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ORIGINAL ARTICLE

Reliability and construct validity of the ACTIVLIM-Hemo and Haemophilia Activities List (HAL) questionnaires in individuals with haemophilia

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Abstract

Objective: The objective of this study is to assess the reliability and construct validity of ACTIVLIM-Hemo, a newly developed Rasch-built questionnaire designed to evaluate activity limitations in people with haemophilia (PwH), in comparison with the Haemophilia Activities List (HAL), which was developed using Classical Test Theory.

Methods: A total of 130 participants with haemophilia A or B were included. They underwent various assessments, including joint health scoring (HJHS), functional tests (TUG and 2MWT) and completed questionnaires such as the BPI, IPAQ, HAL and ACTIVLIM-Hemo. Reliability indices and the minimum detectable change (MDC95) were determined for ACTIVLIM-Hemo and for HAL. Construct validity was evaluated through correlations and multiple linear regression, considering demographic and clinical factors.

Results: Both ACTIVLIM-Hemo (Person Separation Index = 0.92) and HAL (Cronbach's $\alpha = 0.98$) demonstrated high reliability. The MDC95 for ACTIVLIM-Hemo represented 11.6% of its measurement range, while for HAL, it amounted to 18/100 score points. Activity limitations measured by both instruments were significantly correlated with demographic and clinical factors. Joint health (HJHS), pain severity (BPI) and walking performance (2MWT) emerged as the main predictors of activity limitations, explaining 75% of the variance in ACTIVLIM-Hemo and 60% in HAL.

Conclusion: ACTIVLIM-Hemo stands as a reliable and valid instrument for assessing activity limitations in PwH. Both instruments exhibited significant correlations with demographic and clinical factors, but ACTIVLIM-Hemo displayed a more homogeneous construct. Given its linear scale and lower MDC95 and better targeting, ACTIVLIM-Hemo shows promise as a patient-centric instrument for assessing responsiveness to treatment during individual follow-up.

KEYWORDS
activity limitations, bleeding disorder, haemophilia, International Classification of Functioning disability and health (ICF), outcome assessment, questionnaire, Rash analysis

1 | INTRODUCTION

People with haemophilia (PwH) often experience pain, musculoskeletal damage and functional limitations as a result of recurrent bleedings in the muscles and the joints. As recommended by the World Health Organization, functional assessment should be performed according to the International Classification of Functioning, Disability and Health (ICF),[1] which provides a framework including the 'body structures and functions', 'activities' and 'participation' domains. A global functional assessment of PwH should therefore not only include aspects of joints' structure and function, but should also capture how their degradation affects the persons' ability in executing daily activities, that is 'activity limitations'. Moreover, with the advent of new therapies and subsequent improvements in joint health in PwH,[2] it is essential to target activities that are more challenging and explore the whole functional spectrum ranging from minimal to very high. In addition, functional limitations persisting in PwH are mostly impacting the ankle,[3] especially in activities where the body weight is no longer supported by both feet such as jumping and running.

Unlike observable variables such as joint's range of motion, 'activity limitations' is a latent variable that cannot be directly observed; it is hidden within the individual such as intelligence or pain and can only be measured using specific instruments such as questionnaires. These questionnaires typically report ordinal scores (e.g. frequency of limitations reported as 'always', 'sometimes' or 'never', respectively scored as 0, 1 and 2). However, ordinal scores do not support standard arithmetic operations such as computing the average performance within a sample of PwH or the change of performance over time but merely support non-parametric operations on ranks.[4–6] Nevertheless, ordinal scores have been widely used in Classical Test Theory (CTT) to develop assessments of patients' functional status in various diagnoses including haemophilia, while modern psychometric approaches rely on a latent variable (e.g. activity limitations). Additionally, one of the main advantages of modern psychometry over CTT, is that the latent variable is linear and is amenable to usual arithmetic. Indeed, probabilistic models such as the Rasch model formulate the probability of a PwH with a given level of activity limitations to select a given response to a given item (e.g. running or riding a bicycle).[7–9] This probabilistic formulation can then be used to determine[1] the level of activity limitations of each PwH and[2] the level of difficulty (or the weight) of each item. According to Langley,[6] the Rasch model is the only model providing the necessary and sufficient transformations, if possible, between ordinal observations and interval measures of patient-reported outcome or cost effectiveness claims.

