Health status development in a cohort of preterm children

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Objective: To determine the impact of preterm birth on health status (HS) development at the ages of 5 and 10 years in a cohort of children born before term.

Sample: Six hundred eighty-eight children, born in 1983 with a gestational age of <32 weeks and a birth weight of <1500 g.

Design: Prospectively collected HS variables, obtained from the parents, were analyzed in a longitudinal perspective by using principal component analyses.

Results: One third of the sample had minor to severe HS problems at both ages of measurement. One third had problems on one assessment only. The remainder of the sample had no HS problems at either age. The analyses grouped the HS variables into 3 combinations. Problems in basic functioning, such as mobility or speech, decreased with age. Negative moods substantially increased, and concentration problems increased slightly. Specifically at risk were preterm born children with handicaps, boys, and children who were small for gestational age.

Conclusion: According to the parents, one third of the cohort had no HS problems at either age. The pattern of HS problems of the preterm born children changed between 5 and 10 years of age. (J Pediatr 2000;137:534-9)

Since neonatal intensive care was introduced in the 1960s, the survival rate of very preterm (<32 weeks) and very low birth weight (<1500 g) infants has substantially improved. However, the prevalence of major disabilities and handicaps has remained stable.[1-4] It is well documented that VPT or VLBW birth can result in psychologic, social, and physical problems.[3,5-9] In 1948 The World Health Organization defined health as a combination of physical, psychologic, and social functioning; and health status is a combination of these 3 domains.[10,11] The HS domains are most often divided into subdomains: physical functioning into physical complaints and motor functioning or daily functioning, psychologic functioning into cognitive functioning and emotional functioning, and social functioning into functioning toward peers and functioning toward adults.[10,11] However, in studies of HS in preterm born children, the use of a combination of these domains is rare. Most studies have focused primarily on the relation between perinatal factors and an HS outcome in a specific domain at a certain age in childhood. It is of interest to clinicians and parents to know whether these problems in childhood are stable or in which HS domain problems will decrease or increase.

Our aim was to study, in a large national cohort of VPT and VLBW children, the relations between the HS domains, the changes in HS with age, and the impact of factors such as gestational age on changes in HS.

HS	Health status
SES	Social economical status
VLBW	Very low birth weight (<1500 g)
VPT	Very preterm (<32 weeks)

METHODS

Sample

In a nationwide cohort of VPT and VLBW infants, 94% (n = 1338) of all infants, born alive in 1983 in The Netherlands, with a gestational age of <32 completed weeks and/or a birth weight <1500 g were enrolled. Prospective data collection was performed during infancy and at 5 and 10 years of age. Of the 966 survivors, 96% (n = 927) could be enrolled at 5 years of age, and 74% (n = 688) at 10 years of age. The non-response group at 10 years of age included more children with low social economic status, handicaps, and disabilities at 5

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Table I. Distribution of clinical and demographic variables

Perinatal factor	No.	%
Gestational age (wk)		
<28	62	9
28-30	159	23
30-32	275	40
>32	190	28
Percentile of birth weight against gestational age*		
≤2.3 (VSGA)	128	19
<10 (SGA)	122	18
≥10 (AGA)	437	64
Sex		
Female	353	51
Handicap		
None	550	80
Motor	22	3
Sensory	8	1
Cognitive	91	13
Combination	17	3
SES[14]		
Low	205	37
Medium	217	39
High	137	24
Maternal age at enrollment		
<25 y	200	29
25-29 y	253	37
>29 y	235	34

VSGA, Very small for gestational age; *SGA,* small for gestational age; *AGA,* appropriate for gestational age.
*Controlled for sex and parity.[15]

Table II. Grouping of the 16 HS variables before and after analyses

Theoretical HS sub-domains	Result of principal component analyses*
Physical complaints	Basic functioning problems
Vision problems	Speech problems (key variable)
Hearing problems	Vision problems
Respiratory problems	Hearing problems
	Moving problems
Motor functioning	
Moving problems	Concentration problems
Clumsiness	Not concentrated (key variable)
	School problems
Cognitive functioning	Clumsiness
Not concentrated	Unsociable
School problems	Wriggling
Speech problems	Reticent
	Afraid
Emotional functioning	
Unhappy	Negative moods
Worried	Tense (key variable)
Tense	Unhappy
Afraid	Worried
	Felt picked on
Social functioning	
Felt picked on	
Unsociable	
Reticent	
Wriggling	

*Respiratory problems not necessarily as HS indicator.

years of age. This resulted in a positive selection bias.[12] The history of the cohort is described in more detail in previous publications.[1,12,13]

