

CDDUX: A Disease-specific Health-related Quality-of-life Questionnaire for Children With Celiac Disease

*†Roesja K. van Doorn, †Lex M.F. Winkler, ‡Koos H. Zwinderman, *§M. Luisa Mearin, and
*Hendrik M. Koopman

*Department of Pediatrics, Leiden University Medical Center, Leiden, †Dutch Foundation Doctors for Children, ‡Department of Biostatistics, University of Amsterdam, and §Department of Pediatrics, Free University Medical Center, Amsterdam, The Netherlands

ABSTRACT

Objective: The development of a disease-specific, health-related, quality-of-life questionnaire for children ages 8 to 18 with celiac disease (CD), together with a parent-as-proxy version.

Materials and Methods: We used a focus-group method (bottom-up approach) to investigate the impact of CD on children's everyday lives and selected 24 items to create a preliminary disease-specific questionnaire. This questionnaire, together with the complementary generic quality-of-life questionnaire DUX-25, was sent to 756 children with CD in the Netherlands and was returned by 530 of them. With the help of statistical analyses (Cronbach α , factor analysis, Pearson correlation, Student *t* test, paired samples *t* test, and item response theory), we tested the psychometric performance of the 24 items.

Results: We reduced the questionnaire to 12 items: the Celiac Disease DUX (CDDUX). The CDDUX has 3 subscales: "Communication" (3), "Diet" (6), and "Having CD" (3).

This questionnaire proved to be reliable, valid, and feasible and able to discriminate between perception of severity in cases of CD as assessed by parents.

Conclusions: Children with a better perception of their own health status have a higher score on the CDDUX questionnaire. The whole group seems to have a lower quality of life than the healthy reference group on all domains of the DUX-25. The new disease-specific questionnaire CDDUX provides information about how children with CD think and feel about their illness. The questionnaire may enable researchers and clinicians to determine the consequences of this illness and the effects of clinical interventions on several aspects of daily living. *JPGN* 47:147–152, 2008. **Key Words:** Celiac disease—Quality of life—Disease-specific questionnaire—Proxy. © 2008 by European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

Celiac disease (CD) is an inflammatory chronic disease of the small intestine caused by gluten ingestion in genetically susceptible individuals. It may cause many symptoms, such as malabsorption of important nutrients (1,2). The diagnosis is confirmed by characteristic histological findings in small bowel biopsy specimens. The treatment for CD is consistent exclusion of gluten from the diet. After starting a gluten-free diet, most children show a rapid clinical response, with improvement of symptoms within weeks. However, complete recovery of the mucosa can take months or years, especially in adults (3). Following a gluten-free diet is difficult and

complex (4). Untreated CD may be complicated by, among other things, osteoporosis, infertility, miscarriage, malignancy, and autoimmune diseases (1,3). With an incidence of 0.5% to 1.0% in the general population (1,5–7), it seems much more frequent than was formerly presumed.

Having a chronic illness like CD may reduce a child's quality of life (QOL) (8). Health-related QOL (HRQOL) is a multidimensional concept containing physical, emotional, social, and cognitive domains that vary over time, and it has received increasing attention in medical and health care settings (9). What matters in HRQOL is the way patients that feel about their functioning, not their functioning itself (10). HRQOL can be measured by generic, disease-generic, and disease-specific instruments. Generic HRQOL instruments such as the DUX-25 (11) and the TACQOL (12) allow comparison with normative data and across disease populations. Disease-generic questionnaires can be handed out to children with any disease (9). Disease-specific instruments have

Received October 2, 2006; accepted November 8, 2007.

Address correspondence and reprint requests to Luisa Mearin, Department of Pediatrics, Leiden University Medical Center, PO Box 9600, 2300 RC Leiden, the Netherlands (e-mail: m.l.mearin_manrique@lumc.nl).

Supported by the Dutch Foundation Doctors for Children, Amsterdam.

