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Comparing two measures of quality of life for children with haemophilia: the CHO-KLAT and the Haemo-QoL

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Summary. Disease-specific measures of quality of life (QoL) for children with haemophilia are now available for use in clinical studies [*Haemophilia*, **10**, 2004, 9–16]. One of these measures, the Canadian Haemophilia Outcomes – Kids' Life Assessment Tool (CHO-KLAT), was developed in Canada with emphasis on the perspectives of children [*Pediatr Blood Cancer*, **47**, 2006, 305–11; *Haemophilia*, **10**, 2004, 34–43]. Another, the Haemo-QoL, was developed in Europe, with emphasis on the perspectives of clinicians [*Haemophilia*, **8**, 2002, 47–54; *Haemophilia*, **10**, 2004, 17–25]. While these two measures are unique and independent, researchers from both studies were collaboratively linked throughout development and testing. This study presents the results of a joint assessment of the two measures with respect to their strengths, limitations and unique contributions.The primary questions addressed were:

1 What is the relationship between the CHO-KLAT and the Haemo-QoL in terms of summary scores and item content?

2 What are the methodological strengths, limitations and unique contributions of each measure?

We conducted a retrospective analysis of data from field testing of both measures. The analysis included a comparative assessment of the basic validity, reliability and items used in each measure. Overall, the CHO-KLAT and the Haemo-QoL are promising and valuable measures of QoL for children with haemophilia. Our analyses confirmed the basic psychometric properties of both tools, but identified some discrepancies between them. Additional data will allow for greater understanding of these discrepancies and lend clarity to how the tools should be used in clinical studies (separately or merged). The present recommendation is that the measures be run independently, but preferably concurrently in studies of children with haemophilia.

Keywords: haemophilia, paediatrics, quality of life, questionnaires, self-report

Introduction

Haemophilia is a bleeding disorder caused by an inherited deficiency of factor VIII (FVIII) or factor IX (FIX), leading to impaired clotting [1]. Often there is a family history of haemophilia, but the disorder occurs as a new mutation in approximately 30% of cases [1]. Haemophilia A (FVIII deficiency) affects approximately 1/5000 males and haemophilia B (FIX deficiency) affects approximately 1/30 000 males; both are extremely rare in females [2]. The three recognized levels of severity of haemophilia – mild, moderate and severe, are defined by the level of measurable plasma coagulation factor activity in the circulation; >5% is mild, 1–5% moderate and <1% severe [1].

The quality of life (QoL) of children with haemophilia is expected to vary. The World Health Organisation defines QoL as 'the net consequence of life characteristics on a person's perception of their position in life, in the context of the culture and

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value systems in which they live, and in relation to their goals, expectations, standards and concerns' [3]. Haemophilia may have a significant impact on QoL for many reasons, including: lifestyle issues such as restrictions in physical activities; parental concerns about organ or life-threatening bleeding such as intracranial haemorrhage; musculoskeletal complications of recurrent bleeding into joints leading to disabling arthropathy; development of high-titre inhibitors rendering infused FVIII/FIX ineffective; and, fortunately now much less frequent, therapy-related infectious complications such as hepatitis and human immunodeficiency virus.

The presumption that haemophilia affects children's QoL prompted two groups of researchers, clinicians and other interested parties to begin developing disease-specific tools for measuring the QoL of boys with haemophilia. Disease-specific measures were needed to be sensitive to the issues and changes in QoL that relate specifically to haemophilia. In Canada, researchers sought to develop a tool by focusing on children's perspectives throughout measure development [4,5]. In Germany, researchers sought to develop a tool that would be culturally relevant in six European countries, in each of the six respective dominant languages, working from the perspectives of clinicians [6,7].

Development of the measures

The Canadian Haemophilia Outcomes – Kids' Life Assessment Tool The Canadian measure, the Canadian Haemophilia Outcomes – Kids' Life Assessment Tool (CHO-KLAT) [4,5] was developed using a clinimetric approach [8] with emphasis on the perspectives of children. Details of the development of the CHO-KLAT are provided in Young *et al.* [4] and Young *et al.* [5]. In brief, items were identified and assessed for relative importance through literature review, discussion sessions and structured focus groups that included children and a survey of Canadian haematologists. Items from the developing Haemo-QoL were considered as part of the CHO-KLAT item pool. A preliminary 79-item version of the CHO-KLAT (CHO-KLAT$_{79}$) for boys 4–18 years old and a complimentary parent version were generated, pilot tested and then assessed through field testing for reliability and validity. The 79-item version was subsequently reduced to 35 items. Overall summary scores range from 0 to 100, with 100 representing best QoL. The 35-item measure has been validated against the Pediatric Inventory of Quality of Life (PedsQL) [9–11]; a Visual Analogue Score (VAS) of global QoL [12]; and a provisional Haemo-QoL (what was available at the time of Canadian field testing). For the purposes of this paper, the provisional 35-item Haemo-QoL for 8–16 year olds used in the Canadian study will be denoted as Haemo-QoL$_{35*}$ and the provisional 16-item Haemo-QoL for 4–7 year olds will be denoted as Haemo-QoL$_{16p*}$. The commonalities between the provisional and current versions of the Haemo-QoL are detailed later in this article.