At present time, activity limitations in PwH are typically assessed with the Functional Independence Score in Haemophilia (FISH) and the Haemophilia Activities List (HAL).[10,11] The FISH is a performance-based test calibrated for PwH with significant musculoskeletal impairments and is therefore hardly used in countries with access to regular haemophilia treatments.[10] The HAL is a self-reported questionnaire covering seven domains of activity limitations but also includes some items of participation[11] To date, although the HAL has been developed and validated with CTT, it remains the most widely used patient-reported outcome thanks to its well documented relationship with the clinical and functional status in PwH.[11–16]

Recently, the ACTIVLIM-Hemo has been developed with the Rasch model to assess activity limitations in PwH.[17] The ACTIVLIM-Hemo questionnaire reports the patient-perceived difficulty in executing 22 daily activities. The ACTIVLIM-Hemo reports a linear and unidimensional measure of activity limitations that is amenable to usual linear analysis such as correlations or regressions. The linear scaling of ACTIVLIM-Hemo meets the requirements for objective measurement[6] and allows quantitative comparisons of activity limitations between different PwH, between treatments and over time.

While ACTIVLIM-Hemo demonstrates a high correlation with the HAL, it offers a lower ceiling effect (1% rather than 9% for the HAL) allowing less limited PwH to be targeted by this instrument.[17] This study aims to consolidate the clinical applicability of ACTIVLIM-Hemo by investigating its reliability and construct validity in correspondence with the HAL.

2 | METHODS

2.1 | Participants

Overall, 130 PwH of the Belgian Hemophilia Comprehensive Treatment Centers of the *Cliniques universitaires Saint-Luc* Brussels and *Universitair Ziekenhuis Antwerpen* were screened between June 2020 and April 2022. Inclusion criteria were males aged over 18 years with mild, moderate or severe haemophilia A or B, on unmodified haemophilia therapy over the last 6 months. The study was approved by local ethical committees of both hospitals (2019/28OCT/469, B3002011942304). Written informed consent was obtained from all participants. The study sample is presented in Table 1.

2.2 | Procedures

The same investigator (VAC) performed the Haemophilia Joint Health Score 2.1 (HJHS),[18] the Timed Up and Go (TUG)[19] and the two-minute walking test (2MWT).[20] Afterwards, participants were asked to fill in the Brief Pain Inventory (BPI),[21] the International Physical Activity Questionnaire (IPAQ),[22] the HAL[11] and the ACTIVLIM-Hemo.[17]

TABLE 1 Characteristics of the haemophilia group ($n = 130$).

Age (years)	45 [29;61]
Weight (kg)	80 [69;89]
Height (m)	1.77 [1.73;1.81]
BMI (kg/m^2)	25.4 [22.6;28.7]
Haemophilia type	
A	101
B	29
Factor deficiency	
Severe (FVIII or IX activity < 1 IU/dL)	80
Moderate (FVIII or IX activity between 1 and 5 < IU/dL)	29
Mild (FVIII or IX activity 5 ≥IU/dL)	21
Current medical treatment	
On-demand	41
Prophylaxis	68
Emicizumab	20
Gene therapy	1
Patients with upper limb surgery	7
Unilateral elbow synovectomy	2
Bilateral elbow synovectomy	3
Elbow replacement	1
Radial head excision	1
Patients with lower limb surgery	45
Unilateral THR	6
Bilateral THR	1
Unilateral TKR	17
Bilateral TKR	14
Unilateral ankle synovectomy	4
Unilateral ankle arthrodesis	11
Bilateral ankle arthrodesis	1
Unilateral TAR	2
Hemophilia Joint Health Score 2.1 (/120 pts)	14 [4;37]
BPI-Pain Severity item (/10 pts) ($n = 127$)	1.5 [.3;3.3]
TUG (s) ($n = 126$)	9.1 [8.3;10.1]
2MWT (m) ($n = 126$)	191 [171;213]
IPAQ (min/week) ($n = 123$)	500 [200;1260]
Hemophilia Activities List (/100pts) ($n = 127$)	77 [57;91]
ACTIVLIM-Hemo (/100 pts)	65 [48;88]

Values are *n* or median [P25;P75].
Abbreviations: 2MWT, 2-Minutes Walk Test; BMI, Body Mass Index; BPI, Brief Pain Inventory; IPAQ, International Physical Activity Questionnaire; TAR, total ankle replacement; THR, total hip replacement; TKR, total knee replacement; TUG, Timed-Up-and-Go test .

