

# Validation of the Haemophilia & Exercise Project-Test-Questionnaire (HEP-Test-Q)—An instrument for the assessment of subjective physical functioning in children with haemophilia

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**Introduction:** Contemporary haemophilia management recommends sport and physical activity in children with haemophilia. Assessment of subjective physical functioning requires standardized and validated instruments.

**Aims:** To adapt and psychometrically test the adult Haemophilia & Exercise Project-Test-Questionnaire (HEP-Test-Q) for children (aged 6-17 years).

**Methods:** In discussion rounds with children, single items of the adult HEP-Test-Q were reformulated to make them understandable without changing the item concept. The validation of the child-adapted version in children with haemophilia (n = 228) included pre-testing with feasibility testing, cognitive interviewing (n = 34), pilot-testing of the revised version in the EIS Study (n = 67) and field-testing in the SO-FIT Study (n = 127).

**Results:** *Pre-testing* revealed a completion time of  $8.2 \pm 4.1$  minutes and children liked the instrument. Cognitive interviews demonstrated that most items were easy to understand; 9 items were reformulated. *Pilot-testing* demonstrated good psychometric characteristics in terms of reliability ( $\alpha = .94$  Total Score) and validity. Convergent validity testing showed moderate correlations with the Haemo-QoL ( $r = -.491$ ), but low correlations with the Petrini Score ( $r = -.293$ ). Known groups' validity revealed significant differences in clinical subgroups; chronic pain ( $P < .002$ ) and target joints ( $P < .021$ ). *Field-testing* confirmed psychometric characteristics; Cronbach's alpha ranged from  $\alpha = .80$  ("endurance") to  $\alpha = .94$  (Total Score). The child-adapted HEP-Test-Q showed moderate correlations with the PedHAL ( $r = .634$ ,  $P < .0001$ ) and the Haemo-QoL SF ( $r = -.575$ ,  $P < .0001$ ). Known groups' validity testing proved that the HEP-Test-Q could discriminate between clinical subgroups.

**Conclusion:** The child-adapted HEP-Test-Q is a short, practical and acceptable instrument for the assessment of subjective physical functioning. Outcomes can be compared to adults because item concepts are identical to the adult version.

## KEYWORDS

children, exercise, haemophilia, physical functioning, questionnaire, self-assessment, validation

## 1 | INTRODUCTION

Musculoskeletal bleeding in children with haemophilia (CWH) results in reduced mobility and physical performance, which impacts on daily life.<sup>1</sup> Prophylaxis with factor concentrates has been the standard of care for children with severe haemophilia in the Western world since the 1990s<sup>2</sup> and is supported by the World Health Organisation.<sup>3</sup> In turn, this has allowed CWH to participate in sport and physical activity more than any other generation of CWH.<sup>4</sup> Prophylaxis offers protection from bleeding, especially if, treatment can be tailored around “risky” activities such as sport with a goal of maintaining joint health.<sup>5</sup> Physical activity is important for a healthy lifestyle, but in CWH it can cause injury and pain, therefore, it is important to define the activity risk in order to match the child’s interest and abilities with appropriate sporting activities.<sup>6</sup>

The assessment of Patient-Reported Outcomes (PROs) is important both to demonstrate the value of treatment to the subject and to justify treatment costs to payers.<sup>7</sup> Physical outcome measures were historically driven by health care providers undertaking assessments of joint health using validated instruments such as the Haemophilia Joint Health Score (HJHS),<sup>8</sup> however, self-reported PROs, either stand-alone or in combination with clinician-reported outcomes (ClinROo), are now recommended.<sup>9</sup>

The only validated instrument for the assessment of self-perceived functional health in CWH is the Pediatric Haemophilia Activities List (PedHAL), which was adapted from the adult Haemophilia Activities List (HAL).<sup>10</sup> Whilst this is a well-recognized instrument, it is complex to use, is lengthy and can be challenging for children to complete as it has been documented that complex questionnaires result in low completion rates in children.<sup>11</sup> Moreover, questionnaires focussing on physical ability may not appeal to CWH who have been treated exclusively with prophylaxis and who do not consider themselves “disabled”. Furthermore, data entry and analysis of questionnaires can be time-consuming for clinicians; thus these instruments are used more for research than to monitor clinical outcomes.

