Received: 6 January 2022 | Revised: 29 June 2022 | Accepted: 1 July 2022

DOI: 10.1111/hae.14628

Haemophilia WFH WILEY

ORIGINAL ARTICLE

Clinical haemophilia

Validation of the pedHAL$_{short}$ and HAL$_{short}$ in Dutch children and adults with haemophilia

Isolde A. R. Kuijlaars[1] | Janjaap van der Net[2] | Lize F. D. van Vulpen[1] | Mariette H. E. Driessens[3] | Saskia E. M. Schols[4,5] | Melanie Tan[6] | Samantha C. Gouw[7,8] | Kathelijn Fischer[1]

[1]Center for Benign Haematology, Thrombosis and Haemostasis, Van Creveldkliniek, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands

[2]Center for Child Development, Exercise and Physical Literacy, University Medical Center Utrecht, Utrecht University, University Children's Hospital, Utrecht, the Netherlands

[3]Netherlands Haemophilia Society (NVHP), Nijkerk, the Netherlands

[4]Department of Haematology, Radboud University Medical Center, Nijmegen, the Netherlands

[5]Haemophilia Treatment Center Nijmegen-Eindhoven-Maastricht, Radboud University Medical Center, Nijmegen, the Netherlands

[6]Department of Vascular Medicine, Amsterdam Cardiovascular Sciences, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, the Netherlands

[7]Emma Children's Hospital, Amsterdam UMC, University of Amsterdam, Pediatric Hematology, Amsterdam, the Netherlands

[8]Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, the Netherlands

Correspondence
Isolde A. R. Kuijlaars, Heidelberglaan 100, 3584 CX Utrecht, the Netherlands.
Email: i.a.r.kuijlaars-2@umcutrecht.nl

Abstract

Introduction: The Haemophilia Activities List (HAL) and paediatric HAL assess self-reported limitations in various daily activities. To reduce patient burden, shorter versions of the pedHAL (22 items) and HAL (18 items) have been developed.

Aim: This study aimed to determine the agreement between the pedHAL/HAL$_{full}$ and pedHAL/HAL$_{short}$ and construct validity and internal consistency of the pedHAL/HAL$_{short}$ in persons with haemophilia (PWH).

Methods: A cross-sectional secondary analysis of the Hemophilia in the Netherlands-6 national survey was performed. Adult and paediatric PWH completed the original pedHAL/HAL$_{full}$, from which pedHAL/HAL$_{short}$ were derived. Score differences between the original and short versions were calculated. Construct validity was studied by testing hypotheses regarding the relationship of the pedHAL/HAL$_{short}$ with the pedHAL/HAL$_{full}$, Haemophilia & Exercise Project Test-Questionnaire (HEP-Test-Q), Canadian Haemophilia Outcomes-Kids' Life Assessment Tool (CHO-KLAT) and RAND 36-item Health Survey (RAND-36) (convergent/discriminant validity) as well as its ability to discriminate between subgroups (known-group validity). Internal consistency was assessed with Cronbach's α.

Results: We included 113 children (median 10y [range 4–17], 53% severe haemophilia) and 691 adults (median 51y [range 18–88], 35% severe). Scores of the pedHAL/HAL$_{full}$ and pedHAL/HAL$_{short}$ were similar with high correlations (>0.9). Construct validity was confirmed for the pedHAL/HAL$_{short}$. The HAL$_{short}$ was able to discriminate between different disease severities and ages. Cronbach's α of the pedHAL/HAL$_{short}$ was 0.95–0.97.

Conclusion: This study confirmed the agreement between the pedHAL/HAL$_{full}$ and the pedHAL/HAL$_{short}$ and the construct validity of the pedHAL/HAL$_{short}$. The next step

is to study construct validity of the pedHAL/HAL_{short} when administered as short forms.

KEYWORDS
activities, haemophilia, participation, patient-reported outcome, validity

1 | INTRODUCTION

The paediatric Haemophilia Activities List (pedHAL) and Haemophilia Activities List (HAL) assess self-reported limitations in various activities of daily living, which are relevant to children and adults with haemophilia.[1–4] The pedHAL consists of 53 items and the HAL of 42 items, both distributed over seven domains: '(lying down)/sitting/kneeling/standing', 'functions of the legs', 'functions of the arms', 'use of transportation', 'self-care', 'household tasks' and 'leisure activities and sports'. Since these questionnaires are routinely used for outcome assessment, feasibility is crucial. Especially within the constraints of a clinical practice, it may take too much time to administer questionnaires. Time was mentioned as a barrier for clinical use of outcome measures in general as well as within the field of haemophilia.[5–7] Ideally, patients complete questionnaires before the outpatient consultation, which the clinician discusses with patients during the consultation (e.g. KLIK Patient Reported Outcome Measures [PROM] portal [www.hetklikt.nu]).[8] In order to enhance feasibility, we developed shorter versions of the pedHAL (22 items) and HAL (18 items).[9,10] For both the pedHAL and HAL, the short versions are derived from the original versions which allows for longitudinal studies that use the pedHAL/HAL to switch to the pedHAL/HAL_{short}. The item reduction of >50% for both questionnaires will substantially reduce the burden of time for completing the questionnaires. Before widespread introduction of the pedHAL$_{short}$ and HAL$_{short}$, further validation is needed. For children the pedHAL$_{short}$ was developed in an international dataset but was not validated in other datasets.[9] For adults the HAL$_{short}$ was developed and validated in data from American persons with haemophilia (PWH) only.[10]

This study aimed to determine the (1) agreement between the pedHAL/HAL_{full} and pedHAL/HAL_{short}, (2) construct validity and (3) internal consistency of the pedHAL/HAL_{short} to assess limitations in activities and participation in Dutch PWH.