Measures and Analysis Strategy

Objective clinical and demographic variables were assessed by trained pediatricians. Table I shows the distribution of gestational age, birth weight, sex, handicaps, SES, and maternal age that could influence HS development.[14,15] HS variables were prospectively collected from the parents by means of a questionnaire. To study HS development between 5 and 10 years of age, 16 variables were used in the analyses; these variables were assessed at both ages and covered all HS domains according to experts. The association between these variables was computed by using principal component analysis (SPSS Category 8.0; SPSS Inc, Chicago, Ill).[16,17] This kind of analysis (also known as *factor analysis* and *PRINCALS*) is often used in data reduction to identify a small number of dimensions that explain most of the variance observed in a larger number of variables. Variables with a strong correlation form a cluster in the outcome of the principal component analysis. These clusters of variables were labeled according to their content. In Table II, the 16 variables are grouped according to theoretical HS sub-domains and according to the results of the principal component analysis. From each cluster, a key variable was selected to represent the other variables in the cluster in further analyses. The influence of clinical and demographic factors (Table I) on HS changes with age was assessed by relating them to the key variables. Statistical significance was tested with repeated-measures analysis of variance.

RESULTS

Relationships Between HS Variables With Age

The average proportion of variance accounted for by the principal component analysis in 2 dimensions is 31%. Dimension 1 accounts for 21%, which is equivalent to a Cronbach's α of .76, and dimension 2 accounts for 10%, which is equivalent to an α of .46.[18] According to the principal component