A shorter, quicker and easier to use instrument, to assess self-reported physical function in CWH is required to show changes over time with repeated assessments. The purpose of this study was to develop an instrument for the assessment of subjective physical functioning in children; we adapted the adult HEP-Test-Q (Haemophilia & Exercise Project Test-Questionnaire)<sup>12</sup> for use in children, and tested its feasibility and determined its psychometric characteristics in different populations of CWH.

## 2 | MATERIALS AND METHODS

The adaptation and psychometric validation of the HEP-Test-Q for use in CWH was performed in 3 phases: (i) instrument adaptation and pre-testing, (ii) pilot-testing and (iii) field-testing.

### 2.1 | Instrument adaptation

The HEP-Test-Q child version is based on the published HEP-Test-Q adult instrument<sup>12</sup> and was adapted for children in discussion rounds

with children reflecting the child’s understanding and capturing comments about statements used in the questions. Each formulation of the single items of the adult HEP-Test-Q was discussed with 5 children for comprehension and reformulated as necessary without changing the item concept.

The child-adapted HEP-Test-Q consisted of 25 items pertaining to 4 dimensions (“mobility”, “strength & coordination”, “endurance” and “body perception”) with a recall period of “in the past 4 weeks” and 1 single item assessing changes in physical activity “compared to the last year”. Answers were provided on a 5-point Likert scale from “never” to “always”. Negative formulated items were re-coded; subscales and the total score were transformed to a scale of 0-100 with high scores indicating better physical functioning.

The child-adapted HEP-Test-Q was forward translated from German into English by 2 native speakers and then back translated into German; inconsistencies were discussed with the developer of the HEP-Test-Q. After translation concurrence was achieved, the HEP-Test-Q was pre-tested.

### 2.2 | Pre-testing

Pre-testing included preliminary psychometric testing, feasibility testing and cognitive interviewing of 34 CWH A and B, of any severity, aged 6-17 years from Germany, USA and the UK conducted in 2008-2009. Cognitive pretest methods were used to probe how each question was understood and why a particular response was given.<sup>13</sup> In feasibility testing, children were asked to complete the entire child-adapted HEP-Test-Q to assess completion time, acceptance, comprehension and completeness. Next, cognitive interviews were conducted to probe their understanding of each individual item and obtain suggestions for rewording if they found the item difficult to understand or if they preferred another formulation. Importantly, the relevance of the item to the child was also assessed.

### 2.3 | Pilot testing

The child-adapted HEP-Test-Q instrument was pilot-tested (2009-2010) in the paediatric arm of the “Evaluation of the Impact of Sport Activities on Health-Related Quality of Life of Haemophilia Patients’ Study” (EIS Study) in which 84 boys with mild ( $n = 23$ ), moderate ( $n = 19$ ) or severe ( $n = 42$ ) haemophilia A or B aged 6-17 years participated in the UK<sup>14</sup>; the HEP-Test-Q was only administered to children at least 8 years of age ( $n = 69$ ). Orthopaedic joint status (OJS) was recorded using the ClinRO Petrini Score ranking 6 joints (right and left elbow, ankle and knee) on swelling, muscle atrophy, axial alignment, crepitus with motion, flexion and extension loss, instability, joint pain, gait and strength. Scores ranged from 0 indicating no joint complications to 156 indicating severe joint damage and immobility.<sup>15</sup> Health-related quality of life (HRQoL) was assessed with the PRO Haemo-QoL, a disease-specific instrument for CWH.<sup>16</sup> It consisted of 8-12 domains depending on the age group version with values ranging from 0-100; high values indicated high impairments in HRQoL.