The authors report no conflicts of interest.

been praised for their discriminating properties and their sensitivity to small differences and changes (9–14). QOL questionnaires are usually designed as top-down instruments. This means that they are developed by researchers and attending physicians who have used their own experience as guidelines. The DUX-25 assesses the influence of the disease on daily activities and is designed for children in the age group 5 to 16 years. It contains 25 items on 4 domains: emotional, physical, social, and functioning at home (11). The interest in HRQOL instruments developed from the bottom up is increasing in medical health care settings. Such a questionnaire uses a focus group–based approach that allows us to perceive the situation from the child’s point of view. It can be seen as a child-centered method, designed to ensure that the children, rather than their parents or health care professionals, generate, prioritize, and explain the issues of interest to them. It can produce data that adult investigators and even parents have never considered. Until now, as far as we are aware, no bottom-up disease-specific questionnaire for CD has been designed (15). Our research group had previously assessed the HRQOL of children with CD, making use of the TACQOLCD (16), a questionnaire especially designed for CD in which the child’s well-being was estimated by the researchers and attending physicians. The TACQOLCD did not provide information about the children’s view or that of their parents, and it was limited because it contained only symptomatic questions. The questionnaire was mainly useful for the investigation of physical symptoms; its discriminating properties were lacking. In the absence of symptoms, thanks to compliance with the gluten-free diet or to coping with the disease, the results gave an optimal score, which may not have given an accurate view of the HRQOL. Together with the Dutch foundation Doctors for Children, a foundation that works for the improvement of the QOL of children with chronic illness, we aimed to develop an improved questionnaire, developed from the bottom up, to assess the QOL of children with CD.

MATERIALS AND METHODS

Phase 1: Construction of a Disease-specific HRQOL Questionnaire for Children With CD, Using Focus Groups

To develop a new questionnaire on CD-related QOL, we looked at the experiences of children with CD, and that of their parents, and used a bottom-up approach. To do this we used focus groups with interactive discussions among participants that approximated a “normal” social context more closely than do individual interviews. We used the following inclusion criteria for the participating children: diagnosis of CD by means of at least 1 small bowel biopsy showing the histological alterations characteristic of the disease, no other chronic disease(s), and no mental impairments. The Dutch Celiac Patients Society randomly invited 52 of its members from the district of Leiden, south

Holland, and their parents, to participate in the study. The children were stratified by 3 age categories: latency (8–11 years), early adolescence (12–15 years), and late adolescence (16–18 years). Of those children, 51 received their diagnoses an average of 12 months before the invitation to participate. One child received the diagnosis 4 months before the invitation. A total of 50% accepted the invitation. Reasons not to participate were, first, a lack of motivation and, second, the burden this would create in addition to their gluten-free diet and the confrontation with their disease, or an unknown reason. The participating group consisted of 3 subgroups: latency (10 participants, of whom 3 were girls), early adolescence (12 participants, of whom 7 were girls), and late adolescence (4, all of whom were girls). The number of 26 children complies with the standards accepted to generate qualitative data to construct a questionnaire when one is working with focus groups (17). In general, 8 to 12 participants is a suitable number in a focus group; smaller groups equal to 4 to 6 participants may sometimes be used (18). Under the direction of 2 trained facilitators, the focus group members (girls and boys separately) were encouraged to express their perceptions and opinions about living with CD. Children and parents were interviewed separately. The group discussions were tape recorded. The trainers subsequently selected the relevant information about living with CD, using a card sorting system with the following themes: “Home situation,” “School,” “Peers,” “Going out/parties,” “Holidays,” “Feeling different,” “Future,” “Sports,” “General statements,” “Advantages,” “Disadvantages,” and “One wish to be happier.” We did not use the information concerning coping with the disease because we were interested in the feelings and experiences around CD, not in the mechanisms used to gain control over stressful situations. After checking for comprehensibility, relevance, and age appropriateness by the participating families (cognitive debriefing), the selected information was used to construct a CD-specific 24-item questionnaire (pilot CDDUX) with 2 versions, 1 for children and 1 for parents (proxy). The layout conformed to the generic QOL questionnaire, DUX-25, which has been described before (Fig. 1) (9,11).

