Clinical and humanistic burden of people with severe haemophilia A treated with prophylaxis in Europe: A longitudinal analysis from the CHESS studies

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Objectives

- Haemophilia A is a rare, congenital X-linked bleeding disorder marked by a deficiency in clotting factor VIII (FVIII). Severe haemophilia A (SHA; residual FVIII activity <1% of healthy levels) manifests clinically as frequent spontaneous bleeding episodes, predominantly in joints and soft tissues[1]
- Understanding how real-world decisions pertaining to prophylactic treatment for SHA impacts the clinical outcomes of people with SHA (PwSHA) is crucial for patients, treating healthcare professionals (HCPs), and policymakers
- This analysis describes changes in outcomes for a multi-country cohort of PwSHA receiving prophylaxis using FVIII replacement therapy and/or non-factor replacement therapy (NRT; emicizumab [HEMLIBRA®]), using data from two waves of the "Cost of Haemophilia: A Socioeconomic Survey" (CHESS) study
  - CHESS is a cross-sectional burden of illness study in adult men (≥18yrs) with haemophilia A or B, which has been serially conducted in the US and EU[2,3,4,5]
  - Specifically for the CHESS II (2019/2020) and CHESS III (2022) waves, n=176 PwSHA participated in both waves, allowing for description of changes between study waves

Methods

- Data for the subset of prophylaxis-treated PwSHA with no inhibitor history recruited in CHESS II ("initial" in this analysis) and subsequently followed up in CHESS III ("follow-up") (n=35) were linked across study waves and described
  - Sample attrition (n=141) was due to a prior/active history of inhibitors and/or reporting of an on-demand treatment regimen during one or both waves
- Demographic, clinical and treatment-pattern information (including adherence) was reported by treating HCPs
  - *Target joints*: Joints in which three or more spontaneous bleeds had occurred within a consecutive 6-month period prior to study capture[6]
  - *Problem joints*: Chronic joint pain and/or limited range of movement due to compromised joint integrity (i.e. chronic synovitis and/or haemophilic arthropathy), with or without persistent bleeding[7]
- Bleeding outcomes for specific treatment patterns (patients receiving FVIII replacement therapy across both study waves and those who had switched to NRT at follow-up) were also described

Results

- Mean patient age was 37.1 years, with data generally from Spain or Italy (**Table 1**)
- All patients were initially receiving prophylactic FVIII replacement therapy, per analysis design.
  - Fifteen patients had switched to NRT at follow-up. All had switched from standard half-life or plasma-derived FVIII (**Table 2**)
- The proportion of patients with some level of chronic pain remained consistent at follow-up (82.9%). Mild pain (45.7%) was more commonly reported at follow-up versus moderate pain initially (40.0%). A small increase in adherence was observed (**Table 3**)
- ABR was higher during the initial wave among the subgroup of patients who subsequently switched to NRT. Mean annual bleed rate (ABR) decreased at follow-up across all patients, most notably in those switching to NRT (**Table 4**)
- Improvement or stabilisation of target joints were observed in two-thirds of patients. A similar proportion had experienced some increase in reported problem joints at follow-up (**Figure 1**)
- Mean FVIII usage decreased at follow-up for patients switching to NRT (mean [SD] -417,710 IU [240,973]). Mean increase for those remaining on FVIII at follow-up was 62,860 IU (281,092) (**Figure 2**)

Table 1. Patient characteristics

		n=35
Age, y	mean (SD)	37.1 (13.4)
BMI, kg/m^2	mean (SD)	24.8 (2.7)
Country	n (%)	
Spain		20 (57.1)
France		1 (2.9)
Italy		14 (40.0)
Ethnicity	n (%)	
White/Caucasian		35 (100.0)

BMI, body mass index; SD, standard deviation.

Table 2. Treatment class at initial and follow-up waves, n (%)

Initial	Follow-up		
	SHL/PD FVIII	EHL FVIII	NRT
SHL/PD FVIII (n=30)	5 (16.7%)	10 (33.3%)	15 (50%)
EHL FVIII (n=5)	5 (100%)	0	0

EHL, extended half-life; NRT, non-factor replacement therapy; PD, plasma-derived.

Table 3. Clinical outcomes

		Initial	Follow-up	Δ
ABR	mean (SD)	4.5 (2.8)	1.0 (0.8)	–3.5 (2.9)
Target joints	mean (SD)	1.5 (1.8)	0.6 (0.7)	–0.9 (1.5)
Problem joints	mean (SD)	0.7 (0.7)	1.5 (1.2)	0.8 (0.7)
Chronic pain[a]	n (%)			
None		6 (17.1)	6 (17.1)	0.0%
Mild		11 (31.4)	16 (45.7)	45.5%
Moderate		14 (40.0)	13 (37.1)	–7.1%
Severe		4 (11.4)	0 (0.0)	–100.0%
Prophylaxis adherence[b]	n (%)			
Fully adherent		24 (68.6)	27 (77.1)	12.5%
Sub-optimal		9 (25.7)	6 (17.1)	–33.3%
Non-adherent		2 (5.7)	2 (5.7)	0.0%

[a]Pain levels defined using the WFH Physical Examination Score[8] [b]Fully adherent: missing no administrations; Sub-optimally adherent: missing 15–25% of administrations; Non-adherent: missing >25% of administrations. ABR, annualised bleed rate; SD, standard deviation.