## 2.4 | Field testing

Field testing of the child-adapted HEP-Test-Q was conducted as part of the “Study Of physical Function In adolescents with Haemophilia” (SO-FIT Study), in which 127 boys with severe haemophilia A or B between 8-17 years from 16 UK haemophilia centres participated (2014).<sup>17</sup>

Physiotherapists assessed the OJS using the *HJHS* (vs2.1), an 8-item tool assessing swelling/duration of swelling, muscle atrophy, crepitus on motion, range of movement loss, joint pain, strength in knee, elbow and ankle joints and gait. Item scores were combined to provide an overall score of 0-124, with 0 representing healthy joints.<sup>8,18</sup> The *HJHS* was used in this study, rather than the Petrini score as clinical practice in the UK had changed.

Subjective assessment of the impact of haemophilia on self-perceived functional abilities was assessed with the *PedHAL* consisting of 53 items categorized into 7 domains (sitting/kneeling/standing, functions of the legs, function of the arms, use of transportation, self-care, household tasks, leisure activities and sports). High values (range 0-100) indicate better physical functioning.<sup>10</sup>

Health-related quality of life was assessed with the short form of the *Haemo-QoL*,<sup>15</sup> which contained 35 items. High scores (range 0-100) indicated greater degrees of impairment in *HRQoL*.

Ethical approval for pilot testing and field-testing was granted in the context of the respective parent studies.<sup>13,17</sup>

## 2.5 | Data analysis

Statistical analyses were performed using the *SPSS* programme version 24 (Statistical Package for Social Science; IBM®). Testing of the child-adapted HEP-Test-Q included analysis of the results from the pre-testing phase retaining information from patients’ evaluation in the feasibility testing and from the cognitive interview on item-level concerning comprehensibility and relevance as well as preliminary psychometric testing. Further, psychometric testing was performed on scale level in terms of reliability (internal consistency) and validity (convergent and known groups) in the context of pilot testing and field-testing. Reliability was calculated for internal consistency (Cronbach’s alpha). Test-Retest Reliability was only tested in the SO-FIT Study and only after 6 months in contrast to the recommended time period of 2 weeks.<sup>19</sup> Intra-Class-Coefficients (ICCs) were used, which can be interpreted as: ICC < 0.40 (“poor”), 0.40-0.59 (“fair”), 0.60-0.74 (“good”) and 0.75-1.0 (“excellent”).<sup>20</sup>

Construct validity was tested applying convergent validity and known groups’ validity testing. Different measures for convergent validity testing were included for pilot-testing and field testing, due to the different projects and changes in routine clinical assessment of joint status over time in which the child-adapted HEP-Test-Q was psychometrically tested (see Table 1). Convergent validity was determined by means of Pearson or Spearman correlation coefficients depending on the distribution, comparing the child-adapted HEP-Test-Q scales with ClinRO measures, such as the *HJHS* or Petrini Score, as well as with PRO measures, including the *PedHAL* and the

**TABLE 1** Instruments used in the different studies

Concepts	Instruments	
	Pilot-testing (EIS Study) 2009-2010	Field-testing (SO-FIT Study) 2014
ClinROs		
Orthopaedic joint status	Petrini Score <sup>15</sup>	HJHS Score <sup>8</sup>
PROs		
Subjective physical functioning	-	PedHAL <sup>10</sup>
Health-related quality of life	Haemo-QoL long version <sup>16</sup>	Haemo-QoL SF <sup>16</sup>

ClinRO: Clinician-Reported Outcome; PRO: Patient-Reported Outcome

*Haemo-QoL* (long, short forms). As a rule for the interpretation of correlation coefficients, we used the following values:  $r = .30-.50$  low correlation,  $r = .50-.70$  moderate correlation and  $r = .70-.90$  high correlation.<sup>21</sup>

For known groups’ validity testing, patients were classified into different clinical subgroups according to the data collected in the respective studies (eg age, BMI, OJS, target joints, severity, treatment intensity, inhibitor, pain, joint bleeds, doing sport, sedentary lifestyle).