Phase 2: Validation of the Disease-specific HRQOL Questionnaire for Children With CD: the CDDUX

The Dutch Celiac Patients Society invited all of its members with CD ages 8 to 18 years and their parents to fill in the new CD-specific 24-item questionnaire (pilot CDDUX), the generic QOL questionnaire, DUX-25, and a questionnaire for demographic features and general health. The inclusion-exclusion criteria were the same as in phase 1. There were 756 eligible children with CD: group 1 (latency) with 407 children; group 2 (early adolescence) with 275 children, and group 3 (late adolescence) with 74 children. Of the families who were invited, 70% gave informed consent to participate in the study. The response differed according to the age groups: 71% in groups 1 and 2 ($n = 291$ and 195 , respectively) and 63.5% in group 3

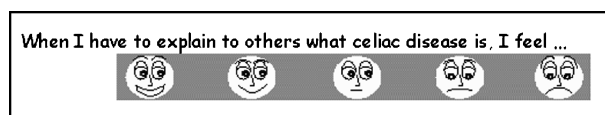


FIG. 1. Example of an item in the CDDUX.

($n = 47$). Of the returned questionnaires, 96% were fully completed and could be used for further statistical analysis.

Statistical Analysis

The data were statistically processed by means of SPSS for Windows, version 10.7. The psychometric properties of the instrument were analyzed by use of classic psychometric methods. First we calculated the Cronbach α coefficient for reliability and dimensionality, and the internal consistency for the entire scale of 24 items. Dimensionality, construct validity, and explained variances of the final item subset were investigated with factor and component analysis with varimax rotation. Our aim was to describe the important CD-specific aspects of QOL with simple sum scores calculated from a limited number of items. Agreement between the scores of the children and the parents and criterion validity were quantified with a correlation coefficient and were tested for difference with the paired samples t test. The Student t test was used for comparison of the variables. Differences between mean scores in different patient subgroups were evaluated with the unpaired t test. The association of the CDDUX scores and the DUX-25 scores was quantified with the correlation coefficient. Overall, $P \leq 0.05$ was accepted as a statistically significant result. For comparison of the results with former data (16), the scores on the DUX-25 and the CDDUX were recoded into a scale from 1 to 100, with 1 = very bad to 100 = very good. When a 5-point Likert scale is used, a score of 1–20 is considered very bad, 21–40 is bad, 41–60 is neutral, 61–80 is good, and 81 to 100 is very good. We also tested the reliability of the generic questionnaire, the DUX-25.

We compared the scores of the CDDUX questionnaire with the health status. Through dichotomization of the health status in very healthy (50%) and otherwise (healthy to very ill, 50%) individuals, we defined the discriminative validity. Finally, we compared the results on the DUX-25 with a reference population of 991 healthy children and with children with asthma, rheumatoid arthritis, and diabetes in the 8 to 15 years age group.

RESULTS

The characteristics of 510 children with CD are presented in Table 1. The age at diagnosis was significantly higher in the groups of older children. The mean age of the parents was 42 years (range 30–59). Nearly all of the participants (98%) were of Dutch origin. In 88% of cases the mother filled in the questionnaire. Most of the parents

TABLE 1. Characteristics of 510 children with celiac disease in the Netherlands

	Female		Age		Age at diagnosis	
	n	%	Mean	SD	Mean	SD
Group 1: 8–11 y	278	60	9.1	0.9	2.9	2.3
Group 2: 12–15 y	184	63	13.1	0.9	4.5	4.1
Group 3: 16–18 y	48	64	16.7	0.7	5.5	4.8
Total	510	62	11.3	2.7	3.7	3.5