The Haemo-QoL The European tool, the Haemo-QoL was developed using a psychometric approach [13] with primary emphasis on the perspectives of clinical experts. The stages of Haemo-QoL development have been discussed in Bullinger *et al.* [6], and von Mackensen *et al.* [7]. In brief, items were identified and assessed for relative importance from a generic measure of child QoL, literature review and by expert consensus. A 119-item English language pilot version of the questionnaire was compiled and then translated into French, Spanish, Italian, German and Dutch. The questionnaire was divided into three age versions (4–7, 8–12 and 13–16 years) and complimentary parent proxy versions were developed. Pilot testing involved cognitive debriefing by obtaining child feedback on items, followed by field testing with children for the assessment of reliability and validity. The Haemo-QoL for children aged 4–7 years was then subsequently reduced to 16 items in eight domains, and the Haemo-QoL for children aged 8–12 and 13–16 have been reduced to a common 35-item set with nine domains. Overall summary scores range from 0 to 100, with 0 representing best QoL. The Haemo-QoL has been validated against the global health item, 'In general, how would you say your health is?', taken from the Child Health Questionnaire (CHQ) [14] and the KINDer Lebensqualitätsfragebogen (KINDL) [15] (generic and chronic generic).

Primary questions

While the CHO-KLAT and Haemo-QoL are unique and independent measures of QoL for children with haemophilia, Canadian and European researchers were willing to share the data from field testing to address the following questions of how the two measures perform individually and in comparison with each other:

1 What is the relationship between the CHO-KLAT and the Haemo-QoL in terms of the summary scores and item content?
2 What are the methodological strengths, limitations and unique contributions of each measure (reliability, validity and feasibility)?

Materials and methods

We conducted a retrospective analysis of existing data from the field testing of both the CHO-KLAT (Canadian data: $n = 52$) and the Haemo-QoL (European data: $n = 301$). The European data set was divided into two subsamples that reflected the age-specific versions of the Haemo-QoL that were used in the clinical field testing ($n = 211$ children aged 8–16 years, and $n = 90$ children aged 4–7 years). The characteristics of the three resulting samples were summarized including: demographic and medical data such as age range, type of haemophilia, severity of haemophilia and use of prophylaxis. Next, the summary scores were calculated using the algorithms described by the developers. A 75% minimum data rule was adhered to during summary score calculation, meaning that summary scores were only calculated if <25% of items were missing, and individual mean item scores were imputed for any missing item(s). The distributions of summary scores for each of the measures were then reviewed. The measures for which summary scores were calculated were: the child and parent reported CHO-KLAT$_{35}$, the Haemo-QoL$_{35}$, the Haemo-QoL$_{35*}$ (provisional included in Canadian study), the Haemo-QoL$_{16}$, and the Haemo-QoL$_{16*}$ (provisional included in Canadian study).

In addition, summary scores were calculated using Canadian data ($n = 52$) for the Pediatric Quality of Life Inventory 4.0 (PedsQL) [9–11] and the global visual analogue scale (VAS) of QoL [12]. Briefly, the PedsQL [9–11] is a widely used generic measure of QoL for children with three self-reported age versions (5 years and older) and parent proxy versions. Summary scores are provided from 0 to 100 with 100 representing best QoL. The VAS of QoL [12] asks children and parents to rate their overall QoL from 'the worst' to 'the best' on a VAS, with summary scores reported from 0 to 100 and 100 representing best QoL. Summary scores were calculated using European data ($n = 211$ for ages 8–16 years; $n = 90$ for ages 4–7 years) for the global health item taken from the CHQ [14] and the KINDL (generic and chronic generic) [15]. The CHQ [14] is a generic measure of QoL/health status for children. Children and parents in the Haemo-QoL study were asked to answer the general health item: 'in general, how would you say your health is?' and the results of this are assessed in this study. The KINDL [15] is a generic measure of child QoL with three age versions and corresponding parent proxy versions. Summary scores are provided from 0 to 100 with 100 representing best QoL. The KINDL also contains items that specifically relate to having a chronic condition and are included to form a 'chronic generic' score also from 0 to 100.

Data analysis

Data from each source was compiled, aggregated and verified, leading to a data set comprising both measures. Variations in data manipulation methods were avoided by having one member of the Canadian team (CB) review and consolidate all data under the supervision of a member of the European team (MB).

Data analysis was run in SPSS and was directed to address the primary research questions. Pearson correlations were run to assess the overall relationship between the CHO-KLAT and the Haemo-QoL summary scores in the Canadian data set ($n = 52$), where both measures were available.[1] The *a priori* hypothesis was that if the Pearson correlation was greater than −0.80, the measures would be considered to measure the same construct without much variation. If the correlation was ≤−0.5, the measures would be judged to measure different constructs and if so, the differences required further exploration. If the correlation was between −0.5 and −0.8, it would be deemed that they both measured the construct of QoL, but that each was unique. Additionally, a table of items was created to map out the similarities in item content between the CHO-KLAT$_{35}$, the Haemo-QoL$_{35*}$, the Haemo-QoL$_{16*}$, the Haemo-QoL$_{35}$ and the Haemo-QoL$_{16}$ and to facilitate the assessment of the relationship of the CHO-KLAT and Haemo-QoL in terms of item content.

