Haemophilia (2004), **10,** (Suppl. 1), 17–25

Development and testing of an instrument to assess the Quality of Life of Children with Haemophilia in Europe (Haemo-QoL)

S. VON MACKENSEN, M. BULLINGER and the HAEMO-QOL GROUP*
Institute and Policlinic for Medical Psychology, University Hospital of Hamburg-Eppendorf, Hamburg, Germany

Summary. In spite of an increased interest in the assessment of quality of life (QoL) in children, so far no instrument for children with haemophilia is available. Because of the low prevalence of the condition, such an instrument should also be cross-culturally applicable. In the study presented, a (QoL) assessment instrument for children with haemophilia (the Haemo-QoL questionnaire) was developed and tested in six countries (France, Germany, Italy, the Netherlands, Spain and the United Kingdom) for psychometric properties in 339 children with haemophilia and their parents. The Haemo-QoL is a self-reported questionnaire for children in the age ranges 4–7 (I: 21 items), 8–12 (II: 64 items), 13–16 years (III: 77 items) as well as for parent rating containing 9–11 subscales (depending on age-group versions). Psychometric testing involved the examination of reliability and validity. The three age-group versions of the Haemo-QoL had acceptable internal consistency and retest reliability values, as well as possessing sufficient discriminant and convergent validity. However, in young children when compared to older children, these indicators were less satisfactory. The Haemo-QoL full version is now available for children of three age groups and their parents and is ready for use in clinical research (http://www.haemoqol.org).

Keywords: children, haemophilia, quality of life, questionnaire validation

Introduction

The term 'health-related quality of life' was coined to represent the subjective perception of health. Health indicators refer traditionally to clinical signs and symptoms, morbidity and mortality. The perception of health by patient self-report has only recently been the focus of medical research. While in anthropology and social sciences quality of life (QoL) is a long-standing concept, representing structural indicators of living conditions or the evaluation thereof in terms of life satisfaction, the focus on quality of life in medicine is relatively recent. However, within the last 30 years, after an initial phase of philosophically orientated theoretical debates, QoL measures have been developed and applied in a variety of research contexts. In relation to the QoL literature in adult patients, QoL research in children is even more

*The Haemo-QoL Group was comprised as follows: Pilar Arranz, Hospital La Paz, Madrid, Spain; Günther Auerswald, Zentralkrankenhaus, Bremen, Germany; José Aznar, Hospital Universitario La Fe, Valencia, Spain; Marijke van den Berg, Academisch Ziekenhuid Utrecht, the Netherlands; Annie Borel-Derlon, Centre de l'Hémophilie, Caen, France; Hervé Chambost, Centre de l'Hémophilie, Marseille, France; Edith Fressinaud, Centre de l'Hémophilie, Nantes, France; R. Perez Garrido, University Hospital Virgen del Rocio, Seville, Spain; Eduard Gorina, Clinical Development Biological Products Bayer HealthCare, USA; Alessandro Gringeri, IRCCS Maggiore Hospital and University of Milan, Milan, Italy; Claude Guerois, Centre de l'Hémophilie, Chambray Lés Tours, France; Kate Khair, Great Ormond Street Hospital for Children NHS Trust, London, UK; Karin Kurnik; von Haunerische, Kinderklinik, München, Germany; Harald Lenk, Klinik für Kindermedizin, Universität Leipzig, Germany; Giovanni Longo, Centro Emofilia, Firenze, Italy; Felix Lucia, Servicio de Haematologia, Zaragoza, Spain; Laura Perugini, Ospedale Infantile 'Regina Margherita', Torino, Italy; Marijolein Peters, Academish Medish Centrum, Amsterdam, the Netherlands; Eduardo Remor, Hospital La Paz, Madrid, Spain; Chantal Rothschild, Centre de l'Hémophilie, Hôpital Necker, Paris, France; Marc Trossaert, Centre de l'Hémophilie, Nantes, France; Monique Vicariot, Centre de traitement de l'hémophilie, CHU de Brest, France; Ana Villar, Hospital La Paz, Madrid, Spain; Cornelia Wermes, Pädiatrische Hämatologie und Onkologie, Medizinische Hochschule, Hannover, Germany.

