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Study of physical function in adolescents with haemophilia: The SO-FIT study

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Introduction: Contemporary haemophilia care demands Patient-Reported Outcomes. SO-FIT is a UK multi-centre study, assessing self-reported function, health-related quality of life (HRQoL) and joint health in boys with severe haemophilia.

Methods: Subjective physical function (PedHAL, HEP-Test-Q) and HRQoL (Haemo-QoL Short Form [SF]) were assessed alongside joint health using the objective Haemophilia Joint Health Score (HJHS v2.1). Demographic and clinical data were collected.

Results: Data from 127 boys mean age 12.38 ± 2.5 (range 8-17) treated at 16 sites were analysed. One-hundred-and-thirteen had haemophilia A, 25/9 past/current inhibitor, 124 were treated prophylactically (46.8% primary) and three on-demand. In the preceding 6 months, boys reported median 0 joint bleeds (range 0-8) with a median HJHS score of 1 (range 0-30). Boys reported good physical functioning; HEP-Test-Q (M = 80.32 ± 16.1) showed the highest impairments in the domain "endurance" (72.53 ± 19.1), in PedHAL (M = 85.44 ± 18.9) highest impairments were in the domains "leisure activities & sports" (M = 82.43 ± 23.4) and "lying/sitting/kneeling/standing" (M = 83.22 ± 20.3). Boys reported generally good HRQoL in Haemo-QoL SF SF (M = 22.81 ± 15.0) with highest impairments in the domains "friends" (M = 28.81 ± 30.5) and "sports & school" (M = 26.14 ± 25.1). HJHS revealed low correlations with the Haemo-QoL SF (r = .251, P < .006), the PedHAL (r = −.397, P < .0001) and the HEP-Test-Q (r = −.323, P < .0001). A moderate correlation was seen between HEP-Test-Q and Haemo-QoL SF of r = −.575 (P < .0001) and between PedHAL and Haemo-QoL SF r = −.561 (P < .0001) implying that good perceived physical function is related to good HRQoL.

Conclusions: The SO-FIT study has demonstrated that children with severe haemophilia in the UK report good HRQoL and have good joint health as reflected in low HJHS scores.

KEYWORDS

adolescents, haemophilia, haemophilia joint health score, haemo-QoL, health-related quality of life, HEP-Test-Q, PedHAL, physical function, subjective assessment

*SO-FIT Study Group details are given in the Acknowledgements section.

1 | INTRODUCTION

Severe haemophilia (with factor levels of <1 iu/dl)[1] is an X-linked, usually inherited disorder of coagulation factors VIII (haemophilia A) or IX (haemophilia B) which occurs in approximately 1:5000-1:10 000 births in the United Kingdom (UK).[2] Children and young people with haemophilia (CWH) experience spontaneous or trauma-related bleeding from early childhood, joint damage results in haemophilic arthropathy by early adulthood.[3]

Primary prophylactic replacement therapy, commenced before the age of 2 years and/or before the second joint bleed, is the standard care for CWH in the UK,[4] thus CHW are growing up to be active members of society with near-normal lifestyles and life-spans. Physiotherapists in the UK routinely use the Haemophilia Joint Health Score (HJHS) to assess joint health in clinical practice. These assessments are usually performed at routine follow up clinics provided no bleeds have occurred in the preceding 4 weeks. The HJHS is a well-validated tool accurately reflecting early joint changes and can be used to monitor joint health, damage and improvement.[5–7]

Healthcare commissioners increasingly require justification of haemophilia treatment using measures of functional outcome and quality of life (QoL). Evaluation of haemophilia care includes collection of Patient-Reported Outcomes (PROs) evaluating patient's views of care and overall health. PROs assess the quality of care delivered to patients from their perspective.[8] Many of the questionnaires that CWH are asked to complete are long and unengaging, resulting in low completion rates.[9] Furthermore, questionnaires that focus on the assessment of subjective physical function may not be fully appropriate for those who have benefited from prophylaxis and who do not consider themselves "disabled". It is unclear whether these questionnaires add to the clinical data that are routinely collected in haemophilia centres, and indeed if they are acceptable to boys with haemophilia.