TABLE 2. Items of the disease-specific CDDUX

Item	Question
Scale "Communication"	
1	Talking about celiac disease I find ...
2	When I have to explain to others what celiac disease is, I feel ...
3	Talking about my celiac disease with others my age, I find ...
Scale "Having CD"	
4	When at school I am given food containing gluten, I find it ...
5	When someone offers me food that I can't have, I feel ...
6	When I think of food containing gluten, I feel ...
Scale "Diet"	
7	Not being able to eat anything I want, I find ...
8	Having to follow a lifelong diet, I find ...
9	Having to pay attention to what I eat, I find ...
10	Having celiac disease is ...
11	Not being able to eat all the things other people eat, I find ...
12	Following a diet for my celiac disease is ...

were married, 9% were divorced, and 2% were single. The parents indicated the health state of their children as very healthy (51%), healthy (38%), not healthy/not ill (6%), ill (4%), or very ill (1%). These results were similar in the 3 age groups.

Development and Validation of the CDDUX Questionnaire

Classic psychometric analysis allowed a reduction of the 24 items from the pilot CDDUX questionnaire to 12 items (Table 2). The 12 deleted items either were not informative or were referred to the effects of CD on the functioning of the child, not to how the child (and the parent as proxy) felt about his or her own functioning. Analysis showed that the 12-item questionnaire formed a valid instrument (Table 3). A rotated component matrix of the 12 items made a clear distinction in 3 scales: "Diet" (6 items), "Communication" (3 items), and "Having CD" (3 items). These showed good variances, both for the child version and for the parent version. The scale "Diet" yielded the highest proportion in variances

TABLE 3. Reliability and variance of the CDDUX and the 3 scales

	Parent form		Child form	
	Reliability	Variance	Reliability	Variance
CDDUX (12 items)	0.88	68.5	0.88	67.8
CDDUX Diet (6 items)	0.87	43.8	0.88	44.2
CDDUX Having CD (3 items)	0.77	10.9	0.77	10.3
CDDUX Communication (3 items)	0.85	13.8	0.71	13.3

TABLE 4. Report of quality of life of children with CD assessed by the CD-specific CDDUX and the generic DUX-25 compared with children 8–15 years old from a healthy norm group and children with asthma, rheumatoid arthritis, or diabetes

	n	DUX-25					CDDUX			
		Emotion M (SD)	Social M (SD)	Physical M (SD)	Home M (SD)	Total M (SD)	Communication M (SD)	Having CD M (SD)	Diet M (SD)	Total M (SD)
CD parents	510	72* (15)	76* (12)	73* (16)	81* (13)	75* (12)	53* (20)	30* (18)	33* (18)	39* (15)
CD children	510	73† (15)	77† (12)	75† (17)	84† (13)	77† (12)	59 (21)	36 (21)	36 (16)	44 (15)
Asthma	71	71 (14)	75† (14)	73 (16)	86 (14)	76† (11)				
Rheumatoid arthritis	49	71 (15)	77 (12)	63† (20)	86 (13)	74† (12)				
Diabetes	29	68 (11)	71 (13)	70† (13)	78 (15)	74 (11)				
Healthy norm	991	75 (15)	79 (14)	79 (16)	86 (14)	80 (12)				

* Differences with children with CD were significant (2-tailed) at 0.05 level.

† Differences with healthy norm group were significant (2-tailed) at 0.05 level.

explained (Table 3). This scale gives an impression of how the child feels about compliance, the restrictions of the diet, and the lifelong aspects. The “Communication” scale tells the caregiver how the child feels when talking about CD to others and when explaining the disease to others. The scale “Having CD” gives information on how the child feels when offered food containing gluten or when he or she thinks about food containing gluten.