Correspondence: Dr Sylvia von Mackensen, Institute and Policlinic for Medical Psychology, University Hospital of Hamburg-Eppendorf, Martinistraße 52, S35, D-20246 Hamburg, Germany. Tel: + 49 40 42 803 6430; fax: + 49 40 42 803 4940;
e-mail: s.mackensen@uke.uni-hamburg.de

recent. According to a literature research only about 13% of approximately 20 000 publications in QoL-focused on children [1]. This is due certainly to several problems posed by assessment of QoL in children, which not only include the adequate representation of relevant domains or dimensions of QoL, but also the age dependency of the possible self-report, in terms of cognitive capacity, consistency of answers and the role of external parental reports. While in adult QoL literature relevant dimensions and domains have been consensually identified [2], their application in children's QoL concepts has been a challenge [3]. Serious doubts have been raised about whether children below the age of 8 years can reflect and report on their perceived health. The value of parental report has been stressed therefore as an approximation (proxy) for children's feelings and behaviours. Discussion has been extensive, especially concerning so-called generic assessments of QoL in children. Such assessment is applicable to a wide range of health states and has led to the development of generic instruments. These are available as self-report or proxy ratings. Disease-specific or targeted measures for children have been developed in several clinical areas, such as asthma, atopic dermatitis or diabetes. Haemophilia is a congenital coagulation disorder due to the genetically transmitted defect of clotting factor (factor VIII in haemophilia A and factor IX in haemophilia B). These haemostatic defects lead to spontaneous and post-traumatic internal bleeding events, particularly frequent in joints and muscles, but also possible in any tissue and organ, including the central nervous system. Recurrence of bleeding events in joints is the cause of the progressive deterioration of joint function with the development of arthropathy. The treatment is based on substitutive therapy with intravenous clotting factor concentrates to administer 'on-demand', i.e. when a bleeding event occurs, or prophylactically, to prevent the bleeding, two to three times a week. The treatment of haemophilia as well as related complications might influence the QoL of children and their families [4–6].

Targeted QoL measures for children with haemophilia have not been identified so far. For example, in over 300 publications on QoL research in children available between 1995 and 2003, many of them introducing or testing instruments assessing generic QoL in children, only some were disease-specific but none of them related to children with haemophilia. The few studies on QoL in children with haemophilia have not used standardized or psychometrically tested instruments, but rather *ad hoc* questions, or have inferred QoL information from clinical data [7–10].

QoL assessment in children with haemophilia will profit from the availability of quality of life measures for epidemiological reasons (describing the quality of life of this patient group with reference to children with other chronic conditions), for clinical trials (to evaluate the potential benefits of new treatments for haemophilia with regard to QoL), for quality assurance (identifying the quality of care given to children with haemophilia, for example, in haemophilia centres), for health-economic studies (assessing costs and benefits of haemophilia treatment with regard to economic indicators) and for routine treatment (identifying individual treatment options from which specific patients might benefit). Some data are available on QoL in haemophilia with regard to effectiveness of prophylactic home treatment which suggested that prophylactic treatment is associated with higher treatment costs, but is expected to lower costs in the course of the lifetime of a person, i.e. by reducing adverse consequences such as immobility and therefore preventing disability, handicap and impairment. Studies have shown that prophylactic treatment may improve QoL because it leads to reduced hospitalization rates, fewer joint bleeds and less time off school or work [11–13].

The question of how haemophilia and its care may impact on children's health-related QoL stimulated the development of a haemophilia-specific QoL questionnaire. A specific feature of the work was the simultaneous development of such a questionnaire starting from clinical expertise and patients' experience, not only in one country but simultaneously in several European countries. Such an international and cross-cultural perspective is necessary because haemophilia is a relatively rare condition affecting one in 10 000 children in the general population. The present paper describes the development and testing of the QoL questionnaire for children with haemophilia (the Haemo-QoL questionnaire) in a cross-cultural sample of children from six European countries. The aim of this paper is to describe the psychometric properties of the questionnaire with regard to reliability and validity, to understand factors influencing scale scores and to evaluate critically the potential and limitations of the newly developed questionnaire.

Methods

Study design and patient population

In this cross-sectional study, children with haemophilia and their families were included from one to six haemophilia centres in each of the six countries

(France, Germany, the Netherlands, Italy, United Kingdom and Spain). Inclusion criteria were severe (< 1% or between 1 and 2%, but clinically severe) haemophilia A or B, absence of inhibitors and informed consent from both parents and children. With regard to treatment, no restrictions were made. The only exclusion criterion was lack of ability to speak and understand the language of the respective country.

The Haemo-QoL questionnaire

The Haemo-QoL questionnaire is a modular instrument that was developed in expert discussions and from literature review. It has been tested in a pilot study within three age groups (children aged 4–7 years: interviews with the children and their parents' self-report; children aged 8–12 years: self-report by children and by parents; and adolescents aged 13–16 years: self-report by adolescents and parents). The pilot testing of the Haemo-QoL questionnaire was carried out with 58 children from six European countries and has been described recently [14]. The field-test version of the questionnaire was produced after modification of the pilot version and consists of 29 items for the younger children conducted as an interview. The version for the children aged 8–12 consisted of 84 items, and the version for adolescents consisted of 91 items. The difference of the number of items between the older age groups is due to the additional inclusion of two scales to assess the dimensions of specific relevance to adolescents, namely 'relationships' and 'future'.

