

# Quality of Life and its Determinants in Preschool Children with Down Syndrome

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**Abstract:** *Objective:* Children with Down syndrome (DS) show a delay in cognitive and motor development and have various concomitant health problems. We compared Health-Related Quality of Life (HRQoL) in preschool children with DS with a reference group, and investigated child-related factors (i.e., developmental quotient, adaptive function, health problems, problem behaviour), and maternal level of education on HRQoL.

*Method:* In a cohort of 55 children with DS, HRQoL was measured with the TNO-AZL preschool children Quality of Life Questionnaire (TAPQoL). Data from a reference group were used for comparison. Developmental Quotient (DQ) was assessed with the Bayley Scales of Infant Development II, adaptive function with the Pediatric Evaluation of Disability Inventory, health problems were derived from the medical file, and behavioural problems were measured with the Child Behaviour Checklist.

*Results:* Children with DS (N=55; mean age 41.7 months) scored significantly lower on the TAPQoL domains lung and stomach problems, motor function and communication compared to the reference group. DQ had a significant negative correlation with the domains lung problems and liveliness. Children with DS with respiratory or gastro-intestinal problems showed significant lower scores on lung problems and communication. Problem behavior had a significant negative correlation with the domains sleeping, appetite and social function. A low level of maternal education correlated negatively with positive mood. Adaptive function and congenital heart defect (CHD) did not significantly correlate with HRQoL.

*Conclusion:* Preschool children with DS show a lower HRQoL on particular domains of functioning compared to a normative sample. HRQoL of children with DS is correlated to DQ, respiratory and gastro-intestinal health problems, problem behaviour and maternal education, but not to CHD and adaptive function.

**Keywords:** Down syndrome, Quality of life, Developmental Preschool children, Children.

## INTRODUCTION

Down syndrome (DS) is the most prevalent chromosomal cause of intellectual disability. It occurs worldwide in a range of 1 out of every 625-1000 births [1, 2]. The syndrome results in higher risk for associated medical conditions, as well as cognitive, language, and behavioral problems. Health problems in young children with DS consist mainly of congenital heart defects (CHD), congenital anomalies of the gastrointestinal tract and respiratory problems. Recent decades have shown a significant improvement of mortality and morbidity, especially as a result of the successful early treatment of CHD [1-7]. Preventive health care programs have also contributed to the overall improved medical outcome [3-7]. Outcome assessments of children with a chronic disease that receive treatment should be focused more on health

related quality of life (HRQoL) and well-being [8]. HRQoL is defined as health status in 12 domains weighted by the impact of the health status problems on well-being [8]. HRQoL can be described according to four domains: physical, social, emotional and cognitive functioning. Medical issues like CHD, specific behavior problems, age and family context may play a role in HRQoL of children with DS.

A recent study on the HRQoL of 8-year-old children with DS revealed that their HRQoL was lower for the domains of motor functioning, autonomy, social functioning and cognitive functioning [9]. Knowledge about the HRQoL in younger children and the factors that might influence their HRQoL is lacking. To define the possible influences on HRQoL in young children with DS the delay in motor development is an important domain to study. In young children with DS this delay substantially affects functional performance most and is on average more affected than cognitive development [10, 11]. The more challenging language development in children with DS play an important role in their

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cognition as well. Particularly the expressive language lags behind while the receptive language is usually mental age appropriate [12-14]. A specific behavior phenotype of DS emerges around 2 years of age as a result of the relative strengths in aspects of visual processing, receptive language and nonverbal social functioning and weaknesses in gross motor skills and expressive language skills. Furthermore motor milestones in children with DS follow a specific sequence in their performance, mainly caused by disturbances in the system of postural control and tone [12, 15-18]. Development of children with disabilities can also be influenced by the family context, the level of education of the parents is part of this [19].

Finally children with DS show a wide variation in functional performance and ability levels, regardless the extent of the delayed fine motor skills [20, 21].

Compared to normally developing controls, specific behavior patterns of DS consist of stubbornness, oppositionality, inattention, difficulties in concentrating and impulsivity [22]. Children with DS have overall a relative predictable behavior and a good mood as favorable qualities [12].

In the present study we investigated HRQoL in children with DS aged 1 to 5 years old, compared to typically developing children, as well as the relation with child-related factors, such as, developmental age, adaptive function, health problems, problem behavior, and maternal level of education.

