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Real-world clinical and patient-centric outcomes in people with haemophilia A in the United Kingdom: Findings from the CHESS II study

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Background

- Haemophilia A (HA; factor VIII [FVIII] deficiency), characterised by prolonged trauma-related and/or spontaneous intra-articular bleeding events, is associated with adverse impacts on physical functioning and health-related quality of life (HRQoL).[1]
- Previous research has suggested a high incidence of joint bleeds in people with HA (PWHA) in the United Kingdom (UK) relative to that of other European countries,[2] with levels of HRQoL falling below that of the general population.[3]
- Little research has focused on differential outcomes for PWHA in the UK across the spectrum of condition severity.[2,4]
- This analysis describes variation in clinical and patient-centric outcomes for a cohort of mild (>5-40% normal FVIII activity), moderate (1-5%) and severe (<1%) PWHA in the UK, using real-world data.

Methods

- Data for PWHA living in the UK with no active inhibitor at the time of study capture were extracted from "Cost of Haemophilia in Europe: A Socioeconomic Survey – II" (CHESS II), a burden of illness study of adults with HA and haemophilia B in Europe. An interim dataset with study capture period Nov 2018 – Jul 2019 was used for this analysis.
- Patient demographics and clinical and patient-centric outcomes were assessed in total and stratified by baseline endogenous FVIII (mild, moderate, severe).
- Clinical outcomes of interest were as follows:
  - *FVIII replacement:* Strategies categorized as follows:
    - Patients on **Primary** treatment regimens (prophylaxis or on demand) were defined as managing their HA with the same regimen from treatment initiation, with no switch (of prophylaxis to on demand or vice-versa).
    - Patients on **Secondary** regimens at some stage switched to an alternative regimen (prophylaxis to on demand or vice versa).
  - *Annual bleed rate (ABR):* Physician-report, based on the 12 months prior to study capture.
  - *Target joints:* Joints in which three or more spontaneous bleeds had occurred within a consecutive 6-month period prior to study capture.[5]
  - *'Problem joints':* Joints exhibiting symptoms of HA-related damage: chronic synovitis; arthropathy; reduced range of motion; recurrent bleeding.[6]
  - *Hospital admissions:* For joint procedures and/or bleeding events in the 12 months prior to study capture.
  - *Chronic pain:* Physician-report of the patient's level of chronic pain relating to their HA ('None', 'Mild', 'Moderate', 'Severe'), based on functional deficit and use of analgesics.
- HRQoL was captured in a subset of patients via the EQ-5D-5L. Respondents select from five levels of impairment (ranging from "no problems" in performing a particular activity to "extreme problems/being completely unable") across five dimensions of health (mobility, self-care, usual activities, pain/discomfort, anxiety/depression).[7]
- EQ-5D-5L responses were converted to a single 0–1 index score using the UK-specific EuroQoL value set, with 0 representing a state "equivalent to death" and 1 representing "perfect health".[8]
- Outcomes by condition severity were compared using descriptive statistics (mean ± standard deviation [SD] or freq. [n; %]).
- Study methodology and interpretation of results were informed by representatives [DM, WM] from the UK Haemophilia Society patients' organisation.

Results

- Sixty-nine patients with HA and without active inhibitors were included in the analysis (mild n=11, moderate n=22, severe n=36). No patients were recorded with HIV coinfection; one patient with severe HA had a HCV diagnosis. (**Table 1**)
- Mean age ranged from 27.8 years in the severe subgroup to 43.8 in those with mild HA. Mean body mass index (BMI) was largely similar across severity subgroups (mean 24.3), though the proportion of patients reported as overweight or obese (BMI >25) increased inverse to condition severity (mild [55%] – severe [39%] (**Table 1**).
- Similarly, the proportion of patients in full-time employment decreased with increasing condition severity (mild [36%] – severe [8%]) (**Table 1**).
- One-third of patients with mild HA and 64% of patients with moderate HA were receiving FVIII replacement. Treatment was used on demand in these subgroups. For patients with severe HA, a mixture of on demand and prophylaxis regimens was reported (**Table 1**).
- Frequency of HA-related complications generally increased with increasing condition severity: ABR (mild mean [1.18] – severe [4.28]); reporting of moderate or severe chronic pain (mild [0%] – severe [66%]); problem joints (mild [0.00] – severe [0.36]) and bleeding event-related hospital admissions (mild [0.18] – severe [1.39]) (**Table 2 / Figs 1, 3 & 4**).
- EQ-5D-5L index scores appeared to decrease with increasing condition severity (mild [0.88] – severe [0.61]) (**Table 2**).
- No trends were observed in target joints or joint procedure-related hospital admissions (**Table 2 / Fig 2 / Fig 4**).

Table 1. Cohort demographics and characteristics by HA severity

	Severity subgroup			Total (n=69)
	Mild (n=11)	Moderate (n=22)	Severe (n=36)	
Age (mean ± SD)	43.8 ± 18.3	29.7 ± 10.4	27.8 ± 8.4	30.9 ± 12.3
BMI score (mean ± SD)	24.5 ± 3.4	23.9 ± 5.4	24.5 ± 4.4	24.3 ± 4.6
BMI >25 (n [% of patients])	6 [55%]	11 [50%]	14 [39%]	31 [45%]
Employment status (n [% of patients])				
Employed full time	4 [36%]	4 [18%]	3 [8%]	11 [16%]
Employed part-time	1 [9%]	5 [23%]	9 [25%]	15 [22%]
Self-employed	2 [18%]	5 [23%]	14 [39%]	21 [30%]
Unemployed	0 [-]	2 [9%]	1 [3%]	3 [4%]
Student	1 [9%]	2 [9%]	4 [11%]	7 [10%]
Other	3 [27%]	4 [18%]	5 [14%]	12 [17%]
Treatment strategy (n [% of patients])				
Receiving FVIII replacement	4 [36%]	14 [64%]	36 [100%]	54 [78%]
Primary on-demand	4 [100%]	8 [57%]	6 [17%]	18 [33%]
Primary prophylaxis	0 [-]	0 [-]	8 [22%]	8 [15%]
Secondary on-demand	0 [-]	6 [43%]	13 [36%]	19 [35%]
Secondary prophylaxis	0 [-]	0 [-]	9 [25%]	9 [17%]
Coinfection (n [% of patients])				
HIV	0 [-]	0 [-]	0 [-]	0 [-]
HCV	0 [-]	0 [-]	1 [3%]	1 [1%]

