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Functional decline in persons with haemophilia and factors associated with deterioration

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Abstract

Introduction: The World Haemophilia Federation advises regular musculoskeletal assessment covering all International Classification of Functioning and Health (ICF) domains, including limitations in activities and participation in persons with haemophilia (PWH). This enables clinicians to detect changes early and enable adjustments in personalized healthcare when needed. However, data on the course of physical functioning and occurrence of decline is lacking. The aim of this study is to describe changes in perceived limitations in activities of PWH and to identify factors associated with a change.

Methods: Data were collected from medical health records of regular check-up visits of adults with moderate and severe haemophilia in two time periods. Perceived limitations in activities was measured with the Haemophilia Activities List (HAL). Association between variables (e.g., age, body mass index, bleeding rate and synovitis) and change in perceived limitations was assessed using a generalized linear model.

Results: A total of 104 PWH were included. At T0, the median HAL sum score was 79.5 (IQR 62.1–93.6) and at T1 the median HAL sum score was 74.2 (IQR 57.5–88.3). A functional decline was found in 35.6% of PWH, 55.8% remained stable and 8.7% improved. Among other variables, a BMI > 30 kg/m^2 appeared to be an important factor that negatively influenced the change in perceived functioning in adult PWH. With the included factors we could only explain a small part of this decline (R^2_{adj}: .12).

Conclusion: The majority of PWH remained stable in their perceived functional ability over mid-long term (median 3.5 years). However, about a third showed a clinical relevant decline in their functional ability.

KEYWORDS
activities of daily living, haemophilia

1 | INTRODUCTION

Haemophilia is a congenital bleeding disorder which results in a deficiency in coagulation factor VIII or IX.[1] This leads to a limited ability to form clots, causing an increased bleeding time after a surgery, easy bruising and an increased risk of bleeding into joints and muscles.[1] Even though the risk of bleeds is reduced by advanced treatment options such as prophylactic factor replacement and increasingly non-replacement treatment options, bleeding still occurs in persons with haemophilia (PWH). Bleeds in joints and muscles lead to acute

pain and limitations in activities. Recurrent bleeding in joints can lead to chronic joint conditions such as haemophilic arthropathy.[1,2] Haemophilic arthropathy is a disabling joint condition characterized by chronic pain, reduced range of motion and muscle atrophy.[2] Consequently, this arthropathy limits a person's quality of life and ability to participate in society.[3,4]

In the past decades, there is an increasing recognition for the importance to look beyond bleeds by assessing physical functioning and quality of life in PWH.[5,6] Regular outcome assessment covering all domains of the International Classification of Functioning and Health (ICF) is therefore advised by the World Haemophilia Federation.[7] This implies looking beyond body function and structures like bleeding rate or joint assessment and also include assessment of limitations in activities and participation and personal and environmental factors.[8] In current care assessment of bleeding rate combined with physical functioning and evaluation of limitations in activities and participation are important to determine a personalized healthcare plan.[9]Whereas an increase in bleeding rate is an indication to review the clotting factor regimen, an increase in limitations in activities may be an indication to consider a physiotherapy or orthopaedic intervention. To our knowledge, no literature regarding changes over time of perceived limitations in activities is available in the adult PWH. Knowledge on these topics can enable healthcare providers to identify people at risk of a decline in an early stage and develop interventions with the aim to detain this decline.

A previous study on changes in joint functioning over time in adult persons with severe and moderate haemophilia indicated that the number of bleeds and development of synovitis are related to a deterioration of joint functioning.[10] However, it is not yet determined if this deterioration also affects the perceived functioning. In paediatric PWH limitations in activities remained stable over 3–5 years with only little limitations found in this group. The small proportion of children that deteriorated over time showed higher bleeding rates.[11] However, it is uncertain if these results can be generalized to the adult population, as the impact of the disease might be different for adults. Studies in people with knee, hip and ankle osteoarthritis revealed that among other factors avoidance of activities, higher pain levels, higher morbidity count, higher BMI, more affected joints, worse joint status and a higher age are strongly associated with an increase in limitations in activities and a progression of the disease.[12–15] Given the similarities in pathophysiology and clinical characteristics between osteoarthritis and haemophilic arthropathy,[2] it can be hypothesized that these factors could also apply to adult PWH.