3 | STATISTICAL ANALYSES

3.1 | Reliability

The reliability of the HAL score was determined according to the CTT with Cronbach's alpha.[23] The reliability of ACTIVLIM-Hemo was determined according to the Rasch Measurement Theory,[7,24] with the Person Separation Index (PSI),[8] which can be interpreted like Cronbach's alpha. This analysis was performed with RUMM2030 (RUMM Laboratory, Perth, Australia). Both reliability analyses were performed in order to compare the error of both instruments. The error for each instrument was used to determine the minimum detectable change with a 95% confidence interval (MDC_{95}).[25]

3.2 | Construct validity

The correlation between HAL scores and ACTIVLIM-Hemo measures was determined with Spearman correlation coefficient. Correlations of demographic and clinical indices with activity limitations as measured by HAL and by ACTIVLIM-Hemo were determined with Spearman correlation coefficients (ρ) for ordinal and categorial variables or with Pearson correlation coefficients (r) for continuous and interval variables. The level of statistical significance was set to .05 for all analyses.

Variables that correlated significantly and at least weakly with activity limitations (conservative significance threshold of 0.2) were included in a forward stepwise linear regression to build the best predictive equations of activity limitations as reported by ACTIVLIM-Hemo and HAL. All statistical analyses were performed with SPSS 23 (IBM Corp. Armonk, New York, USA).

3.3 | Dependent variables

The HAL includes 42 items covering seven domains of daily life activities[11] reporting a total score ranging from 0 to 100, where higher scores indicate better functional status. The ACTIVLIM-Hemo includes 22 activities[17] where participants self-reported their perceived difficulty in performing each activity as 'impossible', 'difficult' or 'easy'. The responses to ACTIVLIM-Hemo were converted into a 0-100% linear measure (%range) using the online engine available at www.rehab-scales.org. Higher measures indicate lower activity limitations.

3.4 | Independent variables

The HJHS was used to assess structure and function in six joints (elbows, knees and ankles). The total score (20 points per joint) ranges from 0 to 120.[13,18]

Physical functioning was assessed with the 2MWT and the TUG.[26] The 2MWT was administered in a quiet hallway where participants