Descriptive data are shown as frequency distribution in percentage or as mean (M) ± standard deviation (SD) and range. Data were tested for normal distribution using the Kolmogorov-Smirnov test. Differences between clinical subgroups were analysed utilizing unpaired Student’s *t* test or Mann-Whitney *U* test according to distribution.  $P < .05$  was defined as statistically significant.

## 3 | RESULTS

### 3.1 | Pre-testing

The child-adapted HEP-Test-Q was pre-tested in 34 children from Germany (n = 5), USA (n = 9) and the UK (n = 20). The median age of the children was 11 years (range 6-17). Most had haemophilia A (91.2%), with severe disease (85.3%), received prophylaxis (76.5%) and participated in physical education in school (91.2%). Children reported complaints due to pain (32.4%) and limitations in mobility (17.6%); the median number of reported hemarthroses was 0 (range 0-8). Five children received physiotherapy, mostly once weekly.

*Feasibility testing* revealed that children needed on average  $8.2 \pm 4.1$  minutes (range 1-20) to complete the child-adapted HEP-Test-Q. On a visual analogue scale, ranging from 0 (“poor”) to 100 (“excellent”), they liked the questionnaire (M =  $71.1 \pm 21.0$ , range 25-100), found it easy to complete (M =  $81.5 \pm 23.8$ , range 20-100), considered the answer categories easy to understand (M =  $79.1 \pm 25.3$ , range 25-100), and considered the questionnaire relevant and comprehensive, covering almost all aspects of physical

Items	Child-adapted formulation	New formulation
Body 1	How do you rate your <i>actual</i> physical ability	How do you rate your <i>current</i> physical ability
Mobility 4	My physical ability was not so good because of <i>chronic</i> pain	My physical ability was not so good because of <i>constant</i> pain
Coordination 2	I <i>am</i> walking safely	I <i>could</i> walk safely
Coordination 7	I had problems with my balance on <i>rough</i> ground	I had problems with my balance on <i>uneven</i> ground
Endurance 2	I was weak after <i>not too much</i> physical activity	I was weak after <i>moderate</i> physical activity
Endurance 7	I did a lot with others	I did a lot of <i>physical activities</i> with others
Endurance 8	I did <i>physically more</i> than usual	I did <i>more physically</i> than usual
Perception 1	I felt physically OK	I felt physically <i>fit</i>
Perception 2	I felt fine <i>in</i> my body	I felt fine <i>with</i> my body

**TABLE 2** Reformulation of items based on children's recommendations during cognitive interviews in the context of the pre-testing phase (n = 34)

functioning ( $M = 82.7 \pm 17.7$ , range 47-100). Nine out of 34 children wanted to change or add something in the questionnaire, eg adding comment fields that child could explain more, having I-pad rather than paper-and-pencil version, adding questions about treatment and pain.