The aim of this current study is to describe changes in perceived limitations in activities of adult PWH over time and to identify factors associated with a change in perceived limitations in activities.

2 | METHODS

2.1 | Study design and data collection

The current study is a monocenter retrospective cohort study using systematically collected healthcare data. Data from medical health records of regular check-up visits of all adult patients (≥18 years) with moderate or severe haemophilia A or B, who visited the regular check-up with a physiotherapist at the Van Creveldkliniek, University Medical Centre Utrecht between February 2014 and July 2016 were used. Within the Van Creveldkliniek comprehensive check-ups are scheduled with the physician, physiotherapist, nurse and social worker approximately every 3–4 years. Data from two subsequent visits in two time periods; February 2014–July 2016 (T0) and February 2018–May 2021 (T1), were used. Data from participants were excluded if they experienced a major joint or muscle bleed <6 weeks before the check-up, underwent total knee or total hip replacement <12 months before the check-up or underwent an ankle arthrodesis <6 months before the check-up. The study was approved by the Institutional Review Board of the UMC Utrecht (IRB number: 21/675).

2.2 | Dependent variable

The main outcome measurement was change in perceived limitations in activities. Perceived limitations in activities was measured using the Hemophilia Activities List (HAL); a disease specific questionnaire containing 42 questions regarding everyday activities.[16] An overall sum score and three subscales ranging from 0 to 100 (lower scores indicate more limitations) specific to upper extremity activities, basic lower extremity activities and complex lower extremity activities can be calculated. The HAL has a good test-retest reliability.[17] The change (Δ) between the HAL scores of two subsequent visits is calculated (ΔHAL = HAL T1−HAL T0). As the smallest detectable change of the questionnaire is 10.2 for the sum score,[17] a ΔHAL sum score >10.2 was classified as an improvement and a ΔHAL sum score < −10.2 as deterioration in functioning. A ΔHAL sum score between −10.2 and 10.2 is considered as no meaningful change. The smallest detectable change for the subscales of the HAL are 9.2, 16.7 and 13.4 respectively for the upper extremity, basic lower extremity and complex lower extremity scores.[17]

2.3 | Independent variables

Independent variables included in the analysis were determined a priori and were based on clinical experience and previous research in haemophilia and osteoarthritis.[10,12,14] We included the following independent variables measured at baseline; age (years), haemophilia severity (severe vs. moderate), presence of comorbidities (presence of ≥1 comorbidities, excluding osteoarthritis),[18] body mass index (classified as normal weight, overweight and obese), joint status (Haemophilia Joint Health Score [HJHS]), HAL score at baseline, movement behaviour (measured with accelerometer, classified as sedentary vs. non-sedentary based on method described by Timmer et al.).[19] In addition the following factors of haemophilia-related events that happened between the two visits were included in the analysis; annualized bleeding rate in joints and muscles (total number of bleeds divided by follow-up time in years), development of synovitis,

musculoskeletal surgery (e.g. joint replacement surgery, ankle arthrodesis), switch in clotting factor treatment regime (i.e. switch from on-demand to prophylactic treatment, from standard half-life to extended half-life product, started treatment with emicizumab or underwent gene therapy) and the time between the two visits in months.

2.4 | Statistical analysis

Data were analysed using R version 1.3.1093. Descriptive statistics of participants are presented as proportion (N, %), mean (± standard deviation) for normally distributed data or median (IQR) for not normally distributed data. Normality of the data was checked by visual inspection of the histograms. As routinely collected data were used and missing data were unavoidable. In cases that had missing data of bleeding episodes for a certain period, the annualized bleeding rate was calculated based on available bleeding periods. For other missing variables a multivariate imputation by chained equations (MICE) was used with a total of 25 iterations to create a complete dataset.[20,21] A total of 10 imputed datasets were created and pooled according to Rubinst's rule.[22,23]

We stratified the data based on three subgroups of the outcome measure ΔHAL sum score; decline, no change or improvement. Characteristics of the complete sample and stratified groups were presented and differences between groups were tested using ANOVA for normal distributed data, Kruskal–Wallis test for non-normal distributed data and Chi-square for categorical data. To examine the association between ΔHAL and the independent variables, a multivariable backward stepwise generalized linear model regression was used. For the stepwise model, a *p*-value threshold of .05 was used.[21] Before the analysis problematic multicollinearity was checked by calculating the variance inflation factor (VIF), with a cut-off of 5 indicating a possible problematic multicollinearity. As proposed by van Buuren et al.[21] the majority method was used in which variables that appear in at least half of the models derived from each individual dataset were selected. Subsequently, the Wald statistic was used to determine which variables are included in the final model. Final models of both the ΔHAL sum score and all subscales are presented.

