

# **Quality of life in adolescents with 22q11 deletion syndrome**

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Cursusjaar 2008-2009



# Quality of life in adolescents with 22q11 deletion syndrome

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The aim of the present study was to study the relationship between parental and child reports of quality of life (QoL) and the relationship of child- and parent characteristics on QoL. In a sample of 22q11DS adolescents and their parents, information concerning QoL, child characteristics and parent characteristics was obtained. Evaluation of the internal consistency of the subscales of the CHQ showed that several subscales were unreliable. However, reliable reports concerning the subscales bodily pain, general behavior, self esteem and family activities could be done. Against the expectation, mean QoL subscale scores of adolescents with 22q11DS were almost equal to the control group and the general norm group. In line with the hypothesis, it was found that the majority of the QoL (inter)subscale scores of the adolescents were significant. In the parent reports though, the subscales were less associated. Furthermore, it appeared that parents' and adolescents' reports of QoL were not strongly correlated with the (less observable) general behavior and self esteem subscales. Good agreement between adolescents and mothers was found on the (observable) subscale bodily pain; fair agreement between adolescents and fathers was found on the subscale family activities. Against the expectation, adolescent reports of QoL were not associated with child- and parent characteristics. Mother reports of the general behavior of their child were associated with the intelligence of the adolescent and mother reports of the self esteem of their child were associated with educational level of the mother. Father reports of the self esteem of their child were correlated with internalizing problems as reported by the adolescent. The findings in the present study partly fit with the expectations. In future research, examining factors associated with QoL assessing information concerning psychopathology of the child via parent-reports could be complementary. Also, future research with a larger sample of 22q11DS adolescents and with comparable control groups are needed to explore the usefulness of the CHQ-CF87 in the 22q11DS sample. Specific research into the relation between internalizing problem behavior and self esteem and possible appropriate interventions is necessary. When future research focuses on these and other (possible associating) factors, this will contribute to the perceived QoL of adolescents with 22q11DS.

**KEY WORDS:** *22q11DS; quality of life; child health questionnaire; psychopathology; youth self report; adolescence.*

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## Introduction

Research concerning 22q11 deletion syndrome (DS) has so far mainly focused on genetic, medical and psychiatric aspects of 22q11DS and the development of intelligence and behavior (Antshel et al., 2006; Gothelf et al., 2007; Niklasson, Rasmussen, Oskarsdottir, & Gilberg, 2009; Paylor & Lindsay, 2006; Robin & Sphrintzen, 2005; Swillen et al., 1997). Nowadays, most severe physical manifestations related to 22q11DS can be treated and almost all patients survive into adulthood (Paylor & Lindsay, 2006). Therefore, long term medical care is increasingly directed towards outcome measures such as behavioral and social consequences of (medical) treatments and recognition and

(early) treatment of behavioral and psychiatric disorders. This may contribute to the quality of life (QoL) of the 22q11DS patients (Theunissen, Vogels, Koopman, & Verrips, 1998).

22q11DS is a genetic disorder with an estimated prevalence at birth of approximately 1 in 4000 live births, making it the most common micro deletion syndrome and the second most common chromosomal disorder after Down's syndrome (Antshel et al., 2006; Devriendt, Fryns, Mortier, van Thienen, & Keymolen, 1998; Oskarsdottir, Vuijic, & Fasth, 2004; Paylor & Lindsay, 2006). The syndrome is caused by a structural genetic abnormality characterized by a deletion on the long arm of chromosome 22. Fluorescent in situ hybridization is a cytogenetic technique that is used to detect and localize the specific deletion. It has been a routine diagnostic test for over a decade and has resulted in increased awareness of the syndrome and in a rapidly growing group of patients (Paylor & Lindsay, 2006). Early diagnosis of 22q11DS is important because of the wide and variable phenotype of the syndrome. At this moment there are more than 180 structural and functional known abnormalities that can be associated with the syndrome (Robin & Sphrintzen, 2005).

The most common physical manifestations of 22q11DS include congenital heart defect, structural and/or functional palatal abnormalities, characteristic facial features, hypocalcaemia, delay in growth and immunodeficiency (Oskarsdottir et al., 2004; Ryan et al., 1997). In addition to the physical abnormalities, 22q11DS patients have characteristic cognitive, behavioral and developmental problems, speech abnormalities and a high risk for developing psychiatric disorders (Arnold et al., 2001; Jansen et al., 2007; Vorstman et al., 2006). The 22q11DS behavior phenotype includes poor social skills, introversion, disinhibition, impulsivity, anxiety and emotional instability (Niklasson et al., 2009; Swillen et al., 1997).

The extensive research into the development of psychopathology in patients with 22q11DS reveals that they are a specifically high-risk group for developing attention-deficit/hyperactivity disorders (ADHD), affecting approximately one third to one half of the population (Gothelf et al., 2007; Niklasson et al., 2009). Furthermore, 22q11DS patients are a high-risk group for developing schizophrenia, since approximately 30% have at least one incident of psychosis and about a quarter develop actual schizophrenia (Baker & Skuse, 2005; Murphy, Jones, & Owen, 1999; Swillen et al., 1997; Vorstman et al., 2006). In addition to schizophrenia, autism spectrum disorders (ASD), anxiety and affective disorders, and obsessive-compulsive disorder (OCD) are observed at increased prevalence rates compared with the general population (Baker & Skuse, 2005; Feinstein, Eliez, Blasey, & Reis, 2002; Gothelf et al., 2007; Murphy et al., 1999; Niklassen et al., 2009; Swillen et al., 1997).

The mean full-scale intelligence quotient (IQ) of patients with 22q11DS is about 70, indicating a borderline intelligence (De Smedt et al., 2007; Swillen et al., 1997; Vorstman et al., 2006). However, a wide range of cognitive abilities (mild mental retardation to average IQ) has been seen in 22q11DS patients. Mild mental retardation (MR) is common, while severe MR is rare. Psychiatric disorders are common in patients with developmental delay. However, within the

22q11DS group there seems to be no relationship between psychopathology and IQ (Baker & Skuse, 2001; De Smedt et al., 2007; Jansen et al., 2007). This finding suggests a specific vulnerability to psychiatric disturbance in the 22q11DS that is independent of cognitive disability.

Because the phenotype of the 22q11DS is wide and variable, decisions about supportive interventions should incorporate a broad range of relevant indicators of outcome, including QoL.

In recent years, there has been an extraordinary growth in research on pediatric perceived QoL and Health-related QoL (HRQoL) (Bastiaansen, Koot, & Ferdinand, 2005; Mandzuk & McMillen, 2005; Meuleners, Lee, Binns, & Lower, 2003). Although there is considerable variability in how QoL is operationalized across studies, many researchers assert that their measure of QoL encompasses the dimensions described by the World Health Organization. Recent conceptualizations recognize the multidimensional nature of QoL, including physical and psychological health, personal beliefs, social relationships and their relationship to important aspects of their environment. HRQoL is considered to be a sub-domain of the more global construct of QoL (Mandzuk & McMillen, 2005; Theunissen et al., 1998; WHOQoL Group, 1995).