Table 4. Mean (SD) ABR by treatment pattern

	Initial	Follow-up	Δ
FVIII prophylaxis at follow-up (n=20)	3.7 (2.7)	0.8 (0.9)	-2.9 (3.1)
NRT at follow-up (n=15)	5.5 (2.7)	1.2 (0.6)	-4.3 (2.4)

ABR, annualised bleed rate; SD, standard deviation

Figure 1. Change in target joints (a) and problem joints (b)

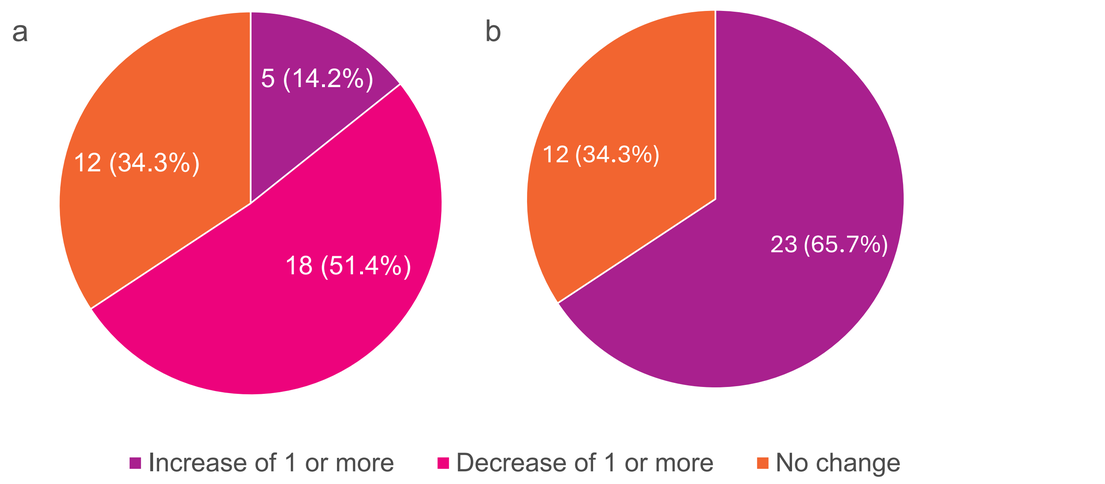
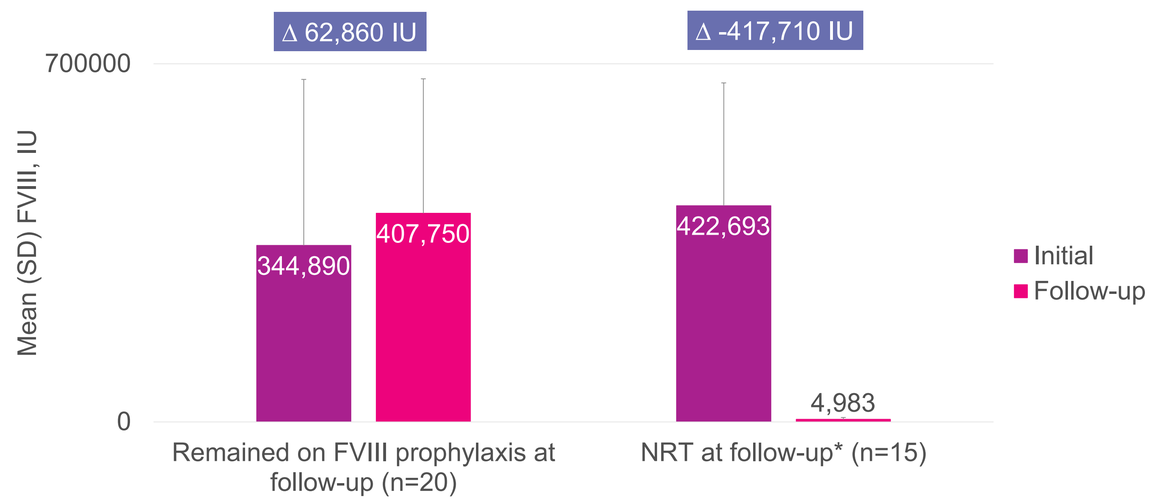


Figure 2. Mean (SD) FVIII use by treatment pattern



*On-demand use for bleeding events. IU, international units; SD, standard deviation

Conclusions

- Residual unmet need within this cohort of PwSHA is suggested by an increased use of FVIII among those remaining on FVIII prophylaxis, despite availability of EHL FVIII; incremental continued use of on-demand FVIII among PwSHA switching to NRT; and an increase in reported problem joints at follow-up
- Modest improvements in ABR, target joints, and chronic pain were observed in PwSHA receiving prophylaxis at three-year follow-up

References

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