3 | RESULTS

3.1 | Characteristics

A total of 104 participants were included in the study. In total 4.9% of all data points were missing and 10.1% of HAL data were missing; 9 participants had a missing HAL score at baseline only, 8 participants had a missing HAL score at follow up and 2 participants were missing both HAL scores. The participant characteristics of the whole group and stratified subgroups are presented in Table 1 and Appendix 2. Mean age of participants was 42.1 (SD 13.1) years at baseline, 85% had severe haemophilia, 92% had haemophilia A and 73% received prophylactic treatment at the time of baseline measurement. The median HJHS sum score at baseline was 16 points (IQR: 6.5–31) and most participants were classified as sedentary (59.6%). Of the 11 participants that underwent surgery between the two measurements, 3 had a multiple joint procedure (e.g., combined arthrodesis and total knee replacement), 2 had arthrodesis of the ankle joint, 3 had total knee replacement, and 3 had other surgeries performed (reversed total shoulder prosthesis, synovectomy, distraction of the ankle joint). No important differences were observed between the three stratified groups.

3.2 | Changes in scores

The median time between T0 and T1 was 3.5 years (range 24–82 months). At T0, the median HAL sum score was 79.5 (IQR 62.1–93.6) and at T1 the median HAL sum score was 74.2 (IQR 57.5–88.3). At T1, the mean decline in the HAL sum score was 5.9 (SD 13.9) points. A total of 35.6% of the participants showed a decline in their HAL scores between T0 and T1 larger than the SDC; 55.8% was classified as no change and a minority (8.7%) improved between T0 and T1. The subscales (upper extremity, lower extremity basic, lower extremity complex) showed a mean decline of −3.8 (SD 15.0), −4.9 (SD 20.4) and −4.3 (SD 18.2), respectively. The distribution of ΔHAL sum score and all subscales is shown in Figure 1.

3.3 | Factors associated with decline—HAL sum score

Results from the multivariable analysis with ΔHAL sum score as dependent variable are presented in Table 2. Results of the univariable analysis can be found in Appendix 1. The VIF test revealed that none of the VIF scores exceeded the cut-off point of 5. The multivariable analysis showed a decrease of .34 points in ΔHAL sum score for every point of increase in HAL sum score at T0 (β −.34, $p < .01$). A 30.0 points higher HAL sum score at T0, therefore, results in a decrease in HAL score between T0 and T1 of (the SDC) 10.2. The analysis showed a decrease of .37 points in ΔHAL sum score for every point of increase in HJHS score at T0 (β −.37, $p < .01$). A 27.6 point higher HJHS score, therefore, results in a decrease in HAL score between T0 and T1 of 10.2. Furthermore, participants with a BMI higher than 30 had 10.99 ($p = .01$) lower ΔHAL sum score compared to participants with a healthy weight (BMI < 25). The model with these variables included was only able to explain a small portion of the variation in the data (R^2_{adj}: .12).

3.4 | Factors associated with decline—HAL subscales

Results from the multivariable analysis on ΔHAL subscales are presented in Table 3. An increase in the ΔHAL upper extremity subscale is associated with a BMI ≥30 (β −13.07, $p < .01$), a higher HAL score at T0 (β −.41, $p < .01$) and with a higher HJHS score at T0 (β −.38, $p = .01$).

TABLE 1 Participant characteristics.