Measurement of QoL could be an important addition in research and clinical practice, encouraging clinicians to think about issues beyond the physical and psychological well-being of the patient. A measure of QoL could also provide information regarding the effects of treatment, and so guide choices and perhaps encourage new developments (Bastiaansen et al., 2005). Since 22q11DS involves an increased risk for developing psychopathology, and as the behavioral issues are likely to become more problematic with increasing age (Arnold et al., 2001; Feinstein et al., 2002; Swillen et al., 1997), research into the relationship between QoL and psychopathology among patients with 22q11DS seems therefore relevant.

Studies that have examined the QoL in children and adolescents with 22q11DS are currently not available. However, extensive QoL research in similar populations is available, through which it is possible to get a better insight into the relationship between parental and child reports of QoL and the influence of several factors such as behavioral problems, IQ and more remote variables on QoL.

Parents' QoL assessments of children with 22q11DS raise many issues. It has been noted that adolescents are indispensable informants about their (behavior) problems because many of the problems they experience go unnoticed by their parents. In general, they report more psychological and behavioral symptoms about themselves than their parents do, with the symptom count discrepancy increasing with age (Stawsky et al., 1995). It may be that the accuracy of proxy ratings is dependent on the specific domains of QoL. Inconsistent proxy reports between children and parents have been reported frequently in the literature (Bastiaansen et al., 2005; Drotar, 1998; Eiser & Morse, 2001; Theunissen et al., 1998). Parent's perceptions of child-wellbeing (operationalized as QoL) may reflect for instance a clinical status, but this is not necessary so for the adolescent (Eiser & Morse, 2001). Furthermore, parents may also underestimate the complaints of their child. During puberty, hormonal changes and increased social demands may play a role in the development of psychological problems

and can affect the perceived QoL. Especially during adolescence, parents may have difficulty identifying the problems related to the functioning of their child.

Although many studies demonstrate that parent perspectives alone are insufficient to measure their child's QoL, any comprehensive assessment of the child's QoL is likely to include information from both the child and caregiver. Given the unavoidable differences between adults and children in their understanding of health and illness, and in experience of different situations, it is important to collect QoL data from multiple informants (Eiser & Morse, 2001; Mandzuk & McMillen, 2005). Therefore, many studies assert a combination of both proxy and self reports in QoL research.

To examine why parents and children report different levels of QoL, Davis et al. (2007) undertook a qualitative study. The results showed that children tend to have different response styles compared to parents. For example, children tend to provide extreme scores (highest and lowest score) and base their response on one single example, more than parents. However, parents and children seem to interpret the meaning of the items very similarly. This study suggests that concordance or discrepancies among parent-child ratings on QoL may be a result of different reasoning and different response styles, rather than interpretation of QoL items.

Research into the relationship between QoL and psychopathology, found that parents are able to judge the adolescents' externalizing problems, but are less accurate when it comes to internalizing problems. It is possible that parents underestimate the internalizing problems of their child (Bastiaansen et al., 2005; Eiser & Morse, 2001).

In a study of Bastiaansen et al. (2005) concerning determinants of QoL in children with psychiatric disorders, no significant association between intelligence and QoL was found. The results of this study indicate however, that the association between QoL and IQ is mediated by psychopathology. Child psychopathology indeed, was strongly associated with QoL. Over and above the association between psychopathology and QoL demonstrated in this study, several other child- and parent factors contributed to the variance in QoL reports, such as self-esteem and family functioning.

Although research on the effect of environmental, i.e. remote factors, on QoL is limited, it has been found that socioeconomic-status (SES) is associated with various QoL dimensions. Lower family educational level and single parent family are associated with decreased general health and problem behavior (Drukker, Kaplan, Feron, & van Os 2003). Therefore, it may be that environmental factors also affect the emotional and physical development of adolescents with 22q11DS.

Against the above background, the purpose of the present study is fourfold. First, QoL scores of adolescents with 22q11DS will be compared to those of a healthy norm group and to those of a general norm group using normative data from Landgraf, Abetz, & Ware (1996). Adolescents with 22q11DS are expected to experience a lower QoL than both control groups.

The second aim is to determine the associations between the subscale scores of the QoL measurements of successively adolescents, mothers and fathers. Positive associations between the subscale scores are expected within the adolescent, mother and father groups.

Third, the strength of concordance between parent and adolescent reports of QoL in adolescents with 22q11DS will be examined. Research suggests that agreement between adolescent and parent rating is higher for physical than for psychosocial health. Parents may have limited knowledge concerning their child's social and emotional well-being (Eiser & Morse, 2001).

The final aim is to examine whether QoL is related to psychopathology, social competence, IQ, gender, marital status and family educational level. Adolescent psychopathology is expected to be associated with poorer QoL in both adolescent and parent reports. Furthermore, QoL is expected to be negatively influenced by poor social competence and low intelligence, and by single parent families and low occupational level of the parents (Bastiaansen et al., 2005; Daliento, Mapelli, & Volpe, 2006).

## **Method**

### **Participants**

This comparative study is part of a longitudinal study on intelligence and behavior in children with 22q11DS in the age of 1½ - 15½ years<sup>1</sup>. Since the start of the study in 2000, over 200 children and adolescents from the Netherlands have been included.

The participants in this study consisted of the adolescents with 22q11DS and their parents. Inclusion criteria included the confirmation of the 22q11 deletion with fluorescence in situ hybridization or multiplex ligation-dependant probe amplification, age of 15½ years, the ability to complete the questionnaires concerning QoL and problem behavior and a cognitive evaluation of the adolescent.

The adolescents with 22q11DS were asked to evaluate their QoL using a standardized questionnaire. A total of 20 (10 males) out of 38 adolescents returned this questionnaire completely, leaving a final response of 53%. Of this group with a complete QoL- and behavior evaluation ( $n = 20$ ), a total of 18 adolescents participated in a cognitive evaluation (IQ). Data on intelligence were also present for 11 adolescents (out of 18 adolescents) with missing CHQ-CF87 reports. There were no significant differences between adolescents with missing data ( $M = 61$ ,  $SD = 11.6$ ) versus adolescents with complete data ( $M = 66$ ,  $SD = 12.0$ ) in intelligence (IQ) ( $t(24) = 1.86$ ,  $p = .075$ ).