2 | MATERIALS AND METHODS

2.1 | Study design and study population

This study was a secondary analysis of the cross-sectional Hemophilia in the Netherlands-6 (HiN-6) nationwide survey.[11] All PWH A (congenital factor VIII deficiency) and B (congenital factor IX deficiency) of all severities aged ≥4 years (n = 2192) were invited to complete a survey, in the period from June 2018 until July 2019. The response rate was 46% (n = 1009). For the current analysis (from June 2021 to December 2021) PWH who completed the HAL or pedHAL were included (n = 804). In the HiN population the median age at initiation of prophylaxis in patients with severe haemophilia was three (range 0–79). In patients with haemophilia A 7% was treated with extended half-life FVIII products and in patients with haemophilia B 29% was treated with extended half-life FIX products.[11]

In children (4–17 years) data on the pedHAL$_{full}$, pedHAL$_{short}$, Haemophilia & Exercise Project Test-Questionnaire (HEP-Test-Q) and Canadian Haemophilia Outcomes-Kids' Life Assessment Tool version 2.0 (CHO-$KLAT_{2.0}$) were analysed. For children aged 4–11 years parents were asked to complete the questionnaires. Children aged 12–17 years completed the questionnaires by themselves. In adults (≥18 years) data on the HAL$_{full}$, HAL$_{short}$, HEP-Test-Q and RAND 36-item Health Survey (RAND-36) were analysed. Patients completed the original pedHAL/HAL, from which the pedHAL/HAL$_{short}$ was derived.

The HiN-6 study was approved in 2018 by the Medical Ethics Committee at Leiden University Medical Center.

2.2 | Measurements

2.2.1 | Pediatric haemophilia activities List$_{(short)}$

The pedHAL assesses self-reported limitations in activities and participation in children with haemophilia.[3,4] It consists of a patient version (8–17 years) and parent version (4–17 years). The original pedHAL contains 53 items and the pedHAL$_{short}$ contains 22 items, distributed over seven domains. Patients score the items on a 6-point Likert scale (In the previous month, did you have any difficulty, due to haemophilia, with: 'impossible', 'always', 'usually', 'sometimes', 'almost never', 'never'), with a 'not applicable (N/A)' scoring option. Domain scores and sum scores are converted to a normalized domain score ranging from 0 (worst possible functional abilities) to 100 (best possible functional abilities) according the scoring tool available at www.vancreveldkliniek.nl. Domain, component and sum scores are only calculated if a minimum of 50% of items of a domain or component are scored on the 6-point Likert scale. For the pedHAL$_{short}$ only the sum score should be used since some domains only have one or two items in the pedHAL$_{short}$.[9]

2.2.2 | Haemophilia activities List$_{(short)}$

The HAL is a validated instrument for assessment of self-reported limitations in activities and participation in PWH.[1,2] The original HAL contains 42 items and the HAL$_{short}$ contains 18 items, distributed over

seven domains. Patients score the items on a 6-point Likert scale (In the past month, did you have any difficulty, due to haemophilia, with: 'impossible', 'always', 'mostly', 'sometimes', 'rarely', 'never'), with a 'not applicable (N/A)' scoring option for some items. Domain scores, component scores and sum scores are converted to a normalized domain score ranging from 0 (worst possible functional abilities) to 100 (best possible functional abilities). Domain, component and sum scores are only calculated if a minimum of 50% of items of a domain or component are scored on the 6-point Likert scale. For the HAL_{short} only the sum score should be used since some domains only have one or two items in the HAL_{short}.[10]

2.2.3 | Haemophilia and exercise project test-questionnaire

The HEP-test-Q is a validated questionnaire for the assessment of self-reported physical performance in children and adults with haemophilia.[12,13] The HEP-test-Q consists of 25 items pertaining to four domains ('mobility', 'strength & coordination', 'endurance' and 'body perception'). The response options are a 5-point Likert scale ('never' to 'always'). Subscales and the total score were transformed to a scale ranging from 0 to 100 with high scores indicating better physical performance.[12,13] Convergent and discriminant validity of the HEP-test-Q were moderate to good in children and adults. The internal consistency of the HEP-test-Q was high in children and adults (Cronbach's α 0.94–0.96).[12,13]

2.2.4 | Canadian haemophilia outcomes-kids' life assessment tool

The $CHO\text{-}KLAT_{2.0}$ measures disease specific quality of life in children with haemophilia.[14,15] The $CHO\text{-}KLAT_{2.0}$ consists of a patient version and a parent version, both with 35 items. The response options are a 5-point Likert scale. Scores range from 0 to 100, with higher scores indicating better health status.[14,15] Content validity, test–retest reliability and construct validity of the CHO-KLAT were good.[16] According to the developers the CHO-KLAT was not intended to contain homogeneous items. Therefore, assessment of internal consistency was considered not to be appropriate.[17]

2.2.5 | RAND 36-item health survey

The RAND-36 measures health related quality of life across 8 domains ('physical functioning', 'role limitations due to physical health problems', 'bodily pain', 'general health', 'energy/fatigue', 'social functioning', 'role limitations due to emotional health problems' and 'emotional well-being') and construct validity has been studied in PWH.[18,19] In 6/8 domains patients score the items on a 3–6-point Likert scale and in 2/8 domains patients score 'yes' or 'no'. Scores range from 0 to 100, with higher scores indicating better health status.[18,20] The internal consistency of the RAND-36 was high (Cronbach's α 0.78–0.95).[19]

2.2.6 | Patient characteristics

Patient characteristics included age at pedHAL/HAL assessment, type of haemophilia (A or B), severity of the disease (mild [factor VIII/IX activity 0.06–0.40 IU/ml], moderate [factor VIII/IX activity 0.01–0.05 IU/ml] or severe [factor VIII/IX activity <0.01 IU/ml]), current clotting factor regimen (prophylaxis yes/no) and inhibitor status (never/current/former).