Using classical psychometric approaches, reliability and validity indicators were obtained for both measures. This involved analyses within each of the data sets. Internal consistency was assessed using Cronbach's-alpha for the child self-report and parent proxy versions of the measures [16]. Random effect interclass correlation coefficients (ICCs) [17] were used to assess concordance: between children and their parents (inter-rater reliability); between time 1 and time 2 for children and between time 1 and time 2 for parent proxy-report (repeated measures intra-rater or test–retest reliability).

Basic validity testing was run on each of the measures. Pearson correlation matrices were run in the Canadian data set for the child and parent data respectively. The variables included were the CHO-KLAT, the provisional versions of the Haemo-QoL

[1]We hypothesized a negative relationship due to the different scoring directions of the two measures.

(35 and 16 items), the PedsQL and the VAS of QoL. Pearson correlation matrices were run in the European data set for the child and parent data respectively. Variables included the Haemo-QoL (35 and 16 items), the global health item score from the CHQ, the KINDL and the KINDL chronic generic scores.

Finally, the response burden was reviewed as an indicator of feasibility. Completion time of the CHO-KLAT$_{35}$ had previously been determined during Canadian pilot testing to be <10 min [5]. However, the Haemo-QoL$_{35}$ and Haemo-QoL$_{16}$ had not been run as independent measures and accordingly, no data existed on specific completion times. As such, a secondary measure of response burden was used for each of the measures to provide a general indication of the number of 'choices' a respondent must make when completing the questionnaires. The number of items per response set was multiplied by the number of response options and the products summed.

Response burden by measure

$$\text{CHO-KLAT}_{35} = (\text{no. items with six response options} \times 6) + (\text{no. items with five response options} \times 5),$$

$$\text{Haemo-QoL}_{35} = \text{no. items} \times \text{five response options},$$

$$\text{Haemo-QoL}_{16}(\text{children}) = \text{no. items} \times \text{three response options},$$

$$\text{Haemo-QoL}_{16}(\text{parent}) = \text{no. items} \times \text{five response options}.$$

Results

The sample characteristics of the Canadian and European data sets are presented in Table 1. Nine characteristics were captured in all data sets: severity of haemophilia, type of haemophilia, age of the child, use of prophylaxis, use of home infusion, use of self-infusions, presence or history of an inhibitor, presence of a port-a-catheter and target joint. All children included were male.

The distribution of baseline summary scores is shown in Table 2. Of note, both the CHO-KLAT and Haemo-QoL are both scaled from 0 to 100. However, 100 is the highest possible score on the CHO-KLAT$_{35}$,and represents best QoL. On the Haemo-QoL, 0 is the highest possible score and represents best QoL.

The relationship between the CHO-KLAT and the Haemo-QoL

Summary score data from both the CHO-KLAT and the Haemo-QoL were only available in the Canadian data set ($n = 52$). The overall relationship between the two measures was moderate, with most correlations falling between −0.5 and −0.80. Specifically, the Pearson correlation coefficients between the CHO-KLAT$_{35}$ and Haemo-QoL$_{35*}$ (8–18 year olds) were $r = -0.74$ for children ($n = 40$) and $r = -0.82$ for the parents ($n = 38$). For 4–7 year olds the correlations between the CHO-KLAT$_{35}$ and Haemo-QoL$_{16*}$ were $r = -0.53$ for the children ($n = 11$) and $r = -0.84$ for the parents ($n = 12$).

Table 1. Sample characteristics of boys with haemophilia.

	Severity	Type	Mean age in years (range)	Treat by prophylaxis	Home infusion	Self-infusion	Presence or history of an inhibitor	Have a port-a-catheter	Target joint	Total *n*
Canadian sample ($n = 52$)	Moderate	A	11.6 (4.4–18.9)	8.6%	10.8%	12.5%	0.0%	0.0%	17.6%	23.1%
		B	13.4 (8.9–16.2)	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	7.7%
	Severe	A	11.1 (5.4–17.7)	80.0%	81.1%	87.5%	100.0%	100.0%	70.6%	57.7%
		B	10.6 (6.9–17.6)	11.4%	8.1%	0.0%	0.0%	0.0%	11.8%	11.5%
	Total *n*		11.3 (4.4–18.9)	35	37	8	8	12	17	52
European sample (4–7 year olds) ($n = 90$)	Moderate	A	5.3 (4.0–7.0)	7.9%	13.1%	0.0%	5.6%	0.0%	2.9%	10.0%
		B	5.3 (4.0–7.0)	1.6%	1.6%	0.0%	0.0%	0.0%	0.0%	3.3%
	Severe	A	5.4 (4.0–7.0)	81.0%	75.4%	100.0%	88.9%	94.7%	80.0%	74.4%
		B	5.7 (4.0–7.0)	9.5%	9.8%	0.0%	5.6%	5.3%	17.1%	12.2%
	Total *n*		5.4 (4.0–7.0)	63	61	4	18	19	35	90
European sample (8–16 year olds) ($n = 211$)	Moderate	A	12.1 (8.0–16.0)	9.2%	10.9%	8.0%	6.7%	5.6%	10.1%	10.4%
		B	11.4 (8.0–16.0)	2.1%	2.9%	2.7%	0.0%	0.0%	3.4%	3.3%
	Severe	A	12.0 (8.0–16.0)	81.7%	79.3%	85.3%	90.0%	94.4%	79.8%	78.7%
		B	11.7 (8.0–16.0)	7.0%	6.9%	4.0%	3.3%	0.0%	6.7%	7.6%
	Total *n*		12.0 (8.0–16.0)	142	174	75	30	18	119	211