Furthermore, the Youth Self Report (YSR) was used to obtain standardized reports of problem behavior and social competence in adolescents with 22q11DS. A total of 20 (53%) out of 38 adolescents returned this questionnaire completely. The final 22q11DS sample with a complete QoL-, cognitive- and behavior evaluation consisted of 18 adolescents. Descriptive information of the cognitive and behavior characteristics from the 22q11DS group is presented in Table 1.

Parents of adolescents with 22q11DS were asked to evaluate the QoL of their child. A total of 51 (67%) out of 76 parents returned this questionnaire completely. It concerned 28 mothers (55%) and

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23 fathers (45%). Descriptive information of the demographic characteristics of the parents is presented in Table 2.

The control group (n = 58, 50% males) consisted of adolescents recruited from the department of Child and Adolescent Psychiatry<sup>2</sup>. It concerns adolescents from the control group of a still ongoing study on prodromal symptoms of psychosis. An examination of the background characteristics showed that there were significant differences between the 22q11DS and control group in terms of age (M = 14.64, SD = 1.35 for the control group and M = 15.59, SD = .09 for the 22q11DS group; ( $t(59) = 5.35, p < .001$ )).

Furthermore, the intelligence of the control group adolescents and the 22q11DS adolescents was assessed using the Dutch version of the WISC-III-NL (Wechsler et al., 2002). There was a significant difference between the 22q11DS and control group in terms of total intelligence (M = 107, SD = 13.7 for the control group and M = 66, SD = 12.0 for the 22q11DS group; ( $t(74) = -11.46, p < .001$ ). Reports of problem behavior in the control group are not available.

Data from the general norm group was obtained from the CHQ manual (Landgraf et al., 1996) and concerned U.S. adolescents.

*Table 1. Age, intelligence and behavior of 22q11DS adolescents.*

	n	Mean	SD	Range
<i>Adolescents 22q11DS</i>				
Age	18	15.59	.09	15.43 - 15.78
Verbal IQ*	18	70	11.4	55 - 96
Performance IQ*	18	68	11.7	55 - 89
Total IQ*	18	66	12.0	47 - 92
Internalizing (T score)**	20	15.35	5.68	6 - 27
Externalizing (T score)**	20	10.50	4.33	2 - 20

\* Data from the WISC-III-NL

\*\* Data from the YSR

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Table 2. Demographic characteristics of the parents of 22q11DS adolescents.

	Fathers (n=23)	Mothers (n=28)
<i>Marital status</i>		
Married/ living together	21 (91%)	26 (93%)
Divorced	2 (9%)	2 (7%)
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<i>Family educational level</i>		
High	6 (26%)	7 (25%)
Middle	8 (35%)	10 (35%)
Elementary/ low	9 (38%)	11 (40%)

## Measures

### *Child Health Questionnaire-Child Form (CHQ-CF87).*

One of the best known and most widely used non-categorical measures of perceived QoL for children and adolescents (10-18 years) is the Child Health Questionnaire Child Form (CHQ-CF87; Landgraf, Abetz, & Ware, 1996). Research demonstrated that the CHQ-CF87 can be used for adolescents with or without health conditions/ illnesses, and has been translated, validated and used in many different countries, including the Netherlands (Landgraf et al., 1996).

The 87 items included in the CHQ-CF are intending to reflect the broad domains of children's psychosocial health and physical health, from the perspective of the child. Participants are asked to rate each item using a four- or five-point scale. All positively scored subscales range from 0 to 100, with higher scores indicating higher QoL.

In addition to a total score, the CHQ-CF87 contains two broad domains: physical and psychosocial health. The Physical Health domain has three subscales (Physical Functioning (PF); General Health (GH); Bodily Pain (BP)) and the Psychosocial Health domain comprises five subscales (Role Functioning Emotional (RE); Role Functioning Behavioral (RB); General Behavior (GB); Mental Health (MH); Self Esteem (SE)). Besides these eight subscales, the CHQ-CF87 comprises a ninth' separate scale Family Activities (FA) (Landgraf et al., 1996).

### *Child Health Questionnaire-Parent Form (CHQ-PF50).*

The CHQ-PF50 consists of 50 items and is a widely used questionnaire to describe a child's physical, emotional and social well-being from the perspective of a parent or guardian.

Equally to the CHQ-CF87, the parent form of the CHQ contains two broad domains: physical and psychosocial health. Unlike the CHQ-CF87, the parent form comprises two more subscales; Parental Impact-Time (PT) and Parental Impact-Emotional (PE). Furthermore, the subscale Role functioning Emotional (RE) and Role Functioning Behavior (RB) are combined to form the subscale Role functioning Emotional/Behavioral (REB) (Landgraf et al., 1996).



*Youth Self Report Form (YSR 11-18 years).*

The Dutch version of the Youth Self Report (YSR; Verhulst, Koot, Akkerhuis, & Veerman, 1996) was completed by the 22q11DS adolescents. It consists of 17 competence items and 112 behavior (problem) items and is a widely used standardized questionnaire to describe the competence and behavior in adolescents from an adolescent's point of view. It asks adolescents to rate their competence and behaviors on a three-point scale (0 = not true; 1 = somewhat or sometimes true; 2 = very true or often true).

In order to measure the competence of the adolescent, the YSR contains three subscales: social competence, activities and a total competence scale.

In addition to a total score, the YSR investigates two broad domains to measure the behaviour: internalizing problems (anxious/depressed, withdrawn/depressed, somatic complaints) and externalizing problems (attention problems, rule-breaking behavior and aggressive behavior). Furthermore, the checklist yields scores on six DSM-IV orientated scales: affective problems, anxiety problems, somatic problems, attention deficit/hyperactivity problems, oppositional defiant problems and conduct problems.

The outcomes are expressed as T-scores, based on sex and age norms. The T-scores have a mean of 50 (SD = 10). A T-score of 64 or higher on the internalizing, externalizing and total scale is classified as scoring in the 'clinical range', indicating psychopathology.

## **Procedure**

The children with 22q11DS participating in the longitudinal study were referred by medical genetic departments or child cardiology and cleft palate teams. Members of the Dutch Parent support group of children with 22q11DS also referred their children for participation in the assessments. Questionnaires concerning behavior (YSR) and quality of life (CHQ-CF87 and CHQ-PF50) were sent to the parents. Behavior questionnaires were also sent to parents (CBCL) and teachers (YSR); data concerning these questionnaires are reported elsewhere. Data on intelligence were acquired by means of the appropriate IQ-tests for the specific age (BSID-II-NL, SON-R-2 ½-7, WPPSI-R, and WISC-III-NL). Written informed consent was obtained from all parents or guardians.

## **Data- analysis**

All statistical analyses were conducted using SPSS version 16.0. Reliability of the CHQ-CF87, CHQ-PF50 and YSR scales was tested using Cronbach's alpha coefficient. Internal consistency was considered satisfactory if the coefficient was at least 0.70. Statistical significance was defined as  $\alpha < 0.05$  (Field, 2005; Landgraf et al., 1998).

