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Pilot testing of the 'Haemo-QoL' quality of life questionnaire for haemophiliac children in six European countries

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Summary. In a multinational working group, an instrument (Haemo-QoL) to assess quality of life in children/adolescents with haemophilia and their parents has been developed. In co-operation with haemophilia treatment centres in six European countries, approximately 10 children/adolescents with haemophilia per country and their parents were asked to participate in the pilot-testing. Both self-reported and parent-reported questionnaires were provided for two age-groups of children (4–16 years). Medical data was collected from physicians from patient files. Answers to open questions from participants (58 children and 57 parents) confirmed the content of 116 of the preliminary items. Cognitive debriefing revealed that the majority of the Haemo-QoL was rated favourably, but 29 questions were recommended to be omitted and several items to be reformulated. Preliminary psychometric testing of the revised 77 item questionnaire in the same sample showed acceptable reliability and validity, which will be examined in a subsequent study with a larger patient sample.

Keywords: quality of life, questionnaire, haemophilia, children/adolescents, assessment

Introduction

Health-related quality of life is increasingly considered a relevant health outcome parameter in medicine. In adults, concepts on quality of life, assessment methods and applications of respective instruments in various types of studies have been published within the past 20 years [1]. As concerns the concept, consensus has been reached with regard to the main components of the operationally defined term for quality of life, namely well-being and function in physical, social and emotional domains [2]. Self-reporting by respondents is important to capture the individual perception of health conditions and treatment regimes. Standardized, psychometrically tested and internationally available measurement instruments include the short form SF-36 Health Survey [3], the Nottingham Health Profile [4] or the EuroQol [5] questionnaire amongst others. While generic instruments measure quality of life across health conditions, condition-specific measures do so with regard to a specified disease, treatment or symptom.

In comparison to adults, children's quality of life assessment is a more recent area of research. A Medline literature search involving papers published from 1995 to 2000 identified a total of 319 publications on quality of life research in children [6], few publications introducing or testing instruments to assess quality of life in children.

Generic measures to assess quality of life in children are existent, examples are the Child Health Questionnaire [7], the TAQOL questionnaire [8] or the KINDL questionnaire [9]. Disease-specific instruments, however, have not been developed for children with haemophilia.

Generally, only few studies referring to quality of life in children with haemophilia are published and these

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rarely used standardized and psychometrically tested quality of life questionnaires. Available data on quality of life in haemophilia evaluate the effectiveness of prophylaxis and home treatment. Prophylactic treatment is associated with higher direct treatment costs, but is expected to lower costs in the course of lifetime of a person with haemophilia by reducing adverse consequences of the disease such as immobility, pain and therefore disability, handicap and impairment (e.g. [10]). Studies have shown that prophylactic treatment improved quality of life in terms of less hospitalization, fewer joint bleeds and less time off school or work (e.g. [11]). In children where both types of treatment, prophylactic and on-demand, are administered, health condition and treatment may affect well-being and function of patients and families.

The question of how haemophilia and its care may impact on children's health-related quality of life, motivated the development of a haemophilia-specific quality of life questionnaire with the goal to have at hand an instrument with which different treatment modalities maybe evaluated for their effect on children and families in clinical studies. In this paper the development of such an instrument and results from its pilot test are presented. The work presents a European effort to (a) develop a disease-specific self-report instrument (Haemo-QoL) for children and adolescents with haemophilia and their parents available in different languages; (b) to cognitively debrief it to understand how children respond to the questions; and (c) to preliminarily test it for basic psychometric properties in terms of reliability and validity.

Materials and methods

Within a European collaborative working group of haematological and psychosocial experts from six countries a condition-specific questionnaire for children with haemophilia and their parents was developed. In the development of QoL instruments care was taken to comply with guidelines pertaining to quality-controlled translations (including forward/backward translations and comparison of the retranslated versions with the original) as well as focus group work (ensuring the comprehensibility, relevance and acceptance of the instrument). In addition, testing of psychometric properties (including indicators of reliability, validity and sensitivity) and obtaining reference data for the study population is recommended [12]. These guidelines are especially important in multinational, cross-cultural work to ascertain the equivalence of items and scales across countries. Within the international instrument development, the cognitive debriefing of questionnaires is increasingly considered important. It involves an evaluation of each question of the instrument (item per item) and feedback on comprehensibility, relevance and modification needs [13]. Preliminary psychometric testing helps to select items that best represent the constructs to be measured.