Variables in addition to the Haemo-QoL questionnaires

In addition to the questionnaire described above, clinical variables as well as psychosocial and sociodemographic information were collected. Specifically for clinical documentation, an effort was made to standardize reporting relevant indicators across countries, using a specific clinical documentation sheet. Sociodemographic information was obtained primarily from parents and included a wide range of information also useable to identify indicators of social class. Psychosocial variables related to instruments assessing coping (KID-Cope [15]), social support (SSS adapted for children [16]), health locus of control (adapted for children [17]), as well as life satisfaction (FLZ adapted for children [18]). Care was taken to include not only the newly developed Haemo-QoL questionnaire [14], but also generic measures of QoL that can be used for convergent psychometric validation, namely the KINDL [19] for child self-report and the Child Health Questionnaire (CHQ) [20], which assesses QoL in children from the parents' perspective, and the SF-12 [21], which related to the perceived health status. An overview over the instruments is given in Table 1.

Conduct of the study

The preparation of the questionnaires in six different languages included the Haemo-QoL questionnaire together with a generic quality of life questionnaire and other instruments, which included psychosocial information, to be administered in the centres and in a take-home questionnaire for retest reliability testing. Clinical data were collected at the haemophilia centre. All data collection was carried out by a nurse or student helping in the project, either by specific appointments with participants or by routine visits through the haemophilia centre. Following information about the study and a signed consent form, the children in the two older age groups sat in a quiet room to fill in the questionnaire; however, they could

Table 1. Domains of the Haemo-QoL and additional questionnaires with number of items per age group (I: 4–7, II: 8–12, III: 13–16 years).

	Age groups				Age groups		
Haemo-QoL	I	II	III	Additional questionnaires	I	II	III
Dimension	4–7	8–12	13–16	Questionnaire	4–7	8–12	13–16
Physical health	5	9	9	KINDL	18	30	30
Feeling	3	6	6	CHQ	1	1	1
Attitude	3	7	7	FLZ	–	11	11
Family	5	11	11	SSS	–	9	9
Friends	2	8	8	Kids-Cope	3	9	9
Other people	5	13	13	KKG	–	7	7
Sport and school	4	11	11	Open questions	5	6	6
Coping	–	10	10	Total	27	73	73
Treatment	2	9	9				
Future	–	–	4				
Relationship	–	–	3				
Total	29	84	91				

ask if they had questions. In parallel, parents, if available, were asked to fill in the respective questionnaire. Young children (4–7 years) were interviewed by trained staff. All children received a small present for participation. Take-home questionnaires – to be filled in separately by children and parents only in age groups II (ages 8–12) and III (ages 13–16) – were provided with a free stamped return envelope so that returning the follow-up questionnaire after 1 week was made as easy as possible. In each centre one responsible person was identified who could be addressed for logistical matters. All centres were visited to introduce and train for the study and were monitored continuously by the project staff.

Data analysis

Upon central data input and plausibility checking, descriptive statistics were performed using the SPSS program (SPSS/PC version 10.0) followed by psychometric testing with the so-called 'multi trait analysis' program (MAP) [22]. The MAP program allows identification of the item characteristics in terms of item distributions and the confirmatory analyses of the scale fit, which gives an indicator of the percentage with which items correlate with the scales to which they are supposed to belong, in comparison to another scale. The MAP program also provides information on floor/ceiling effects of scales, reliability indicators (Cronbach's α) and scale intercorrelations. Other statistical analyses, including comparisons between subgroups using *t*-test or variance analytical methods or correlational analyses, were performed using the SPSS/PC program.

Results

A total of 24 centres in the six countries had expressed interest in participation and contributed patients to the study. Due to organizational reasons, four centres could not participate so that a total of 20 centres were active. Table 2 shows the distribution of centres and sample size per centre across countries. Within these centres, a total of 339 children and their parents were recruited into the study. With regard to an expected number of 476 children, this represents a 70% response rate.

Sociodemographic data

The children's mean age was 10.00 (SD = 3.7) years ranging from 5.56 years in the youngest age group I (4–7) over 10.00 years in the age group II (8–12) to 14.09 in the age group III (13–16). Half of the children had one sibling, 19.0% had no siblings and 17.7% had two siblings (see Table 3).

Table 2. Participating centres (number of children).

Country	Centres	No. of patients
Spain	Valencia	17
	Zaragoza	10
	Sevilla	14
	Madrid	35
France	Nantes	12
	Caen	10
	Tours	15
	Paris	29
	Marseille	15
	Brest	5
Germany	Bremen	26
	Leipzig	14
	Hannover	12
	Munich	8
Italy	Firenze	11
	Milano	41
	Torino	18
the Netherlands	Utrecht	19
	Amsterdam	6
UK	London	22
Total no. of patients		339

The parents' characteristics (see Table 4) show that mainly mothers responded (77.2%). Most of the parents were married (83.0%) and 90.9% of the parents lived with a partner. In terms of schooling the high school level was predominant in 30.1% of the parents and 66.1% of the parents were employed.