Table 2. Distribution of time 1 summary scores.

	n	Range	Mean (SD)
Canadian data set (4–18 year olds)			
CHO-KLAT$_{35}$: child	52	33.9–97.2	74.6 (14.0)
CHO-KLAT$_{35}$: parent	52	47.9–92.9	74.5 (11.6)
Haemo-QoL$_{35}$*: child	40	80.7–0.0	17.4 (15.4)
Haemo-QoL$_{35}$*: parent	38	50.0–0.0	23.8 (13.4)
Haemo-QoL$_{16}$*: child	11	42.9–3.6	16.4 (11.7)
Haemo-QoL$_{16}$*: parent	12	30.4–5.4	17.4 (7.7)
European data set (4–7 year olds)			
Haemo-QoL$_{16}$: child	90	78.6–0.0	23.6 (17.2)
Haemo-QoL$_{16}$: parent	90	76.9–0.0	22.4 (14.5)
European data set (8–16 year olds)			
Haemo-QoL$_{35}$: child	211	72.1–0.7	22.0 (11.3)
Haemo-QoL$_{35}$: parent	211	80.0–0.0	27.1 (14.4)

CHO-KLAT, the Canadian Haemophilia Outcomes – Kids' Life Assessment Tool; QoL, quality of life.

The mapping of items across the CHO-KLAT$_{35}$, Haemo-QoL$_{35}$*, Haemo-QoL$_{16}$*, Haemo-QoL$_{35}$ and Haemo-QoL$_{16}$ is provided in Appendix 1. Overall, the difference between the provisional Haemo-QoL$_{35}$* and the current Haemo-QoL$_{35}$ was the substitution of four items. The difference between the provisional Haemo-QoL$_{16}$* and the current Haemo-QoL$_{16}$ was that item 9 (I was unable to do as much with my friends because of my haemophilia) of the Haemo-QoL$_{16}$ was not included in the Haemo-QoL$_{16}$*. However, item 9 was not included in the Haemo-QoL$_{16}$ during European (4–7 years old) field testing. Subsequently, there is no item 9 data in either the Canadian or European (4–7 years old) data sets and this item was therefore treated as missing data throughout the analysis.

The strengths, limitations and unique contributions of each measure

The internal consistency, tested in the separate Canadian ($n = 52$, aged 4–18 years) and European ($n = 211$, aged 8–16 years; $n = 90$, aged 4–7 years) data sets was high for all versions of both measures (range of cronbach's-alpha 0.81–0.91) [16]. However, the ICCs varied significantly, the details of which are shown in Table 3.

The validity in relation to other measures (Pearson correlation coefficients) are shown in Tables 4–6 and is specifically addressed in the discussion section of this article. The most relevant correlations in the Canadian data (Table 4; $n = 52$) that were significant at the 0.05 level were as follows: between the CHO-KLAT and the PedsQL were 0.59 for children and 0.54 for parents; between the HaemoQoL$_{35*}$ and the PedsQL were −0.76 for children and −0.63 for parents; between the CHO-KLAT and the VAS were 0.61 for children and 0.67 for parents; between the HaemoQoL$_{35*}$ and the VAS were −0.78 for children and −0.75 for parents; between the HaemoQoL$_{16*}$ and the VAS was −0.61 for children. The most relevant correlations in the European data set with children aged 4–7 years (Table 5; $n = 90$) who were significant at the 0.05 level were as follows: between the HaemoQoL$_{16}$ and the KINDL were −0.22 for children and −0.32 for parents; between the HaemoQoL$_{16}$ and the KINDL chronic generic was −0.44 for parents. The most relevant correlations in the European data set with children aged 8–16 years (Table 6; $n = 211$) who were significant at the 0.05 level were as follows: between the HaemoQoL$_{35}$ and the CHQ global health item were −0.36 for children and −0.20 for parents; between the HaemoQoL$_{35}$ and the KINDL were −0.48 for children and −0.37 for parents; between the HaemoQoL$_{35}$ and the KINDL chronic generic were −0.53 for children and −0.30 for parents.

Response burden ranged from 48 possible choices on the Haemo-QoL$_{16}$ to 186 possible choices on the CHO-KLAT$_{35}$. Since response time for the CHO-KLAT was previously assessed at <10 min [5], it is therefore reasonable to assume that completion time for all versions of the Haemo-QoL is also <10 min, and therefore acceptable.

Table 3. Intraclass correlation coefficients (ICC).