Instrument development

The preliminary version of the Haemo-QoL questionnaire was derived from an expert consensus meeting in which clinicians and social scientists convened to identify relevant dimensions and items of quality of life from the literature, clinical experience and available questionnaires. This resulted in an instrument with 116 items pertaining to 10 domains of quality of life. Item examples of each subscale are shown in Table 1. The questionnaire was professionally translated into all project languages using the forward-backward method.

Pilot-testing

The preliminary version of the Haemo-Qol was given to children/adolescents and their parents in the collaborating haemophilia centres in six different countries (England, France, Germany, Italy, the Netherlands and Spain) together with generic questionnaires. For the children/adolescents these included the Child Health Questionnaire [7], and the KINDL questionnaire [9]. As potential determinants of quality of life, the KID-Cope Questionnaire [14], a treatment motivation questionnaire (M. Bullinger, U.A. Ravens-Sieberer, unpublished data) as well as questionnaires to assess life satisfaction [15], social support [16] and health related locus of control [17] were included. For the parents the parental version of the Child Health Questionnaire [7] and KINDL questionnaire [9] was included in addition to the impact on family scale [18], the SF-12 Health Survey as well as subscales from the SF-36 Health Survey [19].

The testing was performed with the help of staff and trained students at the haemophilia centres. Children included were of two age-groups: younger children (4–7 years) were interviewed by a specially trained student, older children (8–16 years) filled in the questionnaire by themselves as did all parents of the children. A second set of 'take home questionnaires' included the afore mentioned measures of psychosocial predictors of quality of life. All data were checked, plausibility controlled and data inputted.

Cognitive debriefing

The questionnaire was evaluated by children and parents with respect to acceptance, comprehensibility, difficulty and completion time using a standardized feedback evaluation form with visual analogue scales. Feedback was given by children after filling in the

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Table 1. Examples of items for each subscale of the original Haemo-Qol questionnaire (n = 116 items)

Scale	No. items	Subscales	Example
Physical Health	16	pain	I had pain in my joints
		mobility	My joint felt stiff
		anxiety	I was afraid of bleeds
Feeling	12	mood	I was moody
		emotional consequences	I felt under stress because of my haemophilia
		action	I was upset
Attitude	10	relationship to others	I was envious of healthy kids my age
		relationship to own person	I was happy with myself
Family	13	position in the family	I had a special position within our family because of my haemophilia
		restrictions	My parents forbade me doing certain things because of my haemophilia
		problems	There were problems at home because of my haemophilia
		activities of parents	My parents had to limit their activities because they had to look after me
		own feelings in family	I was happy in my family
Friends	13	relationship	I could talk to my friends about my haemophilia
		activities	I was able to participate in the activities I liked
		anxiety	I was afraid of being an outsider
Other Persons	13	social support	Others were understanding towards me because of my haemophilia
		estrangement	I felt different from others
		isolation	I felt left out when others did things together
Sport and School	13	sports & games	Because of haemophilia I had to refrain from sports that I like
		school	I was afraid of fights in the school playground
Coping	10	control	I felt well informed about haemophilia
		emotional acceptance	I felt healthy as anybody else
Treatment	12	quality	I was satisfied with my haemophilia centre
		side-effects	The injections annoyed me
Future	4		I have worried about my health

questionnaires and a break of 15–30 min. For the older children from age 8 onward, open questions were posed in addition to the in-depth cognitive interview, for younger children only an overall evaluation using smileys was obtained.

The cognitive debriefing (as answered by older children) was conducted in the language of the child. The children and adolescents were asked for each item about difficulty to understand and about its relevance with respect to their haemophilia. If an item was not understandable, they were asked to give a suggestion for rewording the item to improve it.