2.3 | Statistical analyses

Data were checked for normality and are presented as median (interquartile ranges [IQR]: P25–P75) or as proportions where appropriate. Statistical analyses were performed with SPSS (version 26, IBM Corp.) and RStudio (version 4.1.2.). The used R package was 'psych' to calculate Cronbach's alpha.

The bootstrapped differences between the $pedHAL_{full}$ versus $pedHAL_{short}$ and HAL_{full} versus HAL_{short} and bias corrected accelerated (BCa) 95% confidence intervals (CI) of the differences were calculated using bootstrapping (1000 iterations) because the scores were left skewed distributed. In addition, the proportions of 'positive' scores (pedHAL ≤95, HAL ≤90) and positive predictive value of the $pedHAL/HAL_{short}$ were calculated and shown in a cross table. The thresholds of ≤95 for the pedHAL and ≤90 for the HAL are based on reported limits of agreement (LoA) of test-retest data[4,21] and in accordance with previous studies.[9,10,22]

Construct validity was studied by testing hypotheses regarding correlations between the sum scores of the $pedHAL/HAL_{full}$ versus $pedHAL/HAL_{short}$ and hypotheses regarding the relationship of the $pedHAL/HAL_{(short)}$ with the HEP-Test-Q and CHO-KLAT (*convergent validity*). Prior to the analysis a consensus based cut-off point of <0.15 was defined, which was used for the differences between the correlations (Δ *r*) of the HEP-Test-Q and CHO-KLAT with the original versus the short versions of the pedHAL/HAL. In addition, the correlations of the $HAL_{(short)}$ with the RAND-36 physical functioning and emotional well-being domains were compared (*discriminant validity*). Finally, hypotheses regarding expected differences in $HAL_{(short)}$ sum scores between subgroups on severity and age were tested for the adults (*known-group validity*). In children, no differences were expected between subgroups on severity and age. This is comparable to data on the CHO-KLAT, Haemo-QoL and Pediatric Quality of Life Inventory (PedsQL) in Canadian children[17] and similar in the CHO-KLAT and HEP-test-Q scores according to severity and age in the current dataset. Hypotheses were defined a priori based on expert opinion (KF, JN, IK). To test hypotheses regarding convergent validity and discriminant validity, Spearman's correlations were calculated because some data showed skewed distributions. Correlation coefficients of ≥0.9 were considered as a very strong correlation, 0.7–0.89 as strong, 0.4–0.69 as moderate, 0.10–0.39 as weak and <0.10 as negligible.[23] To test hypotheses regarding known-group validity, Mann-Whitney *U* tests were performed and score differences were compared to the smallest detectable change of the HAL.[21]

TABLE 1 Patient characteristics

Patient characteristics	Children ($n = 113$)	Adults ($n = 691$)
Median (IQR) or number (%)		
Age (years)	10.0 (7.0–13.5)	51.0 (34.0–62.0)
Haemophilia A[a]	99 (88.4)	610 (88.9)
Haemophilia severity		
Mild	39 (34.5)	337 (48.9)
Moderate	14 (12.4)	110 (15.9)
Severe	60 (53.1)	244 (35.3)
Prophylaxis[b]	66 (58.4)	232 (33.7)
Inhibitor status[c]		
Never	92 (84.4)	585 (88.8)
Current	0 (0)	12 (1.8)
Former	17 (15.6)	62 (9.4)

[a]In children missing data ($n = 1$), in adults missing data/unknown ($n = 5$); [b]in adults missing data ($n = 3$); [c]in children missing data/unknown ($n = 4$), in adults missing data/unknown ($n = 32$).

To determine internal consistency Cronbach's α of the $pedHAL_{short}$ and HAL_{short} was calculated. Cronbach's α should be between 0.70 and 0.95.[24]

3 | RESULTS

3.1 | Patient characteristics

A total of 113 children and 691 adults with haemophilia were included. Patient characteristics are shown in Table 1. Median age at the time of completing the pedHAL/HAL was 10.0 years (range 4–17) in children and 51.0 years (range 18–88) in adults. In children the majority had severe haemophilia (53.1%) and in adults the majority had mild haemophilia (48.9%). All children with severe haemophilia and 35.7% of the children with moderate haemophilia were treated with prophylaxis. In adults, 87.7% of the patients with severe haemophilia and 12.7% of the patients with moderate haemophilia were treated with prophylaxis. In children aged 4–11 years ($n = 70$, 61.9%) parents completed the questionnaires and children aged 12–17 years completed the questionnaires by themselves ($n = 43$, 38.1%). The proportion of severe haemophilia was slightly higher in the older children who completed the questionnaires by themselves (60.5%) compared to the younger children (48.6%).

3.2 | $PedHAL_{full}$ versus $pedHAL_{short}$

3.2.1 | Agreement

The median (IQR) sum score of the $pedHAL_{full}$ was slightly lower than the $pedHAL_{short}$ (99.6 [96.9–100] vs. 100 [96.8 – 100]). The bias corrected mean difference between the $pedHAL_{full}$ and $pedHAL_{short}$ sum scores was −0.3 with 95% CI of −0.5 to −0.1. 'Positive' scores (≤95) were reported in 20.4% for the $pedHAL_{full}$ and 18.8% for the $pedHAL_{short}$. The vast majority (86.4%) of the patients who reported a score ≤95 on the $pedHAL_{full}$, reported a score ≤95 on the $pedHAL_{short}$, which is shown in Table 2.