Comparison	Data set	Measure	Age group (years)	*n*	ICC	Lower limit of 95% CI
Child vs. parent at time 1	Canadian	CHO-KLAT$_{35}$	4–16	52	0.75	0.60
		Haemo-QoL$_{16}$*	4–7	11	0.60	0.37
		Haemo-QoL$_{35}$*	8–16	38	0.55	0.28
	European	Haemo-QoL$_{16}$	4–7	88	0.30	0.10
		Haemo-QoL$_{35}$	8–16	198	0.47	0.35
Time 1 vs. time 2 child	Canadian	CHO-KLAT$_{35}$	4–16	47	0.74	0.57
	European	Haemo-QoL$_{35}$	8–16	85	0.78	0.68
Time 1 vs. time 2 parent	Canadian	CHO-KLAT$_{35}$	4–16	48	0.83	0.71
	European	Haemo-QoL$_{35}$	8–16	78	0.86	0.78

CHO-KLAT, the Canadian Haemophilia Outcomes – Kids' Life Assessment Tool; QoL, quality of life.

Table 4. Correlations of time 1 summary scores – Canadian data (4–18 year olds, $n = 52$).

	CHO-KLAT$_{35}$		Haemo-QoL$_{35*}$		Haemo-QoL$_{16*}$		PedsQL		VAS of QoL	
	Child	Parent	Child	Parent	Child	Parent	Child	Parent	Child	Parent
CHO-KLAT$_{35}$										
Child	1	0.76*	−0.74*	−0.65*	−0.53	−0.42	0.59*	0.50*	0.61*	0.55*
Parent		1	−0.55*	−0.82*	−0.76*	−0.84*	0.40*	0.54*	0.48*	0.67*
Haemo-QoL$_{35*}$										
Child			1	0.56*	N/A	N/A	−0.76*	−0.39*	−0.78*	−0.45*
Parent				1	N/A	N/A	−0.46*	−0.63*	−0.35*	−0.75*
Haemo-QoL$_{16*}$										
Child					1	0.68*	0.26	−0.13	−0.61*	−0.04
Parent						1	0.09	−0.43	−0.27	−0.21
PedsQL										
Child							1	0.60*	0.71*	0.36*
Parent								1	0.37*	0.51*
VAS of QoL										
Child									1	0.51*
Parent										1

CHO-KLAT, the Canadian Haemophilia Outcomes – Kids' Life Assessment Tool; PedsQL, Pediatric Inventory of Quality of Life; QoL, quality of life.
*Significant at 0.05 level, two-tailed.

Table 5. Correlations of time 1 summary scores – European data (4–7 year olds, $n = 90$).

	Haemo-QoL$_{16}$		CHQ (general health item)		KINDL		KINDL (chronic generic)	
	Child	Parent	Child	Parent	Child	Parent	Child	Parent
Haemo-QoL$_{16}$								
Child	1	0.30*	−0.16	0.20	−0.22*	−0.15	−0.51	−0.33*
Parent		1	−0.05	−0.13	−0.01	−0.32*	−0.26*	−0.44*
CHQ								
Child			1	0.13	0.21	−0.05	0.09	0.06
Parent				1	0.07	0.21	−0.17	0.21
KINDL								
Child					1	0.17	0.31*	−0.09
Parent						1	0.10	0.33*
KINDL chronic generic								
Child							1	0.36*
Parent								1

CHQ, Child Health Questionnaire; QoL, quality of life.
*Significant at 0.05 level, two-tailed.

Discussion

The findings of this study suggest that while there are similarities between the measures, each measure has its own specific methodological strengths, limitations and unique contributions. Overall, the data analysis conducted in this study supports the basic reliability, validity and feasibility of the CHO-KLAT and Haemo-QoL. Both tools are therefore promising and valuable measures of QoL for boys with haemophilia.

The CHO-KLAT is distinct in that the perspectives of children were emphasized throughout measure development. This approach is consistent with the conceptual belief that QoL is best measured through the eyes of the individual in question and based on items that are of most relevance to them [3]. Conversely, the Haemo-QoL was developed with emphasis on the perspectives of clinicians and parents, incorporating children's views at a later stage. When reviewing the frameworks and processes from which the measures were developed, the CHO-KLAT has only been validated in Canada, in English, with plans for translation into French in the near future. In contrast, the Haemo-QoL is distinct in that it was developed and is available for use in six languages and in six European countries.

Table 6. Correlations of time 1 summary scores – European data (8–16 year olds, $n = 211$).

	Haemo-QoL$_{35}$		CHQ (general health item)		KINDL		KINDL (chronic generic)	
	Child	Parent	Child	Parent	Child	Parent	Child	Parent
Haemo-QoL$_{35}$								
Child	1	0.48*	−0.36*	−0.13	−0.48*	−0.19*	−0.53*	−0.20*
Parent		1	−0.26*	−0.20*	−0.13	−0.37*	−0.36*	−0.30*
CHQ								
Child			1	0.06	0.35*	0.13	0.19*	0.13
Parent				1	−0.04	0.30*	0.02	0.38*
KINDL								
Child					1	0.06	0.30	−0.03
Parent						1	0.09	0.06
KINDL chronic generic								
Child							1	0.58*
Parent								1

CHQ, Child Health Questionnaire; QoL, quality of life.
*Significant at 0.05 level, two-tailed.