For the CHQ-CF87 in the 22q11DS group, the Cronbach's alpha for four of the ten domains were above 0.70 and ranged from .51 (Physical Functioning) to .95 (General Behavior). For the CHQ-CF87 in the control group, the Cronbach's alpha for eight of ten domains were above 0.70 and ranged

from .26 (Physical Functioning) to .92 (Role functioning Social/Physical). The Cronbach's alpha coefficients for seven of the nine CHQ-PF50 domains were above 0.70 and ranged from .47 (Mental Health) to .96 (Bodily Pain). Only the following domains with a satisfactory reliability (coefficients above .70) in *all* groups are included in the analyses: Bodily Pain (BP), General Behavior (BE), Self Esteem (SE) and Family Activities (FA). As mentioned before, higher subscale scores indicate a higher QoL. To clarify; higher scores on the subscale Bodily Pain and General Behavior indicates *lower* bodily pain complaints and *lower* general behavior problems. Higher scores on self esteem and family activities indicate higher levels of self esteem and higher levels of family activities.

The internal consistency of the YSR was satisfactory in the following domains: internalizing scale (.78) and externalizing scale (.84). As a result of the poor reliability of the remaining scales (social competence scale .18; activity scale .23; total competence scale .29), only the internalizing and externalizing problem scale are included in the analyses. The poor reliability of the three competence scales corresponds with the internal consistency outcomes of population norms (Verhulst et al, 1997).

To answer the first aim of the study, mean scores for each domain for adolescent QoL reports were compared with the scores of a population norm group (Landgraf et al., 1996) and with those of a (healthy) norm group (described above) by means of one-sample and Student's t-tests respectively.

The second aim was to determine the associations between the subscale scores of the QoL measurements of successively adolescents, mothers and fathers. Therefore, Pearson correlations coefficients were computed. The strength of concordance was categorized as follows: 0.30 and below as poor to fair, 0.30-0.50 as moderate and above 0.50 as good (Field, 2005).

Third, the strength of concordance between parent and adolescent reports of QoL in adolescents with 22q11DS was examined, in order to determine whether concordance is greater for physical than for psychosocial subscales. Therefore, Pearson correlation coefficients were computed in order to compare adolescent with parent reports of QoL and interpreted as described above.

The final aim was to examine the influence of several factors on QoL as reported by adolescents with 22q11DS and their parents. Simple linear regression analyses between the QoL subscales as a dependent variable and an internalizing problem behavior-, externalizing problem behavior-, intelligence-, marital status- or family educational level measure as independent factors were performed.

## Results

Table 3 and 4 present the descriptive information for the four QoL subscales by group.

Table 3. Means and standard deviations of the QoL subscale scores<sup>a</sup> by group.

Scale	Adolescents 22q11DS			Control group			Normative sample		
	n	Mean	(SD)	n	Mean	(SD)	n	Mean	(SD)
BP	18	77.22	(21.91)	58	83.45	(15.51)	2361	72.80	(20.82)
BE	19	80.56	(12.27)	58	85.44	(8.43)	2361	77.51	(13.76)
SE	20	74.78	(13.61)	58	78.26	(10.84)	2361	74.64	(17.07)
FA	20	79.38	(19.47)	58	90.16	(11.70)	2361	72.50	(15.92)

<sup>a</sup> BP (Bodily Pain), BE (General Behavior), SE (Self Esteem), FA (Family Activities).

Table 4. Means and standard deviations of the QoL subscale scores<sup>a</sup> from the 22q11DS group parents.

Scale	Fathers			Mothers		
	n	Mean	(SD)	n	Mean	(SD)
BP	23	83.04	(23.24)	28	75.71	(23.32)
BE	23	72.50	(16.73)	28	70.71	(16.79)
SE	23	70.11	(12.48)	27	69.44	(14.29)
FA	23	78.08	(22.90)	28	71.99	(22.62)

<sup>a</sup> BP (Bodily Pain), BE (General Behavior), SE (Self Esteem), FA (Family Activities).

### Comparison with control group and population norms

Mean scores for each QoL subscale for adolescents with 22q11DS were compared with adolescents from the control group and adolescents from a normative sample. No statistical differences were found between the 22q11DS group and the general norm group. Between the 22q11DS group and the control group, a significant difference was found for the subscale Family Activities (FA) ( $t = -2.48$ ;  $df = 19$ ;  $p = .023$ ). Adolescents from the control group obtained a higher mean score on this subscale compared to that of the adolescents with 22q11DS, indicating that adolescents from the control group experience higher levels of family activities than the 22q11DS adolescents (Table 3).

### (Inter-) subscale correlations within the CHQ-CF87 and CHQ-PF50

#### Adolescents 22q11DS

The upper part of Table 5 shows the correlation coefficients of the subscale reports of QoL by the adolescents with 22q11DS. (Inter-)subscale correlations were all positive and ranged from .062 to .697. The majority of the correlations were significant.

Adolescent reports of bodily pain were correlated with general behavior ( $r = .605, p = .004$ ) and self esteem ( $r = .418, p = .042$ ), indicating that adolescents with lower levels of bodily pain complaints experience lower levels of behavior problems and higher levels of self esteem. Furthermore, adolescent reports of general behavior were correlated with self esteem ( $r = .697, p < .001$ ) and family activities ( $r = .583, p = .004$ ), indicating that adolescents with lower levels of behavior problems experience higher levels of self esteem and higher levels of family activities.

*Table 5.* Inter-subscale correlation coefficients for the CHQ-CF87 subscales: 22q11DS adolescents and control group adolescents.

Control group ( <i>n</i> )	Adolescents 22q11DS ( <i>n</i> )			
	BP	BE	SE	FA
Bodily Pain (BP)	1	.605* (18)	.418* (18)	.062 (18)
General Behavior (BE)	.366* (58)	1	.697* (19)	.583* (19)
Self Esteem (SE)	.230* (58)	.521* (58)	1	.368 (20)
Family Activities (FA)	.138 (58)	.569* (58)	.357* (58)	1

*Note:* Higher subscale scores indicate higher perceived QoL. This means that higher scores on the subscale BP and BE indicate lower levels of bodily pain complaints and lower levels of general behavior problems. Higher scores on the subscales SE and FA indicate higher levels of self esteem and higher levels of family activities.

\* Significant at  $p < .05$

#### Adolescents control group

The lower part of Table 5 shows the correlation coefficients of the subscale reports of QoL by the control group adolescents. (Inter)subscale correlations were all positive and ranged from .138 to .569. Similar to the 22q11DS group, the majority of the correlations were significant.

