Clinical and impairment outcomes in non-inhibitor Severe Haemophilia A patients receiving prophylaxis across currently available Haemophilia A treatments: insights from the 'Cost of Haemophilia: a Socioeconomic Survey III' (CHESS III) study

Blenkiron T[1] , Hinds D[2], Santos S[3], Burke T[1,4], Ferri Grazzi E[1]

[1]HCD Economics, Knutsford, UK; [2]BioMarin Pharmaceutical Inc, San Rafael CA, US ; [3]BioMarin Pharmaceutical Inc, London, UK ; [4]Faculty of Social Care, University of Chester, Chester, UK

Background

- Treatment options to manage people with severe haemophilia A (PwSHA) continue to evolve.
- This analysis aimed to quantify the clinical burden and productivity/activity impairment across treatment classes among adult PwSHA receiving prophylaxis and with no inhibitor history in the EU5 and the Unites States using data drawn from 'The Cost of Haemophilia: a follow-up Socio-economic survey III' (CHESS III).

Methods

- CHESS III is a cross-sectional retrospective burden-of-illness study of adult (18+) males with hereditary haemophilia in the EU5 & US.
- Descriptive data on PwSHA without inhibitor history, treated prophylactically, from the CHESS III dataset were analysed, according to current treatment class (extended half-life [EHL] factor VIII (FVIII), standard half-life/plasma-derived [SHL/PD] FVIII, and non-factor treatment [NFT]).
- Demographic, clinical and treatment information were reported by treating physicians.
  - Annual Bleed Rate (ABR) is measured as the sum of all bleeding events in the 12 months preceding data collection. Annual Joint Bleed Rate (AJBR) and Annual Spontaneous Bleed Rate (ASBR) are measured as the sum of joint and spontaneous bleed events, respectively.
  - Chronic pain was categorized as None, Mild, Moderate and Severe according to functional deficit level ("none" to "interferes with occupation/ADL") and use of analgesics ("none" to "frequent use of analgesics")
  - A problem joint (PJ) is defined as a joint exhibiting chronic 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.[1]
    - A target joint is defined as a joint in which three or more spontaneous bleeds occurred within a consecutive 6-month period prior to data capture.[2]
- Impairment was reported by PwSHA via the Specific Health Problem version of the Work Productivity and Activity Impairment tool (WPAI:SHP) via the linked patient questionnaire.[3]
  - Absenteeism is work time missed and presenteeism is the reduced productivity experienced while at work due to haemophilia and in the previous seven days.
  - Work productivity loss (WPL) is a combination of absenteeism and presenteeism. Activity Impairment (AI) is impairment in daily activities due to haemophilia in the previous seven days.

Results

- Overall, 333 PwSHA met the inclusion criteria, with a mean [SD] age of 35.4 [13.7] and BMI of 25.3 [4.0].
- ABR and ASBR were lowest for the EHL cohort (n=62) at 1.3 [1.3] and 0.6 [1.0], respectively, followed by SHL/PD (n=68; 1.7 [3.3]; 1.4 [2.8]) and NFT (n=203; 2.4 [4.9]; 1.6 [3.3]). AJBR was lowest for the SHL/PD cohort (0.7 [1.5]), followed by EHL (0.8 [1.0]) and NFT (1.3 [3.0]) (**Table 1**).
- In the NFT cohort, higher bleeding frequencies were accompanied by higher frequencies of target and problem joints (0.9 [1.5]; 1.0 [1.6] compared to the EHL (0.7 [0.8]; 0.7 [0.9]) and SHL/PD (0.5 [0.6]; 0.9 [1.2]) cohorts (**Table 1**).
  - The NFT cohort had, on average, shorter time on current treatment (24.6 [21.2] months), compared with the other cohorts while substantial proportions of the NFT and EHL cohorts (n=77 [37.9%] and n=18 [29.0%]) had a treatment class switch in the 12 months prior to data collection.
- Seventy percent (n=232) of all patients were reported to suffer from some level of chronic pain, with moderate/severe levels reported in 16% (n=11), 19% (n=12) and 27% (n=54) of the SHL/PD, EHL and NFT cohorts, respectively (**Figure 1**).
- Among those with available patient-reported outcomes (n=75):
  - AI ranged from 42.9 (29.3) for NFT to 56.7 (24.1) for EHL. Among those, 53 (70.7%) were employed and reported WPL ranging from 15.0 (21.2) for SHL/PD to 56.0 (28.6) for EHL, while (**Table 2**).
  - Patients in the EHL and NFT groups experienced similar levels of anxiety as measured by the GAD-7 tool (**Table 2**).[4]

Limitations

- Due to the observational design of the CHESS III study and voluntary nature of participation by physicians and patients, a degree selection or recall bias cannot be excluded

Table 1. Demographic characteristics and clinical outcomes

	EHL	SHL/PD	NFT	Total
N	N=62	N=68	N=203	N=333
Age, *Mean (SD)*	38.5 (14.5)	35.2 (12.7)	34.4 (13.8)	35.4 (13.7)
BMI, *Mean (SD)*	25.7 (3.0)	26.1 (6.8)	24.9 (2.8)	25.3 (4.0)
ABR, *Mean (SD)*	1.3 (1.3)	1.7 (3.3)	2.4 (4.9)	2.1 (4.1)
AJBR, *Mean (SD)*	0.8 (1.0)	0.7 (1.5)	1.3 (3.0)	1.1 (2.5)
ASBR, *Mean (SD)*)	0.6 (1.0)	1.4 (2.8)	1.6 (3.3)	1.4 (2.9)
Time on current TX (months), *Mean (SD)*	35.4 (47.3)	87.7 (111.2)	24.6 (21.2)	39.5 (61.6)
TX class switch in 12 months prior, *n (%)*	18 (29.0%)	2 (5.9%)	77 (37.9%)	99 (29.7%)
Target joints, *Mean (SD)*	0.7 (0.8)	0.5 (0.6)	0.9 (1.5)	0.8 (1.3)
Problem joints, *Mean (SD)*	0.7 (0.9)	0.9 (1.2)	1.0 (1.6)	1.0 (1.4)