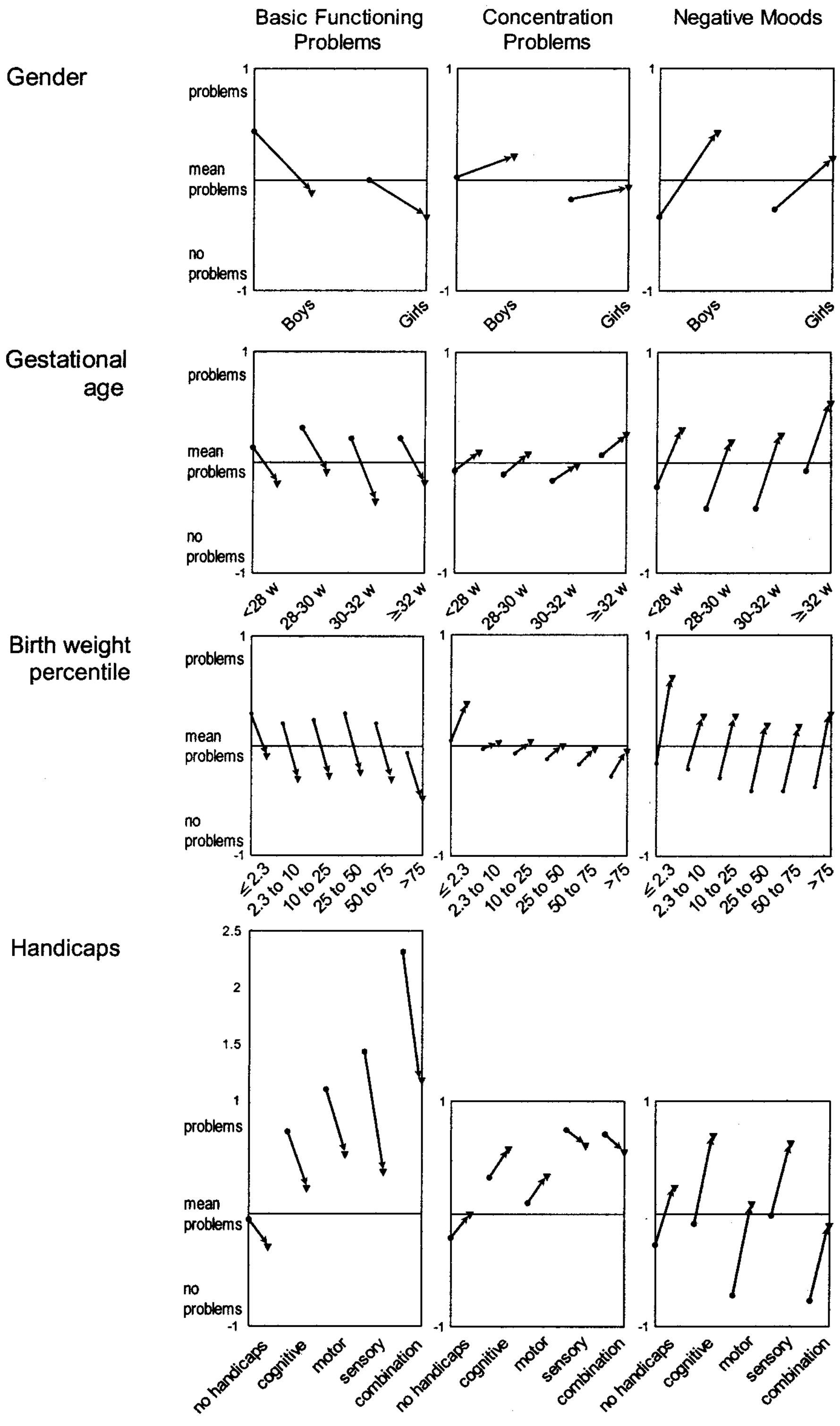

Figure. Clinical and demographic factors at 5 and 10 years of age with respect to basic functioning problems, concentration problems, and negative moods. A score of zero equals the mean HS problem score of the sample. The mean HS score indicates a minor problem level at the 2 time points. A score below zero indicates no HS problems, and a score above zero indicates minor to severe problems. The length of an arrow between the 2 ages of measurement indicates the amount of change in time. The differences between groups are indicated by differences in arrow length, and parallel lines indicate no interaction effects between group and time. A higher score represents more HS problems. *Filled circles* represent assessments at 5 years of age; *filled triangles* represent assessments at 10 years of age.

analysis, 35% of the children had HS problems at both ages and 32% had no HS problems at either age. The remaining third either had problems at age 5 years (16%) or at age 10 years (17%). The variables were clustered by the analyses in 3 main problem areas: basic functioning, concentration, and negative moods (see Table II). The variable "respiratory problems" did not belong to one of these areas and was therefore excluded. From each cluster, one variable was selected to represent the cluster in further analyses. The key variable "speech problems" represents basic functioning problems, "tensed" represents negative moods, and "not concentrated" represents concentration.

Relationships Between Clinical and Demographic Factors and HS Development

The relations between the key variables and the age factor are shown in the Figure. The magnitude of the differences between groups and the magnitude of differences with age with respect to the key variables are given in Table III.

HS appeared to change with age in all groups: problems in basic functioning decrease with age, negative moods increase, and concentration problems increase slightly.

Boys had more problems than girls with one exception: at 5 years of age, boys had fewer negative moods than girls (Figure, *A*). The differences between boys and girls, as well as differences between 5 and 10 years of age, are statistically significant (Table III). It can be concluded that boys overall have more problems than girls and that the change, either positive or negative, is greater for boys than for girls.

More concentration problems and negative moods were found at lower gestational ages, but problems in basic functioning were not linearly related to gestational age (Figure, *B*). Children born at ≥32 weeks' gestation had the most negative moods and concentra-

Table III. Repeated-measures analysis of variance between perinatal factors and age at assessment with respect to the 3 key variables

	Basic functioning problems "speech problems" F	Concentration problems "not concentrated" F	Negative moods "tense" F
Gender			
Between subjects (groups)	88.23*	40.14*	4.61†
Within subjects (age)	450.01*	37.73*	608.41*
Interaction	25.11*	2.82	37.77*
Gestational age (wk)			
Between subjects (groups)	4.99‡	10.30*	20.45*
Within subjects (age)§	286.28*	37.12*	431.32*
Interaction	5.61*	0.38	1.09
Birth weight percentile score			
Between subjects (groups)	4.30*	7.38*	8.58*
Within subjects (age)	353.87*	35.98*	463.59*
Interaction	1.52	2.92‡	4.17*
Handicaps			
Between subjects (groups)	222.98*	43.97*	15.32*
Within subjects (age)	222.58*	1.64	112.25*
Interaction	24.99*	2.63†	4.59*
Maternal age at enrollment by SES group			
Between subjects (groups)	7.69*	6.18*	4.60*
Within subjects (age)	354.12*	28.35*	360.61*
Interaction	8.25*	1.46	1.78

F, F-ratio as a result of the repeated measures analysis of variance.
*$P < .001$.
‡$P < .01$.
†$P < .05$.
§Differences between measurements at 5 and 10 years of age.

tion problems. One explanation could be that because of the inclusion criteria, these children were all small for gestational age. This is confirmed by the significant relationship found between birth weight percentile and HS problems (Table III). HS problems were generally more prevalent in children with lower birth weight percentile scores (Figure, *C*).

Children with handicaps had far more problems in basic functioning and concentration than the children without handicaps at both ages (Figure, *D*). Children with a combination of handicaps had many concentration problems and the most problems in basic functioning. Negative moods were found primarily in children with cognitive and sensory problems and in the children without handicaps. Surprisingly, even in children with handicaps, problems in basic functioning clearly decreased with age. Although negative moods increased in all groups, these problems were significantly less prevalent in children with motor handicaps and in children with a combination of handicaps at 10 years of age.

The overall pattern of a decrease in basic functioning problems and an increase in concentration problems and negative moods also applied to each maternal age and SES group (data not shown). Children of younger mothers have more HS problems. SES (estimated by occupational and educational level) did not have a linear relation with HS.