HRQOL of Children With CD Measured by Use of the New Disease-specific Questionnaire CDDUX

In general, children with CD reported a neutral to low score of 44 to their QOL on a scale from 1 to 100 (1 = very bad, 100 = very good) (Table 4). Their parents found their children’s QOL significantly lower, with a score of 39 ($P < 0.05$). In general, this significantly different appreciation of QOL between children and parents was present for all 3 scales of the CDDUX (ie, “Communication” (child 59 vs parent 53), “Having CD” (child 36 vs parent 30), and “Diet” (child 36 vs parent 33)). These differences gave a correlation of 0.5 to 0.6 and were significant. We found a good correlation between the subjective health status as assessed by the parent and the scores of the CDDUX questionnaire: children with a better health status had a higher score on the CDDUX.

QOL of Children With CD Measured by Use of the Generic Questionnaire DUX-25

The DUX-25 scores of the children and their parents are shown in Table 4. The scores of the parents and children had a high correlation of 0.5 to 0.6. These differences were significant.

In comparing the results of the DUX-25 with those in a reference population, we found that the children with CD found their QOL significantly lower ($P < 0.05$) than the children in the healthy reference group, with the exception of the emotional domain in the 2 younger groups. By

contrast, the children with CD found their QOL higher than did children with other chronic diseases such as asthma, rheumatoid arthritis, or diabetes (Table 3).

DISCUSSION

We have developed a new, bottom-up, disease-specific HRQOL questionnaire for children with CD, together with a parent-proxy version, the CDDUX. We found good psychometric performances. The CDDUX proved to be valid and feasible and allowed discrimination between the perception of severity in cases of CD as assessed by the parents.

The results of the CDDUX indicate that children with CD have a bad to neutral experience of their QOL when they consider living with CD. By contrast, when the generic QOL instrument, the DUX-25, is used, the children with CD perceive their QOL as good. This discrepancy in outcomes can be explained by the different type of information that is obtained from the children when disease-specific or generic QOL questionnaires are used. A disease-specific questionnaire elicits information about those aspects of life that are influenced by the specific disease, in this case CD. These specific aspects may be evaluated by the children as negative, but this does not mean that their perception of their generic QOL is negative as well. These kinds of discrepancies may also be found when disease-specific QOL instruments are used that are designed by different methods. For example, in 2001 our group investigated the HRQOL of children with CD using the TAQOLCD (13,16), which is a disease-specific and top-down–designed questionnaire. Our group found that these children reported a QOL similar to that of the general population. Inasmuch as the TAQOLCD was designed mainly by caregivers taking care of children with CD, the instrument focused primarily on the existence of physical problems and secondarily on the affective evaluation of possible problems. CD patients who follow a strict gluten-free diet mostly have no, or few, physical problems, which explains the

positive scores for QOL when the TAQOLCD was used. Moreover, in cases of chronic disease, an adaptation to physical, social, or emotional problems may evolve through the years from the use of coping mechanisms. Therefore, the TACQOLCD instrument is mostly useful to assess QOL during the phase of diagnosis and at the start of the treatment, when physical problems are often present.

One possible limitation of our study may be that all of the participants were members of the Dutch Celiac Society. The question is whether our results may be considered representative of the general population of children with CD. To our knowledge, our cohort represents the best available homogeneous group of children with CD in our country, inasmuch as 80% of all of the patients with CD in the Netherlands are members of the Dutch Celiac Society. In addition, we had a relatively high rate of participation (70%) in the study. However, the response in our study is clearly higher among the girls (60%) than among the boys. There is also a considerable sex difference between the different age groups used for the focus groups: latency 70% boys, early adolescence 40% boys, and late adolescence 0% boys. This could have influenced the validity and the generalized aspect of the focus groups. In particular, the adolescent focus group consisted only of 4 girls, and the results from this group should be interpreted with caution.