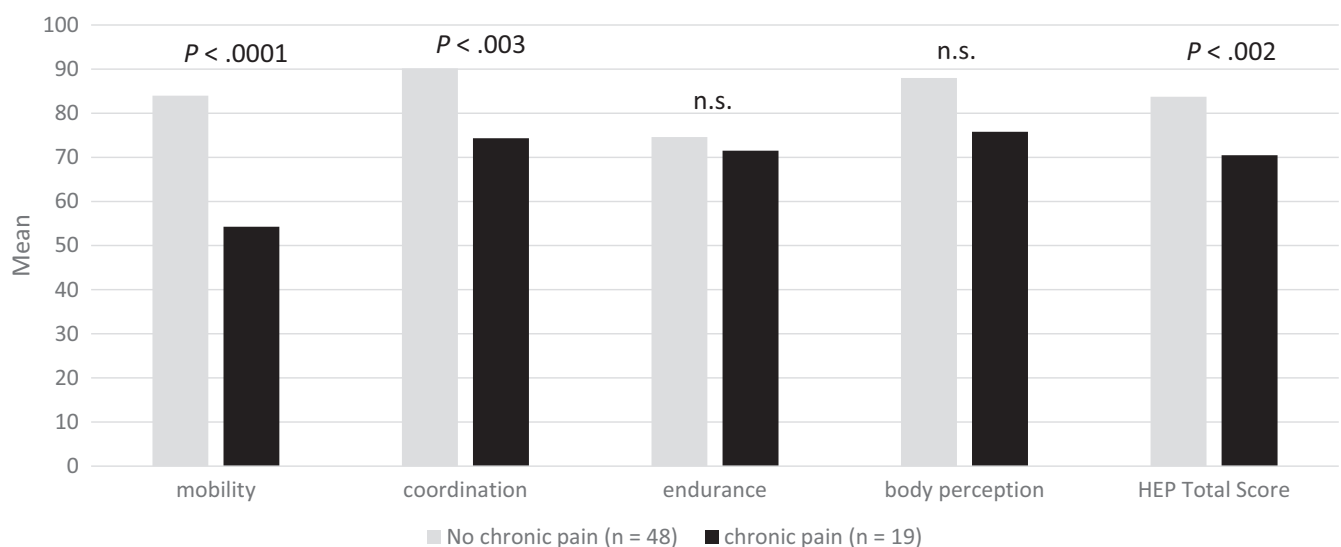
Cognitive interviews revealed that children generally had no difficulty understanding the items. One item in the domain "mobility" ("my physical activity was not so good because of chronic pain") was difficult for 23.5% of children to clearly understand what was intended; this item was reformulated. Overall, nine items were modified based on the findings and suggestions made by the children in order to have a more comprehensible version available (see Table 2). When asking children in the cognitive interview about the importance of the single items in the questionnaire, they considered items in the domain "mobility" most important whilst items in the domain "endurance" were considered least important. This was probably related to the good overall general health in this cohort

of boys; where physical ability ("mobility") was seen to be more functionally relevant than stamina or staying power ("endurance").

Preliminary psychometric testing revealed Cronbach's alpha values ranging from  $\alpha = .72$  ("endurance") to  $\alpha = .84$  ("perception") and a total score of  $\alpha = .89$ . For known groups validity, significant differences were found for clinical subgroups concerning *complaints due to pain and due to limitations, the presence of joint bleed and impairments in the OJS* within the domains "mobility" ( $P < .003$ ;  $P < .037$ ;  $P < .006$ ;  $P < .033$ ) and "strength & coordination" ( $P < .042$ ;  $P < .033$ ;  $P < .004$ ;  $P < .027$ ), respectively; a difference was found also for *participation in physical education in school* in the domain "strength & coordination" ( $P < .010$ ).

### 3.2 | Pilot-testing (EIS Study)

The child-adapted version of the HEP-Test-Q was administered to boys from the UK at least 8 years ( $n = 69$ ) with a median age of 11.5 years (range 8.1-17.9); 67 completed questionnaires were



**FIGURE 1** Known groups validity for chronic pain of the child-adapted HEP-Test-Q in the pilot-testing (EIS Study) (n = 67)

analysed. Psychometric testing revealed excellent reliability ranging from Cronbach's  $\alpha = .86$  ("endurance"),  $\alpha = .87$  ("strength & coordination"),  $\alpha = .88$  ("mobility"),  $\alpha = .94$  ("body perception") to  $\alpha = .94$  for "the HEP-Test-Q total score". Convergent validity testing revealed a moderate correlation of the total score of the child-adapted HEP-Test-Q with the subjective PRO Haemo-QoL Total Score ( $r = -.491$ ) and a low correlation with the clinically assessed ClinRO Petrini Score ( $r = -.293$ ). Good values for known groups' validity were found differentiating clinical subgroups in terms of chronic pain and target joints. Children with chronic pain reported significantly lower subjective physical functioning than those without pain (see Figure 1). Children with target joints reported lower values in the domains "mobility" ( $P < .014$ ) and the "Total Score" ( $P < .021$ ). Significant differences were also found for sporting activity and sedentary lifestyles, which were reported elsewhere.<sup>14</sup> No differences were found for age, severity, inhibitor presence or joint bleeds.

