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Real-world clinical and patient-centric outcomes in people with haemophilia A in Spain: 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]
- Research on the lived experiences of people with HA (PHWA) is often unavailable/very limited and varies within and between countries across Europe. Specifically, little is currently known on the country-specific clinical, treatment, and HRQoL outcomes in PWHA across severity.[2,3]
- 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 Spain, using real-world data.

Methods

- Data for PWHA living in Spain with no active inhibitor at the time of study capture were extracted from the "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 diagnosis, 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.[4]
  - *'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).[6]
- EQ-5D-5L responses were converted to a single 0–1 index score using the Spanish-specific EuroQoL value set, with 0 representing a state "equivalent to death" and 1 representing "perfect health".[7]
- Outcomes by condition severity were compared using descriptive statistics (mean ± standard deviation [SD] or freq. [n; %]).

Results

- One hundred and eighty-seven patients were included in the analysis (mild n=33, moderate n=66, severe n=88) (**Table 1**).
- Mean age of patients was 40.6 years, with small differences from mild [43.6 years] through to severe condition (39.4 years). Body mass index (BMI) was similar across subgroups (**Table 1**). Coinfection of HIV and HCV was reported in 3% and 5% of patients, respectively.
- The proportion of subjects in full-time employment declined with increasing severity (mild [61%] – severe [35%]); the proportion in part-time employment progressively increased with increasing severity (mild [6%] – severe [25%]) (**Table 1**).
- One-quarter and two-fifths of mild and moderate patients, respectively, were receiving on demand regimens of FVIII replacement. A mixture of on-demand (49%) and prophylaxis (51%) regimens were in use within the severe cohort (**Table 1**).

Table 1. Cohort demographics and characteristics by HA severity

	Severity subgroup			Total (n=187)
	Mild (n=33)	Moderate (n=66)	Severe (n=88)	
Age (mean ± SD)	43.6 ± 17.0	40.8 ± 16.0	39.4 ± 14.3	40.6 ± 15.4
BMI score (mean ± SD)	25.1 ± 2.5	24.6 ± 2.7	24.8 ± 2.8	24.8 ± 2.7
BMI >25 (n [% of patients])	15 [45%]	32 [48%]	40 [45%]	87 [47%]
Employment status (n [% of patients])				
Employed full time	20 [61%]	25 [38%]	31 [35%]	76 [41%]
Employed part-time	2 [6%]	8 [12%]	22 [25%]	32 [17%]
Self-employed	3 [9%]	1 [2%]	4 [5%]	8 [4%]
Unemployed	1 [3%]	4 [6%]	3 [3%]	8 [4%]
Student	4 [12%]	7 [11%]	9 [10%]	20 [11%]
Other	3 [9%]	21 [32%]	19 [22%]	43 [23%]
Treatment strategy (n [% of patients])				
Receiving FVIII replacement	8 [24%]	25 [38%]	88 [100%]	121 [65%]
Primary on-demand	8 [100%]	20 [80%]	37 [42%]	65 [54%]
Primary prophylaxis	0 [-]	0 [-]	10 [11%]	10 [8%]
Secondary on-demand	0 [-]	5 [20%]	6 [7%]	11 [9%]
Secondary prophylaxis	0 [-]	0 [-]	35 [40%]	35 [29%]
Coinfection (n [% of patients])				
HIV	0 [-]	1 [2%]	4 [5%]	5 [3%]
HCV	1 [3%]	3 [5%]	5 [6%]	9 [5%]

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

- Mean ABR (mild [1.09] – severe [4.58]) and incidence of target joints (mild [0.06] – severe [1.00]) were suggestive of greater impairment with increasing severity of HA (**Table 2 / Fig 1 / Fig 2**).