The SO-FIT Study was planned in order to answer the following questions.[10] The principal objective of this study was to determine whether self-perceived functional ability and quality of life (QoL) correlate with joint scores measured by the HJHS Version 2.1 in CWH. Secondary aims were to determine whether measures of perceived function (PedHAL, HEP-Test-Q) correlate with accepted quality of life measures (Haemo-QoL SF) *(reported in this paper)* and whether the HEP-Test-Q is as good a measure of perceived function as the PedHAL and acceptable to boys with haemophilia *(will be reported elsewhere)*.

2 | STUDY DESIGN AND METHODS

This was a UK multi-centre, cross-sectional study, assessing self-reported function and HRQoL of young people aged 8-16 years with severe haemophilia, with or without inhibitors, alongside objective assessment of joint health status.

Eligible boys were identified by the participating centre staff using a consecutive approach to limit selection bias. Nurses administered PRO questionnaires and collected medical and demographic data from medical records. Physiotherapists performed the HJHS Version 2.1 and provided raw score data; they had received a one-day training session on how to complete the HJHS before the study started in order to improve standardization.[11,12]

The study was registered with the Research and Innovation office at Great Ormond Street Hospital for Children NHS Trust. Ethical approval was granted by Camberwell St Giles Research Ethics Committee (13/LO/1733).

2.1 | Instruments

Self-reported subjective assessment of physical function was assessed using the HEP-Test-Q and the PedHAL, objective assessment of joint health was assessed using the HJHS Version 2.1. Participants were asked about their haemophilia-specific HRQoL using the Haemo-QoL SF. Medical and demographic data (eg., age, diagnosis, treatment) were collected.

2.2 | Patient reported outcomes

The HEP-Test-Q assesses subjective physical performance and consists of 26 items pertaining to four dimensions (mobility, strength & coordination, endurance and body perception) with high values (range 0-100) indicating better physical performance.[13] The HEP-Test-Q has been validated in children and preliminary psychometric characteristics have been reported in another publication.[14.]

PedHAL measures the impact of haemophilia on self-perceived functional abilities and consists of 53 items pertaining to seven domains (sitting/kneeling/standing, functions of the legs, function of the arms, use of transportation, self-care, household tasks, leisure activities and sports. High values (range 0-100) indicate better physical functioning.[15.]

The disease-specific Haemo-QoL SF assesses self-reported HRQoL of CWH aged 4-17 years (with 35 items for children aged 8-17 years). Answer categories were based on a 5-point Likert scale varying from 1 = never to 5 = always. Values are transformed from 0 to 100 with high values indicating high impairments in HRQoL.[16]

2.3 | Objective physical function

Assessment of joint health status was performed using the Haemophilia Joint Health Score. The HJHS (vs2.1) is designed to assess the knee, elbow and ankle joints of children aged 4-18.[5] It is an 8-item tool assessing swelling/duration of swelling, muscle atrophy, crepitus on motion, range of movement loss, joint pain and strength and gait. Data for each item are scored in an ordinal categorical scale and each joint has a total score of 0-20. The global gait score assesses walking, hopping, running and stair skills with a score range of 0-4.[6] Scores are combined to provide an overall score of 0-124, with 0 representing healthy joints.

2.4 | Statistical analysis

Statistical analyses were conducted using the SPSS program version 24 (SPSS Inc. Chicago, IL, USA). Descriptive data are shown as

frequency distribution in percent or as mean ± standard division SD (range), median and ranges. Correlations between subjective physical functioning and objective joint status and between the PROs were calculated, using the Spearman Rho correlation coefficient. The comparison of differences between groups was examined by Student's test or Mann-Whitney *U*-test according to distribution; $P < .05$ were defined as significant. Clinical subgroups were defined as follows: impairments in HJHS (0 vs ≥1) based on the median split of 1 in this study and published data by Bladen et al.[17] who found a median HJHS of 0 in a similar cohort, BMI categories (very low/low/normal weight vs overweight/obese/severely obese), inhibitor status (yes [past, current] vs no), dosing regimen based on UK guidelines (≥40 IU vs <40 IU), prophylaxis treatment (primary prophylaxis [commenced before the age of 2 years and/or before the second joint bleed] vs secondary prophylaxis [commenced after age 2 or the second joint bleed]); differences in young age (<12.4 years) vs old age (≥12.4 years) and number of joint bleeds (≥1 vs <1) were based on the median split.