## METHOD

### Procedure

The VU University Medical Center (VUmc) has a dedicated outpatient clinic for children with DS, which

accepts children with DS referred by parents themselves, general practitioners, and pediatricians from within and outside the hospital.

Between 2005 and 2007 parents of all children with DS aged 12-60 months attending this VUmc outpatient clinic were asked to participate in this study. Inclusion criteria were a cytogenetic confirmed diagnosis DS and an age of 12-60 months at the start. If the parents were not able to speak and understand Dutch was considered as exclusion criterion. The clinical examinations were performed as part of our standardized clinical routine preventive health care program for children with DS with approval of the parents [5-7].

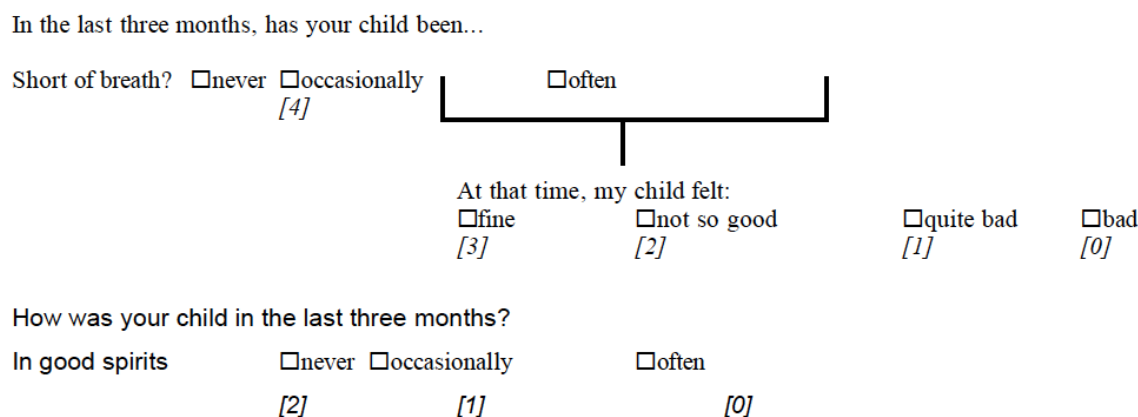
### Ethical Considerations

Under Dutch law, our study involving solely health related questionnaires sent to healthy adults (the parents of the children involved) and was waived submission for full consideration by the institutional review board.

Informed consent was given by the parents of the children with DS who participated.

### Measurements

For assessment of quality of life, the Netherlands Organisation for Applied Scientific Research (TNO-AZL) Preschool children Quality of Life (TAPQoL) form was used [8, 23]. This is a generic instrument consisting of 43 items, covering physical, social, cognitive and emotional functioning in preschool children aged 2 to 48 months. It measures parent's perception of HRQoL, defined as health status in 12 domains weighted by the impact of the health status problems on well-being (Figure 1). Lower scores



**Figure 1:** Item example TAPQOL (the scores attributed to the paired items are in italics). Reprinted with permission of Fekkes *et al.* [8].

indicate a lower HRQoL. The reliability and discriminative validity of its scales for infants as well as toddlers has been reported satisfactory [8, 23]. All parents were sent this questionnaire by mail.

The results of the questionnaires of parents of a randomly selected general population sample of 318 children (192 boys, 56.5%) aged 12–48 months (mean chronological age 30.6 months, sd 11.0 months) were used as normative data, this is the reference group as stated previously by Bunge *et al.* [23].

Cognitive abilities were measured by the mental scale of the Bayley Scales of Infant Development, second version (BSID-II) [24]. The mental scale consists of 178 items. The raw scores of successfully completed items were converted to developmental age scores. Developmental Quotients (DQ) were calculated using the traditional mental age method (Mental Age/Chronological Age x 100).

Children's behavior was measured by the Child Behavior Checklist (CBCL) Parent Form either the CBCL 2-3 for children aged 2-3 years, or the CBCL 4-18 for children aged 4-18 years. The CBCL is a questionnaire containing 113 items about childhood behavior problems [25]. Based on age- and gender-dependent norm tables, the presence of externalizing problem behavior (delinquency, aggression) and internalizing problem behavior (depression, withdrawal and somatization) was assessed. The present study used the Dutch version of the CBCL, which has good psychometric properties, also in children with developmental delays [26, 27].