Another possible limitation is that we compared the generic QOL (DUX-25) of CD children ages 8 to 18 with that of a healthy population ages 8 to 15. This means that we compared the QOL of the adolescent CD group (group 3) with that of a healthy control group that was 3 years younger. As expected, the scores from the older adolescent CD group were significantly lower on every scale and in the total mean score in the DUX-25. This may be explained by the longer time of living with CD present in the group of older adolescents in comparison with the younger children (Table 1) or by the assumption that the adolescents with CD with the best HRQOL are not members of the Dutch Celiac Society. However, the most plausible explanation is the age of this group of patients: older adolescents have a well-known tendency to have a lower appreciation of their QOL (19). Compared with healthy children, children with CD reported a lower QOL on the generic QOL questionnaire DUX-25. Although the differences are statistically significant, reflecting the large size of the studied groups, it is necessary to take into account that these differences may have little clinical relevance, inasmuch as a difference of 2 points on a scale of 1 to 100 may be considered small.

When parents are asked to evaluate the QOL of their children using the CDDUX proxy version, they appraise their QOL significantly more negatively than do the children themselves. This effect is not unique to CD, and it has also been shown in earlier studies (8,13,20–22). Most studies of parents of children with chronic

health problems report decreased marital satisfaction in comparison with parents of healthy children, but no significant decrease in marital stability (23). However, in our population, as many as 89% of the parents were married, which is a much higher percentage than the 63% of married people ages 30 to 50 in the general Dutch population (24).

Our new, bottom-up, disease-specific HRQOL questionnaire for children with CD, the CDDUX, provides information on 3 subscales in the day-to-day life of children with CD: "Having CD," "Communication," and "Diet." The CDDUX does not contain items with respect to feeling guilty if "forbidden" foods are eaten because feelings of guilt were not expressed during the focus groups used to develop the questionnaire. The questionnaire concentrates on the consequences of CD and on how the children think and feel about their illness and treatment over a long time. It may reflect a different appreciation of QOL at different moments in life. The information gained by the use of the CDDUX may enable researchers and clinicians caring for children with CD to determine the effects of illness and clinical interventions on different aspects of their daily living. In addition, the use of the CDDUX may give the physician the necessary opening for communication about the impact of the disease on the daily life of his patients during the outpatient consult, especially when caring for a child with CD who shows a tendency to give socially correct answers to the questions. The CDDUX makes use of "smiley answer" categories, which are short, simple, feasible, and easy to interpret by the pediatrician. If desired, the disease-specific CDDUX can be used in combination with the generic DUX-25, giving the caregiver a better overview of the consequences of CD for the individual. The continuing development of the children, the constant changes in their experience of their illness and health status, and the continuous adjustment of their internal standards regarding QOL make it an issue of interest to monitor the experiences of children with CD throughout their lives. The new CDDUX questionnaire has been developed for pediatricians, dietitians, and other health care providers to give them a better view of how the child experiences his or her life. However, to achieve improved care for the child, the physician has to be prepared to respond to the needs elucidated by the use of the HRQOL instrument. Combined with a generic questionnaire like the DUX-25, the CDDUX questionnaire may enable comparison of the CD population with a healthy population. Further research is mandatory for better insight into specific groups and aspects of the QOL in CD patients, such as adolescents or patients with early and late diagnosis of the disease.

Acknowledgments: The authors thank the Dutch Celiac Patients Society and their members for their cooperation, and Rolanda Baars for moderating the focus groups.