Height, weight, birthdate and date of assessment were used to categorize children's BMI using the UK90 clinical cut points: clinically very underweight: ≤0.4th centile, clinically low weight: ≤2nd centile, clinically healthy weight: >2 to <91st centile, clinically overweight: ≥91st centile, clinically obese: ≥98th centile, clinically extremely obese: ≥99.6th centile.[18]

Since pain was not explicitly assessed from a subjective perspective in the SO-FIT study, and in the pain domain of the HJHS pain is reported only at the moment of joint assessment, when the joint is manipulated; there was a need to create a variable in order to get an impression of subjective pain perception. Three items—"my swelling hurt", "I had pain in my joints" and "it was painful for me to move" from the Haemo-QoL SF were combined into a new "self-reported pain variable (yes vs no)". When a child answered "often" or "always" *in the previous 4 weeks* in one of these three items, he was considered to have PAIN.

3 | RESULTS

3.1 | Demographic and clinical data

One hundred and sixty boys with severe haemophilia were approached to participate with 127 boys from 16 centres agreeing to be in the study. Boys had a mean age of 12.38 ± 2.5 years, most had haemophilia A (89.7%), received prophylaxis (97.6%) and were on home treatment (98.4%). 19.7% had an inhibitor (past or current) and 28.3% were classified as overweight or obese according to their BMI and their age group.[18] According to the HJHS, only 8 boys had documented pain. For more clinical data see Table 1.

3.2 | Joint health status (HJHS Version 2.1)

For 122 boys, the HJHS could be assessed with the HJHS version 2.1; five boys were excluded due to recent bleed (n = 2), medical conditions (n = 2) and coordination difficulties (n = 1). Boys had a good objective joint health status (M = 3.47 ± 6.0) with a median of 1 and a range of 0-30 (see Table 1). Swelling, duration and muscle atrophy were the highest predictors of the HJHS.

We compared boys with a HJHS score of 0 with boys with a score >0 based on the median split and published work by Bladen et al.[6] The mean HJHS total score in the group >0 is M = 6.61 ± 6.9 (Median 4, range 1-30).

3.3 | Subjective physical function

In general, children reported good subjective physical functioning. They had high values in the Total Score of the HEP-Test-Q (M = 80.32 ± 16.1) and reported highest impairments in the domain "endurance" (M = 72.53 ± 19.1). In the PedHAL, a good overall Total Score was reported (M = 85.44 ± 18.9), with highest impairments found in the domains of "leisure activities & sport" (M = 82.43 ± 23.4) and "lying/sitting/kneeling/standing" (M = 83.22 ± 20.3).

3.4 | Health-related quality of life (HRQoL)

Children reported generally good HRQoL in the Total Score of the Haemo-QoL SF (M = 22.81 ± 15.0). They showed highest impairments in the domains "friends" (M = 28.18 ± 30.5) and "sports & school" (M = 26.14 ± 25.1).

3.5 | Correlations of instruments

Total HJHS scores revealed low correlations with the total Haemo-QoL SF Score ($r = -.251$, $P < .006$), the total PedHAL score ($r = -.397$, $P < .0001$) and the HEP-Test-Q ($r = -.323$, $P < .0001$). A moderate correlation was seen between HEP-Test-Q and Haemo-QoL SF of $r = -.575$ ($P < .0001$) and between PedHAL and Haemo-QoL SF $r = -.561$ ($P < .0001$), implying that good physical function is related to low HRQoL impairments. The two subjective measures of physical functioning (HEP-Test-Q, PedHAL) correlated moderately with each other ($r = .634$; $P < .0001$).