Adaptive function was assessed with the Dutch adaptation of the Pediatric Evaluation of Disability Inventory (PEDI). The PEDI is a standardized parent interview that examines adaptive function with regard to three domains: self-care, mobility, and social function [10]. All children with DS were followed up at the outpatient clinic for DS patients at the VU University medical center, the attending pediatrician (MW), who examined all the children at all visits according the international guidelines of children with DS [5-7]. The medical files were used for data collection. Maternal education was defined as less than high school, high school/general equivalency diploma and more than high school.

### Statistical Analysis

Cronbach's  $\alpha$  was used to determine the internal consistency of the TAPQoL scales. A one Sample t-test was applied to compare the TAPQoL domain scores of

children with DS with the mean TAPQoL domain scores of the reference group [23].

Association between TAPQoL domain scores and chronological age and DQ was tested with Spearman's rho rank correlation coefficient. Partial correlation analysis was applied to test the relation between TAPQoL domain scores and PEDI domain scores with chronological age as control variable. A Mann-Whitney U test was applied to test the differences between children with or without CHD, and children with or without respiratory and/or gastro-intestinal problems. A Kruskal-Wallis test was applied to test the effect of maternal education.

Analyses were carried out with SPSS version 16.0 (SPSS Inc., Chicago, IL, USA), level of significance was set at  $\alpha=.05$ .

### RESULTS

In our study 98 children were eligible of which 55 finally participated. Response rate was 56% over the 3 years of data collection (2005-2007). The main reasons for not participating were lack of time ( $n=31$ ), illnesses of the child ( $n=8$ ) and some parents had forgotten their appointment ( $n=4$ ). The children who did participate were randomly distributed among the group of 98 children. The age distribution and characteristics of the participating children are shown in Table 1. Most children (87%) were Dutch Caucasian. In 54 children the diagnosis DS was based on trisomy 21 and one had mosaicism. The mental age is almost half as would be expected according to the chronological age (mean 21.2 vs. 40.6 months respectively).

For the DS sample, Cronbach's  $\alpha$  of the different TAPQoL scales ranged from 0.39 to 0.84 (Table 2). For most scales, the Cronbach's  $\alpha$  was above 0.60. However for the scales measuring stomach problems and skin problems, the Cronbach's  $\alpha$  was low.

### Down Syndrome Group vs. Reference Group

Table 2 shows the mean TAPQoL scores for DS and the reference group. Children with DS scored significantly lower on the domains lung problems ( $t=-3.34$ ,  $p<.01$ ), stomach problems ( $t=-2.17$ ,  $p<.05$ ), motor function ( $t=-8.73$ ,  $p<.001$ ), and communication ( $t=-12.99$ ,  $p<.001$ ) compared to the reference group, indicating a lower HRQoL on these domains. No significant differences were found for sleeping, appetite, skin problems, social functioning, problem behavior, positive mood, anxiety, and liveliness.

**Table 1: Characteristics of Young Children with DS (N=55)**

	DS children
Mean Chronological Age in months (sd; range)	40.6 (12.8; 15-69)
Gender	
Male	30 (54.5%)
Female	25 (45.5%)
Cognition	
Mean BSID Mental Age (sd; range)	21.2 (6.7; 10-37)
Mean BSID DQ (sd; range)	53.8 (10.1; 30-85)
Adaptive function(sd)	
Mean subscale PEDI Self care	36.2 (14.2)
Mean subscale PEDI Ambulation	44.3 (17.0)
Mean subscale PEDI Social function	35.0 (13.4)
Medical problems	
Congenital heart defect	27 (48%)
Respiratory problems	18 (32%)
Gastro-intestinal problems	11 (20%)
Problem behavior (N=30)	
Mean CBCL T-score (sd; range)	52.8 (7.8; 33-64)
CBCL borderline/clinical range (T $\geq$ 60)	N=6 (20%)
Maternal education	
Less than high school	4 (7%)
High school/general equivalency diploma	15 (27%)
More than high school	36 (65%)

**Table 2: Score Distribution and Internal Consistency of TAPQOL Scores for the DS Group (N=55) and Reference Group (N=318) [23]**