TABLE 2 Cross table to show the proportions of 'positive' scores on the pedHAL/HAL_{short} versus pedHAL/HAL_{full}

		$pedHAL_{short}$	
		≤95	>95
$pedHAL_{full}$	≤95	19 (86.4%)	3 (13.6%)
	>95	2 (2.2%)	88 (97.8%)
		HAL_{short}	
		≤90	>90
HAL_{full}	≤90	311 (99.7%)	1 (0.3%)
	>90	19 (5.0%)	360 (95.0%)

Based on reported limits of agreement (LoA) of test-retest data, limitations in activities and participation were defined as ≤95 for the pedHAL and ≤90 for the HAL.

3.2.2 | Construct validity

The hypotheses regarding convergent validity were confirmed and shown in Table 3. The correlation between the $pedHAL_{full}$ and $pedHAL_{short}$ was 0.91 (95% confidence interval [95% CI]: 0.86–0.94) and the sum scores of the $pedHAL_{full}$ and $pedHAL_{short}$ are shown in Figure 1. The differences in correlations were within the criterion of $\Delta r < 0.15$, for both the HEP-test-Q ($pedHAL_{full}$ $r = 0.40$ and $pedHAL_{short}$ $r = 0.42$) and CHO-KLAT ($pedHAL_{full}$ $r = 0.46$ and $pedHAL_{short}$ $r = 0.44$).

3.2.3 | Internal consistency

The internal consistency of the $pedHAL_{short}$ was high with Cronbach's α of 0.95.

3.3 | HAL_{full} versus HAL_{short}

3.3.1 | Agreement

The median (IQR) sum score of the HAL_{full} was slightly higher than the HAL_{short} (92.9 [66.5–100] vs. 92.2 [62.4–100]. The bias corrected mean (IQR) difference between the sum scores of the HAL_{full} and HAL_{short} was 1.2 with 95% CI of 1.1–1.4. 'Positive' scores (≤90) were reported in 45.2% for the HAL_{full} and 47.8% for the HAL_{short}. The vast majority (99.7%) of the patients who reported a score ≤90 on the HAL_{full}, reported a score ≤90 on the HAL_{short}, which is shown in Table 2.

TABLE 3 A priori defined hypotheses to determine construct validity of the $pedHAL_{short}$ and HAL_{short} and known-group validity of the HAL_{short}

$PedHAL_{short}$	**Confirmed**
Convergent validity	
r $pedHAL_{full}$ vs. $pedHAL_{short}$ >0.90	V
r $pedHAL_{full}$ – HEP-Test-Q vs. r $pedHAL_{short}$ – HEP-Test-Q: $\Delta r < 0.15$	V
r $pedHAL_{full}$ – CHO-KLAT vs. r $pedHAL_{short}$ – CHO-KLAT: $\Delta r < 0.15$	V
HAL_{short}	
Convergent validity	
r HAL_{full} vs. HAL_{short} >0.90	V
r HAL_{full} – HEP-Test-Q vs. r HAL_{short} – HEP-Test-Q: $\Delta r < 0.15$	V
Discriminant validity	
r HAL_{short} – RAND-36 physical functioning > r HAL_{short} – RAND-36 emotional well-being	V
Known-group validity	
Severity: severe vs. non-severe haemophilia	V
Age: 18–49 years vs. 50–88 years	V

r = correlation, Δ = delta: the delta in correlations between the pedHAL/HAL_{short} and pedHAL/HAL_{full} with the HEP-Test-Q/CHO-KLAT should be <0.15. CHO-KLAT: Canadian Haemophilia Outcomes-Kids' Life Assessment Tool, HAL: Haemophilia Activities List, HEP-Test-Q: Haemophilia & Exercise Project Test-Questionnaire, pedHAL: paediatric Haemophilia Activities List, RAND-36: RAND 36-item Health Survey.