3.6 | Differences in subjective physical function and HRQoL according to impairments in objective joint health status

Differences in subjective physical function and HRQoL were found with regard to patients' objective physical joint health status. Children in whom *impairments in objective joint health status* (HJHS ≥1) were detected (n = 64) reported significantly worse subjective physical functioning measured by the HEP-Test-Q (see Figure 1) and by the PedHAL (see Figure 2) compared to children with *no impairments (HJHS <1) in their joint health status* (n = 58). They also reported worse HRQoL in the "physical health" ($P < .037$), "view" ($P < .023$) and "sport & sport" ($P < .008$) domains of the Haemo-QoL SF (see Table 2). When looking at a subgroup of patients comparing the HJHS group <1 to patients with a moderate HJHS of 1-5 (n = 40) there were still significant differences in the PedHAL in the domains "household" ($P < .020$), "leisure activities and sports" ($P < .014$) and the total score of the PedHAL ($P < .048$).

TABLE 1 Demographics and clinical data of participants (n = 127)

Clinical data		n	Percentage
Haemophilia			
A		113	89.7%
B		14	10.3%
Inhibitor History *(past, current)*	Yes	25	19.7%
Inhibitor treatment *(8 failed, 1 ITI on-going)*			
Tolerized		16	64%
Current		9	36%
Type of treatment			
On Demand		3	2.4%
Prophylaxis		124	97.6%
Type of prophylaxis			
Primary		58	46.8%
Secondary		66	53.2%
Treatment administration			
Self		47	37%
Family Member		80	63%
Venous access			
Peripheral		120	94.5%
Central line		7	5.5%
Home treatment	Yes	125	98.4%
BMI			
Very underweight		1	0.8%
Low weight		1	0.8%
Healthy weight		89	70.1%
Overweight		22	17.3%
Obese		12	9.4%
Extremely obese		2	1.6%
Presence of target joints or arthropathy	Yes	30	23.6%
Target joints (≥3 bleeds in the same joint in the past 6 months)	Yes	8	6.3%
	M ± SD		**Median (range)**
Age	12.38 ± 2.5		12.35 (8.06-16.99)
Total number of bleeds *in the last 6 months*	1.8 ± 3.3		1 (0-24)
Number of joint bleeds *in the last 6 months*	0.81 ± 1.5		0 (0-8)
Number of sport-related bleeds *in the last 6 months*	0.38 ± 0.8		0 (0-4)
Dosage (IU/kg) (n = 126[a])	35.65 ± 18.1		32 (14-125)
Non-inhibitor patients (n = 102)	32.55 ± 12.1		30.5 (14-75)
Tolerized inhibitors (n = 16)	37.25 ± 23.5		32.5 (15-115)
Current inhibitor (n = 8)[a]	72.0 ± 29.1		63.5 (45-125)
HJHS (n = 122)	3.47 ± 6.0		1 (0-30)

[a]One boy received bypassing agent therapy only.