In terms of the feasibility of each of the measures, the CHO-KLAT has only one version for children aged 4–18 years. While the argument could be made that this decreases its age-specific sensitivity, the questionnaire is simple to administer and comparisons of scores across a broad range of ages and over time are readily possible. In contrast, there are two age versions of the Haemo-QoL that were assessed in this study (35 items for children aged 8–16 years and 16 items for children aged 4–7 years). While this may render the Haemo-QoL more sensitive to relevant issues for children of varying age ranges, it also presents challenges in comparing scores over time and across age groupings as item/domain content is not consistent. Before a definitive decision can be made regarding whether multiple or single age versions are preferred, further work is needed to substantiate the claim that adding subscales/domains by age groups improves a measure's sensitivity while minimally sacrificing other psychometric properties.

There is a proposed all-age version ultra-short eight-item Haemo-QoL under development. While shorter versions are considered attractive for incorporation into clinical trials because of less presumed burden on participants, the Haemo-QoL (35 and 16 items) response times are likely <10 min, thus the time saved by reducing its number of items to a proposed eight items is arguably minimal. Conversely, decreasing the number of items in measures may sacrifice the reliability and face validity (as items that are highly relevant may be deleted) and consequently, may decrease the overall acceptability of the questionnaire. The Canadian team does not plan to develop a shorter version or age-specific versions of the CHO-KLAT. Concern regarding sacrificing reliability and/or validity; with limiting comparisons across ages and over time; and with potentially deleting items that were of particular relevance to the children (a premise for CHO-KLAT development) were felt to outweigh the potential for efficiency/reduced response burden.

Summary score distributions of both measures suggest that there may be concerns with ceiling effects. The CHO-KLAT is consistent with most other measures of QoL that equate 100 as the best possible QoL. The Haemo-QoL is scored with 0 representing best QoL which is opposite of most measures and complicates interpretation. Additionally, the Haemo-QoL is structured with several domains that the authors report can be used for more detailed analysis and for suggesting particular areas of concern with respect to QoL. However, it remains unclear as to whether or not the results of these two measures are better interpreted using summary scores, the explicit focus of the CHO-KLAT or using multiple domains, as is possible with the Haemo-QoL. A future comparison of summary vs. domain scores in the Haemo-QoL may lend better insight into this quandary.

Based on the *a priori* hypothesis, the Pearson correlations between the CHO-KLAT$_{35}$, Haemo-QoL$_{35*}$ and Haemo-QoL$_{16*}$ suggested that the same construct is measured on the parent report versions, but the correlations were not as strong for the child reported data. This may be a result of having different theoretical frameworks from which the measures were developed; however, this finding should be regarded as preliminary because the correlations have only been assessed in 52 children from Canada.

With respect to overall reliability of the tools, several assessments were made. Cronbach's alpha, a measure of internal consistency, was good for both

tools suggesting that overall, the items do represent a single construct [16]. Test–retest ICCs were 'substantial' to 'almost perfect' [18] in both the CHO-KLAT$_{35}$ and the Haemo-QoL$_{35}$ suggesting that they are appropriate for use in studies requiring repeated administrations. Unfortunately, the Haemo-QoL$_{16}$ (for 4–7 year olds) could not be assessed for this property as follow-up data was not available from participants of this age grouping from the original field test. With respect to parent-child reliability, the CHO-KLAT ICCs were also substantial [18] but this was not true for the Haemo-QoL. Overall parent–child ICCs for the Haemo-QoL were poor to moderate [18] and worsened as the measure was shortened (35 item vs. 16 item). This finding may be in part due to greater instability in the shorter version, but may also be a reflection that the Haemo-QoL$_{16}$ was only tested in the youngest children (4–7 year olds) who are presumably the most affected by developmental changes and subsequently the possibility of less consistent scores.

The comparisons of the CHO-KLAT and the Haemo-QoL with other measures were considered to support the basic validity of both measures. For this analysis, the Pearson correlations between the disease-specific tools and the generic measures were expected to range between 0.4 and 0.6 [18]. The CHO-KLAT performed generally as expected in comparison to the PedsQL and the VAS, suggesting that these measures are assessing QoL, but that the disease-specific tool (CHO-KLAT) may be more sensitive to the needs of children with haemophilia.

The Haemo-QoL was more highly correlated with the PedsQL and the VAS scorings of QoL than expected; particularly among children. This suggests that what is measured by the Haemo-QoL may be measured equally well by the generic PedsQL or VAS ratings. As these correlations have only been assessed in the Canadian population, further testing would aid in understanding the potential influence of cultural differences.

The Haemo-QoL correlated slightly lower than expected with the CHQ general health item in both parent and child data. However, the CHQ item may relate more to general health than QoL, and thus a low correlation would be expected. The Haemo-QoL correlated as expected with the KINDL and the KINDL chronic generic items in the children, suggesting that the Haemo-QoL may be more specific to the needs of children with haemophilia than the KINDL.