Clinical characteristics

Of the 339 patients enrolled no medical documentation was available from 13 patients and eight patients were excluded because they did not fulfil the inclusion criteria. From the 318 patients included in the analysis, 85.5% had haemophilia A and 11.6% haemophilia B. The factor level as an indicator of the severity of the condition was less than 1% in 86.5% and between 1% and < 2% in 12.9%. Of the children, 25.8% had had no joint bleeds in the previous 12 months, 41.2% of the children had had less than five joint bleeds and 9.1% had five to 10 joint bleeds; the remaining 9.1% had had more than 10 joint bleeds. A total of 66.7% of the children were on prophylactic treatment and 31.8% received on-demand treatment (see Table 5); 11.3% of the patients had functional impairments, mainly in age group III (15.5%). Chronic pain was reported in 3.1% of the patients and 6.6% had undergone orthopaedic surgery.

Table 3. Sociodemographic data of the children per age group (I: 4–7, II: 8–12, III: 13–16 years).

Characteristics	Σ ($n = 320$)	I ($n = 95$)	II ($n = 122$)	III ($n = 103$)
Age [mean (SD)]	10.00 (3.7)	5.56 (1.2)	10.00 (1.7)	14.09 (1.5)
Number of siblings				
0	19.0%	26.7%	12.3%	19.8%
1	50.5%	44.4%	57.0%	48.5%
2	17.7%	22.2%	18.4%	12.9%
3	6.9%	3.3%	5.3%	11.9%
4	4.3%	3.3%	3.5%	5.9%
5	0.3%	–	–	1.0%
> 5	1.3%	–	3.5%	–

Table 4. Sociodemographic data of the parents.

Characteristics	Σ ($n = 309$)	I ($n = 95$)	II ($n = 110$)	III ($n = 104$)
Age [mean (SD)]	39.30 (6.1)	36.27 (5.5)	39.23 (6.0)	42.54 (5.1)
Gender				
Female ($n = 233$)	77.2%	81.9%	72.6%	77.5%
Marital status				
Single ($n = 16$)	5.8%	12.2%	4.1%	1.1%
Married ($n = 230$)	83.0%	83.3%	79.6%	86.5%
Divorced ($n = 30$)	10.8%	4.4%	15.3%	12.4%
Widowed ($n = 1$)	0.4%	–	1.0%	–
Living with partner				
Yes ($n = 241$)	90.9%	92.3%	90.6%	88.9%
No ($n = 24$)	9.1%	6.8%	9.4%	11.1%
School grade				
Some high school ($n = 31$)	11.1%	7.7%	13.6%	11.2%
High school ($n = 84$)	30.1%	34.1%	28.2%	27.0%
Vocational school ($n = 59$)	21.1%	20.9%	20.4%	21.3%
College ($n = 31$)	11.1%	11.0%	16.5%	7.9%
Professional degree ($n = 47$)	16.8%	16.5%	13.6%	21.3%
Other degree ($n = 20$)	7.2%	8.8%	2.9%	10.1%
No degree ($n = 7$)	2.5%	1.1%	4.9%	1.1%
Employment				
Yes, full time ($n = 107$)	38.4%	35.1%	38.4%	39.6%
Yes, half time ($n = 66$)	22.6%	17.0%	25.3%	27.5%
Yes, < half time ($n = 15$)	5.1%	8.5%	4.0%	3.3%
No, house wife ($n = 76$)	27.1%	30.9%	25.3%	24.2%
No, in training ($n = 1$)	0.3%	–	1.0%	–
No, unemployed ($n = 9$)	3.1%	4.3%	4.0%	1.1%
No, others ($n = 10$)	3.4%	4.3%	2.0%	4.4%

Psychometric characteristics

Psychometric testing involved *a priori* inspection of item distribution and correlation with the supposed scale. Following this information items were deleted or regrouped for each of the age groups, which resulted in psychometric testing in three age groups: young children (age 4–7 years: 21 items), older children (age 8–12 years: 64 items) and adolescents (age 13–17 years: 77 items). Confirmatory psychometric testing using the MAP program was employed to describe the mean and standard deviation of the scale scores as well as ceiling and floor effects, minimum and maximum scale values and the two psychometric indices, namely scale fit and Cronbach's α. This psychometric testing procedure was also performed for the parents' questionnaires, but will be described elsewhere (paper in preparation).

Reliability and scale structure (Table 6) shows the scale structure and reliability coefficients of the revised Haemo-QoL questionnaire for the three age-group versions. Within the Haemo-QoL for age group I ($n = 90$), which now consisted of 21 items, the scale fit was acceptable in four of the scales. Cronbach's α was acceptable in two of the scales as well as the total score. In age group II (ages 8–12) ($n = 117$), analysis of the instrument, which consisted of 64 items, revealed better psychometric

Table 5. Clinical data.