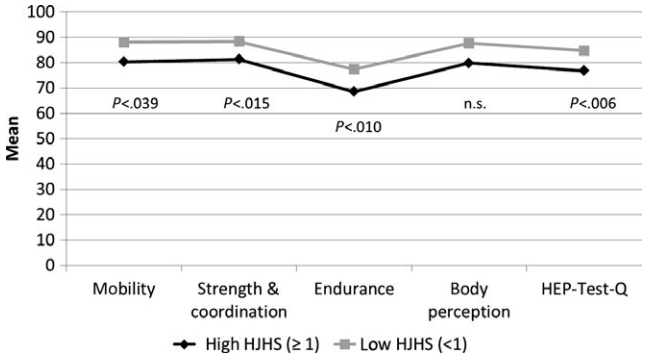

FIGURE 1 Differences in HEP-Test-Q according to HJHS

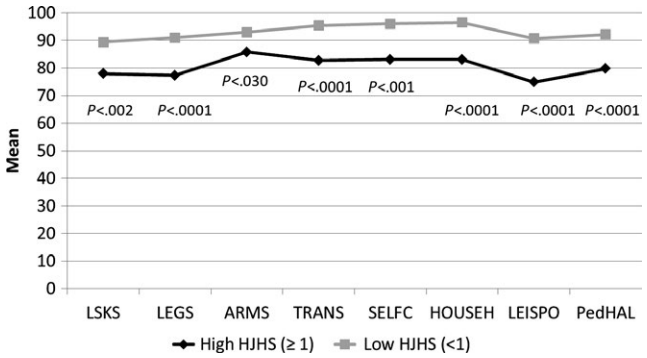

FIGURE 2 Differences in PedHAL according to HJHS

3.7 | Differences in subjective physical function, objective joint health status and HRQoL according to clinical subgroups

Children classified as overweight/obese based on their BMI (n = 36) reported significantly higher impairments in subjective physical function in the domains "mobility" ($P < .026$), "endurance" ($P < .008$) and the Total Score of the HEP-Test-Q ($P < .015$) (see Figure 3). They also reported higher impairments in the domain "functions of legs" ($P < .008$), "self care" ($P < .038$) and the total score of the PedHAL ($P < .036$). Furthermore, overweight/obese boys reported worse HRQoL in the domains "physical health" ($P < .003$) and "dealing" ($P < .043$) of the Haemo-QoL SF compared to *children classified as low/normal weight* (n = 91). No difference was found in the HJHS.

Children *with an inhibitor (past or current)* (n = 25) reported significant higher impairments in their subjective physical function in three domains of the PedHAL: "functions in legs" ($P < .003$), "use of transportation" ($P < .029$) and "self-care" ($P < .029$). Only one difference was seen in the Haemo-QoL SF in the domain "sports & school" ($P < .013$). No differences were found in the HEP-Test-Q and the HJHS.

Children *with ≥1 joint bleed in the last 6 months* (n = 46) reported significant higher impairments in the dimensions "function in the legs" ($P < .017$), "function in the arms" ($P < .044$), "self-care" ($P < .031$), "household tasks" ($P < .030$) of the PedHAL and in the Total PedHAL

TABLE 2 Differences in Haemo-QoL SF according to HJHS

Haemo-QoL domians	High HJHS (≥1)	Low HJHS (<1)	*P* value
Physical health	25.6	16.38	<.037
Feeling	16.53	16.38	ns
View	27.65	18.5	<.023
Family	24.75	23.96	ns
Friends	31.99	26.29	ns
Others	18.54	15.19	ns
Sport & School	31.25	19.07	< .008
Dealing	18.11	16.2	ns
Treatment	26.59	24.03	ns
Haemo-QoL	24.31	19.37	ns

ns, not significant.