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

	Severity subgroup			Total (n=187)
	Mild (n=33)	Moderate (n=66)	Severe (n=88)	
ABR (mean ± SD)	1.09 ± 0.96	2.77 ± 3.57	4.58 ± 10.65	3.34 ± 7.73
Target joints (mean ± SD)	0.06 ± 0.24	0.53 ± 0.83	1.00 ± 1.30	0.67 ± 1.08
Problem joints (mean ± SD)	0.33 ± 0.48	0.86 ± 1.18	0.78 ± 1.12	0.73 ± 1.07
Hospital admissions (mean ± SD)				
Bleeding event related	0.03 ± 0.17	0.61 ± 0.70	0.66 ± 0.97	0.53 ± 0.82
Joint procedure	0.00 ± 0.00	0.58 ± 2.17	0.78 ± 1.98	0.57 ± 1.89
Chronic pain (n [% of patients])				
No pain	22 [67%]	18 [27%]	31 [35%]	71 [38%]
Mild pain	10 [30%]	24 [36%]	26 [30%]	60 [32%]
Moderate pain	1 [3%]	22 [33%]	24 [27%]	47 [25%]
Severe pain	0 [-]	2 [3%]	7 [8%]	9 [5%]
EQ-5D-5L (sample (n); mean ± SD)	15; 0.87 ± 0.19	28; 0.81 ± 0.15	55; 0.77 ± 0.19	98; 0.80 ± 0.18

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

Fig 1. ABR by HA severity

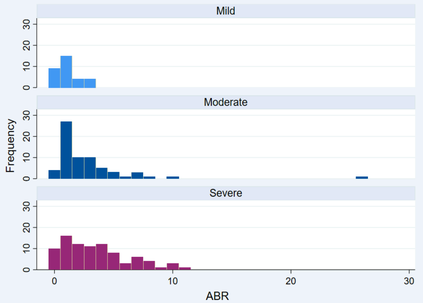


Fig 2. Target joints by HA severity

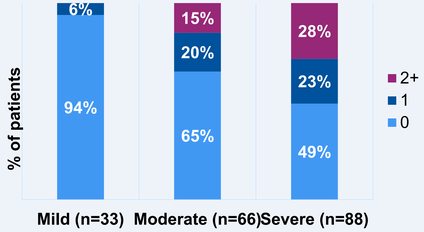
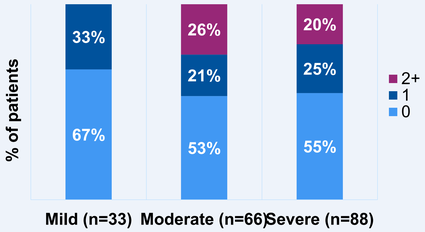
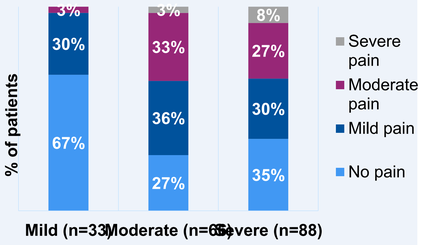


Fig 3. Problem joints by HA severity



- Incidence of problem joints was similar between moderate and severe subgroups, with highest in patients with moderate HA (0.86) (**Table 2 / Fig 3**).
- Physician-report of pain showed majority of patients currently experience chronic pain due to their HA (62%) (**Table 2 / Fig 4**).

Fig 4. Chronic pain by HA severity



- EQ-5D-5L index score (mild [0.87] – severe [0.77]) progressively worsened with increasing condition severity (**Table 2**).

Conclusions

- This analysis observed increasing clinical burden and a lower QoL with greater condition severity, with the exception of the problem joint and chronic pain outcomes.
- The incidence and nature of joint disease in people with moderate haemophilia A identified in this study highlights an unmet need in this subgroup, and should be explored in future research.
- The majority of patients had reported chronic pain relating to their haemophilia A, with almost one in ten of the severe cohort with severe chronic pain. The extent to which this impacts on functional and psychosocial wellbeing warrants further study.
- Further study of the management, outcomes, and life experiences of patients across the clinical spectrum of haemophilia A in Spain would help to validate the trends observed here and to quantify any impact of new therapies available subsequent to this analysis.

References

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