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Real-world clinical and patient-centric outcomes in people with haemophilia A in Germany: 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 Germany, using real-world data.

Methods

- Data for PWHA living in Germany 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 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 German-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; %]).
- Study methodology and interpretation of results were informed by representatives [TB, SB] from the Interessengemeinschaft Hämophiler e.V (IGH) patients' organisation .

Results

- Forty-seven patients with HA and without active inhibitors were included in the analysis (mild n=10, moderate n=16, severe n=21) (**Table 1**).
- Mean age was highest in the moderate HA cohort (44.8); approximately half of patients were reported as overweight or obese (BMI >25) (**Table 1**).
- The proportion of patients in full-time employment decreased with increasing condition severity (mild [80%] – severe [67%]) (**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, primary prophylaxis regimens were most common (38%) (**Table 1**).
- Mean ABR was suggestive of greater impairment with increasing severity of HA (mild [0.70] – severe [1.86]) (**Table 2 / Fig 1**).
- Incidence of target joints (mild [0.00] – severe [0.43]), problem joints (mild [0.10] – severe [0.57]), and hospital admissions (bleeding event-related: mild [0.00] – severe [0.71]) followed a similar trend of increasing impairment (**Table 2 / Figs 2 & 3**).
- The proportion of patients with chronic pain increased with increasing condition severity (mild [20%] – severe [76%]) (**Table 2 / Fig 4**).

Table 1. Cohort demographics and characteristics by HA severity

	Severity subgroup			Total (n=47)
	Mild (n=10)	Moderate (n=16)	Severe (n=21)	
Age (mean ± SD)	40.7 ± 11.1	44.8 ± 15.7	40.0 ± 11.1	41.7 ± 12.8
BMI score (mean ± SD)	24.7 ± 1.8	24.7 ± 2.6	25.5 ± 3.1	25.0 ± 2.7
BMI >25 (n [% of patients])	6 [60%]	8 [50%]	10 [48%]	24 [51%]
Employment status (n [% of patients])				
Employed full time	8 [80%]	12 [75%]	14 [67%]	34 [72%]
Employed part-time	0 [-]	1 [6%]	2 [10%]	3 [6%]
Self-employed	1 [10%]	1 [6%]	4 [19%]	6 [13%]
Unemployed	0 [-]	0 [-]	0 [-]	0 [-]
Student	1 [10%]	1 [6%]	0 [-]	2 [4%]
Other	0 [-]	1 [6%]	1 [5%]	2 [4%]
Treatment strategy (n [% of patients])				
Receiving FVIII replacement	3 [30%]	4 [25%]	21 [100%]	28 [78%]
Primary on-demand	3 [100%]	4 [100%]	7 [33%]	14 [50%]
Primary prophylaxis	0 [-]	0 [-]	8 [38%]	8 [29%]
Secondary on-demand	0 [-]	0 [-]	0 [-]	0 [-]
Secondary prophylaxis	0 [-]	0 [-]	6 [29%]	6 [21%]
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.

- EQ-5D-5L index scores showed a possible trend towards lower HRQoL with increased severity (mild [0.97] – moderate [0.90]) (**Table 2**).

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

	Severity subgroup			Total (n=47)
	Mild (n=10)	Moderate (n=16)	Severe (n=21)	
ABR (mean ± SD)	0.70 ± 0.48	1.25 ± 1.57	1.86 ± 1.53	1.40 ± 1.44
Target joints (mean ± SD)	0.00 ± 0.00	0.19 ± 0.40	0.43 ± 0.81	0.26 ± 0.61
Problem joints (mean ± SD)	0.10 ± 0.32	0.19 ± 0.40	0.57 ± 1.25	0.34 ± 0.89
Hospital admissions (12mth) (mean ± SD)				
Bleeding event related	0.00 ± 0.00	0.50 ± 0.82	0.71 ± 1.23	0.49 ± 0.98
Joint procedure	0.00 ± 0.00	0.19 ± 0.75	0.38 ± 1.16	0.23 ± 0.89
Chronic pain (n [% of patients])				
No pain	8 [80%]	7 [44%]	5 [24%]	20 [43%]
Mild pain	2 [20%]	9 [56%]	7 [33%]	18 [38%]
Moderate pain	0 [-]	0 [-]	9 [43%]	9 [19%]
Severe pain	0 [-]	0 [-]	0 [-]	0 [-]
EQ-5D-5L (sample (n); mean ± SD)	2; 0.97 ± 0.04	4; 0.90 ± 0.08	0; -	6; 0.92 ± 0.08

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

Fig 1. ABR by HA severity

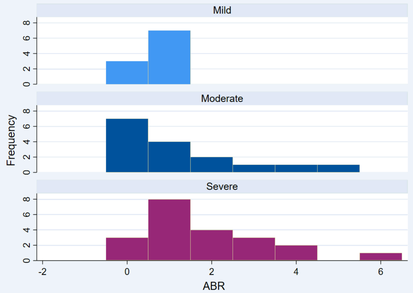


Fig 2. Target joints by HA severity

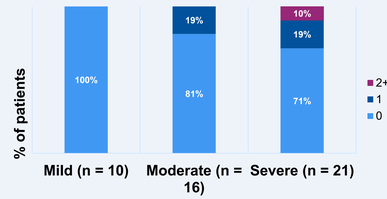


Fig 3. Problem joints by HA severity

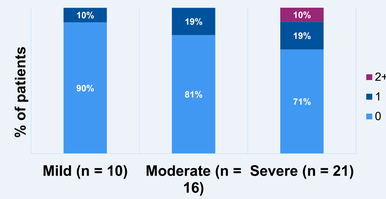
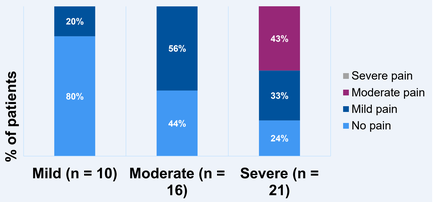


Fig 4. Chronic pain by HA severity



Highlights: the patient community perspective

Interessengemeinschaft Hämophiler e.V

From a patient perspective, the study at hand shows the importance of our continuous joint efforts with physicians and pharmaceuticals for further research and a better life with haemophilia.

For us, the most striking is the high number of patients with on-demand treatment despite the well-established benefits of prophylaxis regimens.

We believe more research is needed in order to better understand patients' motivations when making treatment decisions as well as the guidance they received upon making these decisions.

Additionally, it is concerning to see that only 40% of patients in the study cohort are reported as pain-free. In contrast, reported health-related quality of life is high in the small number of patients who responded. Future studies would benefit from capturing more quality of life data, to explore how it varies between condition severities and how clinical outcomes and management of the condition's impact upon patient wellbeing.

We will continue to advocate for haemophilia patients to live pain-free and regular lives. Studies like CHESS help us make the case why continuous improvements are required.

Conclusions

- Overall, a low frequency of clinical complications was reported in this cohort, though a pattern of increased reporting with increased condition severity was observed.
- Physician reporting of chronic pain in more than half of patients with moderate and severe haemophilia A is suggestive of residual burden warranting further study.
- Limitations of this analysis include the relatively small sample size, particularly for EQ-5D-5L responses; and a lack of data for newer therapies made available in Germany subsequent to this analysis.
- Additional data could provide insight into how clinical outcomes impact upon daily functioning and lived experiences of people with haemophilia A in Germany.

References

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