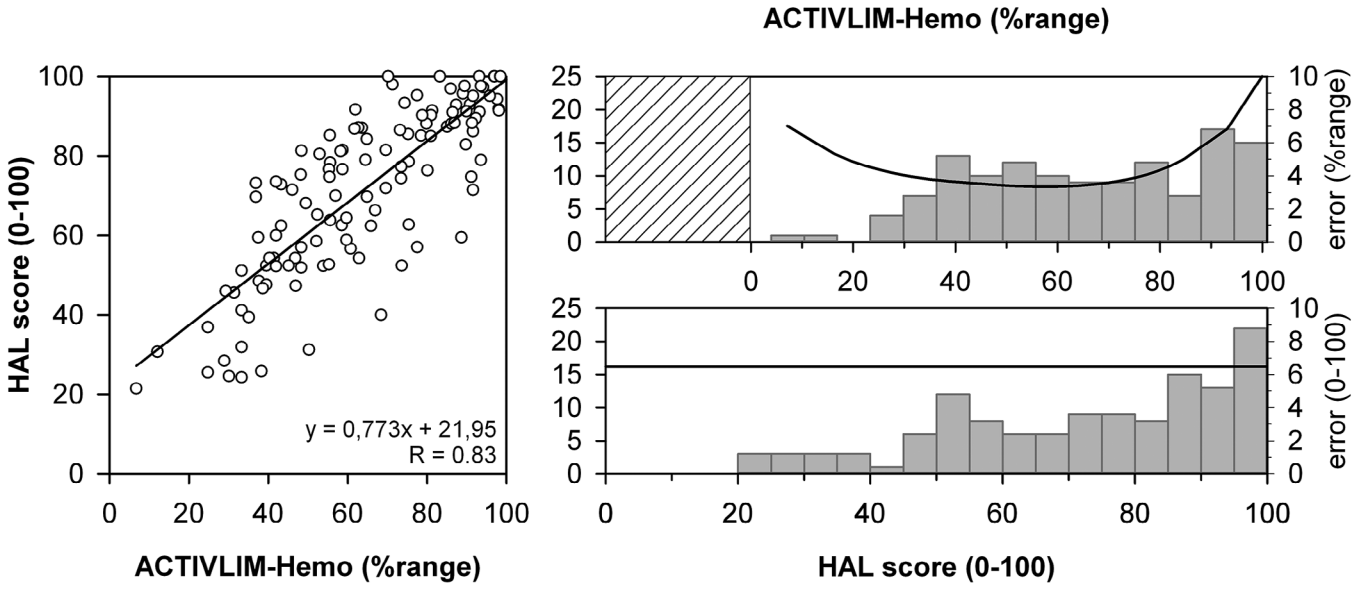

FIGURE 1 Relationship between the ACTIVLIM-Hemo measures and the HAL scores about activity limitations in PwH (left panel). Although the HAL score is ordinal in nature and merely approximates a linear scale, their relationship denotes a high correlation ($R = 0.83$). The distribution of activity limitations reported by both instruments (histogram, left ordinate axis) show an adequate correspondence where ACTIVLIM-Hemo measures ranging from 22 to 99 correspond to HAL scores ranging from 0 to 100 (right panel). Activity limitations corresponding to HAL scores lower than 22 (i.e. very severely affected patients) correspond to levels below the floor of ACTIVLIM-Hemo (hatched area). The error of measurement of both instruments (plain line, right ordinate axis) evolves along the measurement range for ACTIVLIM-Hemo with a minimum of 3.3 %range at a level of activity limitations around 58 %range and an average error of 4.2 %range, while it is only determined on average for HAL as 6.5 score points. Note that the error varies along of measurement range for ACTIVLIM-Hemo, with lower errors in regions where more activities provide information to locate PwH, while for HAL, the error is only known on average along the score range.

were asked to walk as far as they could in 2 min. The distance walked by the participant was recorded in meters. The TUG measured the time required for participants to stand up from a chair, walk 3 m, turn around, walk back to the chair and sit down again. The TUG was repeated twice and the mean time was used.

The IPAQ[22] was used to assess the duration of physical activity during the last week in domains of job-related, transportation, household, recreational activities and sitting. Pain severity within the last 24 h was assessed as the mean score regarding the worst, least, average and current pain self-reported on a scale ranging from 0 ('no pain') to 10 ('worst imaginable pain') using the BPI-Pain Severity item (BPI-PS).[27]

4 | RESULTS

The overall activity limitations measured by ACTIVLIM-Hemo ranged from 7% to 100 % of the full scale; the HAL scores ranged from 21 to 100 demonstrating a high correlation of both instruments ($R = 0.83$) as shown in Figure 1. The results recorded with both instruments report a comparable distribution of activity limitations in our sample of PwH. Nevertheless, the targeting differs between both instruments. Indeed, ACTIVLIM-Hemo includes more difficult activities that are more targeted to the levels of activity in PwH and is overall more challenging than HAL. This also indicates that activity levels corresponding to HAL sores below 22 (corresponding to very severely affected PwH) cannot be measured with ACTIVLIM-Hemo.

4.1 | Reliability

Both instruments demonstrate a high reliability in our sample, with a PSI of 0.92 for ACTIVLIM-Hemo and a Cronbach α of .98 for the HAL. ACTIVLIM-Hemo shows a higher precision around the centre of the scale with an error of 3.3 %range, while its error increases towards the less informative extremities of the scale; the average error being of 4.2 %range and the MDC_{95} of 11.6 %range. HAL demonstrates a larger ceiling effect than ACTILIM-Hemo for higher levels of activity; its average error is of 6.5/100 score points and constant throughout the scoring range; its MDC_{95} is of 18/100 score points.