DISCUSSION

Two thirds of the study group had HS problems, which were mostly minor, at either one or both assessments. Not surprisingly, children without handicaps have far fewer basic functioning and concentration problems than children with handicaps do, and children with a combination of handicaps show the most problems. Negative moods are relevant at 10 years of age in children with a cognitive or a sensory handicap, but also in preterm children without a handicap. A similar result with respect to this non-handicapped group was reported by Schothorst et al.[19] Furthermore, boys had more problems than girls at both ages. Not only is the mortality rate for VPT and VLBW boys higher than that for girls, but boys who survive remain more at risk.[20,21] However, this is found in children born at term as well.[19] Although there was a relation between gestational age and

HS problems, the birth weight percentile appeared to be a more important risk factor. Probably the substantial number of VLBW children of relatively high gestational age in this sample has masked the influence of gestational age. In other studies, small-for–gestational age children had more HS problems than normal-for–gestational age children of similar gestational ages.[22,23] Silva et al expressed it as: "it is better to be born too early than too small."[23]

The non-linear relationship between HS problems and SES that we found is influenced by the age of the mother. Children of young mothers with low SES have the most HS problems. Older mothers may have obtained the maturity and the responsiveness that are important for adequate rearing of preterm children, in spite of low SES.[22,24,25] Another explanation for the ambiguous impact of SES may be the relatively small class differences with regard to exposure to health service created by the health security system in The Netherlands.[21]

The relative importance of HS problems in the cohort of preterm born children appears to change with age. Problems in basic functioning decrease, whereas concentration problems and negative moods increase. Although there are many longitudinal HS studies in preterm born children,[19-30] for several reasons comparison with the results of these studies is complicated. First, these previous studies had small samples of preterm children (range, 30-145), with diverse selection criteria (with or without handicaps and with various cut-off points for gestational age). They used a variety of instruments and informants of HS (eg, clinicians, parents, psychologists, and teachers). Second, studies including a physical domain, a psychologic domain, as well as a social domain in HS, are still limited, and these studies explored the HS domains one by one.[22,23,26,30] We explored new combinations of HS domains to pinpoint the problems that are relevant for preterm born children in particular. Third, in half of the longitudinal studies we found, analyses were restricted to correlations between different time points. Correlations tested the strength of a relation between time points, but not differences in height between the scores at both time points. As a result, changes in HS could not be reported. In the other longitudinal studies, some reported changes similar to ours,[20,23,24,29] and other studies deviated.[19,21,25] From this selection, only Silva et al[23] combined all HS domains. They measured changes in intelligence and problem behavior (social and physical problems) in 31 children born before term (<37 weeks), 71 children who were small for gestational age, and 748 children born at term with normal birth weight. Intelligence appeared stable, and problem behavior increased not only in the preterm groups but also in the control group. Therefore if the scores of the preterm groups had been standardized by the scores of the control group, no increases would have been reported.[25] In our study we cannot prove that the absolute changes we found are relative changes as well when compared with a norm or control group. A limitation of this study is that a norm or control sample was not available. Generalization of the results is limited to some extent by the positive selection bias of the study group. Nevertheless, the dropouts did not influence the HS changes we found, because only children with data up to 10 years of age were included.

The most remarkable HS change we found is the decrease in basic functioning problems, even in the group of children with a combination of handicaps. However, there is a plausible explanation for these results. Parents might develop a tolerance for some problems as their children grow older.[19,21] On the other hand, not all kinds of problems are detected at the same time. The normal development of children at a certain age is reflected in the type of problems the parents reported in this study. Basic functioning (eg, vision and speech) is important from early childhood onward. At "kindergarten age," concentration problems become more important to the parents. When children grow older, they start to communicate more about their moods. Therefore the parents could successively detect problems in basic functioning, concentration, and moods. As a result, when children reached the age of 10 years, the parents could have grown quite accustomed to the first, less to the second, but not to the last kind of HS problems. For instance, parents and children can get used to the burden of a child's handicap. They become physically adjusted with the aid of the available medical treatments and devices, and they become psychologically adjusted because "one can get used to almost anything." The basic functioning problems that appeared to be so overwhelming at 5 years of age were perhaps less intrusive in daily life at 10 years of age. As a result, parents may report fewer basic functioning problems when their handicapped child is 10 years of age, whereas the clinician might report as many problems as before, because the child remains handicapped. Because parents are the main decision makers with respect to the rearing and medical treatment of their children, their perception of their children's HS problems is most relevant.

In conclusion, a VPT or VLBW birth can have long-term effects. Only one third of the cohort born in 1983 had no HS problems at the ages of 5 and 10 years. The rest of the cohort had minor to severe HS problems. Problems in basic functioning decreased, and negative moods and concentration problems increased. Groups at the highest risk were preterm born children with handicaps, those with a birth weight below the 5th percentile, and boys. In the future, new HS follow-up studies, preferably with a control group, are needed to judge the validity of this study's results in current cohorts of preterm born children.

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