Examination and validation of a patient-centric joint metric, the "PROBLEM JOINT": Empirical evidence from the CHESS Paediatrics dataset

Burke T[1,2], Rodriguez-Santana I[1], Chowdary P[3], Curtis R[4], Khair K[5], Laffan M[6], Mclaughlin P[3], Noone D[1], O'Mahony B[7], Pasi J[8], Skinner MW[9,10], O'Hara J[1,2]

[1]HCD Economics, Daresbury, UK; [2]Faculty of Health and Social Care, University of Chester, Chester, UK; [3]Katharine Dormandy Haemophilia Centre and Thrombosis Unit, Royal Free London NHS Foundation Trust, UK; [4]Hematology Utilization Group Study (HUGS), Walnut Creek, USA; [5]Heamnet, London, UK; [6]Centre for Haematology, Imperial College London, UK; [7]Irish Haemophilia Society, Dublin, Ireland; [8]Royal London Haemophilia Centre, Barts and the London School of Medicine and Dentistry, London, UK, [9]McMaster University, Hamilton, Canada; [10]Institute for Policy Advancement Ltd, Washington DC, USA.

Background

- Haemophilia is characterized by spontaneous hemarthrosis often leading to progressive joint deterioration and chronic inflammation of the synovial tissue, with substantial pain and eventually destruction of the joint.[1-3]
- Widely accepted metrics of clinical joint morbidity that focus on bleeding activity, such as the "target joint," are relevant, but may be less sensitive to the totality of patient burden.
- As current treatment strategies look to eradicate hemarthroses altogether, the authors have debated the need for a more patient-oriented measure of haemophilia-related joint morbidity, and have proposed the concept of the "**Problem Joint"**.

Problem Joint (PJ) is defined as having chronic joint pain and/or limited range of movement due to compromised joint integrity (chronic synovitis and/or haemophilic arthropathy), with or without persistent bleeding.

Aims

- To examine the usefulness and validity of the PJ metric in a paediatric haemophilia population as a patient relevant metric in children with haemophilia with respect to two key outcomes (patient quality of life and caregiver burden).

Methods

- We analysed the paediatric European cohort of the 'Cost of Haemophilia: Socioeconomic Survey', a family of datasets containing over 4,000 people with haemophilia.
- CHESS Paeds is a retrospective burden of illness study in male paediatric patients (≤17 years) with moderate or severe haemophilia A or B (Factor VIII or IX deficiency) from Germany, Italy, Spain, France and the UK, conducted in 2018.
- Statistical analysis explored the association of PJ count and location with respect to health-related quality of life (HRQoL) using the EQ-5D-Y, and caregiver burden.
- Individuals with active inhibitors or for whom no patient-reported data on HRQoL or caregiver burden was available were excluded.

Outcomes of interest

Patient HRQoL measured by the EQ-5D-Y

- The EQ-5D-Y consists of five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with three levels of severity from 1 ("no problems") to 3 ("a lot of problems").[4]
  - Utility scores were derived using the UK value set[5] with 0 representing a health state equivalent to death and 1 representing perfect health (negative states "worse than death" are possible).
  - Children and adolescents aged 8–17 completed the questionnaire themselves; caregivers completed the questionnaire for children aged 4-7 (EQ-5D-Y-Proxy 1).

Caregiver burden based on work impact of care provision

- Work impact was derived from the number of hours spent in an average week caring for the child's haemophilia-related needs.

Cohort characteristics

- The pediatric cohort contained information on 198 children with moderate or severe haemophilia (**Table 1)**.
- Approximately 19% of children had ≥1 PJ, (**Table 2**).

Table 1. Sample characteristics

PwH, n (%) unless noted	N = 198
Age	
mean (SD)	11.5 (3.8)
median	3.0
Annualised bleeding rate	
mean (SD)	6.0 (17.4)
median	3.0
Haemophilia type	
A	148 (74.7)
B	50 (25.0)
Haemophilia severity	
Moderate	51 (25.8)
Severe	147 (74.2)
Treatment regimen	
Prophylaxis	147 (74.2)
On Demand	41 (20.7)
No Treatment	10 (5.1)

Impact of Problem Joints

- HRQoL and number of PJs showed a clear negative trend.
- EQ-5D score was 0.71 for those with 0 PJs (n=160), 0.60 for 1 PJ (n=30) and 0.47 for ≥2 PJs (n=8; **Table 3, Figure 1**).
- The impact of having ≥1 PJs is greater, on average, for older children (self-reported EQ-5D) than younger children (proxy-reported EQ-5D).