		Level	Overall ($n = 104$)	Decline[a] ($N = 37$; 35.6%)	No change[a] ($N = 58$; 55.8%)	Improved[a] ($N = 9$; 8.7%)	p-value[b]
Age (years)	Mean (SD)		42.09 (13.07)	43.30 (13.72)	41.07 (13.49)	43.67 (6.12)	.674
Severity	N (%)	Severe	88 (84.6)	29 (78.4)	51 (87.9)	8 (88.9)	.423
Type	N (%)	A	96 (92.3)	32 (86.5)	57 (98.3)	7 (77.8)	.025
Prophylactic treatment	N (%)						
Overall		Yes	76 (73.1)	28 (75.7)	42 (72.4)	6 (66.7)	.849
In group of severe		Yes	73 (83.0)	26 (89.7)	41 (80.4)	6 (75.0)	.469
BMI	N (%)	BMI < 25	59 (56.7)	18 (48.6)	34 (58.6)	7 (77.8)	.227
		BMI 25–30	34 (32.7)	12 (32.4)	20 (34.5)	2 (22.2)	
		BMI > 30	11 (10.6)	7 (18.9)	4 (6.9)	0 (.0)	
Comorbidities	N (%)	Yes	28 (26.9)	7 (18.9)	17 (29.3)	4 (44.4)	.249
HJHS—t0	Median [IQR]		16.00 [6.50, 31.00]	17.00 [8.00, 31.00]	14.50 [3.00, 29.00]	30.00 [16.00, 37.00]	.139
Movement Category—t0	N (%)	Sedentary	62 (59.6)	19 (51.4)	36 (62.1)	7 (77.8)	.210
HAL total score—t0	Median [IQR]		79.50 [62.05, 93.55]	79.50 [62.05, 93.55]	82.25 [66.99, 94.15]	61.00 [58.30, 74.90]	.114
ABR	Median [IQR]		2.75 [1.36, 4.80]	2.86 [1.54, 4.29]	2.38 [1.16, 4.86]	3.00 [1.02, 4.74]	.922
Surgery MSK	N (%)	Yes	11 (10.6)	3 (8.1)	6 (10.3)	2 (22.2)	.465
Developed synovitis	N (%)	Yes	12 (11.5)	5 (13.5)	5 (8.6)	2 (22.2)	.521
Measurement interval (months)	Median [IQR]		42.00 [36.38, 52.50]	42.00 [37.00, 51.00]	41.50 [36.00, 53.50]	41.00 [37.00, 47.00]	.862

Abbreviations: ABR, annualized bleeding rate; HAL, Haemophilia Activity List; IQR, interquartile range; MSK, musculoskeletal; N, number; SD, standard deviation.

[a]Subgroups are based on ΔHAL of the sum score; a value of ← 10.2 was classified as "Decline", a value of > 10.2 as "Improved" and scores between −10.2 and 10.2 as "No change".

[b]ANOVA for normal distributed data, Kruskal–Wallis test for non-normal distributed data and Chi-square for categorical data.

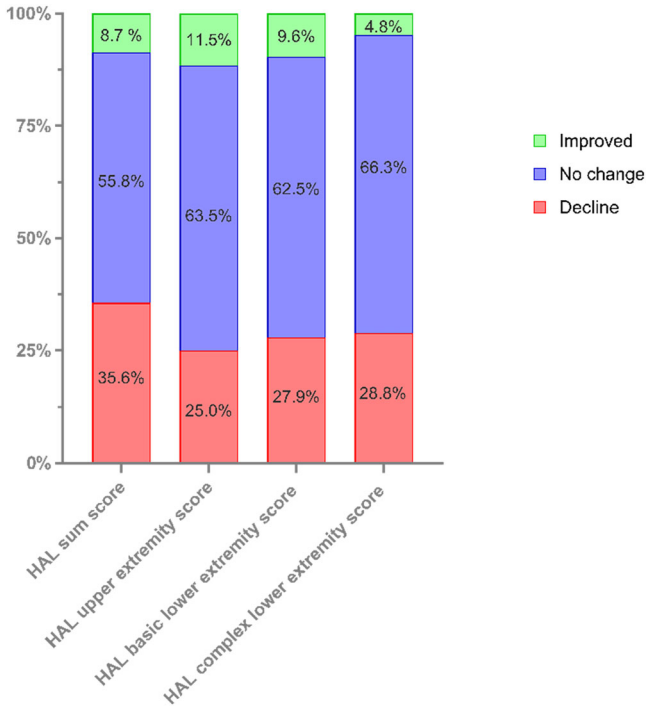

FIGURE 1 Distribution of change on Haemophilia Activities List (HAL) sum score and subscales.