Characteristics	Σ	I	II	III
Type of haemophilia				
A ($n = 272$)	85.5%	84.5%	83.1%	89.3%
B ($n = 37$)	11.6%	14.4%	12.7%	7.8%
Missing data ($n = 9$)	2.9%	1.0%	4.2%	2.9%
Level factor				
≤ 1% ($n = 275$)	86.5%	86.6%	85.6%	87.4%
> 1% ($n = 41$)	12.9%	12.4%	14.4%	11.7%
Missing data ($n = 2$)	0.6%	1.0%	–	1.0%
Treatment scheme				
Prophylactic ($n = 212$)	66.7%	68.4%	68.6%	62.9%
On-demand ($n = 101$)	31.8%	30.5%	30.5%	34.3%
Missing data ($n = 5$)	1.6%	1.1%	0.8%	2.9%
Joint bleeds				
0 ($n = 82$)	25.8%	22.7%	28.8%	25.2%
< 5 ($n = 131$)	41.2%	43.3%	39.0%	41.7%
5–10 ($n = 29$)	9.1%	6.2%	10.2%	10.7%
> 10 ($n = 29$)	9.1%	8.2%	6.8%	12.6%
Missing data ($n = 47$)	14.8%	19.6%	15.3%	9.7%
Impairment				
Yes ($n = 36$)	11.3%	4.1%	13.6%	15.5%
No ($n = 275$)	86.5%	95.9%	84.7%	79.6%
Missing data ($n = 7$)	2.2%	–	1.7%	4.9%
Chronic pain				
Yes ($n = 10$)	3.1%	1.0%	5.1%	2.9%
No ($n = 304$)	95.6%	99.0%	94.1%	94.2%
Missing data ($n = 4$)	1.3%	–	0.8%	2.9%
Orthopaedic surgery				
Yes ($n = 21$)	6.6%	2.1%	5.1%	12.6%
No ($n = 287$)	90.3%	96.9%	91.5%	82.5%
Missing data ($n = 10$)	3.1%	1.0%	3.4%	4.9%

properties assessing between four and nine items and 10 dimensions of health-related QoL. The scale fit approached the optimum of 100 in almost all the scales; the coefficient alpha ranged from 0.60 to 0.79 and was 0.85 for the total score. In addition the Haemo-QoL, re-evaluated 1 week later, produced test–retest reliability results which for most of the scales were beyond $r = 0.70$, with only two exceptions for the subscales 'dealing with haemophilia' and 'treatment'. A total of 100 adolescents responded to the questionnaires in age group III (13–16 years). The item number ($n = 77$) was higher because two dimensions were added, namely 'future' and 'relationship'. The scale fit was near optimum in almost all the scales (the lowest value was 84.1%). The coefficient alpha was satisfactory except for the scales 'future', 'treatment' and 'perceived support'. The test–retest reliability was again largely satisfactory, with the exception of lower scores in three scales (perceived support, treatment and future). The Cronbach's α of the total scale was 0.91 and of the test–retest correlation the total scale was 0.92.

Convergent validity

For the convergent validity of the Haemo-QoL for age group I, correlations between the KINDL total score with the general item (GHQ) from the CHQ as well as the chronic generic item module of the KINDL were examined (see Table 7), showing that these correlations were approximately $r = 0.30$ for correlations between the Haemo-QoL and the KINDL. However, higher scores with the chronic generic module of approximately $r = 0.40$ indicated an acceptable correlation with the Haemo-QoL. The highest correlation was found here for the dimension 'others' of the Haemo-QoL and the chronic generic module of the KINDL ($r = 0.532$, $P = 0.0001$). Only two significant correlations were found between the Haemo-QoL and the GHQ. In age group II, the correlations between the dimensions of the Haemo-QoL and the KINDL total score were higher, averaging $r = 0.30$ in all correlations. The convergent validity of the Haemo-QoL in age group III reached $r = 0.45$-$.50$ in almost all scales, again with high correlation in the total score (see Table 7).

Discriminant validity

Discriminant validity was assessed using clinical information differentiating Haemo-QoL scores within each of the age groups with regard to treatment and condition-related information. Differences between on-demand and prophylactic treatment largely failed to reach significance although, in general, prophylactic treatment seemed to be associated with less impairment in QoL. This is also true for the discriminant validity of the revised Haemo-QoL with regard to joint bleeds. Here differences appeared, especially in the older age groups, indicating higher impairment for children with more than five joint bleeds in the previous 12 months in the dimensions 'physical health', 'view', 'perceived support' and especially 'sports' activity, yielding a significant difference in the total score (see Table 8).