Adolescent reports of bodily pain were correlated with general behavior ( $r = .366, p = .002$ ) and self esteem ( $r = .230, p = .41$ ), indicating that adolescents with lower bodily pain complaints experience lower levels of behavior problems and higher levels of self esteem.

Furthermore, adolescent reports of general behavior were correlated with self esteem ( $r = .521, p < .001$ ) and family activities ( $r = .569, p < .001$ ), indicating that adolescents with lower levels of behavior problems experience higher self esteem and higher levels of family activities. Finally, adolescent reports of self esteem were correlated with family activities ( $r = .357, p = .003$ ), indicating that higher levels of self esteem were correlated with higher levels of family activities.

#### Fathers of adolescents with 22q11DS

The upper part of Table 6 shows the correlation coefficients of the subscale reports of QoL by the fathers of adolescents with 22q11DS. (Inter)subscale correlations were all positive and ranged from .197 to .707. Two significant correlations were found.

Father reports of general behavior were correlated with family activities ( $r = .547, p = .007$ ), indicating that adolescents with lower levels of behavior problems experience higher levels of family activities as reported by the father. Furthermore, father reports of self esteem were correlated with family activities ( $r = .707, p < .001$ ), indicating that higher levels of self esteem correlated with higher levels of family activities as reported by the father.

*Table 6.* Inter-subscale correlation coefficients for the CHQ-PF50 subscales: fathers and mothers of adolescents with 22q11DS.

Mothers ( <i>n</i> )	Fathers ( <i>n</i> )			
	BP	BE	SE	FA
Bodily Pain (BP)	1	.197 (23)	.269 (23)	.266 (23)
General Behavior (BE)	-.015 (28)	1	.294 (23)	.547* (23)
Self Esteem (SE)	.240 (27)	-.048 (27)	1	.707* (23)
Family Activities (FA)	.126 (28)	.363 (28)	.028 (27)	1

*Note:* Higher subscale scores indicate higher perceived QoL. This means that higher scores on the subscale BP and BE indicate lower levels of bodily pain complaints and lower levels of general behavior problems. Higher scores on the subscales SE and FA indicate higher levels of self esteem and higher levels of family activities.

\* Significant at  $p < .05$

#### Mothers of adolescents with 22q11DS

The lower part of Table 6 shows the correlation coefficients of the subscale reports of QoL by the mothers of adolescents with 22q11DS. No statistically significant correlations were found between the subscales.

#### *Strength of concordance between parent- and adolescent reports of QoL*

##### Adolescents and mothers

Good agreement ( $r > 0.50$ ) between child and mother ratings on the same subscale was present only for the physical domain Bodily Pain. Furthermore, higher scores on the subscale Bodily Pain as reported by mothers was associated with higher scores on the subscale Behavior Problems as reported by the adolescent (Table 7).

##### Adolescents and fathers

Only on the subscale Family Activities, scores reported by fathers were in fair agreement with scores reported by adolescents. Furthermore, higher scores on the subscale General Behavior as reported by fathers was associated with higher scores on the subscale Family Activities as reported by the adolescent (Table 7).

Table 7. Pearson's correlation coefficients for the CHQ subscales: adolescents 22q11DS vs. mothers and adolescents 22q11DS vs. fathers.

Parents	Adolescents 22q11DS			
	BP	BE	SE	FA
<i>Mothers</i>	n = 16	n = 17	n = 18	n = 18
Bodily Pain (BP)	.802*	.637*	.370	.083
General Behavior (BE)	.209	-.024	.175	.061
Self Esteem (SE)	.147	.336	.364	-.001
Family Activities (FA)	-.075	-.203	-.277	.074
<i>Fathers</i>	n = 15	n = 16	n = 17	n = 17
Bodily Pain (BP)	.301	.152	-.097	.036
General Behavior (BE)	-.065	.058	.201	.484*
Self Esteem (SE)	-.155	-.120	-.019	.138
Family Activities (FA)	.025	.072	.102	.456*

\* Significant at  $p < .05$

#### *Factors associated with QoL*

##### Adolescents

The present study showed no significant associations between adolescent reports of QoL, child psychopathology and IQ. The presence of internalizing and externalizing problem behavior and the level of intelligence were not associated with the perceived QoL of the adolescent. Also, the influence of more remote factors (marital status and educational level) was almost negligible (Table 9).

Table 9. Regression analyses; the association between child- and parent factors and QoL subscale scores as reported by adolescents.

Factors	QoL subscales <sup>a</sup>			
	BP	BE	SE	FA
<i>Child characteristics</i>				
Internalizing	-.184	.183	.000	.075
Externalizing	.004	-.107	-.175	-.149
IQ	-.102	.252	-.229	.145
<i>Parent characteristics</i>				
Marital status	.129	.199	.252	.033
Educational level mother	.018	-.187	-.084	-.113
Educational level father	.327	-.003	.123	-.171

Note: Betas are standardized betas; both significant and non-significant betas are presented.

<sup>a</sup> BP (Bodily Pain), BE (General Behavior), SE (Self Esteem), FA (Family Activities).

### Mothers

Regarding child characteristics, higher intelligence of the adolescents was significant associated with lower reports of general behavior ( $p = .038$ ). Internalizing and externalizing problem behavior of the adolescent were not associated with the perceived QoL of the adolescent, as reported by the mother. Furthermore, marital status and educational level of the father did not contributed significantly to the QoL reports of the mother. Between educational level of the mother and self esteem a significant association was observed. Lower educational level of the mother was associated with a higher level of self esteem of the adolescent, as reported by the mother ( $p = .050$ ) (Table 10).

Table 10. Regression analyses; the association between child- and parent factors and QoL subscale scores as reported by mothers.

Factors	QoL subscales <sup>a</sup>			
	BP	BE	SE	FA
<i>Child characteristics</i>				
Internalizing	.143	-.363	.296	.073
Externalizing	-.084	-.127	.190	.177
IQ	.230	-.523*	.146	-.134
<i>Parent characteristics</i>				
Marital status	-.150	.343	-.006	.296
Educational level mother	-.118	.331	-.468*	-.115
Educational level father	.310	.187	.157	.115

Note: Betas are standardized betas; both significant and non-significant betas are presented.

<sup>a</sup> BP (Bodily Pain), BE (General Behavior), SE (Self Esteem), FA (Family Activities).

\* Significant at  $p < .05$

### Fathers

According to the hypothesis, a significant association between QoL and child psychopathology was found. Internalizing problem behavior as reported by the adolescent was associated with lower self esteem of the adolescent, as reported by the father ( $p = .021$ ). The other child characteristics, externalizing problem behavior and intelligence, had no significant associations with the QoL of the adolescent. Regarding parent characteristics, no significant associations between marital status, educational level and QoL subscale scores were observed (Table 11).