### 3.3 | Field-testing (SO-FIT Study)

The child-adapted HEP-Test-Q was field tested in 127 children (median age 12.4 years, range 8.1-17.0) with severe haemophilia. Psychometric characteristics are shown in Table 3. Reliability for the total score was  $\alpha = .94$  with all values above the critical value of  $\alpha = .70$  and the range was  $\alpha = .80$  ("endurance") to  $\alpha = .93$  ("body perception"). Due to the SO-FIT study design, Test-Retest Reliability could not be examined in the recommended time frame of 2 weeks; nonetheless, children completed the child-adapted version of the HEP-Test-Q again after 6 months. ICC between baseline and follow-up revealed good ICC for the dimensions "coordination" (ICC = 0.729) and the HEP-Test-Q Total Score (ICC = 0.662); the other dimensions revealed all fair ICC ranging from (ICC = 0.445, "perception") to (ICC = 0.585, "mobility").

Convergent validity testing revealed moderate correlation of the total score of the child-adapted HEP-Test-Q with the PROs PedHAL ( $r = .634$ ) and Haemo-QoL SF ( $r = -.575$ ) and low correlation with the ClinRO HJHS ( $r = -.323$ ) (see Table 4). Known groups' validity revealed significant differences for clinical subgroups in terms of HJHS, BMI, target joints, type of prophylaxis and pain (see Table 5). No significant differences were detected for age, inhibitor status, factor dosing regimen, number of joint bleeds, or total number of bleeding episodes.

**TABLE 3** Psychometric characteristics of the child-adapted HEP-Test-Q in the field study (SO-FIT Study) (n = 127)

Dimensions HEP-Test-Q	No of items	M	SD	Min	Max	Cronbach's $\alpha$
Mobility	4	83.65	20.5	6.25	100	.859
Strength & coordination	8	84.28	16.0	28.13	100	.820
Endurance	8	72.53	19.1	18.75	100	.801
Body perception	5	83.59	22.2	0	100	.925
Total Score	25	80.32	16.1	29.0	100	.935

M: mean; SD: standard deviation

## 4 | DISCUSSION

The child-adapted HEP-Test-Q was developed in 3 phases [pre-testing (n = 34), pilot-testing (n = 67), field-testing (n = 127)] including a total of 228 CWH with (mild [n = 24], moderate [n = 15] and severe disease [n = 189]) from 3 countries. Average completion time for the child-adapted HEP-Test-Q was 8 minutes (demonstrated in the pre-testing phase); in the field-testing the completion times of the child-adapted HEP-Test-Q and the PedHAL were compared; most children needed 5-10 minutes to complete the PedHAL (47.5%), whilst 56.8% reported completing the HEP-Test-Q in <5 minutes. There was a tendency for older children (>10 years) to need <5 minutes (42.9% vs 14.3%) compared to younger children ( $\leq 10$  years), but these data are not statistically significant. Ease of questionnaire completion is an important aspect in paediatric care, as children's motivation and concentration are known to impact on data quality.<sup>22</sup> However, children can and do provide reliable responses to questionnaires that are meaningful to them and that they understand; Kellet & Ding suggest this is best achieved using simple, easy to understand questionnaires with, clear instructions, appealing fonts and layout with use of pictures.<sup>23</sup> The child-adjusted HEP-Test-Q was a pictorial questionnaire which fulfilled these recommendations; it is available at [www.hep-test-q.org](http://www.hep-test-q.org)<sup>24</sup>.