Correlations of the Haemo-QoL with psychosocial determinants were assessed in age groups II and III. Significant correlation of the Haemo-QoL with social support and life satisfaction, but also with coping and less with locus of control were found, indicating that effective social support was associated with a higher QoL score and impairment in the Haemo-QoL was associated with life dissatisfaction. Multiple regression analysis with QoL as a criterion (Haemo-QoL total score) was performed, which took into account specific clinical and psychosocial data. QoL was clearly associated with life satisfaction and social

Table 6. Psychometric characteristics of the revised Haemo-QoL (all age groups).

Scale	No. of items	Min	Max	Mean	SD	Floor effects	Ceiling effects	Scale fit	α	Test–retest
Age group										
Physical health	4	4	16	7.03	3.15	34.8%	0%	85.7%	0.55	–
Feeling	3	3	15	5.13	3.13	58.4%	2.2%	90.5%	0.82	–
View	2	2	10	3.53	2.40	61.8%	7.9%	78.6%	0.69	–
Family	4	4	20	9.47	3.91	18.0%	1.1%	82.1%	0.66	–
Friend	1	1	5	1.74	1.21	69.7%	6.7%	–	–	–
Others	2	2	10	3.87	2.20	48.3%	2.2%	64.3%	0.56	–
Sport	3	3	12	5.48	2.64	42.7%	0%	95.2%	0.49	–
Treatment	2	2	10	4.00	2.34	47.2%	5.6%	64.3%	0.45	–
Total	21	21	81	40.25	13.65	4.5%	0%	82.1%	0.85	–
Age group II										
Physical health	7	7.00	27.00	11.64	4.80	19.7%	0%	98.4%	0.78	0.87
Feeling	7	7.00	25.67	9.56	3.36	41.0%	0%	96.8%	0.69	0.87
View	9	9.00	39.00	14.89	5.86	14.5%	0%	96.3%	0.79	0.84
Family	5	5.00	21.00	9.28	4.02	23.9%	0%	82.2%	0.68	0.76
Friend	4	4.00	20.00	11.03	4.47	7.7%	5.1%	97.2%	0.71	0.81
Perceived support	4	4.00	20.00	11.84	4.07	6.8%	4.3%	94.4%	0.66	0.74
Others	6	6.00	25.00	8.50	3.33	38.5%	0%	96.3%	0.74	0.76
Sport	8	8.00	28.00	15.49	5.53	13.7%	0%	94.4%	0.67	0.79
Dealing	7	7.00	35.00	16.32	5.54	4.3%	0.9%	96.8%	0.66	0.61
Treatment	7	7.00	25.00	12.13	4.06	15.4%	0%	93.7%	0.60	0.67
Total	64	79.00	200.67	120.68	22.66	0%	0%	95.0%	0.85	0.90
Age group III										
Physical health	7	7.00	27.00	12.51	4.46	14.0%	0%	100%	0.76	0.79
Feeling	8	8.00	36.00	11.71	5.15	30.0%	0%	96.6%	0.87	0.89
View	10	10.00	43.00	18.00	6.92	12.0%	0%	97.3%	0.86	0.86
Family	8	8.00	26.00	13.62	4.37	12.0%	0%	90.9%	0.69	0.76
Friend	4	4.00	20.00	11.20	3.90	2.0%	2.0%	97.7%	0.69	0.81
Perceived support	4	5.00	20.00	12.40	3.75	0%	5.0%	97.7%	0.63	0.57
Others	6	6.00	22.00	9.07	3.85	33.0%	0%	89.4%	0.75	0.71
Sport	9	9.00	35.00	19.18	7.24	10.0%	0%	94.9%	0.76	0.78
Dealing	7	7.00	35.00	15.94	5.38	2.0%	1.0%	98.7%	0.68	0.71
Treatment	8	8.00	29.00	15.41	5.14	6.0%	0%	90.9%	0.67	0.63
Future	4	4.00	16.00	8.66	3.00	6.0%	0%	84.1%	0.52	0.64
Relationship	2	2.00	9.00	2.75	1.46	74.0%	0%	100%	0.73	0.90
Total	77	92.00	240.00	150.42	30.62	0%	0%	94.8%	0.91	0.92

support as well as with the number of bleeds. These data are presented in another paper [23].

Discussion

This study presents the results of the psychometric testing of the final long version of the first disease-specific QoL questionnaire (Haemo-QoL), indicating that the three age-related versions of the haemophilia-specific questionnaire with different item numbers across age groups are methodologically acceptable. The reliability of the scales reached the critical alpha of 0.70 in the majority of the scales with, however, lower values in younger children. The same is true for the scale fit, which is an indicator of the factorial validity of the Haemo-QoL questionnaire. Convergent validity with the KINDL questionnaire as well as with the general item (GHQ) from the child health questionnaire (CHQ) showed acceptable correlations. With regard to discriminant validity, indicators of clinical severity also showed that the instrument is able to differentiate between clinical subgroups in the oldest age group.