TABLE 2 Multivariable analysis to identify factors associated with change in perceived limitations in activities—sum score.

Characteristic	β (95% CI)	p
Constant	32.01 (8.81; 55.22)	<.01
BMI		
<25	Reference	
25–30	−3.69 (−9.42; 2.03)	.20
≥30	−10.99 (−19.43; −2.55)	.01
HJHS	−.34 (−.64; −.05)	.02
HAL baseline score	−.37 (−.60; −.15)	<.01

Note: R^2_{adj}: .12. Regression coefficients are unstandardized (i.e., they represent the change in outcome for a unit change in predictor [HAL & HJHS] or category [BMI]). Interpretation: For a person with a BMI ≥ 30, HJHS of 16 and HAL score of 80 the predicted difference after follow-up is −14.02, meaning his HAL score at follow-up is 14.02 points lower compared to the baseline HAL score.

An increase in the ΔHAL lower extremity basic subscale is associated with a higher HAL score at T0 (β −.50, $p < .01$) and with a higher HJHS score at T0 (β −.42, $p = .02$). An increase in the ΔHAL lower extremity complex subscale is associated with a higher HAL score at T0 (β −.41, $p < .01$) and with a higher HJHS score at T0 (β −.54, $p = .01$). In contrast to the sum score and upper extremity subscale, there was no significant association between one of the two lower extremity subscales and BMI. Proportion of variance explained for the upper extremity, lower basic and lower complex subscales by the models are respectively R^2_{adj}: .21, .14 and .17.

TABLE 3 Multivariable analysis to identify factors associated with change in perceived limitations in activities—subscales.

Characteristic	β (95% CI)	p
Upper extremity subscale		
Constant	40.95 (18.59; 63.31)	<.01
BMI		
<25	Reference	
25–30	−2.81 (−8.71; 3.08)	.34
≥30	−13.07 (−21.88; −4.26)	<.01
HJHS	−.38 (−.61; −.16)	.01
HAL baseline score	−.41 (−.63; −.19)	<.01
Lower extremity basic subscale		
Constant	35.27 (11.18; 59.36)	<.01
HJHS	−.42 (−.79; −.05)	.02
HAL baseline score	−.50 (−.73; −.22)	<.01
Lower extremity complex subscale		
Constant	29.49 (10.08; 48.89)	<.01
HJHS	−.54 (−.95; −.12)	.01
HAL baseline score	−.41 (−.61; −.20)	<.01

Note: R^2_{adj}: Upper ext: .21, Lower ext. basic: .14, Lower ext. complex: .17. Regression coefficients are unstandardized (i.e., they represent the change in outcome for a unit change in predictor [HAL & HJHS] or category [BMI]).

4 | DISCUSSION

4.1 | Main findings

This retrospective cohort study shows that more than one-third (35.6%) of the PWH experienced an increase of the perceived limitations in activities during a median period of 3.5 years. Worse joint status at baseline, less limitations in activities at baseline and obesity are associated with more deterioration. This is similar for limitations in upper extremity activities alone. Limitations in activities of the lower extremity were associated with worse joint status at baseline and less limitations in activities at baseline, but not with obesity. Models derived from current research only explained a small part of the variance in changes in limitations in activities of PWH.

4.2 | Comparisons with previous research

In concordance with studies in osteoarthritis, the current study showed that severity of joint damage and BMI are associated with a larger decline in functional ability.[12,14] However, the current study did not reveal evidence of an association between the decline and age or comorbidities. This might be due to the fact that generally, symptoms occur at a much younger age in PWH. Consequently, the proportion of patients without comorbidities is higher. The average age in this study was 42.3 (SD 14.0) years, which is a lot younger compared to mean age of 66.1 years (SD 8.5) in a study investigating

knee osteoarthritis.[12] These differences could explain that changes in functioning occur independently from age and comorbidities.