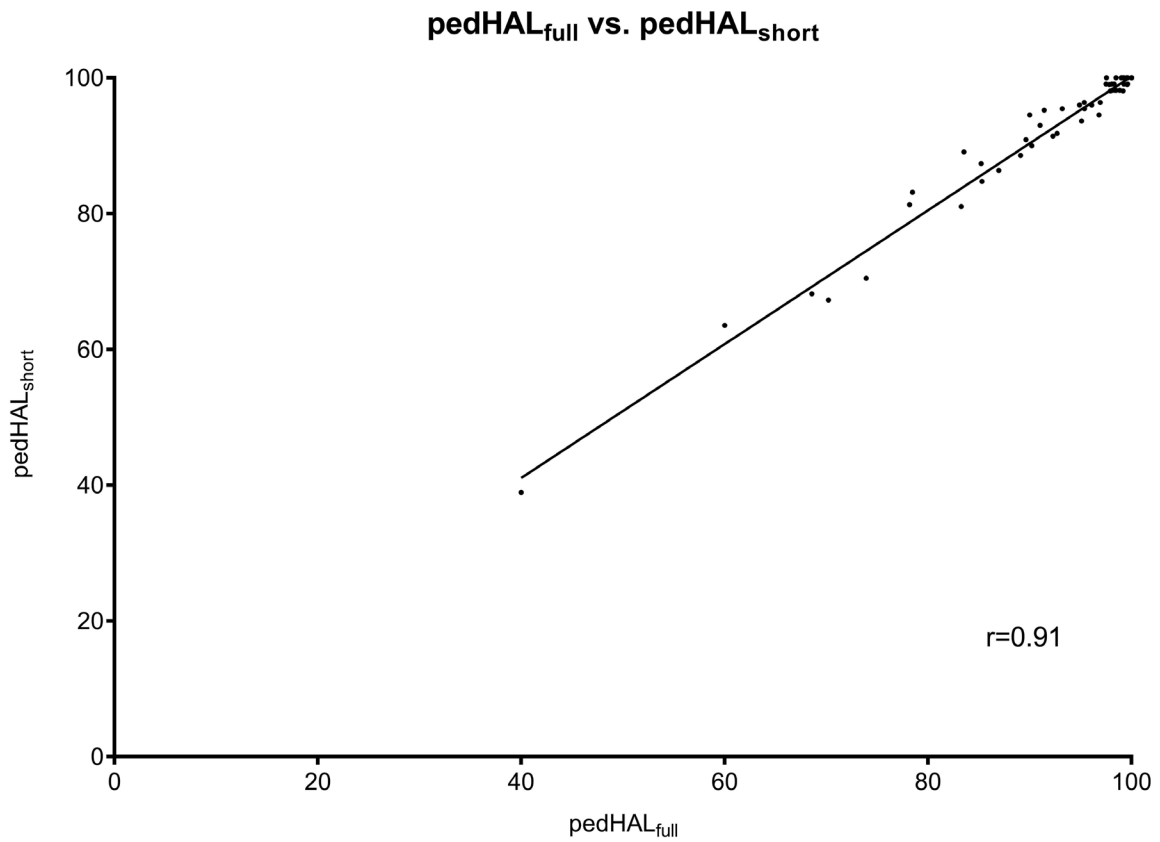

FIGURE 1 Scatterplot of the $pedHAL_{full}$ and $pedHAL_{short}$ sum scores ($n = 112$)

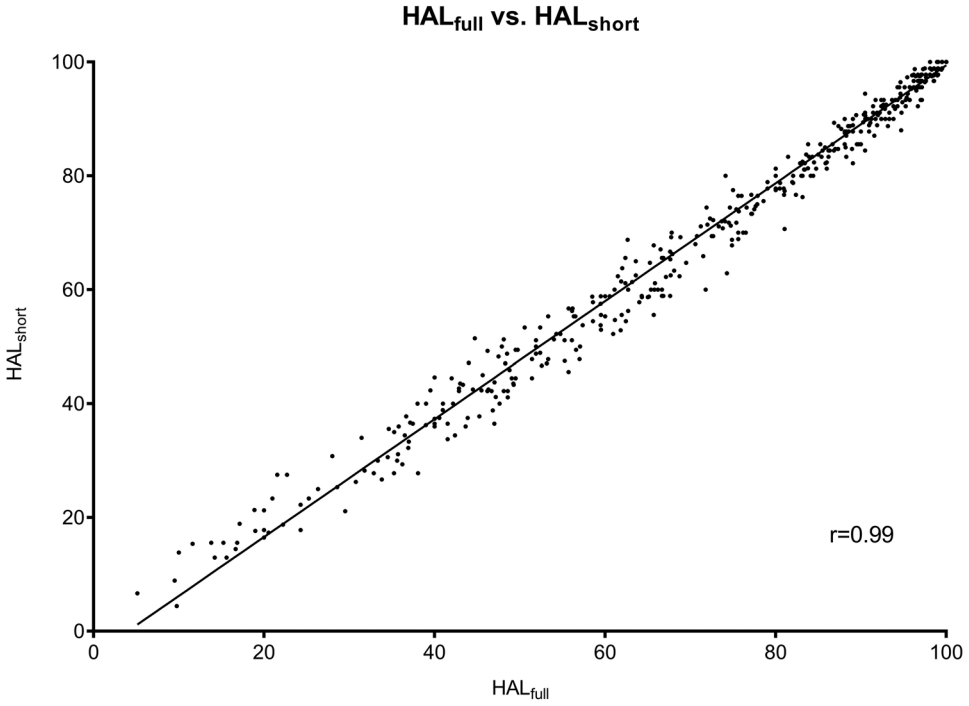

FIGURE 2 Scatterplot of the HAL_{full} and HAL_{short} sum scores ($n = 691$)

3.3.2 | Construct validity

The correlation between the HAL_{full} and HAL_{short} was 0.99 (95% CI: 0.99–0.99) and the sum scores of the HAL_{full} and HAL_{short} are shown in Figure 2. For both adults with mild/moderate haemophilia ($n = 447$) and adults with severe haemophilia ($n = 244$) the correlation was 0.99. For adults aged 18–49 years the correlation was 0.98 ($n = 334$) and for adults aged 50–88 years 0.99 ($n = 357$).

The hypotheses regarding convergent and discriminant validity were confirmed and shown in Table 3. The correlations between the HEP-test-Q and the HAL_{full} ($r = 0.77$) and HEP-test-Q and HAL_{short} ($r = 0.77$) were similar. In accordance with our hypotheses there was a strong correlation with the RAND-36 'physical functioning' ($r = 0.82$) and a weak correlation with the RAND-36 'emotional well-being' ($r = 0.21$).

The hypotheses regarding known-group validity were confirmed for the HAL_{short} and shown in Table 3. Adults with mild/moderate haemophilia reported less limitations than adults with severe haemophilia (median [IQR] HAL_{short}: 97.8 [85.6–100] vs. 62.5 [42.3–87.8], $p < 0.001$) (Table S1). In addition, the HAL_{short} was able to discriminate between adults with mild and moderate haemophilia (Table S2 and Figure S1). Adults aged 18–49 years reported less limitations than adults aged 50–88 years (median [IQR] HAL_{short}: 97.8 [82.2–100] vs. 82.2 [49.4–98.9], $p < 0.001$) (Table S1). Differences between groups were larger than the smallest detectable change of 10.2 of the HAL.[21] Boxplots with sum scores of both the HAL_{short} and HAL_{full} were shown in Figure 3 for subgroups on severity and age.