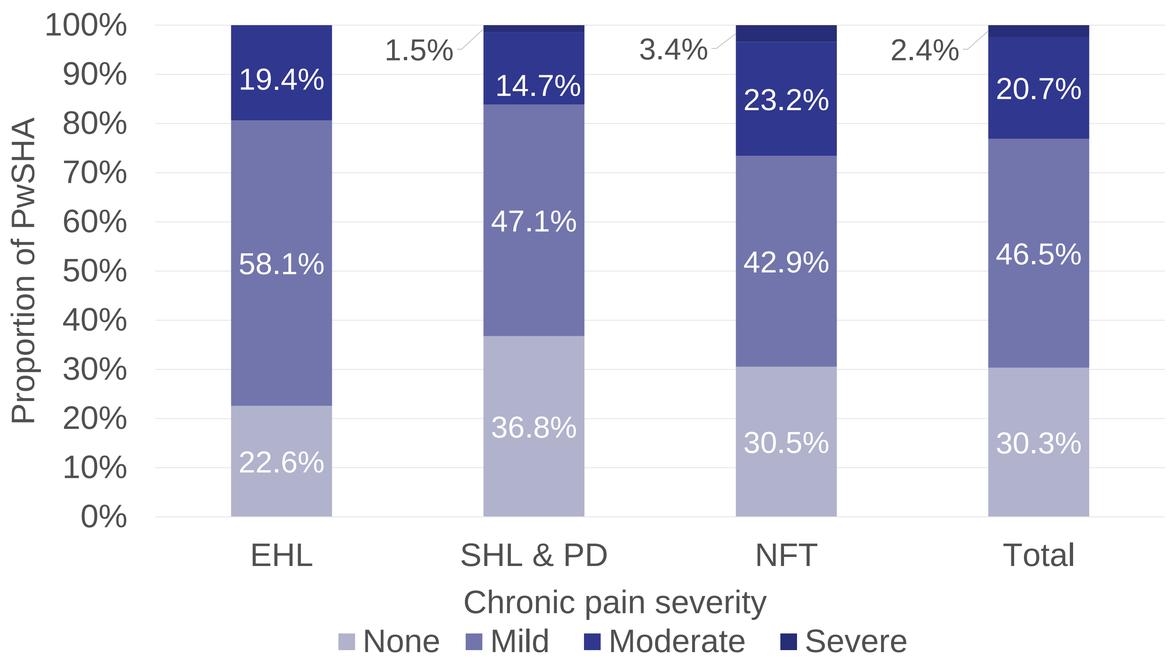
Abbreviations: EHL, Extended half-life; SHL, Standard half-life; PD, Plasma-derived; NFT, non-factor therapy; SD, Standard deviation; BMI, Body Mass Index; ABR, Annual bleed rate, ASBR, spontaneous ABR; AJBR, Joint ABR; TX, treatment

Table 2. Anxiety, employment and WPAI outcomes

	EHL	SHL & PD	NFT	Total
	N=15	N=4	N=56	N=75
Anxiety (GAD-7), *Mean (SD)*	5.6 (4.5)	5.0 (5.2)	5.9 (5.2)	5.8 (5.0)
% AI, *Mean (SD)*	56.7 (24.1)	45.0 (33.2)	42.9 (29.3)	45.7 (28.7)
Employed, *n (%)*	9 (60.0%)	2 (50.0%)	42 (75.0%)	53 (70.7%)
% WPL, *Mean (SD)*	56.0 (28.6)	15.0 (21.2)	34.9 (29.9)	41.3 (30.1)
% Absenteeism, *Mean (SD)*	17.4 (24.4)	0.0 (0.00)	7.2 (11.5)	8.7 (14.6)
% Presenteeism, *Mean (SD)*	47.8 (24.4)	15.0 (21.2)	36.9 (28.2)	37.9 (27.7)

Abbreviations: EHL, Extended half-life; SHL, Standard half-life; PD, Plasma-derived; NFT, non-factor therapy; GAD-7, General Anxiety Disorder 7-item; AI, activity impairment; SD, Standard deviation; WPL, work productivity loss

Figure 1. Proportion of patients with chronic pain, by treatment class



Conclusions

- Clinical outcomes showed variation across treatment classes, with bleeding outcomes highest for those currently on NFTs, possibly related to unfavourable outcomes preceding a recent treatment change as well as existing joint damage levels.
- High levels of AI and WPL were observed across all treatments in this cohort, potentially driven by chronic outcomes and pre-existing joint damage.
- Even with a range of therapeutic options available, these results highlight that PwSHA in this cohort still experience activity impairment, chronic pain and anxiety, suggesting a substantial remaining unmet need to be addressed. Further research is warranted to explore specific areas of residual unmet need.

References

1. Burke T et al. Humanistic burden of problem joints for children and adults with haemophilia. Haemophilia. 2022;12(1).
2. Blanchette VS, et al. Definitions in hemophilia: Communication from the SSC of the ISTH. JTH. 2014;12(11):1935-39.
3. Reilly, M.C. et al. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoeconomics. 1993 4(5).
4. Spitzer R.L. et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006 May 22;166(10):1092-7.

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