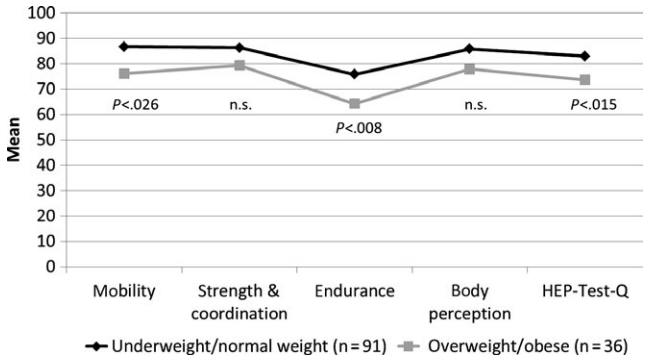

FIGURE 3 Differences in HEP-Test-Q according to BMI categories

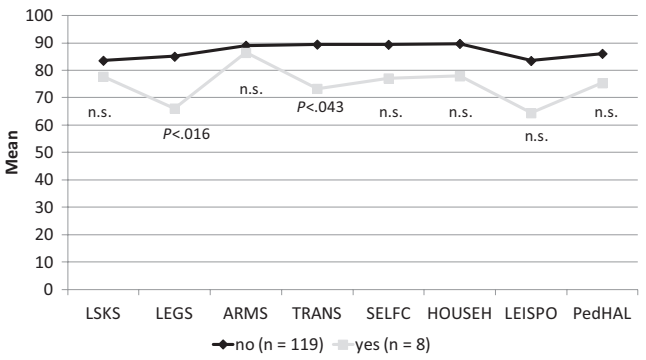

FIGURE 4 Differences in PedHAL according to presence of target joints

score (*P* < .023) than children without joint bleeds (n = 81). Only one difference was found in the dimension "physical health" of the Haemo-QoL SF (*P* < .046). No differences were found in the HEP-Test-Q and in the HJHS.

Boys with a *target joint* (n = 8), defined as three bleeds in the same joint in the preceding 6 months, reported significantly higher impairments in "mobility" (*P* < .033), "strength & coordination" (*P* < .0001), "body perception" (*P* < .003) and the HEP-Test-Q total score (*P* < .0001) compared to those without target joints (n = 119). Significant higher impairments were reported also in the PedHAL in the domains "function of the legs" (*P* < .016) and in "use of transportation" (*P* < .043) (see Figure 4). In the Haemo-QoL SF boys with target joints reported HRQoL impairments in the domains "physical heath" (*P* < .001) and "view" (*P* < .017). Boys with target joints had worse HJHS Scores (M_{target}=12.29 ± 9.3 vs $M_{no\ target}$ 2.93 ± 5.3; *P* < .0001).

When comparing boys who received *primary* (n = 58) vs *secondary (n = 66) prophylaxis* we found differences in "strength & coordination" (*P* < .041) and the HEP-Test-Q Total score (*P* < .038), but no differences were found in the PedHAL or the Haemo-QoL SF.

Age, *dosing regimen* and *total number of bleeds in the previous 6 months* had no influence on children's subjective (HEP-Test-Q, PedHAL) or objective (HJHS) physical functioning or on their HRQoL (Haemo-QoL SF).

3.8 | Differences in subjective physical function and objective joint health status according to self-reported PAIN

Children who were considered to have *PAIN* (n = 33*) in the Haemo-QoL SF in the past 4 weeks* had significantly higher impairments in objective joint health assessment and subjective physical function than children without *PAIN* (n = 89). For 5 boys, the PAIN variable could not be calculated due to missing data in one of the three identified "physical health" items.

Children with self-reported joint PAIN had significantly worse values in all domains of the HEP-Test-Q (*P* < .001) (see Figure 5) and the PedHAL (see Figure 6) and had significantly more joint bleeds (M_{pain}=1.52 ± 2.2 vs $M_{no\ pain}$=0.59 ± 1.1; *P* < .036). They also had a worse HJHS Total Score (M_{pain}=6.28 ± 8.3 vs $M_{no\ pain}$=2.27 ± 4.3; *P* < .018).

4 | DISCUSSION

This study of 127 boys with haemophilia from the UK revealed good overall joint health, good self-reported outcomes of physical function and HRQoL. We discuss each of these findings in more detail here.

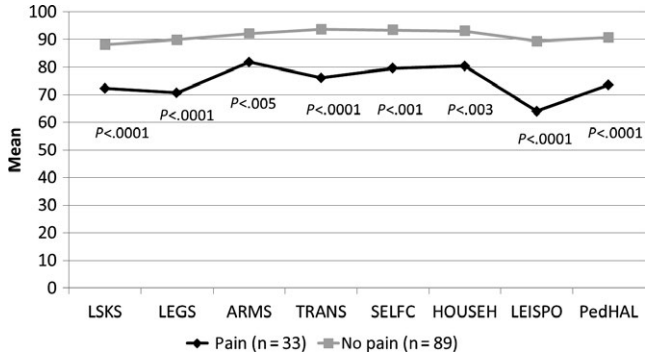

FIGURE 5 Differences in PedHAL according to self-reported PAIN (Haemo-QoL SF)