3.3.3 | Internal consistency

The internal consistency of the HAL_{short} was high with Cronbach's α of 0.97.

4 | DISCUSSION

This study analyzed $pedHAL_{short}$ and HAL_{short} data with the aim to determine their agreement with the original pedHAL/HAL as well as construct validity. The differences between the sum scores of the pedHAL/HAL_{full} and pedHAL/HAL_{short} were not clinically relevant and the sum scores showed high correlations (>0.9). The positive predictive value for the $pedHAL_{short}$ was 86.4% and for the HAL_{short} 99.7%. Compared to the original questionnaires, convergent validity and discriminant validity was confirmed. In addition, the HAL_{short} was able to discriminate between adults with different disease severities and ages (18–49 years vs. 50–88 years). The internal consistency of the $pedHAL_{short}$ and HAL_{short} was high (Cronbach's α: 0.95–0.97).

4.1 | Internal and external validity

The generalizability of the results to PWH with comparable treatment regimens was promoted by inclusion of a heterogeneous group of Dutch children and adults with haemophilia of all severities. However, severe haemophilia was overrepresented in children: 53% had severe haemophilia in the HiN data compared with 33% in the Dutch

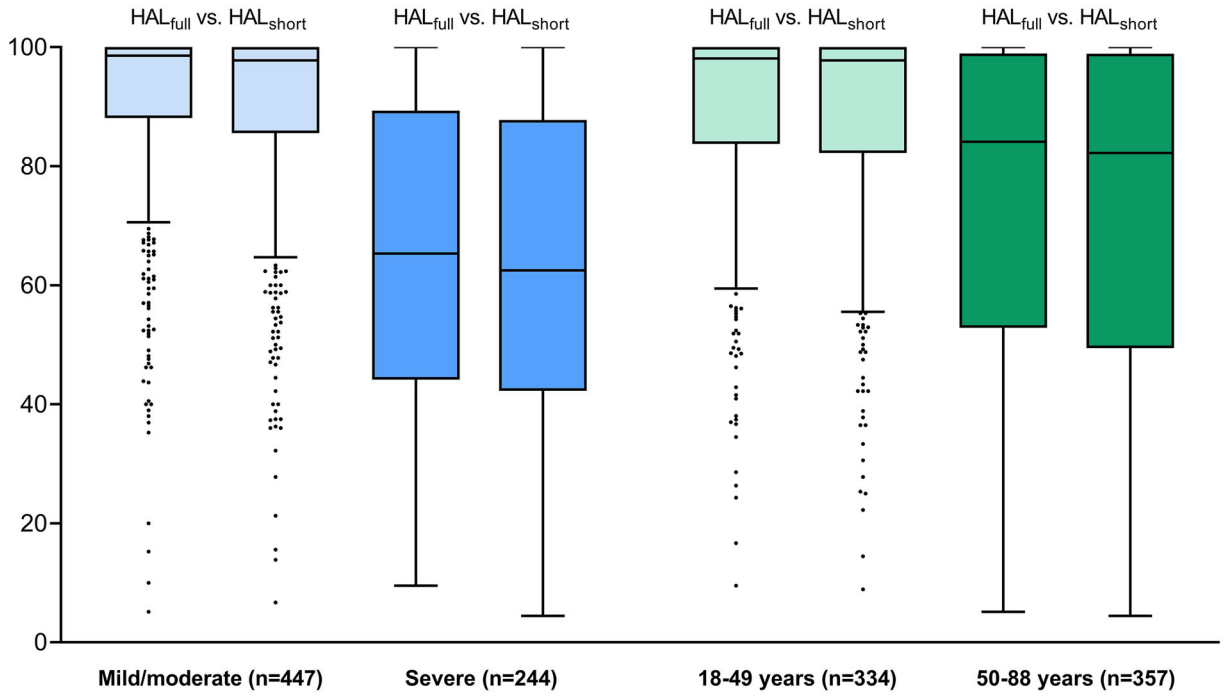

FIGURE 3 Boxplots of the HAL_{full} and HAL_{short} sum scores to show the differences between subgroups on severity and age (known-group validity) in adults

haemophilia population.[11] The high pedHAL scores reported by children suggested that these results are most applicable to intensively treated patients such as Dutch patients receiving early prophylaxis.

When comparing the pedHAL/HAL_{full} and pedHAL/HAL_{short}, the small differences between the sum scores were considered to be not clinically relevant. For the HAL the mean (95% CI) difference was 1.2 (1.1;1.4), which was well below the smallest detectable change of 10.2.[21] The mean (95% CI) difference between the $pedHAL_{full}$ and $pedHAL_{short}$ was even smaller at below 1 point (−0.3 [−0.5; −0.1]) and therefore by default below the smallest detectable change of the pedHAL.

In addition, to determine known-group validity of the HAL_{short} the smallest detectable change of the original HAL was used, because data on the smallest detectable change of the HAL_{short} are not available.

Rather than asking participants to complete two questionnaires, the pedHAL/HAL_{short} scores were derived from the original questionnaires completed for the HiN-6 study. We are unable to predict how this could have influenced the findings in the present study.

4.2 | Comparison with other studies

The construct validity of the HAL_{short} in the current study with Dutch subjects was comparable to the results of the HAL_{short} development study in American subjects (HAL_{short} versus RAND-36 'physical functioning' [$r = 0.82$] and HAL_{short} versus SF-36 Physical component score [$r = 0.77$]).[10] For the $pedHAL_{short}$ the current study was the first validation study and known-group validity was not assessed in the developmental stage of the HAL_{short}.