Table 11. Regression analyses; the association between child- and parent factors and QoL subscale scores of as reported by fathers.

Factors	QoL subscales <sup>a</sup>			
	BP	BE	SE	FA
<i>Child characteristics</i>				
Internalizing	.222	.067	-.553*	-.098
Externalizing	-.216	-.167	-.169	-.003
IQ	-.017	-.152	-.449	-.233
<i>Parent characteristics</i>				
Marital status	-.155	.303	.331	.161
Educational level mother	.206	.006	.390	-.077
Educational level father	.351	-.125	-.010	.159

Note: Betas are standardized betas; both significant and non-significant betas are presented.

<sup>a</sup> BP (Bodily Pain), BE (General Behavior), SE (Self Esteem), FA (Family Activities).

\* Significant at  $p < .05$

## Discussion

The present study compared QoL subscale scores of adolescents with 22q11DS with those of a control group and a general norm group. Furthermore, the study examined the relationship between parental and child reports of QoL and assessed factors possible associated with QoL. The CHQ was used to describe the QoL of adolescents with 22q11DS from the adolescent and parent point of view. Evaluation of the internal consistency of the subscales of the CHQ showed that several subscales were unreliable. Since agreement between respondents can never be high, when the reliability of a measurement is low, only the subscales with an adequate internal consistency were used for further analyses (Field, 2005). As a consequence, the CHQ total scale could not be used. Within the physical domain of the CHQ, the subscale Bodily Pain and within the psychosocial domain, the Self Esteem and General Behavior subscale showed an adequate reliability. Furthermore, the separate subscale Family Activities was used for further analyses. Both the CHQ-PF50 and the CHQ-CF87 have demonstrated strong internal consistency and validity across divers clinical and norm groups in the US and Australia (Landgraf et al., 1996; Waters, Stewart-Brown & Fitzpatrick, 2001). The present study gives rise to some concerns about the internal consistency of several subscales of the CHQ-CF87 in children with 22q11DS, requiring further research. Previous evaluation of the CHQ-CF87 in a healthy Dutch adolescents sample supported the use of the measurement (Raat et al., 2002). Future evaluation of the CHQ-CF87 in atypical samples such as 22q11DS, preferably with a larger sample, is recommended.

Besides the contribution of QoL data, the present study also provided data on the competence and behavioral profile of the adolescents. To this aim, the YSR was used. Analyses of the reliability of



the subscales demonstrated an adequate reliability of the internalizing and externalizing problem scale only. The poor reliability of the three competence scales correspond with the internal consistency outcomes of population norms (Verhulst et al., 1997). Unfortunately, as a consequence of the poor reliability, reports concerning social competence were not possible within the present study.

With reference to the first research question, the present study compared CHQ subscale scores of the 22q11DS sample with those of the control group and a general norm group. Against the expectation, only one significant difference in scale scores was found. Adolescents from the control group experience higher levels of family activities compared to the adolescents with 22q11DS. Previous studies (Bastiaansen et al., 2005; Daliento, Mapelli, & Volpe, 2006; Klassen, Miller, & Fine, 2004; Warschauwski et al., 2001) have noted decrements in QoL among patients with disabilities. Nevertheless, the CHQ-CF87 subscale scores observed in this 22q11DS sample were almost equal to the control group and general norm group. In the present study, the benefit of the presence of a norm group (with a large sample) as well as a control group (from the Netherlands) have made it possible to get a picture of the comparability of the QoL subscale scores of 22q11DS adolescents with other groups. However, an examination of the background characteristics of the control group (of the Netherlands) showed that there were significant differences in terms of age and IQ compared to the 22q11DS group. Future research with more comparable control groups is therefore recommended.

To determine the relationship between QoL subscales, (inter-)subscale correlations were computed for successively adolescents, mothers and fathers. The majority of the subscale correlations of the adolescents, both 22q11DS and control group, were significant. In the 22q11DS adolescent reports, good agreement ( $r > .50$ ) was found between bodily pain and general behavior ( $r = .605$ ) and between general behavior and successively self esteem ( $r = .697$ ) and family activities ( $r = .583$ ). The reports of the control group adolescents showed good agreement between general behavior and successively self esteem ( $r = .521$ ) and family activities ( $r = .569$ ). The majority of the subscale correlations of the mother and father reports one the other hand were, against the expectation, non-significant. In the mother reports, a moderate correlation between general behavior and family activities was found ( $r = .363$ ). In the father reports, good agreement between family activity and successively general behavior ( $r = .547$ ) and self esteem ( $r = .707$ ) was observed. A possible explanation for the degree of differences in correlations within the questionnaires could be that children seem to have different reasoning and response styles, tend to provide extreme scores (highest and lowest score), answer the questions in the same direction, and base their response on one single example, more than parents (Davis et al., 2007).

The third research question aimed at the strength of concordance between child and parent raters. Although the use of both parent and adolescent reports of QoL is desirable (Eiser & Morse, 2001; Mandzuk & McMillen, 2005), research that assesses the agreement between parent and adolescent reports shows that correlations between parent and adolescent reports on the less observable psychosocial measures of QoL are generally low (Theunissen et al., 1997). Discrepancies

between parental and child reports may reflect differences in perspectives. However, they may also reflect a lack of insight on the part of parents into their children's lives. It is plausible that parents' knowledge of their children is limited, particularly with respect to activities or relationships that exist outside the home and with respect to internal feeling state (Eiser & Morse, 2001; Jakovic, Locker, & Guyatt, 2004). The present study shows similar results; parents' and adolescents' reports of QoL were not strongly correlated on the (less observable) general behavior and self esteem subscales. As suggested by others (Davis et al., 2007; Drukker et al., 2003; Waters et al., 2003), differential reporting may result from the different viewpoints of the reporters. For example, reporting may reflect individual biases or viewpoints of family members, or cognitive processes or response styles related to answering questions. Nevertheless, agreement between parents and adolescents seems to be higher in the physical than the psychosocial domain. Good agreement ( $> .50$ ) between mothers and adolescents was found on the subscale Bodily pain; mothers seem to assess the extent of bodily pain of their child properly. Thus, in line with previous research (Davis et al., 2007; Drukker et al., 2003; Eiser & Morse, 2001), there is some evidence for greater agreement between child and parent ratings for observable behaviors such as Bodily Pain (physical functioning) and less for non observable functioning such as Self Esteem and General Behavior (psychosocial functioning). Choice of proxy raters needs to be considered carefully, and differences between raters acknowledged. Given that mothers tend to be more involved in child care, it is possible that they are more aware of the child's views about QoL than fathers (Eiser & Morse, 2001). The present study found contradictory results, since there were also agreements observed between father and adolescent ratings (on the subscale family activities). Hereby, support was found for including fathers as independent sources of information in pediatric psychology research and clinical practice.

