	IQ test	CBCL
Number assessed per test	412	404	402	407
Optimal	275 (67%)	228 (56%)	319 (78%)	314 (77%)
At risk	58 (14%)	86 (21%)	63 (16%)	37 (9%)
Abnormal	79 (19%)	90 (22%)	25 (6%)	56 (14%)

completed all the batteries of the paediatrician's assessment, IQ test, movement ABC, and CBCL. The exact number of children that completed each test is included in the tables.

Mean gestational age (30.2 (SD 2.0) weeks) and mean birth weight (1267 (SD 332) g) were relatively high compared to most follow up studies from the 1990s. This illustrates the selection bias caused by non-inclusion of infants with gestational ages below 30 weeks from one of the three participating hospitals. There were no differences in perinatal data between assessed and non-assessed children, with the exception of multiple births (36% of the assessed versus 21% of the non-assessed children; table 2).

In 412 children a full paediatrician's assessment was performed. The total assessment took approximately one hour and could be performed in a routine outpatient setting. The paediatricians involved felt it contributed highly to their ability to assess development in preschool children. Most children liked the different parts of the assessment and their parents were very satisfied with the thorough examination. The assessment resulted in 275 (67%) children classified as optimal, 58 (14%) as at risk, and 79 (19%) as abnormal. Of the 137 children classified as at risk or abnormal, 82 (60%) had not been identified at earlier follow up assessments.

The IQ test classified 56% of the children as optimal and 24% as non-optimal, the CBCL 77% and 23%. The movement ABC, however, indicated 43% of the children with a motor problem (table 3). The combined results of the three formal assessments indicated significantly more children with developmental disturbances than the paediatrician's assessment. Only 167 children (42%) scored optimal; 228 (58%) were identified as at risk or abnormal by at least one of the tests (table 4).

The specificity (88%) and positive predictive value (85%) of the paediatrician's assessment were adequate, but many children with a developmental disturbance were not identified by it, resulting in a sensitivity of 48% and a negative predictive value of 55% (table 4).

Further investigation of the 20 children classified as abnormal or at risk by the paediatrician's assessment but not by any of the validated tests showed that 10 had delayed language

Table 4 Comparison between the paediatrician's assessment and combined set of standardised tests (n=395 performed each test)

Conclusion of paediatrician's assessment	Conclusion of the combined set of standardised tests		
	At risk or abnormal	Optimal	All
At risk or abnormal	110	20	130
Optimal	118	147	265
All	228	167	395
		95% CI	
Sensitivity	48%	42–55%	
Specificity	88%	83–93%	
Positive predictive value	85%	78–91%	
Negative predictive value	55%	49–61%	
Prior probability (prevalence)	0.58		
Pretest odds	1.4		
Positive test			
Positive likelihood ratio	4.03	2.61–6.21	
Post-test probability	0.85	0.78–0.89	
Post-test odds	5.5		
Negative test			
Negative likelihood ratio	0.59	0.51–0.67	
Post-test probability	0.45	0.41–0.48	
Post-test odds	0.8		

development according to the DDST or the language screening test, in two of them combined with either behaviour or cognitive problems. Three children had an abnormal neurological assessment and four showed abnormal behaviour during the assessment. Three of these children were suspected of a non-optimal cognitive development while their IQs proved to be 89, 95, and 97, respectively. Two children were considered as not optimal without further specification.

Of the 118 children that were incorrectly not identified by the paediatrician's assessment, the majority failed on the movement ABC: 54 scored between the P5 and P15, and 25 below the P5. In 24 of them either behaviour problems or cognitive delay or both accompanied this. One third (n = 43) had a high total problem score on the CBCL, of whom 10 also had other problems. Nineteen children proved to have an IQ score of one SD or more below the mean, also mostly in combination with other problems.

Fifty four children had an abnormal outcome on both the paediatrician's assessment and the validated tests. One third of them (18/54) were not identified before the follow up appointment and did not receive any intervention therapy. Furthermore, multiple problems did not enhance earlier recognition or intervention. Sixty five per cent (55/85) of the children with a failure on more than one test were not identified previously.

DISCUSSION

Follow up of the first survivors of modern neonatal care, that started in the 1970s, showed that preterm birth has an effect well into adulthood.[28] Advances in neonatal care since the early days have led to an increase of survival. Developmental sequelae, however, are still a major problem, mostly because babies who would previously have been expected to die are now surviving neonatal intensive care.[8 29] Follow up studies have shown that developmental problems increase with age, and seemingly healthy toddlers may still have developmental problems and school failure at a later age.[30 31] This makes long term follow up mandatory, both for timely identification of children in need of extra help and to enable a true evaluation of neonatal intensive care. There is no consensus about what should be measured at what age.[30 32] As a result, outcomes in different studies are not always comparable. To achieve reliable outcome measurements, it is necessary to include validated and multidisciplinary instruments into follow up programmes that assess different domains of development. However, funding for such intensive programmes is usually deficient. We therefore tried to develop a comprehensive follow up instrument, manageable by a paediatrician, that could differentiate between preschool children with optimal, and with suboptimal or abnormal development. This instrument proved suitable for use in an outpatient clinic, although it takes approximately one hour to assess a 5 year old child. The assessment enabled the participating paediatricians in this study to identify 137 children with developmental problems, of whom 82 (60%) were not identified at earlier assessments.