Known-group validity was not tested for the $pedHAL_{short}$ as the experts expected no differences between subgroups on severity or age in Dutch children receiving intensive treatment. This is in line with results from the CHO-KLAT, Haemo-QoL and PedsQL, reporting that none of these patient-reported outcomes were able to distinguish between moderate versus severe disease and different ages. This study did not include patients with mild haemophilia.[17] Internal consistency of the HAL_{short} (Cronbach's α 0.97) was comparable to other outcomes on physical functioning like the RAND-36 physical functioning and HEP-test-Q (Cronbach's α: 0.95–0.96).[12,19] Although reduction of one or more items can be considered,[24] the stepwise approach including item deletion based on internal consistency did not result in less items.[10]

To assess haemophilia-specific limitations in physical activities the $pedHAL_{short}$ and HAL_{short} are the shortest patient-reported outcomes. To solve issues like lengthy questionnaires, another development in the field of haemophilia is the introduction of generic Patient Reported Outcomes Measurement Information System (PROMIS) item banks. In adults, the PROMIS Computer Adaptive Test (CAT) 'physical function' was demonstrated to be a feasible, reliable and valid alternative to the HAL_{full} for PWH, with a low number of items (mean number of items was 6.0) which is even lower than the 18 items of the HAL_{short}.[25] However, before implementation of PROMIS CATs in day-to-day care and research several issues need to be addressed like good IT facilities for digital administration of CATs, clear visual feedback and cut-off scores which helps in interpreting, monitoring and discussing individual items or scores, and budget for using CATs.[26,27] Therefore, the HAL_{short} will still be of value for clinical practice. In addition, PROMIS items banks still lack validation in children with haemophilia.

4.3 | Clinical implications and future research

The pedHAL$_{short}$ and HAL$_{short}$ are considered to be valid and more feasible alternatives to the original questionnaires to measure limitations in activities and participation in children and adults with haemophilia. Both short versions can be derived from the original pedHAL/HAL, which allows for use in longitudinal studies. The questionnaires can be requested at www.vancreveldkliniek.nl.

Until now the pedHAL$_{short}$ and HAL$_{short}$ sum scores were calculated from the selected items of the original questionnaires. The next step is to evaluate the pedHAL$_{short}$ and HAL$_{short}$ when administered as short forms. In addition, we recommend to study the discriminative value of the pedHAL$_{short}$ by comparing pedHAL$_{short}$ scores of patients with intensive and less intensive treatment regimens.

5 | CONCLUSION

This study showed the agreement between the original pedHAL/HAL$_{full}$ and the pedHAL/HAL$_{short}$ and the construct validity of the pedHAL/HAL$_{short}$. The pedHAL$_{short}$ (22 items) and HAL$_{short}$ (18 items) were valid, internal consistent and more feasible alternatives to the original questionnaires to measure limitations in activities and participation in children and adults with haemophilia. The next step is to evaluate the construct validity of the pedHAL$_{short}$ and HAL$_{short}$ when administered as short forms.

ACKNOWLEDGEMENTS

We like to acknowledge the HiN-6 steering committee for initiating the HiN-6 project.

CONFLICT OF INTEREST

I.A.R. Kuijlaars does not have any conflict of interest regarding this manuscript other than membership of the group that developed the HAL. L.F.D. van Vulpen has performed consultancy for Sobi, Tremeau, and C.S.L. Behring and received a research grant from CSL Behring and Grifols, all paid to the institution. S.E.M. Schols has received travel grants from Bayer and Takeda, consultancy grants from Takeda and Novo Nordisk and she has received a research grant from Bayer. S.C. Gouw has received an unrestricted research grant from Sobi. The Van Creveldkliniek has received speaker's fees from Bayer, Baxter/Shire, SOBI/Biogen, CSL Behring and NovoNordisk; consultancy fees from Bayer, Biogen, CSL-Behring, Freeline, NovoNordisk, Roche and SOBI; and research support from Bayer, Baxter/Shire, Novo Nordisk, Pfizer and Biogen for work done by K. Fischer. The other authors have no competing interests.

AUTHOR CONTRIBUTIONS

I.A.R. Kuijlaars, J. van der Net, L.F.D. van Vulpen, S.C. Gouw and K. Fischer contributed to the design of the study, I.A.R. Kuijlaars performed the statistical analyses, I.A.R. Kuijlaars, J. van der Net and K. Fischer wrote the first draft of the paper, all authors contributed to interpretation of the data, modification of statistical analyses and the writing of the manuscript.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ORCID

Isolde A. R. Kuijlaars https://orcid.org/0000-0003-2920-2258
Janjaap van der Net https://orcid.org/0000-0003-2606-5104
Lize F. D. van Vulpen https://orcid.org/0000-0003-3242-5524
Samantha C. Gouw https://orcid.org/0000-0002-1957-4122
Kathelijn Fischer https://orcid.org/0000-0001-7126-6613