Within this cross-sectional study, testing of the sensitivity or responsiveness of the newly developed measure was not possible; however, this could be undertaken and will be performed in ongoing studies (e.g. ESCHQoL Project [25]) using the Haemo-QoL questionnaires. In addition, the Haemo-QoL questionnaire is supplemented by an age-related parent version which uses identical items. The psychometric quality of these scales, as described in a paper in

Table 7. Convergent validity of the Haemo-QoL (all age groups, r = correlation coefficient, P = P-value).

		Age group I			Age group II			Age group III		
Haemo-QoL		KINDL	Chronic–generic	GHQ	KINDL	Chronic–generic	GHQ	KINDL	Chronic–generic	GHQ
Physical health	*r*	–	− 0.332	− 0.318	–	− 0.330	− 0.275	− 0.335	− 0.452	− 0.299
	P		0.002	0.002		0.000	0.004	0.001	0.000	0.004
Feeling	*r*	− 0.280	− 0.383	− 0.217	–	− 0.287	–	− 0.517	− 0.563	− 0.359
	P	0.010	0.000	0.036		0.002		0.000	0.000	0.000
View	*r*	− 0.250	− 0.419	–	− 0.345	− 0.368	–	− 0.575	− 0.518	− 0.462
	P	0.022	0.000		0.000	0.000		0.000	0.000	0.000
Family	*r*	–	− 0.435	–	–	− 0.336	–	− 0.257	− 0.508	− 0.269
	P		0.000			0.000		0.014	0.000	0.008
Friend	*r*	–	–	–	–	–	–	− 0.230	–	− 0.260
	P							0.030		0.011
Perceived support	*r*	–	–	–	− 0.296	− 0.357	–	− 0.573	− 0.454	− 0.309
	P				0.003	0.000		0.000	0.000	0.002
Others	*r*	− 0.265	− 0.532	–	− 0.204	–	–	–	–	–
	P	0.015	0.000		0.044					
Sport	*r*	–	–	–	–	− 0.284	− 0.229	− 0.301	− 0.374	− 0.329
	P					0.003	0.017	0.004	0.000	0.001
Dealing	*r*	–	–	–	− 0.266	–	–	–	–	–
	P				0.010					
Treatment	*r*	–	–	–	–	–	–	− 0.325	–	− 0.264
	P							0.002		0.012
Future	*r*	–	–	–	–	–	–	− 0.408	− 0.328	− 0.387
	P							0.000	0.001	0.000
Partner	*r*	–	–	–	–	–	–	− 0.232	− 0.244	–
	P							0.030	0.019	

Table 8. Discriminant validity of the revised Haemo-QoL for number of (joint bleeds) (mean and P-values).

	Age group I			Age group II			Age group III		
Haemo-QoL	< 5	≥ 5	*P*	< 5	≥ 5	*P*	< 5	≥ 5	*P*
Physical health	6.82	6.43	n.s.	11.05	12.47	n.s.	10.95	15.63	0.000
Feeling	5.10	4.86	n.s.	9.14	9.67	n.s.	11.06	12.54	n.s.
View	3.44	3.71	n.s.	15.11	13.58	n.s.	16.54	21.79	0.002
Family	9.22	9.69	n.s.	8.83	11.00	0.042	13.22	14.67	n.s.
Friend	5.32	6.29	n.s.	11.31	11.84	n.s.	11.11	11.46	n.s.
Perceived support	–	–	–	8.16	8.53	n.s.	8.14	10.88	0.002
Others	3.84	3.86	n.s.	12.64	10.89	n.s.	12.56	12.79	n.s.
Sport	5.16	6.23	n.s.	17.28	17.95	n.s.	17.92	23.21	0.004
Dealing	–	–	–	16.44	16.44	n.s.	15.95	16.83	n.s.
Treatment	3.71	4.17	n.s.	13.93	13.89	n.s.	15.13	15.27	n.s.

preparation, is also satisfactory. Using psychosocial determinants of QoL such as coping, locus of control, life satisfaction and social support it was apparent that QoL is dependent not only on clinical but also on psychosocial characteristics. Such an influence of coping strategies on the psychosocial wellbeing of haemophiliacs has already been found in other studies [24].

An attempt at shortening the Haemo-QoL questionnaire was made by empirically identifying, from the total item pool, items that are available in all age groups and that comply with psychometric standards. Using this formal item reduction process, a short version consisting of 35 items with a scale structure retained was identified for children in age groups II and III which could also be used with the youngest age group (paper in preparation). In addition, an ultra-short version consisting of 15 items present in all age groups was produced, which yields only a summary score. Both the short and the ultra-short version must be tested in an independent study.

With the development of the Haemo-QoL simultaneously in several European countries an attempt was made to develop and test a documentation system to assess children's QoL in haemophilia. This

makes it possible to examine, in the long self-report version, age-related aspects in quality of life in haemophilia as well as parental reports, thus enabling the researcher to compare parents' and children's ratings, as well as making available a short form which can be used according to specific study design needs [26]. Considering that no disease-specific tool in haemophilia is available for children and adolescents, it is hoped that this approach will contribute to increased research in this area.