	DS				Reference			
	Mean (Sd)	Range	Median	$\alpha$	Mean	Range	Median	$\alpha$
Sleeping	78.5 (18.9)	25-100	75.0	.72	78.6	13-100	81.3	.89
Appetite	85.3 (15.4)	50-100	91.7	.76	81.9	33-100	83.3	.78
Lung problems	82.4 (22.8)**	17-100	91.7	.78	92.7	0-100	100	.82
Stomach problems	87.3 (15.8)*	50-100	95.8	.57	91.9	50-100	100	.53
Skin problems	90.6 (7.9)	67-100	91.7	.39	91.0	17-100	91.7	.78
Motor function	82.4 (12.7)***	25-100	81.3	.76	97.8	25-100	100	.89
Problem behavior	73.9 (20.3)	14-100	78.6	.84	68.9	14-100	71.4	.78
Social function	93.8 (12.5)	50-100	100	.81	91.8	33-100	100	.69
Communication	68.4 (11.6)***	19-88	68.8	.72	89.4	31-100	93.8	.81
Positive mood	98.5 (6.3)	67-100	100	.64	97.7	0-100	100	.91
Anxiety	78.2 (19.2)	33-100	66.8	.68	75.8	0-100	83.3	.63
Liveliness	96.1 (11.1)	50-100	100	.69	96.1	0-100	100	.80

Note.  $\alpha$  =Cronbach alfa.

\*p&lt;.05, \*\*p&lt;.01, \*\*\*p&lt;.001 measured by a one Sample t-test.

†Average Cronbach alfa for the 12 scales in the DS group was .77.

### Effect of Chronological Age and Developmental Quotient (DQ) on TAPQoL

Table 3 shows a significant positive correlation between chronological age (CA) and the TAPQoL motor function score ( $r_s=.50$ ,  $p<.001$ ), indicating that older children with DS showed a higher score for that domain. A significant negative correlation between CA and the TAPQoL communication score was found ( $r_s=-.30$ ,  $p<.05$ ), indicating that older children had lower scores on communication.

**Table 3: Correlations between TAPQoL Domain Scores and Chronological Age (CA) and Developmental Quotient (DQ)**

TAPQoL scales	CA $r_s$	DQ $r_s$
Sleeping	.18	.13
Appetite	-.14	.14
Lung problems	-.06	.30*
Stomach problems	-.23	.15
Skin problems	.16	-.07
Motor function	.50**	.16
Problem behavior	-.09	.16
Social function	-.03	.22
Communication	-.30*	.26
Positive mood	-.05	.13
Anxiety	-.04	.02
Liveliness	-.20	.41**

Note. \* $p<.05$ , \*\* $p<.01$ .  $r_s$ =spearman's rho rank correlation coefficient.

Correlation analysis of TAPQoL domain scores with BISD II DQ scores revealed significant positive correlations for lung problems and liveliness ( $r_s=.30$ ,  $p<.05$ ,  $r_s=.41$ ,  $p<.01$ , respectively) indicating that children with a lower DQ (i.e. a larger mental developmental delay) had lower scores on these quality of life scales (Table 3). For communication a nearly significant effect was found ( $r_s=.26$ ,  $p=.07$ ), indicating a trend for a lower HRQoL for the children with less communication abilities.

### Effect of Adaptive Function on TAPQoL

The mean scores on the PEDI domains self-care, mobility and social function are presented in Table 1. Partial correlation analysis (controlled for CA) did not reveal any significant relations between PEDI self-care, ambulation and social function scores and the different TAPQoL domain scores.

### Effect of Medical Conditions on TAPQoL

No significant differences on TAPQoL scores were found between children with or without CHD. All the CHD's had been corrected surgically when needed and at the time of the survey, hemodynamically important cardiac defects were no longer present in any of these children. The group children with DS with respiratory or gastro-intestinal problems scored significantly lower on the TAPQoL domains lung problems and communication compared to children without respiratory or gastro-intestinal problems (respectively,  $Z=2.31$ ,  $p<.05$ ;  $Z=2.31$ ,  $p<.05$ ; Table 4), while there was a trend in the same direction for the domain anxiety ( $Z=1.83$ ,  $p=.07$ ). Both groups did not significantly differ in CA. All children had normal vision and hearing functions, no serious defects were seen.