4.2 | Construct validity

The relationship between demographic and clinical indices with activity limitations as measured with ACTIVLIM-Hemo and HAL is presented in Table 2. All factors showed a significant correlation with activity limitations except for type of haemophilia, presence of upper limb surgery and IPAQ. Overall, activity limitations were more related to any demographic or clinical index when measured with ACTIVLIM-Hemo than with the HAL, except for the BPI-PS. A strong relationship was observed with HJHS, with 2MWT for ACTIVLIM-Hemo and with BPI-PS for HAL. A moderate relationship was observed with lower limb surgery, with age, BPI-PS and TUG for ACTIVLIM-Hemo and for 2MWT

TABLE 2 Relation of ACTIVLIM-Hemo and HAL with clinical and functional status.

	ACTIVLIM-Hemo		HAL	
	Correlation coefficient	*p*	Correlation coefficient	*p*
Age[a]	$R = -0.432$	<.001	$r = -0.291$	.001
BMI[a]	$R = -0.206$	.019	$r = -0.223$	.012
Type of haemophilia	$r = -0.047$	.595	$r = -0.103$	.248
Severity[ag]	$r = -0.326$	<.001	$r = -0.328$	<.001
Presence of upper limb surgery	$r = -0.076$	.388	$r = -0.074$	.409
Presence of lower limb surgery[a]	$r = -0.525$	<.001	$r = -0.457$	<.001
HJHS[a]	$r = -0.777$	<.001	$r = -0.676$	<.001
BPI-PS[a]	$r = -0.545$	<.001	$r = -0.624$	<.001
TUG[a]	$R = -0.501$	<.001	$r = -0.383$	<.001
2MWT[a]	$R = 0.634$	<.001	$r = 0.478$	<.001
IPAQ	$r = 0.173$	.056	$r = 0.102$	.261

BMI, Body Mass Index; BPI-PS, Brief Pain Inventory-Pain Severity item; HAL, Hemophilia Activity List; HJHS:,Hemophilia Joint Health Score; IPAQ, International Physical Activity Questionnaire; TUG, Timed-Up-and-Go test; 2MWT, 2-Minutes Walk Test;.

[a]Independent variable included in the stepwise multiple regression. The strength of the relationships between variables were defined as absent or none for $r < 0.2$, weak for $0.2 \leq r < 0.4$, moderate for $0.4 \leq r < 0.6$, strong for $0.6 \leq r < 0.8$ and very strong for $0.8 \leq r < 1$.

for HAL. A weak relationship was observed for BMI and severity of the disease and for age and TUG for HAL.

Four independent predictors were retained in the stepwise multiple linear regressions able predict 75% of the variance in ACTIVLIM-Hemo and 60% of the variance in HAL. Regardless of the assessment tools used to evaluate activity limitations, the three most significant predictors were HJHS, BPI-PS and 2MWT.

The total variance predicted by the regression model for activity limitations as measured by both instruments aligned with the variance predicted solely by the HJHS, that is 0.61 for ACTIVLIM-Hemo and 0.42 for HAL. The regression equation exhibited a similar pattern for both instruments, indicating that the activity level starts off with high levels in PwH and decreases as joint health deteriorates or when experiencing pain (Table 3). However, the activity level increases with higher walking performance. Additionally, a fourth predictor was included for each instrument, namely the TUG for ACTIVLIM-Hemo and the BMI for HAL, which slightly enhanced the explained variance in activity limitations (Table 3).

5 | DISCUSSION

This study aimed to investigate the reliability and construct validity of the ACTIVLIM-Hemo questionnaire originally built as a linear and unidimensional instrument with modern psychometry, in comparison to the HAL which is the most widely used tool to assess activity limitations in PwH and originally built with classical test theory.

By studying the correlation with demographic and clinical indices, factors influencing the performance of both questionnaires have been assessed to compare the performance of both instruments. Although the HAL score is ordinal in nature and only approximates a linear scale, the correlation between both instruments indicates that the HAL score range encompasses a wider range of activity limitations than ACTIVLIM-Hemo. Indeed, the measurement range of the ACTIVLIM-Hemo starts at a HAL score of 22 and it ends at the end of the HAL score range. This observation further illustrates a previous report[17] indicating that ACTIVLIM-Hemo demonstrates a lower ceiling effect (1% of the sample) than the HAL (9%).