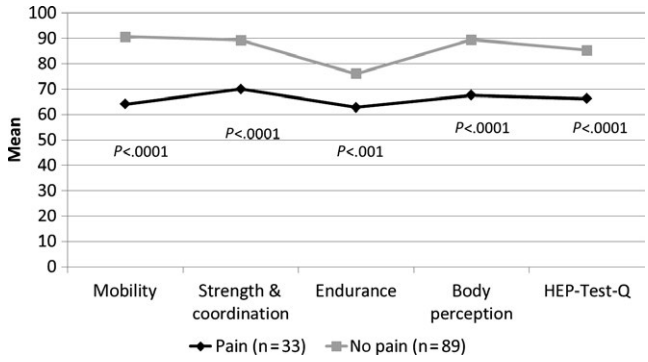

FIGURE 6 Differences in HEP-Test-Q according to self-reported PAIN (Haemo-QoL SF)

4.1 | HJHS

In this study, joint health was relatively good with a median of 1 evaluated with the HJHS Version 2.1. Children with higher physical impairments (demonstrated by HJHS scores ≥1) also reported worse physical functioning on both the PedHAL and HEP-Test-Q scores and worse HRQoL (Haemo-QoL SF). In a recent publication by St Louis et al.[19], youth with haemophilia are reported as having significantly worse physical functioning and bodily pain than Canadian norms, despite early prophylaxis and minimal joint disease.

4.2 | Patient reported outcomes

Boys reported good physical function in the two subjective measures HEP-Test-Q and PedHAL. Children in our cohort showed the highest impairments in their HRQoL in the domains "friends" and "sports & school" of the Haemo-QoL SF; this finding is similar to a European study in which children reported highest impairments in the domains "friends" and "perceived support" of the Haemo-QoL.[20]

In keeping with the findings of St. Louis et al.[19], the boys in this study had minimal joint disease, shown by low HJHS scores and good HRQoL which can be attributed to the initiation of early prophylaxis. Prophylaxis allows children to participate fully in sporting activity[21] with healthy siblings and peers leading to "greater health satisfaction and psychosocial wellness".[22] While the fitness benefits of physical activity in children is recognized, this must be balanced against the risk of bleeding and the impact this may have on long-term joint health and ultimately HRQoL. A recent Australian study revealed no correlation between quality of life and fitness[23] perhaps suggesting fitness and/or physical activity is only one factor impacting on HRQoL.

O'Mahoney et al.[24] stated that patient-reported HRQoL and functional ability data contribute a vital source of evidence for haemophilia care, revealing a deep understanding of the impact of haemophilia on everyday activities. Children are often not included in such patient-reported data due to the perceived difficulties in obtaining views of minors. In this study, the self-reported functional ability and HRQoL were described in a national cohort of 127 boys with severe haemophilia, treated predominantly with prophylaxis in line with UK Guidance.[4]

4.3 | Instrument correlation

Low correlations were found between HJHS and subjective physical function instruments in terms of PedHAL and HEP-Test-Q, and moderate correlations were found between the subjective PROs. In a Romanian study, the PedHAL showed a strong correlation with HJHS (−0.59) and with the domain of physical function of CHQ-50 which is similar to our findings, but not with the mental domains.[25] Conversely, Fischer et al.[26] demonstrated no correlation between HAL and HJHS (2.1) in adults with haemophilia; but found correlation with HRQoL for the physical domains of the SF-36. In our study, we found low correlation between the HJHS and the PedHAL and the HEP-Test-Q which might be due to the HJHS evaluation not detecting early signs of joint damage or the inter-rater variability in the person performing the HJHS.

The findings of Czepa et al.[27]where they found moderate to high correlations between the subjective HEP-Test-Q and objective physical data in terms of 12-minute walk test and one-leg-stand, recommended completion of objective examinations of physical performance in PWH with subjective perceptions since self-assessment did not always correlate highly with objective data. Although this study would appear to be similar to that of SO-FIT, Czepa assessed what would be considered measures of fitness and balance which our study did not. It could be implied that good joint health status allows better fitness, but care must be taken with such extrapolation.