Psychometric testing and evaluation of items by children enabled revision of the adult questionnaire, which was then utilized in pilot and field-testing confirming similar values for reliability and validity to adult studies (Table 6).<sup>12,25</sup> Convergent validity testing revealed moderate correlations between the HEP-Test-Q and the PedHAL, except for the subscale "body perception" which showed a low correlation with the PedHAL demonstrating that both instruments assess similar, but not identical aspects. The HEP-Test-Q is the only instrument measuring subjective "body perception" in both children and adults with haemophilia.

Moreover, we found low correlations between the HEP-Test-Q and ClinRO measures such as the Petrini Score and the HJHS. This finding is in line with the adult data, where low correlations were

**TABLE 4** Convergent validity of the child-adapted HEP-Test-Q in the field Study (So-Fit Study) (n = 127)

Dimensions HEP-Test-Q	PedHAL <i>r</i>	Haemo-QoL SF <i>r</i>	HJHS <i>r</i>
Mobility	.603**	-.465**	-.274*
Coordination	.702**	-.587**	-.296*
Endurance	.477**	-.409**	-.302*
Perception	.422**	-.458**	-.271*
Total	.634**	-.575**	-.323**

Haemo-QoL SF: Haemophilia-specific Quality of Life Questionnaire for children and adolescents Short Form; HJHS: Hemophilia Joint Health Score; PedHAL: Pediatric Hemophilia Activity List;

*r*: Pearson correlation coefficient

\* $P \leq .001$

\*\* $P \leq .0001$



**TABLE 5** Known groups validity of the child-adapted HEP-Test-Q in the field study (So-Fit Study) (n = 127)

Clinical categories	Subgroups	Number of patients	Dimension of the HEP-Test-Q											
			Mobility		Strength & coordination		Endurance		Body perception		Total score			
			M	P	M	P	M	P	M	P	M	P		
OJS	HJHS ≥ 1	61	80.29	.039	81.3	.015	68.49	.010	79.84	n.s.	76.74	.006		
	HJHS < 1	58	88.04		88.37		77.32		87.67		84.74			
BMI	Overweight/obese	36	76.07	.026	79.29	n.s.	64.2	.008	77.86	n.s.	73.66	.015		
	Low/normal	91	86.64		86.24		75.81		85.84		82.94			
Target joint	Yes	8	68.75	.033	64.45	.0001	49.22	.029	61.25	.003	59.63	.0001		
	No	116	84.68		85.65		74.14		85.13		81.75			
Prophylaxis	Secondary	66	81.22	n.s.	81.92	.041	70.56	n.s.	80.61	n.s.	77.96	.038		
	Primary	58	86.59		87.56		75.85		87.91		83.73			
Pain	Yes	33	64.02	.0001	69.98	.0001	62.73	.005	67.58	.0001	66.22	.0001		
	No	89	90.57		89.23		76.00		89.38		85.29			

For transformed scales (0-100), with high scores indicating good physical functioning.

found with the Gilbert Score ( $r = -.48$ ).<sup>12</sup> This is probably because these instruments assess similar, but not identical concepts, therefore combinations of instruments for assessment are recommended. Discrepancies between patient and clinician ratings are recognized in other diseases<sup>26</sup> and therefore it is not the absolute agreement between ClinROs and PROs that is important, but the consistency of their scores.<sup>27</sup>

The HEP-Test-Q was able to discriminate between clinical subgroups revealing reduced physical functioning in children with reduced health status (pain, target joints, orthopaedic status, sedentary life style) and children without limitations. No differences were found concerning age groups in any phase of the validation studies.