REFERENCES

1. Green PHR, Jabri B. Coeliac disease. *Lancet* 2003;362:383–91.
2. Steens RFR, Csizmadia C, Georg E, et al. Better recognition of childhood celiac disease in the Netherlands and its changing clinical picture: a national prospective study 1993–2000. *J Pediatr Gastroenterol Nutr* 2005;40:666–7.
3. Feighery C. Coeliac disease. *BMJ* 1999;319:236–9.
4. Hallert C, Grännö C, Hultén S, et al. Living with coeliac disease: controlled study of the burden of illness. *Scand J Gastroenterol* 2002;37:39–42.
5. Catassi C, Ratsch IM, Fabiani E, et al. Coeliac disease in the year 2000: exploring the iceberg. *Lancet* 1994;343:200–3.
6. Csizmadia CG, Mearin ML, von Blomberg BM, et al. An iceberg of childhood coeliac disease in the Netherlands. *Lancet* 1999;353:813.
7. Maki M, Mustalahti K, Kokkonen J, et al. Prevalence of celiac disease among children in Finland. *N Engl J Med* 2003;348:2517–24.
8. Eiser C, Morse R. Can parents rate their child's health-related quality of life? Results of a systematic review. *Qual Life Res* 2001;10:347–57.
9. Petersen C, Schmidt S, Power M, et al. Development and pilot-testing of a health-related quality of life chronic generic module for children and adolescents with chronic health conditions: a European perspective. *Qual Life Res* 2005;14:1065–77.
10. Gill TM, Feinstein AR. A critical appraisal of the quality of life measurements. *JAMA* 1994;272:619–26.
11. Koopman HM, Theunissen NCM, Vogels TGC, et al. The DUX-25: a short form questionnaire for measuring health related quality of life of children with chronic illness. *Qual Life Res* 1998;7:619.
12. Loonen HJ, Grootenhuis MA, Last BF, et al. Quality of life in paediatric inflammatory bowel disease measured by a generic and a disease specific questionnaire. *Acta Paediatr* 2002;91:348–54.
13. Verrips GHW, Vogels AGC, Verloove-VanHorick SP, et al. Health-related quality of life measure for children: the TACQOL. *J Appl Ther* 1998;1:357–60.
14. Vogels T, Verrips GHW, Verloove-Vanhorick SP, et al. Measuring health-related quality of life in children: the development of the TACQOL-parent form. *Qual Life Res* 1998;7:457–65.
15. The DISABKIDS Group Europe. Quality of life questionnaires for children with chronic conditions. In: *The DISABKIDS Questionnaires*. Lengerich, Germany: Pabst Science; 2006.
16. Kolsteren MMP, Koopman HM, Schalekamp G, et al. Health-related quality of life in children with celiac disease. *J Pediatr* 2001;138:593–5.
17. Sim J. Collecting and analysing qualitative data: issues raised by the focus group. *J Adv Nurs* 1998;28:345–52.
18. Morgan DL. Focus groups. *Annu Rev Sociol* 1996;22:129–52.
19. Compas BE, Orosan PG, Grant KE. Adolescent stress and coping: implications for psychopathology during adolescence. *J Adolesc* 1993;16:331–49.
20. Theunissen NCM, Vogels TGC, Koopman HM, et al. The proxy problem: child report versus parent report in health related quality of life research. *Qual Life Res* 1998;7:387–97.
21. Vance YH, Morse RC, Jenney ME, et al. Issues in measuring quality of life in childhood cancer: measures, proxies and parental mental health. *J Child Psychol Psychiatry* 2001;42:661–7.
22. Addington-Hall JKL. Measuring quality of life: who should measure quality of life? *BMJ* 2001;322:417–20.
23. Sabbeth BF, Leventhal JM. Marital adjustment to chronic childhood illness: a critique of the literature. *Pediatrics* 1984;73:762–8.
24. Dutch Central Bureau of Statistics. Statistics Netherlands, 2005. [http://statline.cbs.nl/StatWeb/publication/VW=T&DM=SLNL&PA=37425ned&D1=a&D2=0,10,20,30,40,50,\(1-1\)-1&HD=080522-2146&HDR=G1&STB=T](http://statline.cbs.nl/StatWeb/publication/VW=T&DM=SLNL&PA=37425ned&D1=a&D2=0,10,20,30,40,50,(1-1)-1&HD=080522-2146&HDR=G1&STB=T).