The final research question examined factors possibly associated with QoL, as reported by adolescents with 22q11DS and their parents. Although support for a significant relationship between child characteristics and QoL has been provided by a number of studies (Bastiaansen et al., 2005; Daliento, Mapelli, & Volpe, 2006; Davis et al., 2007; Eiser & Morse, 2001), the present study found contradictory results. Against the expectation, no significant associations between child characteristics and QoL reports of the adolescents were observed. Internalizing and externalizing problem behavior and IQ does not seem to be related to perceived QoL as reported by adolescents with 22q11DS. The findings support the notion of Robeyn (2004), that perceived QoL is not related to one's capability. Furthermore, adolescent reports of QoL do not seem to be influenced by the marital status and educational level of their parents. Similar results to those of the present study have been found, namely that the contribution of remote factors to explaining QoL is weak, compared to the contribution of intrapersonal variables (Bastiaansen et al., 2005; Meuleners et al., 2003).

QoL reports of the mother showed that higher intelligence of the adolescent seems to be associated with reports of less favourable general behavior, as reported by the mother. This might be explained by the fact that more intelligent adolescents with 22q11DS are possibly more aware of their

impairments, and are for example more likely to realize that they differ from their peers (Bastiaansen et al., 2005). It could be possible that mothers sense these signals and interpret them as problematic behavior. Furthermore, a significant association was found between educational level of the mother and self esteem; lower educational level of the mother seems to be associated with higher reports of self esteem of the adolescent, as reported by the mother. This finding indicates that the (social) environment may have impact on the emotional development of adolescents with 22q11DS. In accordance with the hypothesis, a significant association between father reports of self esteem and internalizing problem behavior was found; internalizing problem behavior seems to be associated with reports of lower self esteem of the adolescent, as reported by the father. Generally, in contrast with previous research, few associations between child characteristics and QoL were found (Bastiaansen et al., 2005; Eiser & Morse, 2001; Klassen et al., 2004). Associations between parent characteristics and QoL were expected to contribute little to the reported QoL. However, several factors tend to contribute to the QoL in the present study and therefore need to be addressed in order to improve QoL in adolescents with 22q11DS, as is suggested in previous studies (Bastiaansen et al., 2005; Davis et al., 2007; Drukker et al., 2003; Eiser & Morse, 2001). For example, a significant association between internalizing problem behavior and self esteem was found in the father reports. This association might be relevant for clinical practice, as clinicians can focus on improving self esteem, too (Bastiaansen et al., 2005; Silverman et al., 1999).

The results of the present study must be interpreted within the limitations of the study. The sample size of the study was relatively small. Although sample size does not impact validity and reliability coefficients, it reduces the power of statistical tests associated with them (Field, 2005). It will be important to replicate the findings with a larger sample. Furthermore, it should be noted, that the information on the internalizing and externalizing problem behavior was not obtained from both child and parent. Information concerning the problem behavior from the parents' point of view was not available. In the present study, psychopathology was only assessed via self-reports. Finally, the representativeness of the sample and generalizability of the findings in the study to the 22q11DS population may be an issue. It is likely that, for instance, parents of the more severely affected children with 22q11DS may join the parents' network of 22q11DS children more often than parents of less affected children (Vorstman et al., 2006).

Because of the small sample of the present study, the results should therefore not be generalized to the entire 22q11DS population. Judging the results of the present study, the CHQ-CF87 seems to be an insufficiently reliable questionnaire to measure all QoL subscales in the 22q11DS sample. However, reliable reports concerning the subscales bodily pain, general behavior, self esteem and family activities could be done. Research with a larger sample of 22q11DS adolescents and with comparable control groups are needed to explore the usefulness of the CHQ-CF87 in the 22q11DS sample. Also, to strengthen the results of the present study, further research with a larger sample is needed.

Furthermore, information concerning psychopathology was only attained via self-reports. In future research examining factors associated with QoL, assessing information concerning psychopathology of the child via parent-reports could be complementary, since parents may observe the behavior of their child in an other way (Eiser & Morse, 2001; Jakovic, Locker, & Guyatt, 2004). Specific research into the relation between internalizing problem behavior and self esteem and possible appropriate interventions is necessary. When future research focuses on these and other (possible associating) factors, this will contribute to the perceived QoL of adolescents with 22q11DS.

## References

- Antshel, K. M., Abdulsabur, N., Roizen, N., Fremont, W., & Kates, W. R. (2005). Sex differences in cognitive functioning in Velocardiofacial syndrome. *Developmental Neuropsychology, 28*(3), 849-869.
- Antshel, K. M., Fremont, W., Roizen, N. J., Shprintzen, R., Higgens, A. Dhamoon., A., & Kates, W. R. (2006). ADHD, Major Depressive Disorder and Simple Phobias Are Prevalent Psychiatric Conditions in Youth With Velocardiofacial Syndrome. *Journal of the American Academy of Child and Adolescent Psychiatry, 45*(5), 596-603.
- Arnold, P. D., Slegel-Bartelt, J., Cytrynbaum, C., Teshima, I., & Schachar, R. (2001). Velo-cardio-facial syndrome: Implications of microdeletion 22q11 for schizophrenia and mood disorders. *American Journal of Medical Genetics, 105*, 354-362.
- Baker, K. D., & Skuse, D. H. (2005). Adolescents and young adults with 22q11 deletion syndrome: psychopathology in an at risk group. *British Journal of Psychiatry, 186*, 115-120.
- Bastiaansen, D., Koot, H. M., & Ferdinand, R. F. (2005). Determinants of quality of life in children with psychiatric disorders. *Quality of Life Research, 14*, 1599-1612.
- Daliento, L., Mapelli, D., & Volpe, B. (2006). Measurement of cognitive outcome and quality of life in congenital heart disease. *Heart, 92*, 569-574.
- Davis, E., Nicolas, C., Waters, E., Cook, K., Gibbs, L., Gosch, A., et al. (2007). Parent-proxy and child self-reported health related quality of life: Using qualitative methods to explain the discordance. *Quality of Life Research, 10*, 863-871.
- Devriendt, K., Fryns, J. P., Mortier, G., Thienen, M. N. van, & Keymolen, K. (1998). The annual incidence of DiGeorge/velocardiofacial syndrome. *Journal of Medical Genetics, 35*, 789-90.
- Drotar, D. (1998). *Measuring Health-related Quality of Life in Children and Adolescents: Implications for Research and Practice*. Manwah, NJ: Lawrence Erlbaum Associations.
- Drukker, M., Kaplan, C., Feron, F., & Os, J. van (2003). Children's health-related quality of life, neighbourhood, socio-economic deprivation and social capital. A contextual analysis. *Social Science & Medicine, 57*, 825-841.
- Eiser, C., & Morse, R. (2001). Can parents rate their child's health-related quality of