Physical functioning in CWH is increasingly evaluated using different Clinical Outcome Assessments (COA).<sup>28</sup> In clinical practice, physical functioning is mainly assessed through ClinROs such as the HJHS<sup>8</sup> and/or PROs such as the PedHAL<sup>10</sup> or the HEP-Test-Q.<sup>12</sup> In research or gait and motion laboratories, physical functioning is evaluated by clinimetric measures,<sup>29</sup> Performance Outcomes (PerfOs) such as 1 leg stand, 6-minute walk test or the Functional Independence Score for Hemophilia (FISH)<sup>30</sup> or apparatus testing such as pedobarography, EMG or motion analysis.<sup>31</sup> The self-reported PedHAL focuses on activities of daily living such as use of transport, self-care and household tasks, whereas the HEP-Test-Q assesses aspects of physical functioning based on motor ability (mobility, strength, coordination and endurance). PedHAL is an internationally recognized instrument with use in clinical trials, yet there is limited published evidence of its use.<sup>10,30,32</sup> FISH has also been used internationally in children and adults and has been shown to be a reliable tool for assessing functional ability in CWH compared to normal controls revealing lower limb functional abnormalities (squatting, walking, and step climbing)<sup>30</sup> and functional "independence" in adolescents.<sup>33</sup> The child-adapted Hep-Test-Q could be used as a complementary instrument to ClinROs and PerfOs in evaluating self-reported outcomes in children as suggested by the ISPOR Clinical Outcome Assessment Emerging Good Practices Task Force.<sup>34</sup>

The development of PROs has helped provide a more comprehensive assessment of health from the patient perspective, however, they are not without limitations; an algorithm for their use in clinical practice has been suggested.<sup>35</sup>

There are some limitations to the current work with the HEP-Test-Q: (i) the pilot and field-testing were undertaken only in the UK, (ii) test-retest within the cohorts was only done in field-testing and not within the required timeframe, (iii) in field-testing, only children with severe haemophilia were included, (iv) the majority of children in all 3 phases of the HEP-Test-Q development were treated with prophylaxis, so that no differences in the subjective physical functioning between different treatment regimen (prophylaxis, on-demand) could be calculated.

The child-adapted HEP-Test-Q is an instrument, which can be used to assess subjective physical performance, in routine clinical practice as well as in clinical trials, but requires further cross-cultural validation in larger studies allowing comparison of children with moderate and mild haemophilia. We also recommend that additional studies are undertaken in countries where

**TABLE 6** Comparison of Cronbach's alpha across the different phases of the development of the child-adapted HEP-Test-Q (pre-test, pilot-test, and field-test) in comparison with the original adult HEP-Test-Q

Dimensions of the HEP-Test-Q	Adults <sup>12</sup>	Children		
	FIELD-Test (n = 43)	PRE-Test (n = 34)	PILOT-Test (n = 67)	FIELD-Test (n = 127)
	Cronbach's $\alpha$			
Mobility	.87	.75	.88	.86
Coordination	.92	.78	.87	.82
Endurance	.87	.72	.86	.80
Perception	.85	.84	.94	.93
Total score	.96	.89	.94	.94
Countries	Germany	UK, US, Germany	UK	UK
Severity	Severe, moderate, mild	Severe, moderate, mild	Severe, moderate, mild	Severe
Prophylactic treatment	48.8%	76.5%	66.2%	97.6%

prophylaxis is not the standard of care, where we expect that CWH would report higher impairments in subjective physical functioning. The authors encourage anyone interested in using this instrument to contact the corresponding author or to visit the HEP-Test-Q website.<sup>24</sup>

## 5 | CONCLUSION

The child-adapted HEP-Test-Q is a short, practical, well-accepted instrument for the assessment of subjective physical functioning in CWH with good psychometric characteristics. Importantly, outcomes can be compared to adults because item concepts are identical in the child and adult versions, allowing continuous study across the age continuum.

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## DISCLOSURES

The authors stated that they had no interests which might be perceived as posing a conflict or bias.

## AUTHOR CONTRIBUTIONS

SvM and TH designed the study. KKh, KKu and LV performed the data collection. SvM analysed the data. SvM and KKh wrote the first draft of the paper; all authors contributed to the paper and reviewed the final version.

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