5.1 | Reliability

The reliability of both instruments was high. The HAL demonstrated a Cronbach α of 0.98 while ACTIVLIM-Hemo showed a PSI of 0.92 in our sample of PwH. Nevertheless, the capacity of both instruments to capture significant functional change over time is higher for the ACTIVLIM than for the HAL. Indeed, the MDC_{95} obtained for both instruments indicates that, for a single patient assessed twice, the safest threshold for identifying a statistically detectable change of ACTIVLIM-Hemo is of 11.6 %range, while a change of 18/100 score points is required for the HAL. Additionally, since the ACTIVLIM-Hemo reports activity limitations on a linear scale, a change of 10% represents the same change of activity at all levels of the scale. Conversely, the HAL reports ordinal scores that are known for their lack of linearity and impedes the measurement of change.[4–9] Also, since the measurement error is only known on average for the HAL, the clinical interpretation of change scores further complicates the assessment of true significant change for a single patient. This stems for a restricted use of the HAL as a cohort descriptive assessment tool while the ACTIVLIM-Hemo, being built with a range-specific known discrimination, offers a larger potential to assess responsiveness to treatment across its measurement range.

TABLE 3 Stepwise multiple linear regression of ACTIVLIM-Hemo and HAL.

ACTIVLIM-Hemo (%range)				
Variables	**B**	**SE**	**D adj. R^2**	**Final model**
Constant	78.91	10.931	–	ACTIVLIM-Hemo(%) = 78.91 – 0.61 * HJHS + 0.11 * 2MWT – 2.82 * BPI-PS – 1.39 * TUG
HJHS (/120 pts)	−0.61	0.058	0.61	
2MWT (m)	0.11	0.036	0.08	
BPI-PS (/10 pts)	−2.82	0.596	0.05	adj. R^2 = .75
TUG (s)	−1.39	0.518	0.01	F = 89.3 p < .001
HAL (0-100)				
Variables	**B**	**SE**	**D adj. R^2**	**Final model**
Constant	87.87	11.094	–	HAL = 87.87 – 0.45 * HJHS – 3.64 * BPI-PS + 0.10 * 2MWT−0.62 * BMI
HJHS (/120 pts)	−0.45	0.070	0.42	
BPI-PS (/10 pts)	−3.64	0.735	0.13	
2MWT (m)	0.10	0.035	0.04	adj. R^2 = 0.60
BMI (kg/m^2)	−0.62	0.265	0.02	F = 46.4, p < .001

2MWT, 2-Minutes Walk Test; BMI, Body Mass Index; BPI-PS, Brief Pain Inventory-Pain Severity item; HAL, Hemophilia Activity List score; HJHS, Hemophilia Joint Health Score; TUG, Timed-Up-and-Go test.

5.2 | Construct validity

The ACTIVLIM-Hemo and the HAL demonstrated significant correlations with demographic and clinical indices. While the correlations of ACTIVLIM-Hemo with other indices have not yet been studied, the present correlations for the HAL strongly align with previous studies. Indeed, the strong correlation of the HAL with joint impairment status as scored with the HJHS 2.1 (ρ = 0.676) is similar to a previous single-centre assessment (ρ = −0.66),[12] even if multicentre studies tend to demonstrate lower correlations.[13,14] The weak correlation of the HAL with the TUG (ρ = −0.383), although slightly lower, is also consistent with the results of the developmental study for the HAL (ρ = −0.59).[11] The HAL shows no significant correlation with the IPAQ in our study (ρ = 0.102) although a weak correlation is reported in a previous study when considering the HAL sub-scores (R = 0.30 for upper limbs and R = 0.36 for lower limbs).[16] The slight differences observed between both studies may be explained by the error inherent to recall-based self-reports used to score activity level with the IPAQ.

Overall, our results show that activity limitations are generally more related to any demographic or clinical index when measured with ACTIVLIM-Hemo or the HAL. This indicates that the nature of the construct underlying the ACTIVLIM-Hemo is more homogeneous than the construct underlying the HAL. Although the HAL mainly includes items related to activity limitations, for example 'Bending forward' or 'Running', some items also involve the patient's participation in life situations, for example 'Going on a holiday'.[28] Such multidimensionality indicates that both activity and participation influence the HAL score and hence deflate its relationship with well-known determinants of activity limitations in PwH.[11,12] As a consequence, a patient change in HAL score could be supported by either a change in activity or a change in participation, leaving the clinician with no ability to determine which domain of functioning has changed more. Conversely, the ACTIVLIM-Hemo was built from activities selected to delineate a unidimensional construct, where each item contributes complementary information of the same nature to determine the level of activity of PwH. In clinical practice, since the ACTIVLIM-Hemo is a unidimensional scale, a patient change affects the odds for the patient to succeed any item of the questionnaire by the exact same amount (actually the odds of passing any given level of difficulty along the linear scale increases by the same amount all along the scale).[6–9]