### Effect of Problem Behavior on TAPQoL

Significant correlations were found between TAPQoL and CBCL scores ( $N=30$ ) for the TAPQoL domains sleeping ( $r_s=-.42$ ,  $p<.05$ ), appetite ( $r_s=-.40$ ,  $p<.05$ ), social function ( $r_s=-.37$ ,  $p<.05$ ) and communication ( $r_s=-.46$ ,  $p<.05$ ). Children with higher scores on problem behavior had lower scores on these TAPQoL scales.

### Effect of Maternal Education on TAPQoL

A significant effect of maternal education on the TAPQoL domain positive mood was found (Chi square=16.1,  $p<.001$ ), indicating a lower HRQoL score for the low education group ( $M=87.5$ ) compared to the middle and high education group (respectively,  $M=100$ ;  $M=99.1$ ).

## DISCUSSION

This study provides an insight into the HRQoL of 55 preschool children with DS and shows the correlation with child-related (developmental quotient, functional status, health problems, problem behavior) and family-related (maternal education) factors. We compared the HRQoL with a normative reference group as well. In comparison with the reference group, children with DS showed a lower HRQoL on the domain of lung and stomach problems, motor function and communication. The HRQoL domains in children with DS were particularly affected by their developmental quotient, health problems (i.e. respiratory or gastro-intestinal), problem behavior, and maternal education. HRQoL in children with DS did not show a correlation with their

**Table 4: TAPQOL Scales for the DS Group with and without Respiratory or Gastro-Intestinal Problems**

TAPQOL Scales	Respiratory and/or Gastro-Intestinal Problems (N=24)		No Respiratory or Gastro-Intestinal Problems (N=31)	
	Mean	SD	Mean	SD
<b>Sleeping</b>	76.0	21.0	80.4	17.2
<b>Appetite</b>	82.3	16.4	87.6	14.4
<b>Lung problems</b>	74.6*	25.0	88.4	19.3
<b>Stomach problems</b>	84.7	17.3	89.2	14.5
<b>Skin problems</b>	92.0	8.7	89.5	7.2
<b>Motor function</b>	83.9	11.8	81.2	13.5
<b>Problem behavior</b>	69.6	21.8	77.2	18.7
<b>Social function</b>	91.0	13.9	96.3	13.8
<b>Communication</b>	64.6*	10.0	71.8	11.9
<b>Positive mood</b>	98.6	6.8	98.4	6.6
<b>Anxiety</b>	72.9	19.3	82.3	18.2
<b>Liveliness</b>	95.8	2.5	96.2	10.2

\* $p < .05$  measured by a Mann-Whitney U test.

adaptive function, and was not affected by the presence of a congenital heart defect.

Children with DS with more mental developmental delay (lower DQ scores) showed a lower HRQoL for lung problems and liveliness, and a trend toward significance for communication.

Recently HRQoL is investigated in a population sample of Dutch eight-year-old children with DS measured with the TACQoL [9]. Children with DS had significantly lower HRQoL scores for the scales gross motor skills, autonomy, social functioning and cognitive functioning compared to a normative sample [9]. Although the scales of the TACQoL are slightly different from those of the TAPQoL, the findings reported comparable with our findings, except for social functioning. Contrary to this study, we did not find a lower HRQoL for social functioning in our sample of young children with DS. That study also reported a developmental delay in cognitive function and more problem behavior in children with DS, however, the association between the individual differences in developmental delay and the observed level of HRQoL was not reported [9].

In our study CHD did not correlate with HRQoL. CHD in children with DS was considered to be the most relevant to morbidity and decisive in infant mortality. However over recent decades, there has been a substantial increase in the life expectancy of children

with DS. The minor role of CHD in morbidity in children with DS has mainly been due to the successful early surgical treatment of the CHD of these children and could be responsible for the favorable HRQoL results in our study [2, 28]. Children with DS scored significantly lower on the domain lung problems compared to the reference group, indicating a lower HRQoL on this domain.