Table 2. Distribution of PJs in CHESS Paeds

PwH, n (%)	
Total number of PJs	**N = 198**
No PJs	160 (80.8)
1	30 (15.2)
2+	8 (4.0)
Lower body PJs*	**n = 38**
0	14 (36.8)
1+	24 (63.2)
Upper body PJs	**n = 38**
0	23 (60.5)
1+	15 (39.5)

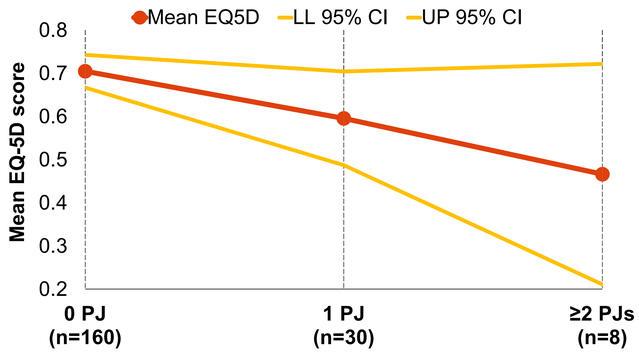
*Distribution of PJs by location for individuals with ≥1 PJ (n=38).
Upper body: neck, shoulders, elbows, wrists and spine. Lower body: hips, knees and ankles.

Table 3. EQ-5D score overall and by number of PJs

	Mean (SD)	Median
Overall (N=198)		
0 PJ (N=160)	0.71 (0.26)	0.73
1 PJ (N=30)	0.60 (0.30)	0.65
2+ PJs (N=8)	0.47 (0.37)	0.42
Self-Reported EQ-5D (n=157)		
0 PJ(N=126)	0.71 (0.25)	0.73
1 PJ (N=27)	0.58 (0.32)	0.64
2+ PJs (N=4)	0.39 (0.41)	0.21
Proxy Reported EQ-5D (n=41)		
0 PJ (N=34)	0.69 (0.21)	0.69
1 PJ (N=3)	0.70 (0.14)	0.66
2+ PJs (N=4)	0.54 (0.36)	0.67

Aggregate EQ-5D score from proxy EQ-5D (patients <8 years) and EQ-5D-Y (patients ≥8 years).

Figure 1. Mean EQ-5D by number of PJs (N=198)



- More PJs was associated with greater caregiver burden.
- Mean 16 h/wk with 0 PJ vs. 26.6 h/wk for ≥1 PJ (**Table 4**).

Table 4. Caregiver time spent (h/wk) by number of PJs

	Mean (SD)	Median
Hours spent caring/week (n=134)		
No PJs (n=107)	16.0 (17.3)	10
≥1 PJ (n=25)	26.6 (31.6)	10

Conclusions

- **The PJ definition provides a patient-centric measure of burden for PwH, applying a holistic and pragmatic view of joint health.**
- **Results from the CHESS Paeds cohort showed increasing humanistic burden in PwH and their caregivers with increasing number of PJs.**
- **Future work will evaluate the appropriateness of the PJ measure in a broader cohort of PwH.**

Acknowledgments

The study was approved by the University of Chester Ethics and conducted in collaboration with HCD Economics. The primary 'CHESS: paediatrics' study was supported by research funding from Bayer, Roche, Swedish Orphan Biovitrum AB (Sobi), Novo Nordisk, and SHIRE. The project was conducted in collaboration with the UK Haemophilia Society (UKHS) and governed by a steering committee chaired by Dr Kate Khair, Haemophilia nurse specialist at Great Ormond Street Hospital.

References

1. National Haemophilia Foundation. Haemophilia A and B. National haemophilia foundation (NHF). Published 2020. Accessed March 12, 2020; 2. O'Hara J, et al. Health Qual Life Outcomes. 2018;16(1):84; 3. Rodriguez-Merchan EC. HSS J. 2010. 6(1):37-42; 4. EQ-5D EuroQoL Research Foundation. 2020; 5. 19, 875–886 (2010). 6. Devlin NJ, et al. Health Economics. 2017; 27(1); 6. Wille, N. et al. Qual. Life Res.