Studies that succeeded in reaching a virtually 100% follow up rate have shown that the disability rate in children that are hard to follow up is considerably higher than in children that are easy to follow up.[33] This selection bias means that the number of children with developmental problems is even higher.

The specificity of the assessment was quite high, 88%. Only 20 children were assessed "false positive". Ten of them were considered to be at risk, and three abnormal because of language or behavioural problems and therefore regarded as not optimal. This means that using this instrument as a screening instrument, unnecessary referral for full assessment will be infrequent.

However, only half of the children with abnormal results on one or more of the standard assessments were identified by the paediatrician's assessment. The majority of them had either motor problems or behaviour problems or a combination; a minority failed on the IQ test. It could be argued that developmental disturbances that do not give rise to suspicion at school or at home and are not identified by a standardised and thorough paediatrician's assessment are not important. On the other hand many of these children encountered delays in more than one domain. Mild impairments at the age of 5 are often not disabling at that age and would perhaps not be insuperable when occurring alone. The combination of problems, however, robs these children from the potential to compensate and puts them at risk for later learning disabilities and social isolation. Some of them may even become more disabled than their peers with a single, but more severe impairment.

Some studies underlined a relation between motor dysfunction at an early age and cognitive problems at school age and later,[34–38] although other studies did not.[39] The failure to recognise motor disturbances at an early age may be one of the reasons for the seemingly increase in developmental problems with increasing age. On the test of motor impairment (TOMI), the predecessor of the movement ABC used in our study, Powls *et al* reported an improvement of motor function in half of the assessed preterm children between the ages of 6 and 8 years. However, at age 12 the percentage of school problems was 34 in children who failed on the TOMI at age 6 versus 5% of the children with optimal results.[40]

Motor disturbances that predict later developmental problems may be found at a much earlier age.[38 41] Hadders-Algra and Groothuis reported an association between mildly abnormal general movements at fidgety age (2–4 months post-term) and the development of attention problems and minor neurological dysfunction at the age of 4–9 years.[38 41] They hypothesised that perinatal hypoxia had resulted in long term changes in the striatic dopaminergic system. These disturbances could have influenced motor fluency and coordination in early childhood and behaviour in later life.

Motor performance is a result of information processing. The more task complexity increases, the more the information

processing becomes important. As the movement ABC tests more than only motor domain, it is, in all likelihood, a good detector of the information processing capacity of the nervous system. We therefore assume that a high impairment score in the movement ABC tests does not only indicate a motor problem, but also identifies children who are at risk for developmental problems in other domains. By inclusion of the movement ABC in the paediatrician's assessment, only six children with cognitive delay would have been missed erroneously, five with IQ scores between −2 and −1 standard deviations and one below 2 standard deviations. Therefore we propose to include the movement ABC in the paediatrician's assessment at age 5, and also base the need for further assessment on the results of this test.

Children of non-Dutch speaking families were far more likely not to participate in the assessment than their Dutch peers (65% versus 19%). The majority of these families belonged to a low socioeconomic class, had low educational levels, and experienced cultural barriers when they looked for medical help. Moreover, an insufficient test result in children of non-Dutch speaking families was in some cases interpreted as a linguistic problem and not as a cognitive problem. Sometimes this interpretation was correct, sometimes it was not. As a result, the tests were often inconclusive in this population. Preterm children in these families are therefore threatened by a combination of biological and social risk factors that may cause long delays before they get the interventions they need.

In conclusion, the systematic and standardised paediatrician's assessment at age 5 years did identify a significant number of children in whom the need for intervention was not recognised by the standard care they received. We also found that inclusion of the movement ABC might be necessary to avoid underestimation of a large number of developmental problems. Non-native children were seldom assessed properly.

Long term follow up studies of adolescents and young adults who were born preterm show that a developmental problem may pose a lifelong burden. Neonatal follow up should therefore aim to identify such problems at an early age and provide intervention therapy when needed. Furthermore, the evaluation of perinatal care should include late sequelae. Early predictors of these late sequelae are necessary in the research aimed at advancing perinatal care. We proved this could only be done with an extensive multidisciplinary assessment. Follow up studies that do not include detailed, standardised tests for several domains will underestimate developmental problems in survivors of neonatal intensive care and may be the reason for incomparability of follow up results and a seemingly increase of developmental problems at later ages. Our study indicates that there is no simple way to identify children in need of extra help or to give a true evaluation of neonatal intensive care.

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