Abbreviations: BMI, body mass index; HIV, human immunodeficiency virus; HCV, hepatitis C virus; SD, standard deviation.

Table 2. Clinical and patient-centric outcomes by HA severity

	Severity subgroup			Total (n=69)
	Mild (n=11)	Moderate (n=22)	Severe (n=36)	
ABR (mean ± SD)	1.18 ± 0.87	3.00 ± 1.54	4.28 ± 1.77	3.38 ± 1.93
Target joints (mean ± SD)	0.00 ± 0.00	0.18 ± 0.50	0.11 ± 0.40	0.12 ± 0.40
Problem joints (mean ± SD)	0.00 ± 0.00	0.18 ± 0.39	0.36 ± 0.49	0.25 ± 0.43
Hospital admissions (12mth) (mean ± SD)				
Bleeding event related	0.18 ± 0.40	0.41 ± 0.50	1.39 ± 1.08	0.88 ± 0.99
Joint procedure related	0.36 ± 1.21	0.05 ± 0.21	0.44 ± 1.84	0.30 ± 1.42
Chronic pain (n [% of patients])				
No pain	7 [64%]	7 [32%]	3 [8%]	17 [25%]
Mild pain	4 [36%]	11 [50%]	9 [25%]	24 [35%]
Moderate pain	0 [-]	4 [18%]	17 [47%]	21 [30%]
Severe pain	0 [-]	0 [-]	7 [19%]	7 [10%]
EQ-5D-5L (sample (n); mean ± SD)	3; 0.88 ± 0.10	8; 0.81 ± 0.18	4; 0.61 ± 0.06	15; 0.77 ± 0.17

Abbreviations: ABR, annual bleed rate; SD, standard deviation.

Fig 1. ABR by HA severity

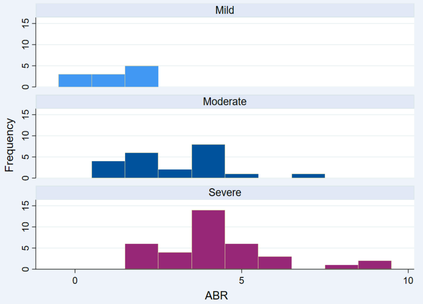


Fig 2. Target joints by HA severity

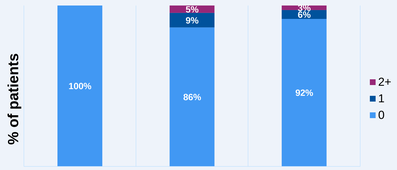


Fig 3. Problem joints by HA severity

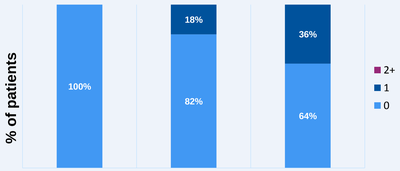
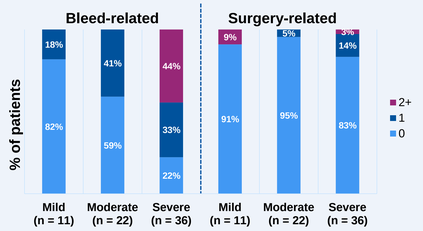


Fig 4. Hospital admissions by HA severity



Highlights: the patient community perspective

The UK Haemophilia Society [WM]

As a 30-year-old patient with severe haemophilia A, I have seen haemophilia care transformed within my lifetime. However, as this analysis highlights, advances in therapeutics have not translated into the expected quality-of-life improvements for all people with haemophilia (PWH).

One particularly worrying example from this research includes rates of full-time employment for people with mild, moderate, and severe haemophilia which stand at 36%, 18% and 8% respectively. The explanation for these concerning employment figures may lie in the annualised bleed rate for PWH which remains very high. As a patient cohort, we should be aspiring to become bleed free and yet, nobody in the moderate and severe cohorts were bleed-free in this analysis.

This research demonstrates the necessity for patient groups, such as the UK Haemophilia Society, to continue advocating for access to treatment and to support patients, along with medical professionals, to fully utilise new therapies. The small numbers included in this analysis should be acknowledged as a potential limitation, particularly regarding quality-of-life outcomes such as EQ-5D.

There is certainly much more work to do to continue evaluating how innovations in haemophilia therapies are actually improving the everyday lives of PWH in the UK. We also need further research to understand more fully why for many PWH, health and economic parity with the general population remains so elusive.

Conclusions

- In this analysis, increased condition severity was associated with greater reporting of haemophilia-related complications. This was observed despite the data comprising a relatively small cohort of patients.
- A notable level of impairment was reported in the subgroup of patients with moderate haemophilia A.
- The results indicate continued burden across the spectrum of condition severity in haemophilia A. Further quality of life and patient-reported data will help to frame the benefits and residual unmet need associated with newer therapies for haemophilia A, made available subsequent to this analysis.

References

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