Bleeding rate and synovitis were not associated with changes in perceived limitations in activities in the current study, which is in contrast to previous studies in PWH investigating changes in joint health and changes in functional ability in a paediatric population.[10,11] In both of these studies the average age was lower and the joint status was better compared to current study. Possibly, the effect of bleeds and subsequent synovitis on the ability to perform activities is smaller in persons who already have significant joint damage. A second explanation might be the effect of subclinical bleeds which could potentially dilute an effect of the bleeds reported by PWH.

Previous studies showed that people with chronic conditions like haemophilia report good or excellent quality of life while external observers might indicate their quality of life less favourable.[24] Theory explains this phenomenon by a change in internal standards and re-prioritization of values of a person living with long term disability also known as a response shift.[25] Changes in perceived limitations in patients with longer existing joint damage could to a greater extend be depended on coping mechanisms than on physical changes. Therefore, in addition to measuring patient reported outcome measurements, it remains important to also keep using performance-based measurements in the future.

4.3 | Strengths and limitations

The current study included a cohort of 104 persons with moderate or severe haemophilia, which is large for a rare disease like haemophilia. Data used in this study were collected in a systematic way during regular consultations with the haemophilia treatment centre. Compared to the haemophilia in the Netherlands study (HIN) and characteristics from all patients in our centre (unpublished data) we included more patients with severe haemophilia and with severe haemophilia receiving on-demand therapy.[26] However, our results showed that this did not lead to an overestimation of the risk of decline as both factors were not related to an increased risk. In addition, our baseline assessment took place in 2014, before the introduction of new less burdensome treatment options that increased the number of severe patients on prophylaxis.

As routinely collected data were used, the factors used in the analysis were limited to factors measured in clinical care. Even though most of the potentially relevant factors identified in literature in both PWH and osteoarthritis in the main analysis were included,[10,12,14] some psychological factors such as pain self-efficacy, kinesiophobia and catastrophizing that are related with functional ability in OA could not be included as they were not measured.[27,28] Second, because of the observational nature of the study design it is possible that changes found in the study are due to regression towards the mean.[29] As functional ability was compared at two moments in time, a linear trend was assumed during analysis. However, a study with more measurement points over a longer time period is needed to determine if this is a likely assumption for all patients or that different trajectories exist. Third, the current study was a monocenter study conducted in the Netherlands in PWH who attended regular clinical visits and have access to prophylactic factor replacement therapies. Findings from the current study might therefore not be generalizable to countries with a different healthcare setting. Lastly, from 11 of the 104 participants included in the study the follow-up data were collected after the covid pandemic. In this group of participants the lockdown measurements could have impacted psychological health and the ability to exercise, which both consequently could result in more perceived limitation.[30–32] However in our sample we could not find evidence for such an effect.

4.4 | Implications for research and practice

Functional ability decreases in more than one-third of the PWH over a period of 3–5 years and precise identification of the people most at risk is not possible. Therefore, healthcare providers should keep monitoring functional ability in all adults with moderate and severe haemophilia in order to timely identify patients that may need an intervention. The current study highlights the importance to raise awareness in PWH about maintaining a healthy weight as it showed that people with a BMI over 30 have a higher probability to experience a meaningful decline in perceived functioning. Future research in this field should focus on longitudinal data collection with three or more measurements in time. Possibly, more variance can be explained with more measurement points and when including psychological and environmental variables. This could help to identify people at risk of decline of their functional ability, who could benefit from an intervention.

5 | CONCLUSION

The majority of PWH remained stable in their functional ability over mid-long term (median 3.5 years). However, about one-third of the patients showed a meaningful decline in their functional ability. Among other variables, a BMI > 30 kg/m^2 appeared to be an important factor that negatively influenced the change in perceived functioning in adult PWH. With the included factors we could only explain a small part of this decline. Therefore, it remains important to monitor functional ability in all adults with moderate and severe haemophilia every 3–5 years.

AUTHOR CONTRIBUTIONS

All authors were involved in the design of the study. Johan Blokzijl and Merel A. Timmer collected the data. Johan Blokzijl, Martijn F. Pisters and Merel A. Timmer analysed the data and wrote the initial version of the report. All authors were involved in data interpretation and review of the paper. All authors approved the final version of the paper.