Data analysis

Analysis involved content analysis for open questions and descriptive analysis on the item feedback during cognitive debriefing, as well as a multitrait analysis program 'MAP:(20)' to identify preliminarily reliability and scale structure of the 116 item original questionnaire. The MAP-analysis program gives information about ceiling and floor effects (dispersion of scores: optimum is a low percentile on the bottom or top of the scale), the scalefit (correlation of items with their own rather than another scale, optimum is 100%) and reliability (Cronbach's alpha, optimum is $\alpha > 0.70$). Together with the cognitive debriefing information the preliminary psychometric analysis results were used to decide on retention, modification or rejection of items using the following criteria:

1. missing values: the item was to be deleted if more than 5% of persons had failed to respond to it;
2. item difficulty: items which did not discriminate between persons, i.e. that were endorsed only by 20% of the respondents or were agreed to by more than 80% of the respondents were omitted;

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3. item total correlation: items were omitted if the correlation of the item with the scale was below $r = 0.30$, meaning that the item does not contribute substantially to the quality of scale;
4. changes in alpha: the coefficient Cronbach's alpha is an indicator of the reliability of a scale and should be at least $\alpha = 0.70$. Since deleting a poorly performing item may lead to an increase in α-coefficients, this criterion was applied to omit such items;
5. cognitive debriefing: judgements in terms of comprehensibility and relevance from the cognitive debriefing were used. If these judgements were negative in more than 25% of respondents, the item was rejected.

If at least one of the above criteria applied, the item was omitted from the questionnaire. For the revised and item reduced questionnaire reliability was assessed via the internal consistency coefficient Cronbach's alpha, which gives information about the correlation of the items belonging to one scale. Convergent validity was inferred from correlations of the Haemo-QoL with other instruments measuring similar concepts, such as the KINDL.

Results

The questionnaire was responded to by a total of 58 children (57 male and one female) and 57 parents. Of these 51 children had haemophilia A, five haemophilia B and two were diagnosed with von Willebrand disease. As concerns health status, 56.4% of the children had had 1–3 bleedings in the last 6 months, six children developed an inhibitor and three children had hepatitis C. Of the older children, two children did not participate in the cognitive debriefing because of language problems and/or acute bleeding. Three younger children stopped because of tiredness, problems of cognitive ability or maternal intervention.

Open questions

With regard to open questions, 36 children gave information about problems and restrictions due to haemophilia. In the youngest age group (4–7 years, $n = 10$) this involved four main issues concerning restrictions in sports and play, injections, pain and visits to the hospital. In the older age group (8–16 years, $n = 26$) these issues were also described in addition to three more issues, namely bleeds, comments of other persons and overprotection by the family.

The parents ($n = 44$) also described problems with haemophilia for the child as well as for themselves. For the child restrictions and injections as well as relationship to others were viewed as most problematic ranging between 16 and 36% of the responses. For the parents themselves burden, stress and anxiety with 32%, but also to be within reach and acceptance of the disease and treatment (each 16%) were mentioned. However, 20% of the parents saw no problems for themselves and 16% saw no problems for their child.

Cognitive debriefing

Cognitive debriefing showed that several items in the subscales 'Feeling', 'Attitude', 'Friends', 'Other Persons' and 'Sport & School' obtained up to 30% of negative responses in terms of incomprehensibility or were rated as not relevant by more than 20% of the children. Interestingly, there were country differences with regard to the numbers of suggestions that were made for rewording items. In Germany and England only a few suggestions were made, in France and the Netherlands the children made some suggestions and in Italy and Spain many suggestions were given, which were related to translation problems. Also, country differences were noticed with regard to type and number of items found relevant and with regard to the number of children on prophylactic vs. on-demand treatment.

Overall feedback

The feedback on the overall questionnaire for older children was rated with a visual analogue scale from 0 (lowest rating) to 100 (highest rating). With regard to acceptance the children rated the questionnaire as 'rather good' ($M = 71.49$, $SD = 26.62$), found it 'rather simple' ($M = 26.08$, $SD = 26.62$), thought that the questionnaire relates to haemophilia ($M = 78.29$, $SD = 23.24$), understood the questions or knew, what was meant ($M = 65.80$, $SD = 27.41$) and could cope well with the answer possibilities ($M = 71.20$, $SD = 29.05$). The parents rated the questionnaire 'good' to 'acceptable', but stated that it is difficult to subsume both treatment options in the same questionnaire, feeling that haemophilia is different with or without prophylactic treatment and stating that haemophilia is not a disease but a health condition. The parents found some questions difficult for very young ages and recommended to change these questions.