- life? Results of a systematic review. *Quality of Life Research*, 10, 347-357.
- Field, A. (2005). *Discovering statistics using, 2nd ed.* London: SAGE Publications.
- Feinstein, C., Eliez, S., Blasey, C., & Reis, A. L. (2002). Psychiatric disorders and behavioral problems in children with velocardiofacial syndrome: usefulness as phenotypic indicators of schizophrenia risk. *Society of Biological Psychiatry*, 51, 312-318.
- Gothelf, D. G., Feinstein, C., Thompson, T., Gu, E., Penniman, L., Stone, E. van, et al. (2007). Riskfactors for the emergence of psychotic disorders in adolescence with 22q11 deletion syndrome. *American Journal of Psychiatry*, 164, 663-669.
- Jakovic, A., Locker, D., & G. (2004). How well do parents know their children? Implications for proxy reporting of child health-related quality of life. *Quality of Life Research*, 13, 1297-1307.
- Jansen, P. W., Duijff, S. N., Beemer, F. A., Vorstman, J. A., Klaassen, P. W., Morcus, M. E., et al. (2007). Behavioral problems in relation to intelligence in children with 22q11.2 deletion syndrome: A matched control study. *Journal of Medical Genetics*, 143A(6), 574-580.
- Klassen, A. F., Miller, A., & Fine, S. (2004). Health-related Quality of Life in children and adolescents who have a diagnosis of Attention-Deficit/Hyperactivity disorder. *Pediatrics*, 114(5), 541-547.
- Landgraf, J. M., Abetz, L., & Ware, J. E. (1996). *The CHQ User's Manual*. Boston, MA: The Health Institute, New England Medical Center.
- Mandzuk, L. L., & McMillen, D. E. (2005). A concept analysis of quality of life. *Journal of Orthopaedic Nursing*, 9, 12-18.
- Meuleners, L. B., Lee, A. H., Binns, C. W., & Lower, A. (2003). Quality of life for adolescents: Assessing measurement properties using structural equation modeling. *Quality of Life Research*, 12, 283-290.
- Murphy, K. C., Jones, L. A., & Owen, M. J. (1999). High rates of schizophrenia in adults with velo-cardio-facial syndrome. *Archives of General Psychiatry*, 56, 940-945.
- Niklasson, L., Rasmussen, P., Oskarsdottir, S., & Gillberg, C. (2009). Autism, ADHD, mental retardation and behavior problems in 100 individuals with 22q11 deletion syndrome. *Research in Developmental Disabilities*, 30, 763-773.
- Oskarsdottir, S., Vujic, M., & Fasth, A. (2004). Incidence and prevalence of the 22q11 deletion syndrome: a population-based study in Western Sweden. *Archives of Disease in Childhood*, 89, 148-151.
- Paylor, R., & Lindsay, E. (2006). Mouse models of 22q11 deletion syndrome. *Biological Psychiatry*, 59, 1172-1179.
- Robin, N. H., & Shprintzen, R. J. (2005). Defining the clinical spectrum of deletion 22q11.2. *Journal of Pediatrics*, 147, 90-96.
- Ryan, A. K., Goodship, J. A., Wilson, D. I., Philip, N., Levy, A., Seidel, H., et al.

- (1997). Spectrum of clinical features associated with interstitial chromosome 22q11 deletions: A European collaborative study. *Journal of Medical Genetics*, 34, 798-804.
- Raat, H., Landgraf, J. M., Bonsel, G. J., Gemke, R. J. B. J., & Essink-Bot, M. L. (2002). Reliability and validity of the child health questionnaire-child form (CHQ-CF87) in a Dutch adolescent population. *Quality of Life Research*, 11, 575-581.
- Robeyn, I. (2004). De kwaliteit van het leven: drie politiek-filosofische benaderingen. *Ethiek en Maatschappij*, 7(1), 3-16.
- Robinson, K. E., Gerhardt, C. A., Vanatta, K., & Noll, R. R. (2007). Parent and family factors associated with child adjustment to pediatric cancer. *Journal of Pediatric Psychology*, 32(4), 400-410.
- Silverman, W. K., Kurtines, W. M., Ginsberg, G. S., Weems, C. F., Lumpkin, P. W., & Carmichael, D. H. (1999). Treating anxiety disorders in children with group cognitive-behavioral therapy: A randomized clinical trial. *Journal of Consulting and Clinical Psychology*, 67(6), 995-1003.
- Stawski, M., Auerbach, J. G., Barasch, M., Lerner, Y., Zimin, R., & Miller, M. S. (1995). Behavior problems of adolescents with chronic physical illness: A comparison of parent-report and self-report measures. *European Child and Adolescent Psychiatry*, 4(1), 14-20.
- Swillen, A., Devriendt, K., Legius, E., Eyskens, B., Dumoulin, M., Gewillig, M., et al. (1997). Intelligence and psychosocial adjustment in velocardiofacial syndrome: a study of 37 children and adolescents with VCFS. *Journal of Medical Genetics*, 34, 453-458.
- Theunissen, N. C. M., Vogels, T. G. C., Koopman, H. M., Verrips, G. H. W., Zwinderman, K. A. H., Verloove-Vanhorick, S. P., et al. (1998). The proxy problem: Child versus parent report in health-related quality of life research. *Quality of Life Research*, 7, 387-397.
- Verhulst, F. C., van der Ende, J., & Koot, H. M. (1997). *Handleiding voor de Youth Self Report (YSR)*. Afdeling Kinder- en jeugdpsychiatrie, Sophia Kinderziekenhuis/ Acedemisch Ziekenhuis Rotterdam/ Erasmus Universiteit Rotterdam.
- Vorstman, J. A., Morcus, M. E., Duijff, S. N., Klaassen, P. W., Heineman-deBoer, J. A., Beemer, F. A., et al. (2006). The 22q11.2 deletion in children: high rate of autistic disorders and early onset of psychotic symptoms. *Journal of the American Academy of Child and Adolescent Psychiatry*, 45(9), 1104-1113.
- Warchausky, S., Kay, J. B., Buchman, S., Halberg, A., & Bergen, M. (2001). Health Related Quality of Life in children with craniofacial anomalies. *Plastic and Reconstructive Surgery*, 110(2), 409-414.
- Waters, E., Stewart-Brown, S., Fitzpatrick, R. (2003). Agreement between adolescent

self report and parent reports of health and well-being: Results of an epidemiological study. *Child: Care, Health and Development*, 29(6), 501-509.

WHOQOL Group (1995). The world Health Organization Quality of Life Assessment (WHOQOL): Position paper from the World health Organization. *Social Science and Medicine*, 41, 1403-1409.