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CONFLICT OF INTEREST STATEMENT

M.T. has received an unrestricted research grant, paid to the institution from NovoNordisk and SOBI and payment for educational events from SOBI, paid to the institution. R.S. has received an unrestricted research grant, paid to the institution from Bayer, Baxalta, CSL Behring, NovoNordisk, Octapharma, Pfizer and SOBI.

DATA AVAILABILITY STATEMENT

Data are available on reasonable request from the authors.

ETHICS STATEMENT

Current study has received ethical approval from the Internal Review Board of the UMC Utrecht (approval number: 21/675).

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APPENDIX 1

TABLE A1 Factors association univariable with functional decline (HAL sum score).

Characteristic	Univariable β (95% CI)	p
Age (years)	−.06 (−.30; .16)	.56
Severity		
Moderate	Reference	
Severe	4.78 (−3.38; 12.96)	.25
Comorbidities		
No	Reference	
Yes	5.16 (−.89; 11.23)	.09
BMI		
<25	Reference	
≥25	−2.23 (−8.58; 4.11)	.48
≥30	−7.78 (−17.17; 1.60)	.10
HJHS (t0)	.03 (−.16; .22)	.72
Movement category		
Active	Reference	
Sedentary	4.72 (−1.02; 10.46)	.11
HAL baseline score	−.18 (−.33; −.02)	.02
Medication change		
No	Reference	
Yes	2.89 (−3.76; 9.53)	.39
Surgery		
No	Reference	
Yes	8.54 (−.63; 17.72)	.06
Developed synovitis		
No	Reference	
Yes	.97 (−8.51; 10.44)	.84
Annualized num. bleeds in joint or muscle	.05 (−1.15; 1.25)	.93
Measurement interval (months)	.01 (−.22; .25)	.91

Note: Regression coefficients are unstandardized (i.e., they represent the change in outcome for a unit change in predictor (Age, HAL & HJHS, Measurement interval) or category (Severity, Comorbidities, BMI, Movement category, Medication change, Surgery, Synovitis).

APPENDIX 2

TABLE A2 Factors association univariable with functional decline (HAL sum score).

	Overall (n = 104)	Decline (n = 37)	No change (n = 58)	Improved (n = 9)	p-value
BMI					
BMI t0	25.1 (3.96)	26.3 (4.56)	24.66 (3.41)	23.49 (3.82)	.060
BMI t1	25.7 (4.41)	26.9 (5.42)	25.2 (3.55)	24.1 (4.17)	.100
Change of BMI (t0-t)	.52 (1.45)	.55 (1.72)	.49 (1.27)	.61 (1.53)	.965
HJHS					
HJHS t0	18.99 (15.15)	19.76 (13.74)	17.31 (16.14)	26.67 (12.71)	.212
HJHS t1	21.21 (16.65)	24.81 (16.92)	18.60 (16.89)	23.22 (11.60)	.195
Change of HJHS sum score (t0-t1)	2.22 (6.88)	5.05 (8.01)	1.29 (5.25)	−3.44 (6.78)	.001

TABLE A2 (Continued)

	Overall ($n = 104$)	Decline ($n = 37$)	No change ($n = 58$)	Improved ($n = 9$)	*p*-value
Movement behaviour					
Frequency of active bouts t0 (per day)[a]	10.19 (4.20)	9.41 (4.46)	10.87 (4.21)	9.56 (2.37)	.287
Frequency of active bouts t1 (per day)[a]	9.82 (4.56)	9.66 (4.11)	10.19 (5.04)	5.25 (3.35)	.623
Change in frequency of Active bouts (t0-t1)	−.37 (4.67)	−.31 (3.30)	−.31 (5.52)	−.87 (5.19)	.963
Average duration of active bouts t0 (min)[a]	12.69 (3.04)	12.89 (2.87)	12.66 (3.29)	12.05 (2.48)	.782
Average duration of active bouts t1 (min)[a]	11.69 (3.33)	12.12 (4.15)	11.71 (2.89)	9.78 (.76)	.307
Change of duration of active bouts (t0-t1)	−.48 (3.31)	−.53 (3.38)	−.26 (3.51)	−1.43 (1.91)	.729

[a]An active bout is defined as a period of five consecutive minutes in which the participant performed an activity measured with the activity monitor (walking, running, biking) with an allowance of standing <5 min.