Item reduction

In addition to the analysis of cognitive debriefing, data quality and preliminary psychometric testing of the 116 items was used to describe about retaining or omitting items. Taking into account the selection criteria described in the method section, 29 items were omitted from the questionnaire and several items were identified as candidates for rephrasing. With the omissions, the

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Table 2. Rejection of items from the original Haemo-QoL-Questionnaire for the children aged 8–16 years

Scale	Item	Missing values above 5%	Item difficulty index (%)	Item total correlation below $r = 0.30$	Changes in α if item is omitted	Cognitive debriefing	
						Comprehensiveness: not clear (%)	Relevance not relevant (%)
Physical health	Had to stay lying down		86.5	*			27
	Did not care whether...			*	⇑		
	Afraid of the injections		86.5	*			
Feeling	Cranky and irritable	7%					65
	In a good mood						57
	Moody			*	⇑	22	51
	Didn't mind about...			*	⇑		
	Tried to test my limits	10%					22
	Upset						60
Atitude	Too vulnerable for...	7%		*	⇑	26	41
	In harmony with my body	10%				29	
	Dissatisfied with myself						24
Family	Not let me do sports...			*	⇑		
	Had to stay off work		81.1				32
	Felt left alone...		100				
Friends	Spend my time indoors					24	
	Not go to other children						32
	Able to participate			*	⇑		
	Being an outsider	7%	88.6	*	⇑	24	
	Afraid of being rejected		83.8				
Other persons	In touch with other...						27
	Embarrassed						22
	Difficult to get on...		89.2	*	⇑		
Sports and school	Active in school			*	⇑	24	
	Careful at school			*	⇑		
Coping	Didn't make a secret			*	⇑		
treatment	Afraid of hospital			*	⇑		22
	Had to lie in bed			*	⇑		
Future	Any profession			*	⇑		

If one of the criteria of rejection is fulfilled = omission of item.

questionnaire could be reduced to 77 items reflecting 10 scales of quality of life with haemophilia. Table 2 gives an overview over deleted items and the respective exclusion criteria across all countries.

Psychometric analysis

Results showed that the scale structure of the reduced Haemo-Qol questionnaire could be confirmed with reliability ranging from $\alpha = 0.67$ for the subscale 'Feeling' to $\alpha = 0.89$ for the 'Haemo-QoL total score'. The confirmatory testing results suggest scaling successes in the majority of the scales approaching 100% (scalefit) and reaching few ceiling and floor effects (see Table 3).

In terms of convergent validity correlations of the scales of the Haemo-QoL and scales of the KINDL and SF-36 subscales were calculated. The correlations of the subscales of the Haemo-QoL with the corresponding subscales of the KINDL and the SF-36 showed to be acceptable and ranged between $r = -0.33$ ('School') and $r = -0.63$ ('Physical Health').

Discussion

Only recently effects of haemophilia and its treatment on quality of life have been addressed in the literature. Rosendaal *et al.* [21] obtained information from 935 Dutch adult haemophiliacs. Data from this study revealed that the patients were less often married, 22% were not employed and home treatment had a positive influence on quality of life. Royal *et al.* [22] found that patients? treated prophylactically report a higher quality of life in the SF-36 scales 'Pain', 'General Health' and 'Mental Health' in comparison to a group with on-demand treatment. Most of the studies assessed quality of life

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Table 3. Scale structure and internal consistency for the reduced Haemo-Qol questionnaire (n = 77 items/children aged 8–16 years)

Scale	No. Items	Min. Value	Max. Value	Mean	SD	Floor Effects	Ceiling Effects	Scalefit	Cronbach's α
Physical health	10	10	30	16.22	6.1	16.7%	0%	93.0%	0.85
Feeling	6	6	16	9.31	3.0	13.9%	0%	88.3%	0.67
Attitude	7	6	24	11.97	4.4	19.4%	0%	88.6%	76
Family	10	11	35	18.22	5.4	0%	0%	70.0%	0.71
Friends	7	7	26	14.89	4.9	0%	0%	45.0%	0.69
Other persons	7	5	20	10.00	3.8	33.3%	0%	91.4%	0.71
Sports and school	11	10	38	19.46	6.1	8.3%	0%	53.3%	0.71
Coping	9	9	35	19.92	6.7	0%	0%	53.3%	0.76
Treatment	7	7	21	11.35	4.1	0%	0%	41.1%	0.70
Future	3	3	11	5.65	2.7	11.1%	2.8%	33.3%	0.75
Haemo-QoL Total Score	77	87	207	136.41	28.0	0%	0%	65.9%	0.89