One third of children with DS were reported to have difficulties with breathing or have other Respiratory problems [29]. Both wheeze ever, wheeze during the last 12 months and recurrent wheeze were more commonly reported in DS than in their siblings or controls [29, 30]. Respiratory problems are the most common reason for children with DS to be admitted and causes the excess in mortality [31, 32]. In a recent study of Verstegen *et al.*, 8-year-old children with DS with parent-reported recurrent respiratory tract infections (RRTI) showed more delayed development, behavioral problems and had a lower HRQoL compared with children with DS without RRTI [33]. The lower lung related scores found in our study underscore the importance of appropriate treatment and follow up of lung problems. Asthma and allergy do not seem to play an important role in this respect [30].

In our study we explored problem behavior and found a significant correlation between problem behavior and the TAPQoL domains sleeping, appetite,

social function and communication. Unexpectedly this was not found on the TAPQoL domain problem behavior. In our study 20% of the children with DS had CBCL borderline/clinical range ( $T$ -score > 60), which is lower but comparable with the 27% found in the study of van Gasteren *et al.*, in 8 year old children with DS [9, 25]. Eisenhower *et al.* found in children with DS at age 3, an age comparable with the children in our study, only 8% in the borderline/clinical range [33]. The problem behavior in children with DS ranked lowest among the groups of children with development delay, like autism and even showed fewer problem behavior than typically developing children. The behavior problems in children with DS described in this study increased over time up to age 5, while typically developed children showed a decrease in total  $T$  scores in time [34]. These results demonstrate that children with DS have more behavior problems when they get older and this may be the result of the increased expression of their externalizing behavior, like stubbornness [22, 32]. In our study the problem behavior had already a correlation with the HRQoL at the preschool age period.

In the present study we did not find any significant correlations of adaptive function (PEDI self-care, PEDI ambulation and PEDI social function scores) with HRQoL of children with DS, comparing different TAPQoL domain scores. In a study of 5 year old children with DS, Dolva *et al.* found a disadvantage of self care activities in those children with delayed fine motor skills [20]. Furthermore the children with DS appeared to be less affected in their functional mobility skills. In our study we did not find a correlation of mobility on the TAPQoL and motor function. Studies up to now report a variation in ability levels in children with DS. The children in our study population were relative young, as a result the differences and their functional performance could be less pronounced because of this age [20].

Finally we studied the education level of the mothers of the children with DS. Mothers from the low level education group reported a lower HRQoL for positive mood compared to the middle and high education group. Studies of typically developing children show the impact of aspects of families in promoting children's functioning and this may help to predict the development of children with disabilities. Hauser *et al.* found a significant positive correlation with mother's education level and growth in socialization domains [19]. On average, higher maternal education was associated with better

developmental (HRQoL) perspectives for their child with DS [19]. The family environment composite can be important in this matter and may be a significant determinant of growth in three domains: communication, daily living, and social skills [19]. The HRQoL domain mood in our study had a negative correlation, when the mothers had a lower education level. These mothers may have more problems with coping and as such have lower well being and positive mood, which influences their child with DS. At the same time having a child with DS may be a potential source of distress. The amount of care of the partner and the support from the environment play an important role in this matter [35]. The present study has several limitations. Especially the small sample size of 55 children and the relative young age of the group children. The HRQoL information has been collected by proxy and may be influenced by the mood of the reporting parent [34, 35]. Also we cannot exclude that the response rate may have introduced a selection bias. Although the most important results show significant differences our results should be interpreted with caution. Compared to 10-20 years ago these children had substantial limited life expectancy and a different morbidity spectrum. The current improvement of the medical issues obliges us to look into new medical issues and new opportunities for these children regarding long term developmental outcome and HRQoL.

## CONCLUSION

Preschool children with DS show a lower HRQoL on particular domains of functioning compared to a normative sample. HRQoL of children with DS is correlated to DQ, respiratory and gastro-intestinal health problems, problem behaviour and maternal education, but not to CHD and adaptive function.

## CONFLICTS OF INTEREST

There are no conflicts of interest

## WHAT'S KNOWN

Recent decades showed a significant improvement of mortality and morbidity in children with Down syndrome (DS). The substantial increase in life expectancy in DS, due mainly to the successful early treatment of congenital heart disease, caused a change in morbidity. Research in children with DS has focused on the medical issues and moves into Health Related Quality of Life (HRQoL) issues.

## WHAT'S ADDED

A lower HRQoL in the children with DS is correlated with developmental quotient, respiratory and gastrointestinal problems, problem behaviour and maternal education, but not with a CHD and adaptive function.

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