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Real-world clinical and patient-centric outcomes in people with haemophilia A in France: 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]
- In France, guidelines for the management and care of people with haemophilia, developed collaboratively by clinicians and patients and published by the national health authority (HAS), highlight the importance of prevention, detection, and early treatment of haemophilia-related complications.[2]
- Nevertheless, high incidence of joint bleeds relative to that of other European countries has previously been reported for people with HA (PWHA) in France,[3] with levels of HRQoL falling below that of the general population.[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 France, using real-world data.

Methods

- Data for PWHA living in France 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 treatment initation, 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 French-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 a representative [GD] from Association Française des Hémophiles (AFH) patients' organisation.

Results

- Sixty patients with HA and without active inhibitors were included in the analysis (mild n=10, moderate n=19, severe n=31) with a mean age of 26.4 years (**Table 1**).
- Mean body mass index (BMI) was similar across subgroups; the proportion of overweight or obese patients was highest in individuals with moderate HA (BMI >25; 42%) (**Table 1**).
- Forty-five percent of subjects were full-time students; for the remainder of the cohort, full-time employment decreased with increasing condition severity (**Table 1**).
- Approximately one-third of patients with mild HA and one-quarter of patients with moderate HA were reported as receiving FVIII replacement. For patients with severe HA, secondary prophylaxis regimens were most common (45%) (**Table 1**).
- Mean ABR was lowest in patients with moderate HA (1.06) and highest in severe HA (2.94) (**Table 2 / Fig 1**).
- Mean number of target joints progressively increased with increasing condition severity (mild [0.10] – severe [0.68]) (**Table 2 / Fig 2**).
- Incidence of 2+ problem joints was observed only in the cohort of severe HA patients (**Table 2 / Fig 3**).

Table 1. Cohort demographics and characteristics by HA severity

	Severity subgroup			Total (n=60)
	Mild (n=10)	Moderate (n=19)	Severe (n=31)	
Age (mean ± SD)	25.1 ± 4.4	23.7 ± 4.9	28.5 ± 13.0	26.4 ± 10.1
BMI score (mean ± SD)	23.4 ± 2.7	25.0 ± 2.0	23.8 ± 2.2	24.1 ± 2.3
BMI >25 (n [% of patients])	3 [30%]	8 [42%]	7 [23%]	18 [30%]
Employment status (n [% of patients])				
Employed full time	6 [60%]	6 [32%]	6 [19%]	18 [30%]
Employed part-time	0 [-]	1 [5%]	2 [6%]	3 [5%]
Self-employed	0 [-]	0 [-]	2 [6%]	2 [3%]
Unemployed	1 [10%]	0 [-]	1 [3%]	2 [3%]
Student	3 [30%]	8 [42%]	16 [52%]	27 [45%]
Other	0 [-]	4 [21%]	4 [13%]	8 [14%]
Treatment strategy (n [% of patients])				
Receiving FVIII replacement	3 [30%]	5 [26%]	31 [100%]	39 [65%]
Primary on-demand	3 [100%]	3 [60%]	8 [26%]	14 [36%]
Primary prophylaxis	0 [-]	0 [-]	2 [6%]	2 [5%]
Secondary on-demand	0 [-]	2 [20%]	7 [23%]	9 [23%]
Secondary prophylaxis	0 [-]	0 [-]	14 [45%]	14 [36%]
Coinfection (n [% of patients])				
HIV	0 [-]	0 [-]	0 [-]	0 [-]
HCV	0 [-]	0 [-]	0 [-]	0 [-]

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

- The proportion of patients experiencing chronic pain due to their HA increased with increasing condition severity (mild [10%] – severe [55%]) (**Table 2 / Fig 4**).
- EQ-5D-5L index scores were similar across subgroups (**Table 2**).