From these assessments, both research teams have agreed that more data, from a variety of sources, is required to fully assess the similarities, strengths and weaknesses of both tools. From this, a decision on keeping the tools separate or merging them based on the best items available can be ascertained. Such studies will provide an opportunity to further compare QoL assessment tools in haemophilia. The present recommendation is that the two measures are suitable for use in clinical studies and should be run independently, but preferably concurrently in studies of children with haemophilia [19]. However, because of the high child–parent concordance and child-centric wording of the CHO-KLAT, it may be favoured at present when the priority is to obtain child self-report or when respondents vary (i.e. child at time 1, parent at time 2 or 3) during a study. Alternatively, because the Haemo-QoL is available in six languages, it presently may be favoured when the priority is to obtain data from children in a study requiring multiple languages.

It is hoped that the information provided in this article contributes to the increasing knowledge in QoL research for children with haemophilia and that more data on the performance of different QoL tools will help guide clinicians and researchers in the choice of measures used in clinical studies.

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References

1 Mannucci PM, Tuddenham EGD. The hemophilias – from royal genes to gene therapy. *N Engl J Med* 2001; **344**: 1773–9.

2 Tuddenham EGD, Cooper DN. *The Molecular Genetics of Haemostasis and its Inherited Disorders. Oxford Monographs in Medical Genetics no. 25*. Oxford, UK: Oxford University Press, 1994.

3 WHO QOL. Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychol Med* 1998; **28**: 551–8.
4 Young NL, Bradley CS, Wakefield CD, Barnard D, Blanchette VS, McCusker PJ. How well does the Canadian Hemophilia Outcomes – Kids' Life Assessment Tool (CHO-KLAT) measure the quality of life of boys with haemophilia. *Pediatr Blood Cancer* 2006; **47**: 305–11.
5 Young NL, Bradley CS, Blanchette V *et al*. Development of a health-related quality of life measure for boys with haemophilia: the Canadian Hemophilia Outcomes – Kids' Life Assessment Tool (CHO-KLAT). *Haemophilia* 2004; **10**(Suppl. 1): 34–43.
6 Bullinger M, von Mackensen S, Fischer K *et al*. Pilot testing of the 'Haemo-QoL' quality of life questionnaire for haemophilic children in six European countries. *Haemophilia* 2002; **8**(Suppl. 2): 47–54.
7 von Mackensen S, Bullinger M and the Haemo-QoL Group. Development and testing of an instrument to assess the quality of life of children with haemophilia in Europe (Haemo-QoL). *Haemophilia* 2004; **10**(Suppl. 1): 17–25.
8 Feinstein A.R. *Clinimetrics*. New Haven, CT: Yale University Press, 1987.
9 Varni JW, Seid M, Rode CA. The PedsQL: measurement model for the Pediatric Quality of Life Inventory. *Med Care* 1999; **37**: 126–39.
10 Varni JW, Seid M, Kurtin PS. PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory Version 4.0 Generic Core Scales in healthy and patient populations. *Med Care* 2001; **39**: 800–12.
11 Varni JW, Seid M, Knight TS, Uzark K, Szer IS. The PedsQL 4.0 Generic Core Scales: sensitivity, responsiveness, and impact on clinical decision-making. *J Behav Med* 2002; **25**: 175–93.
12 Feldman BM, Grundland B, McCullough L, Wright V. Distinction of quality of life, health related quality of life and health status in children referred for rhuematologic care. *J Rheumatol* 2000; **27**: 226–33.
13 Nunnally JC, Bernstein IH. *Psychometric Theory*, 3rd edn. Toronto, ON: McGraw-Hill Publishing Company, 1994.
14 Landgraf J, Abetz L, Ware J. *Child Health Questionnaire (CHQ): A Users Manual*. Boston, MA: The Health Institute Press, 1997.
15 Ravens-Sieberer U, Bullinger M. Assessing health-related quality of life in chronically ill children with the German KINDL: first psychometric and content analytical results. *Qual Life Res* 1998; **7**: 399–40.
16 Portney LG, Watkins MP. *Foundation of Clinical Research: Applications to Practice*, 2nd edn. New Jersey: Prentice Hall, 2000.
17 Fleiss JL. *The Design and Analysis of Clinical Experiments*. New York: John Wiley & Sons, 1986.
18 Landis RJ, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977; **33**: 159–74.
19 Bullinger M, von Mackensen S. Quality of life assessment in haemophilia. *Haemophilia* 2004; **10**(Suppl. 1): 9–16.

Appendix 1. Mapping of items across the Haemo-QoL versions [6,7] and the CHO-KLAT [4,5].