The more homogeneous nature of ACTIVLIM-Hemo compared to the HAL is also supported by the results of the multiple linear regression. Indeed, four predictors were retained for both instruments, with a fair amount of variance explained (adj R^2 = 0.75 for ACTIVLIM-Hemo and 0.60 for HAL). The results show that activity limitations in PwH, whether measured with ACTIVLIM-Hemo or with HAL, are mainly related to joint structure and function as measured by the HJHS, pain as measured with the BPI-PS and walking performance as measured with the 2MWT. This common set of predictors is completed either by lower extremity function as measured with the TUG for the ACTIVLIM-Hemo or by morphology as expressed by the BMI for HAL. This suggests that joint health is the primary factor influencing activity limitations in PwH, with an even greater impact on ACTIVLIM-Hemo (61% of the variance explained) than on the HAL (42% of the variance explained). A post-hoc multiple linear regression was performed by including the joint structure component (extent of swelling, duration of swelling, muscle atrophy and crepitus on motion) and the joint function component (flexion/extension loss, joint pain and strength) of the HJHS as two separate predictors. The variance explained by the joint function component of the HJHS remained at

0.61 for ACTIVLIM-Hemo and at 0.42 for HAL, leaving the coefficients of other predictors than the HJHS unchanged. The joint structure component of the HJHS was not retained as a significant predictor of activity limitations. This observation confirms that joint structure and joint function are related, though independent, components of functioning in PwH. In addition to other factors than joint health, only joint function is related to activity limitations in PwH and is, by itself, the most important factor of activity limitations in haemophilia.

5.3 | Conclusion and perspectives

This study compares the reliability and the construct validity of ACTIVLIM-Hemo and of HAL. ACTIVLIM-Hemo showed a lower ceiling effect in comparison with HAL. With measures reported on a linear scale, ACTIVLIM-Hemo offers an easier interpretation of functional change as compared to HAL. Although, both instruments demonstrate a high reliability in our sample which reinforces their interest for cohort studies in PwH, ACTIVLIM-Hemo demonstrates a lower MDC_{95} than HAL indicating a higher potential to assess responsiveness to treatment in individual follow-up. Given its intrinsic psychometric properties,[17] ACTIVLIM-Hemo delineates a more homogeneous construct than HAL, which also facilitates the clinical interpretation of the patient's functional status. Altogether, ACTIVLIM-Hemo is a measure of activity limitations in PwH that fills the lack of instruments that meet the minimum standard for measurement as claimed by Langley.[6] With its unique psychometric properties, ACTIVLIM-Hemo is a very promising patient centric instrument to assess activity limitations in haemophilia, especially in PwH with access to regular haemophilia treatments.

AUTHOR CONTRIBUTIONS

Sébastien Lobet and Massimo Penta designed the research study, analysed the data and wrote the manuscript. Anthe Foubert and Valérie-Anne Chantrain acquired the data. Anthe Foubert, Valérie-Anne Chantrain, Cedric Hermans and Catherine Lambert reviewed the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the manuscript and there is no financial interest to report. We certify that this submission represents original work and is not currently being considered for publication elsewhere.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The study was approved by local ethical committees of both hospitals involved in the study (2019/28OCT/469, B3002011942304).