Min., max., mean scores and SD based are raw data.
Floor-/Ceiling-effects = percentage of respondents at lowest/highest scale level (optimum is 0%).
Scalefit = percentage of items correlating with own scale (optimum is 100%).
Cronbach's α = reliability indicator (expected is $\alpha = 0.70$ or higher).
All results obtained via MAP analysis.

with the Short Form SF-36 Health Survey (SF-36). Tusell *et al.* [23] found impairments in the SF-36 scales 'Pain', 'General Health' and 'Physical Role Functioning' in a sample of 190 haemophilia patients. The SF-36 was also used by Szucs *et al.* [10] in a study evaluating the socio-economic impact of haemophilia care. Djulbegovic *et al.* [24] assessed quality of life with the Quality of Well-Being Scale (QWB) and the SF-36 and Miners *et al.* [25] used the SF-36 and the EuroQol (EQ-5D). The orthopaedic status of severe haemophilia A and B was assessed by Molho *et al.* [26] using the SF-36 in a sample of 116 patients. Impairments in the scales 'Vitality', 'Pain' and 'General Health' were identified. A major consideration in haemophilia research was infection with hepatitis viruses or HIV from infected blood products. Brown [27] investigating coping strategies of 297 HIV infected adolescents, states that distress about reminders of HIV was associated with ineffective coping strategies (e.g. blaming others).

Bussing *et al.* [28] pointed out that HIV-positive children with haemophilia have not received sufficient attention. Psychosocial sequelae to haemophilia in children and their families have been described from the clinical–apsychological viewpoint referring, for example, to functional problems in everyday life, stigmatization or social isolation. However, studies into the quality of life of patients or families as a function of haemophilia treatment are still rare. In a study on prophylactic treatment of children with haemophilia, Liesner *et al.* [29] examined 27 children (age: 1.3–15.9 years) and found that prophylaxis improved the quality of life of the families. Carnelli *et al.* [30] compared three different prophylactic treatment programmes in haemophiliac children (n = 52) and concluded that the high costs of the treatment can be justified by the better quality of life of the patients. Pabinger *et al.* [31] examined 88 children and adults with haemophilia and found that home treatment is widely accepted by the patients and improved quality of life [32].

Within the emerging area of quality of life research in children with haemophilia, the question of how to assess quality of life in children is yet to be resolved. The current pilot study attempted to develop and gather information about a condition-specific quality of life instrument for young haemophiliacs in different age-groups, using self-report as well as a proxy report by parents. The questionnaire items were conceptualized, collected and pretested internationally in six European countries with younger (4–7 years) and older (8–16 years) children and their parents. In terms of cognitive debriefing, three quarters of the questions were regarded appropriate and understandable by both parents and children. Surprising, however, was the rejection of almost all items suggesting problems with regard to self-esteem, social acceptance or emotional well-being. This could either be due to the positively viewed health of the respondents as expressed in statements such as 'Haemophilia is a health condition but not a disease' or by the feelings of patients and their family that management is possible so that the condition is not major problem. However, social desirability bias in answers cannot be excluded. Comparing answers to open questions with standard questions of the Haemo-QoL showed that problems with haemophilia are experienced by participants, but are not rated highly in their importance. In general, the newly developed questionnaire was largely considered acceptable.

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Psychometric testing and cognitive debriefing results were used to screen items for potential omission. Inspection of all items according to psychometric and cognitive debriefing criteria resulted in a reduced questionnaire version with sufficient reliability coefficients for the scales, adequate convergent correlation with corresponding generic quality of life measures and indication of discriminant validity according to clinical scores. The preliminary work with children's haemophilia questionnaire thus yielded in two age-related versions for children's self-report and parents report on quality of life of children with haemophilia in six languages (German, English, French, Italian, Spanish and Dutch). These versions will be psychometrically tested in the main study involving 50 children per country, i.e. a total of 300 children. In this upcoming study, cross-cultural differences in addition to psychometric criteria and content-related aspects with regard to perceptions of haemophilia will be evaluated further. The pilot work, presented in this paper, is unique in that to the authors knowledge no paper has been published in which cognitive debriefing and psychometrical pretesting to develop a health-related quality of life measure have been conducted simultaneously in six countries in haemophilic children. Although due to sample size, psychometric data has to be carefully interpreted, the results are encouraging. It is hoped that the condition-specific Haemo-QoL questionnaire is reliable, valid and sensitive assessment of quality of life in paediatric haemophilia is available for future clinical studies.

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