Haemo-QoL$_{16}$	Haemo-QoL$_{16*}$	Haemo-QoL$_{35}$	Haemo-QoL$_{35*}$	CHO-KLAT$_{35}$
2. I was afraid of bleeds	2. I was afraid of bleeds	4. I was afraid of bleeds	3. I was afraid of bleeds	11.I was afraid of a serious joint bleed
8.My parents forbade me to do certain things because of my hemophlia	8.My parents forbade me to do certain things because of my hemophlia	15.My parents forbade me to do certain things because of my hemophlia	15.My parents forbade me to do certain things because of my hemophlia	4.My parents wouldn't let me do certain things
12.Because of hemophilia I had to refrain from sports that I like	12.Because of hemophilia I had to refrain from sports that I like	24.Because of hemophilia I had to refrain from sports that I like	24.Because of hemophilia I had to refrain from sports that I like	3.I couldn't play the sports that I like
15. The injections annoyed me	15. The injections annoyed me	34.the injections annoyed me	34.the injections annoyed me	26.Treatments were annoying
1.My swellings hurt	1.My swellings hurt	1.My swellings hurt	2.My swellings hurt	
3. I was sad because of my hemophilia	3. I was sad because of my hemophilia	5. I was sad because of my hemophilia	5. I was sad because of my hemophilia	
4. My hemophilia made me angry	4. My hemophilia made me angry	7. My hemophilia made me angry	7. My hemophilia made me angry	
5. I envied healthy boys my age	5. I envied healthy boys my age	9. I envied healthy boys my age	9. I envied healthy boys my age	
6.My mother protected me too much	6.My mother protected me too much	13.My mother protected me too much	13.My mother protected me too much	
7.My parents told me off when I hurt myself	7.My parents told me off when I hurt myself	14.My parents criticised me (told me off) when I hurt myself	14.My parents criticised me (told me off) when I hurt myself	
10. I felt different from others because of my hemophilia	10. I felt different from others because of my hemophilia	20. I felt different from others because of my hemophilia	20. I felt different from others because of my hemophilia	
11.I felt left out when others did things together	11.I felt left out when others did things together	23.I felt left out when others did things together	23.I felt left out when others did things together	
13. I did just as much sports as many other kids	13. I did just as much sports as many other kids	27. I did just as much sports as any other kid	26. I did just as much sports as any other kid	
14. I disliked visiting the hemophilia centre	14. I disliked visiting the hemophilia centre	33.I disliked visiting the hemophilia centre	33.I disliked visiting the hemophilia centre	
16. There was a best friend that I felt very close to	16. There was a best friend that I felt very close to	18.there was a best friend that I felt very close to	18.there was a best friend that I felt very close to	
		11. I felt as well as other boys my age	11. I felt as well as other boys my age	1.I felt as well as other boys my age
9. I was unable to do as much with my friends because of my hemophilia	9	32. The treatment I got was okay	32. The treatment I got was okay	22.The treatment I got was okay
		2. I had pain in my joints	4. I had pain in my joints	2.I was happy about my body
		3.It was painful for me to move	1.It was painful for me to move	5.I kept some things from my parents about my hemophilia
		6. my hemophilia was a burden (real problem) for me	6. my hemophilia was a burden (real problem) for me	6.I worried about my health
		8. I felt lonely because of my hemophilia	8. I felt lonely because of my hemophilia	7.I was happy in spite of my hemophilia
		10. I felt physically weaker than other boys	10. I felt physically weaker than other boys	8.I tried to forget that I have hemophilia
		12.I felt contented about my body	12.I felt contented about my body	9.I worried that if I were hurt my body wouldn't be the same again

Appendix 1. Continued

Haemo-QoL$_{16}$	Haemo-QoL$_{16}$*	Haemo-QoL$_{35}$		Haemo-QoL$_{35}$*	CHO-KLAT$_{35}$
		16. I felt I was causing my family trouble because of my hemophilia	→	16. I felt I was causing my family trouble because of my hemophilia	10.I got upset that some health care professionals didn't really understand hemophilia
		17. my best friend cared about how I was feeling	→	17. my best friend cared about how I was feeling	12.I liked playing pick up games with my friends
		19. my friends took care of me when I felt bad	→	19. my friends took care of me when I felt bad	13.I was able to talk to my friends about my hemophilia
		21.Other kids teased me because of my hemophilia	→	21.Other kids teased me because of my hemophilia	14.I was able to talk to others about my hemophilia
		22,people behaved different towards me because of hemophilia	→	22,people behaved different towards me because of hemophilia	15.I couldn't do special school events (like outings)
		26. I had to refrain from sports like rollerblading and soccer	→	25. I had to refrain from sports like rollerblading and soccer	16.I felt overprotected by others
		29.hemophilia was a normal part of my life	→	31.hemophilia was a normal part of my life	17.My parents nagged me about wearing the right protective equipment (like helmets)
		35. I was annoyed about the amount of time spent having injections	→	35. I was annoyed about the amount of time spent having injections	18.I needed to know more about hemophilia
		28. I was in control of my complaints due to hemophilia	→	28. I tried to recognise early on when a bleed developed	19.I liked feeling in control of my own life
		30.I felt healthy in spite of my hemophilia	→	29. I was able to tell whether or not I was bleeding	20.I knew that I could help myself if I got hurt
		31.I accepted having hemophilia	→	30. I felt well-informed about hemophilia	21.I liked it when I was included in decisions about my care
		25.I had to do indoor activities more than other kids with hemophilia	→	27. I was able to participate at school in spite of my hemophilia	23.I had to stay still during bleeds
					24.I put off treatment
					25.Factor infusions were a bother
					27.I got upset with my limits in physical activity
					28.I hid my pain
					29.I told my parents right away about my bleeds
					30.Home infusions made my life easier
					31.Having to take factor with me when I travelled was a bother
					32.I didn't like it when strangers were nosy about my hemophilia
					33.I was upset because sports keep getting harder for me
					34.Having a bleed away from home was frightening
					35.Self infusions let me have more freedom