4.4 | Subgroups

Some significant differences in subjective physical functioning and HRQoL were found for clinical subgroups such as BMI categories (high vs low), presence of inhibitors (yes vs no), presence of joint bleeds and presence of target joints. No differences were found for age or dosing regimen.

In this study, there was no loss of range of movement in those children classified as obese in comparison to those who were not. This finding is not consistent with the literature. Soucie et al.[28] reported in a 10-year follow-up study, that increased body fat resulted in reduced

and accelerated loss of joint mobility in boys aged 20 years and under. The difference in findings between these studies may reflect the younger age population in our study and the differences in duration of follow up.

Significant differences were also found for subjective and objective physical function and HRQoL concerning self-reported PAIN in the Haemo-QoL SF. In our study, 33 boys subjectively reported having PAIN in the Haemo-QoL SF compared to only 8 boys in whom pain was documented in the objective HJHS. In our opinion, this difference is due to (i) the timeframes asked (4 weeks in Haemo-QoL SF vs HJHS pain on day of assessment) and (ii) pain in the Haemo-QoL is asked as a subjective perception, whereas in the HJHS, the physiotherapist assesses pain based on range of movement and palpation, these two concepts are different. Since in our study no validated subjective assessment of pain was undertaken and joint pain was only assessed as one part of the objective HJHS assessment, we considered the approach to create a self-reported pain variable to be appropriate. However, we do not consider it to be a validated pain assessment tool which could be used in clinical practice or research, but it was helpful in our study to understand the situation of patients related to their pain perception. In hindsight we should have included a validated pain scale in the study, which was a study methodology error. For future research we recommend including a validated pain measure such as used in the PROBE project.[29]

Pain in children with haemophilia is probably unrecognized and under treated. A recent study revealed that 20.8% of children and adolescents with bleeding disorders suffered from moderate pain most commonly involving joints in a non-acute bleeding state[30] this may impact on functional ability and HRQoL. In our cohort, 26% of boys reported pain in the Haemo-QoL SF in the last six months. A significant difference was found concerning the number of joint bleeds between boys reporting pain compared to those not reporting pain ($P < .036$). However, as joint status on physical examination did not score highly for many of these boys, it suggests that other multifactorial influences on pain perception may be at play. This highlights the need to utilize more appropriate instruments to assess pain in each individual within a bio-psychosocial approach.

This study collected data on boys with severe haemophilia treated at 16 UK haemophilia centres. The centres volunteered to participate in the study, thus bias may have been introduced by including boys treated more intensively. To limit this possibility, consecutive boys were recruited to limit site selection of boys with "better" joint health.

Based on the recommendations of both Czepa et al.[27] and Fischer et al.[26] outcome assessment in patients with haemophilia treated with prophylaxis should include objective assessment as well as self-reported limitations in activities and HRQoL. Outcome assessment tools should be based on the World Health Organisation's International classification of functioning, disability and health. This would ensure a comprehensive understanding of the complexity of haemophilia on body, structure and function, activities, participation, environmental and personal factors.[31]

Although the subjective and objective data in the literature did not always correlate, they have value in their own right and as such, the authors advocate that the assessment of subjective physical functioning should become a routine assessment in haemophilia care in order to get a deeper insight into the specific problems of the individual patient.

5 | CONCLUSION

The SO-FIT study has demonstrated that children with severe haemophilia in the UK generally report good HRQoL and subjective physical functioning, which is also reflected in objective assessment of joint health. Subjective measures such as the PedHAL and the HEP-Test-Q are able to detect differences across clinical subgroups.

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AUTHOR CONTRIBUTIONS

KK and MH designed the study. MB and PMcL designed and analysed physiotherapy data, MH coordinated the centres in the UK. AG performed data entry. SvM analysed the data. KK and SvM wrote the first draft of the paper, all authors contributed to the paper and reviewed the final version.

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