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

	Severity subgroup			Total (n=60)
	Mild (n=10)	Moderate (n=19)	Severe (n=31)	
ABR (mean ± SD)	1.40 ± 0.97	1.06 ± 0.94	2.94 ± 2.35	2.10 ± 2.01
Target joints (mean ± SD)	0.10 ± 0.32	0.11 ± 0.46	0.68 ± 1.05	0.40 ± 0.85
Problem joints (mean ± SD)	0.10 ± 0.32	0.00 ± 0.00	0.19 ± 0.48	0.12 ± 0.37
Hospitalisations (12mth) (mean ± SD)				
Bleeding event related	0.00 ± 0.00	0.00 ± 0.00	0.16 ± 0.45	0.08 ± 0.33
Joint procedure	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Chronic pain (n [% of patients])				
No pain	9 [90%]	13 [68%]	14 [45%]	36 [60%]
Mild pain	1 [10%]	6 [32%]	16 [52%]	23 [38%]
Moderate pain	0 [-]	0 [-]	1 [3%]	1 [2%]
Severe pain	0 [-]	0 [-]	0 [-]	0 [-]
EQ-5D-5L (sample (n); mean ± SD)	3; 0.98 ± 0.02	8; 0.96 ± 0.04	22; 0.96 ± 0.06	33; 0.96 ± 0.05

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

Fig 1. ABR by HA severity

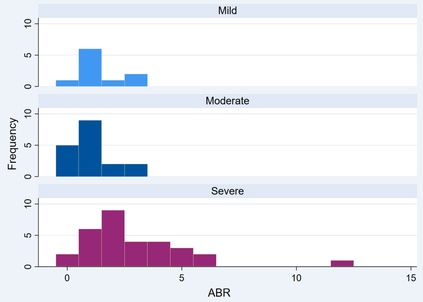


Fig 2. Target joints by HA severity

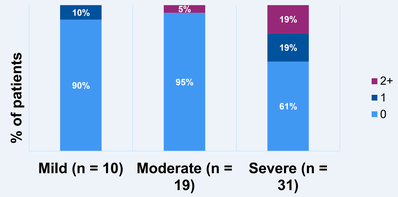


Fig 3. Problem joints by HA severity

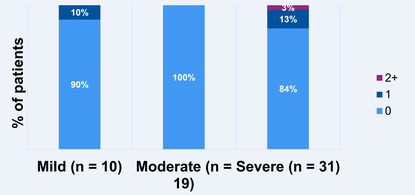
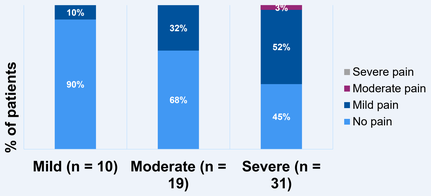


Fig 4. Chronic pain by HA severity



Highlights: the patient community perspective

l'Association Française des Hémophiles (AFH)

- *A notable finding of this research is the high prevalence of chronic pain among haemophilia A patients. This is despite the average age of this study cohort being relatively young, with only a minority of patients having evidence of joint disease.*
- *Additional research with this dataset could explore the characteristics of patients with moderate haemophilia A in greater depth, particularly with respect to low and high bleeding phenotypes, and its relationship with patient quality of life and clinical outcomes.*
- *Further study of clinical outcomes in older patients with haemophilia A in France is also needed, as well as a better understanding of the relationship of joint health with availability of physiotherapy, given a recent study suggesting that physiotherapists in France have some of the lowest engagement with haemophilia patients in Europe.*[8]

Conclusions

- Patients enrolled comprised a young cohort with low frequency of haemophilia-related complications and high health-related quality of life relative to that reported previously.[4] This is despite presence of chronic pain being reported frequently in this cohort.
- Limitations of this analysis include the relatively small sample size, particularly for EQ-5D-5L responses and for the cohort of patients with mild/moderate haemophilia A; and a lack of data for newer therapies made available in France subsequent to this analysis.
- Further research is needed to contextualize the burdens experienced by people with haemophilia A in France, including greater study of outcomes in older patients and those with non-severe condition.

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