Acknowledgements

We would like to thank Bayer for the sponsorship of the Haemo-QoL validation study.

References

1 Ravens-Sieberer U. Verfahren zur Erfassung der gesundheitsbezogenen Lebensqualität bei Kindern und Jugendlichen. *Bundesgesundheitsbl-Gesundheitsforsch-Gesundheitsschutz* 2000; **3**: 198–209.
2 Bullinger M. Quality of life-definition, conceptualization and implications – a methodologist's view. *Thero Surg* 1991; **6**: 143–9.
3 Eiser C, Morse R. A review of measure of quality of life for children with chronic illness. *Arch Dis Child* 2001; **84**: 205–11.
4 Brown LK, Schultz JR, Gragg RA for the Hemophilia Behavioral Intervention Evaluation Project. HIV-infected adolescents with hemophilia: adaptation and coping. *Pediatrics* 1995; **96**: 459–63.
5 Solovieva S. Clinical severity of disease, functional disability and health-related quality of life. Three-year follow-up study of Finnish patients with coagulation disorders. *Haemophilia* 2001; **7**: 53–63.
6 Barr RD, Saleh M, Furlong W *et al.* Health status and health-related quality of life associated with haemophilia. *Am J Hematol* 2002; **71**: 152–60.
7 Rosendaal FR, Smit C, Varekamp I *et al.* Modern haemophilia treatment: medical improvements and quality of life. *J Intern Med* 1990; **228**: 663–40.
8 Nillson IM. Is haemophilia prophylaxis achievable in the context of self-sufficiency? *Blood Coag Fibrinol* 1994; **5**: 71–5.
9 Liesner RJ, Khair K, Hann IM. The impact of prophylactic treatment on children with severe haemophilia. *Br J Haematol* 1996; **92**: 973–8.
10 Tusell J, Molho P. Evaluation of clinical, radiological, economic and quality of life parameters related to orthopaedic status in haemophilic patients in Spain and France. *Haemophilia* 1998; **4**: 175.
11 Bohn RL. The economics of bleeding disorders. *Haemophilia* 1999; **5**: 378–85.
12 Miners AH, Sabin CA, Tolley KH *et al.* Assessing health-related quality of life in patients with severe haemophilia A and B. *Psychol Health Med* 1999; **4**: 5–15.
13 Miners AH, Sabin CA, Tolley KH, Lee CA. Cost–utility analysis of primary prophylaxis versus treatment on-demand for individuals with severe haemophilia. *Pharmacoeconomics* 2002; **20**: 759–74.
14 Bullinger M, von Mackensen S, Fischer K *et al.* Pilot testing of the Haemo-QoL quality of life questionnaire for haemophiliac children in six European countries. *Haemophilia* 2002; **8**(Suppl 2): 2, 47–54.
15 Spirito A, Stark LJ, Williams C. Development of a brief coping checklist for the use with pediatric populations. *J Pediatr Psychol* 1988; **13**: 555–74.
16 Sherbourne CD, Stewart AL. The MOS Social Support Survey. *Social Sci Med* 1991; **32**: 705–14.
17 Lohaus A, Schmitt GM. Kontrollüberzeugungen zu Krankheit und Gesundheit. Bericht über die Entwicklung eines Testverfahrens. *Diagnostica* 1989; **35**: 59–72.
18 Henrich G, Herschbach P, von Rad M. Lebensqualität in den alten und neuen Bundesländern. *Psychother Med Psych* 1992; **42**: 31–2.
19 Ravens-Sieberer U, Bullinger M. Assessing the health related quality of life in chronically ill children with the German KINDL: first psychometric and content-analytical results. *Quality Life Res* 1999; **7**: 399–408.
20 Landgraf I, Abetz L, Ware JE. Child Health Questionnaire (CHQ): a user's manual. Boston: The Health Institute Press, 1997.
21 Gandek B, Ware J, Aaronson N *et al.* Cross-validation of item selection and scoring for the SF-12 Health Survey in nine countries. Results of the IQOLA-Projekt. *J Clin Epidemiol* 1998; **51**: 1171–8.
22 Hays R, Hayashi T, Carson S, Ware J. *User's Guide for the Multitrait Analysis Program (MAP)*. Santa Monica: Rand Corporation Report no. N-2786-RC, 1988.
23 Bullinger M, von Mackensen S and the Haemo-QoL Group. Quality of Life in children and families with bleeding disorders. *J Pediatr Haematol Oncol* 2003; **25**: 64–7.
24 Santavirta N, Bjorvell H, Koivumaki E *et al.* The factor structure of coping strategies in hemophilia. *J Psychosom Res* 1996; **40**: 617–24.
25 http://www.eschqol.org
26 http://www.haemoqol.org