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REFRENCES

1. WHO. *The International Classification of functioning, disability and health*. World Heal Organ; 2001;18:237.
2. Kiialainen A, Niggli M, Kempton CL, et al. Effect of emicizumab prophylaxis on bone and joint health markers in people with haemophilia A without factor VIII inhibitors in the HAVEN 3 study. *Haemophilia*. 2022;28(6). [Internet]. [cited 2022 Dec 22].
3. Hmida J, Hilberg T, Ransmann P, et al. Most subjectively affected joints in patients with haemophilia—what has changed after 20 years in Germany? *Haemophilia*. 2022;28(4):663-670.
4. Merbitz C, Morris J, Grip J. Ordinal scales and foundations of misinference. *Arch Phys Med Rehabil*. 1989;70(4):308-312.
5. Wright B, Linacre J. Observations are always ordinal; measurements, however, must be interval. *Arch Phys Med Rehabil*. 1989;70(12):857-860.
6. Langley PC. Rasch measurement and patient reported value claims: a primer for hemophilia. *Inov Pharm*. 2022;13(4):16. [Internet]. [cited 2023 Jul 15].
7. Rasch G. *Probabilistic Models for Some Intelligence and Attainment Tests*. MESA Press; 1980.
8. Wright B, Masters G. *Rating Scale Analysis*. Mesa Press; 1982.
9. Bond T, Fox C. *Applying the Rasch Model: Fundamental Measurement in the Human Sciences*. Lawrence Erlbaum Assoc; 2001.
10. Poonnoose PM, Manigandan C, Thomas R, et al. Functional independence score in haemophilia: a new performance-based instrument to measure disability. *Haemophilia*. 2005;11(6):598-602.
11. 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(1):36-46.
12. McLaughlin P, Morris R, Chowdary P>. Investigating the relationship between the HJHS and HAL in routine clinical practice: a retrospective review. *Haemophilia*. 2018;24(6):988-994.
13. St-Louis J, Abad A, Funk S, et al. The Hemophilia Joint Health Score version 2.1 Validation in Adult Patients Study: a multicenter international study. *Res Pract Thromb Haemost*. 2022;6(2). [Internet]. [cited 2022 Sep 27].
14. Fischer K, Nijdam A, Holmström M, et al. Evaluating outcome of prophylaxis in haemophilia: objective and self-reported instruments should be combined. *Haemophilia*. 2016;22(2):e80-e86.
15. Poonnoose PM, Thomas R, Keshava SN, et al. Psychometric analysis of the Functional Independence Score in Haemophilia (FISH). *Haemophilia*. 2007;13(5):620-626.
16. Sherlock E, O'Donnell JS, White B, Blake C. Physical activity levels and participation in sport in Irish people with haemophilia. *Haemophilia*. 2010;16(1). [Internet]. [cited 2022 Sep 27].

17. Lobet S, Lambert C, Foubert A, et al. ACTIVLIM-Hemo: a new self-reported, unidimensional and linear measure of activity limitations in persons with haemophilia. *Haemophilia*. 2022. [Internet]. [cited 2022 Dec 22].
18. Hilliard P, Funk S, Zourikins N, et al. Hemophilia joint health score reliability study. *Haemophilia*. 2006;12(5):518-525.
19. Yeung TS, Wessel J, Stratford PW, MacDermid JC. The timed up and go test for use on an inpatient orthopaedic rehabilitation ward. *J Orthop Sports Phys Ther*. 2008;38(7):410-417.
20. Brooks D, Parsons J, Hunter JP, Devlin M, Walker J. The 2-minute walk test as a measure of functional improvement in persons with lower limb amputation. *Arch Phys Med Rehabil*. 2001;82(10):1478-1483.
21. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singapore*. 1994;23(2):129-138.
22. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*. 2003;35(8):1381-1395.
23. Streiner DL. Starting at the beginning: an introduction to coefficient alpha and internal consistency. *J Pers Assess*. 2003;80(1):99-103.
24. Andrich D. A rating formulation for ordered response categories. *Psychometrika*. 1978;43(4):561-573.
25. Jette AM, Tao W, Norweg A, Haley S. Interpreting rehabilitation outcome measurements. *J Rehabil Med*. 2007;39(8):585-590.
26. Yuksel E, Kalkan S, Cekmece S, Unver B, Karatosun V. Assessing minimal detectable changes and test-retest reliability of the timed up and go test and the 2-minute walk test in patients with total knee arthroplasty. *J Arthroplasty*. 2017;32(2):426-430.
27. Stanhope J. Brief Pain Inventory review. *Occup Med (Lond)*. 2016;66(6):496-507.
28. Poonnoose P, Keshava S, Gibikote S, Feldman BM. Outcome assessment and limitations. *Haemophilia*. 2012;18(4):125-130.

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