REFERENCES

1. van Genderen FR, van Meeteren NLU, van der Bom JG, et al. Functional consequences of haemophilia in adults: the development of the Haemophilia Activities List. *Haemophilia*. 2004;10:565-571.
2. van Genderen FR, Westers P, Heijnen L, et al. Measuring patients' perceptions on their functional abilities: validation of the Haemophilia Activities List. *Haemophilia*. 2006;12:36-46.
3. Groen W, Van der Net J, Lacatusu AM, et al. Functional limitations in Romanian children with haemophilia: further testing of psychometric properties of the paediatric haemophilia activities list. *Haemophilia*. 2013;19:116-125.
4. Groen WG, van der net J, Helders PJM, Fischer K. Development and preliminary testing of a Paediatric Version of the Haemophilia Activities List (pedhal). *Haemophilia*. 2010;16:281-289.
5. Fischer K, Poonnoose P, Dunn AL, et al. Choosing outcome assessment tools in haemophilia care and research: a multidisciplinary perspective. *Haemophilia*. 2017;23:11-24.
6. Swinkels RAHM, Van Peppen RPS, Wittink H, Custers JWH, Beurskens AJHM. Current use and barriers and facilitators for implementation of standardised measures in physical therapy in the Netherlands. *BMC Musculoskelet Disord*. 2011;12:106.
7. Duncan EAS, Murray J. The barriers and facilitators to routine outcome measurement by allied health professionals in practice: a systematic review. *BMC Health Serv Res*. 2012;12:96.
8. van Muilekom MM, Teela L, van Oers HA, et al. Patients' and parents' perspective on the implementation of patient reported outcome measures in pediatric clinical practice using the KLIK PROM portal. *Qual Life Res*. 2022;31:241-254.
9. Kuijlaars IAR, van der Net J, Bouskill V, et al. Shortening the paediatric Haemophilia Activities List (pedHAL) based on pooled data from international studies. *Haemophilia*. 2021;27:305-313.
10. Kuijlaars IAR, Net J, Buckner TW, et al. Shortening the Haemophilia Activities List (HAL) from 42 items to 18 items. *Haemophilia*. 2021;27:1062-1070.
11. Hassan S, van Balen EC, Smit C, et al. Fifty years of hemophilia treatment in the netherlands. *J Thromb Haemost*. 2021; (Accepted for publication).
12. Von Mackensen S, Czepa D, Herbsleb M, Hilberg T. Development and validation of a new questionnaire for the assessment of subjective physical performance in adult patients with haemophilia – the HEP-Test-Q. *Haemophilia*. 2010;16:170-178.
13. von Mackensen S, Hilberg T, Valentino LA, Kurnik K, Khair K. Validation of the Haemophilia & Exercise Project-Test-Questionnaire (HEP-Test-Q) – an instrument for the assessment of subjective physical functioning in children with haemophilia. *Haemophilia*. 2018;24:1-8.

14. Manco-Johnson M, Morrissey-Harding G, Edelman-Lewis B, Oster G, Larson PJ. Development and validation of a measure of disease-specific quality of life in young children with haemophilia. *Haemophilia*. 2004;10:34-41.
15. Young NL, Wakefield C, Burke TA, et al. Updating the Canadian hemophilia outcomes-kids life assessment tool (CHO-KLAT version2.0). *Value Heal*. 2013;16:837-841.
16. Limperg PF, Terwee CB, Young NL, et al. Health-related quality of life questionnaires in individuals with haemophilia: a systematic review of their measurement properties. *Haemophilia*. 2017;23:497-510.
17. Young NL, Bradley CS, Wakefield CD, et al. How well does the Canadian haemophilia outcomes-kids' life assessment tool (CHO-KLAT) measure the quality of life of boys with haemophilia? Nancy. *Pediatr Blood Cancer*. 2006;47:305-311.
18. VanderZee KI, Sanderman R, Heyink JW, De Haes H. Psychometric qualities of the RAND 36-item health survey 1.0: a multidimensional measure of general health status. *Int J Behav Med*. 1996;3:104-122.
19. Solovieva S, Santavirta N, Santavirta S, Konttinen YT. Assessing quality of life in individuals with hereditary blood coagulation disorders. *Qual Life Res*. 2004;13:987-1000.
20. van der Zee KI, Sanderman R. Het meten van de algemene gezondheidstoestand met de Rand-36. 2012.
21. Kuijlaars IAR, van Emst M, van der Net J, Timmer MA, Fischer K. Assessing the test–retest reliability and smallest detectable change of the haemophilia activities list. *Haemophilia*. 2021;27:108-112.
22. Kuijlaars IAR, van der Net J, Schutgens REG, Fischer K. The paediatric haemophilia activities list (pedHAL) in routine assessment: changes over time, child-parent agreement and informative domains. *Haemophilia*. 2019;25:953-959.
23. Schober P, Schwarte LA. Correlation coefficients: appropriate use and interpretation. *Anesth Analg*. 2018;126:1763-1768.
24. Terwee CB, Bot SDM, de Boer MR, et al. Quality criteria were proposed for measurement properties of health status questionnaires. *J Clin Epidemiol*. 2007;60:34-42.
25. Kuijlaars IAR, Teela L, Vulpen LFD, et al. Generic PROMIS item banks in adults with hemophilia for patient-reported outcome assessment: feasibility, measurement properties, and relevance. *Res Pract Thromb Haemost*. 2021;5:1-14.
26. Foster A, Croot L, Brazier J, Harris J, O'cathain A. The facilitators and barriers to implementing patient reported outcome measures in organisations delivering health related services: a systematic review of reviews. *J Patient-Reported Outcomes*. 2018;2:1-16.
27. van Muilekom MM, Luijten MAJ, van Oers HA, et al. From statistics to clinics: the visual feedback of PROMIS® CATs. *J Patient-Reported Outcomes*. 2021;5:55.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Kuijlaars IAR, van der Net J, van Vulpen LFD, et al. Validation of the pedHAL$_{short}$ and HAL$_{short}$ in Dutch children and adults with haemophilia. *Haemophilia*. 2022;28:1007–1015. https://doi.org/10.1111/hae.14628