Exploring the level of congruence between patient- and haematologist-reporting of anxiety and depression in people with haemophilia A

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Background

- Suboptimal prevention and treatment of bleeding events in haemophilia A (HA; factor VIII deficiency) is associated with long-term joint inflammation and deterioration, and chronic pain.[1]
- Psychosocial challenges are a recognised issue faced by people with HA (PWHA) and can significantly impact therapy adherence and clinical outcomes.[2-5] Nevertheless, limited research exists on the reporting of mental health challenges by PWHA and their treating physicians.[6-7]
- The aim of this analysis is to explore congruence between patient and haematologist reporting of anxiety and depression in PWHA using data from the 'Cost of Haemophilia in Europe: a Socioeconomic Survey - II' (CHESS II) study.

Methods

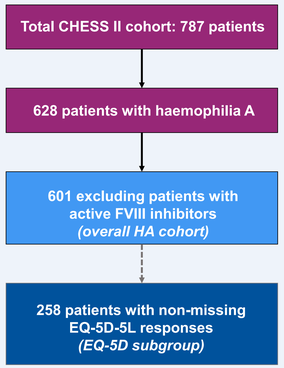
- Data on PWHA without active inhibitors at time of study capture was extracted from CHESS II, a retrospective burden-of-illness study in 787 adult males with HA and haemophilia B in Europe. An interim dataset with study capture period November 2018 – July 2019 was used for this analysis.
- Participating haematologists completed a 'clinical record form' (CRF), containing demographics and medical history, for up to eight PWHA in their care; these patients voluntarily completed a corresponding 'patient and public involvement and engagement' (PPIE) questionnaire, covering non-medical costs, work and activity impairment, and health-related quality of life (HRQoL).
- Patient comorbidities (at the time of study capture), including "Anxiety" and "Depression", were selected by the respondent physician from a pre-specified list. For the purposes of this analysis, a diagnosis of anxiety and/or depression was grouped into a single "anxiety/depression" indicator.
- The generic EQ-5D-5L health status measure was included in the PPIE. Respondents indicate their level of impairment "today" ("no [problems]", "slight", "moderate", "severe", "extreme/completely unable"; level range 1–5) on five dimensions of health (mobility, self-care, usual activities, pain/discomfort, anxiety/depression).[8] A number of studies recognize the performance of the EQ-5D for public health screening of anxiety and depressive symptoms.[9,10]
- Patient report of anxiety/depression was determined via the respective dimension of the EQ-5D-5L using two approaches:
  1. any level of impairment ≥2 ("slight to extreme problems" grouping); and
  2. any level ≥3 ("moderate to extreme problems" grouping).
- For both approaches, the level of congruence (agreement in reporting of anxiety/depression) between patient and haematologist was assessed using 2x2 matrices.
- Demographic and clinical characteristics were reported for the CHESS II HA cohort as a whole and for the subgroup of EQ-5D-5L respondents:
  - *Demographics:* Age, body mass index (BMI), country of residence
  - *Condition severity:* Mild (>5-40% baseline factor VIII activity), moderate (1-5%), severe (<1%).
  - *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.
  - *Treatment strategy (for patients receiving 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.[11]
  - *'Problem joints':* Joints exhibiting symptoms of HA-related damage: chronic synovitis; arthropathy; reduced range of motion; recurrent bleeding.[12]
- Results are presented as mean (± standard deviation) or n (% of patients).

Results

Demographics

- Of the 601 non-inhibitor PWHA enrolled in CHESS II (*overall HA cohort*), 258 (43%) completed the EQ-5D-5L (*EQ-5D subgroup*) (**Fig 1**).
- Age, BMI, and condition severity were largely similar between the overall HA cohort and EQ-5D subgroup (**Table 1**).
- Country representation in the EQ-5D subgroup was similar to the overall HA cohort, though comprising a slightly larger proportion of patients from Spain and Italy, and fewer patients from Germany, France, and the United Kingdom.
- Clinical characteristics were largely similar between the overall HA cohort and EQ-5D subgroup (**Table 1**).

Fig 1. CHESS II sample: EQ-5D-5L



Overall reporting of anxiety/depression

- A diagnosis of anxiety and/or depression was indicated by respondent haematologists in 17% of patients (n=45) (**Table 2 / Figure 2**).
- Levels of anxiety/depression from "slight problems" to "extreme problems" (≥2) were reported by 51% (n=132) of the EQ-5D subgroup (**Table 2 / Figure 2**).
- When excluding those patients reporting "slight" anxiety or depression, the rate of reporting decreased to 13% (n=34) of the EQ-5D subgroup reporting "moderate" to "extreme" (≥3) levels of anxiety or depression (**Table 2 / Figure 2**).

Congruence in reporting of anxiety/depression

- For the patients reporting any level of anxiety or depression (≥2), congruence between patient and haematologist reporting occurred in 54% of instances (**Table 3**).
- Reporting congruence increased to 77% when restricting the EQ-5D subgroup to those reporting moderate to extreme problems (≥3) (**Table 3**).
- Among the 213 patients for whom neither anxiety nor depression were indicated by the respondent haematologist, 19 patients (9%) reported moderate problems in the corresponding EQ-5D-5L dimension, four patients (2%) reported severe problems, and one patient reported extreme problems (**Table 3**).
- Of the 45 patients with a haematologist-reported comorbidity of anxiety/depression, more than one third (36%; n=16) reported no problems in the corresponding EQ-5D dimension (**Table 3**).

Table 1. Demographics and clinical characteristics

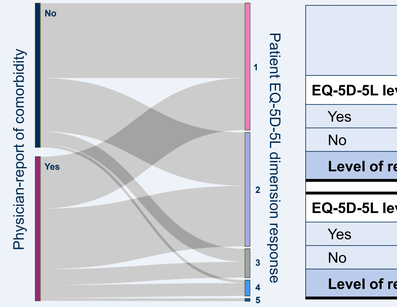
	HA cohort (n=601)	EQ-5D subgroup (n=258)
Age (mean ± SD)	37.7 ± 14.5	38.4 ± 15.0
Body mass index, BMI (mean ± SD)	24.5 ± 2.9	24.7 ± 2.6
Condition severity (n [% of patients)		
Mild	100 [17%]	42 [16%]
Moderate	202 [34%]	72 [28%]
Severe	299 [50%]	144 [56%]
Country (n [% of patients)		
Germany	47 [8%]	6 [2%]
Spain	187 [31%]	98 [38%]
France	60 [10%]	33 [13%]
Italy	232 [39%]	106 [41%]
United Kingdom	69 [11%]	15 [6%]
Netherlands	1 [<1%]	0 [0%]
Romania	5 [1%]	0 [0%]
Chronic pain (n [% of patients])		
None	202 [34%]	84 [33%]
Mild	233 [39%]	102 [40%]
Moderate	135 [22%]	59 [23%]
Severe	31 [5%]	13 [5%]
Treatment strategy (n [% of patients])		
Receiving FVIII replacement therapy	398 [66%]	181 [70%]
Primary on-demand	186 [47%]	80 [44%]
Primary prophylaxis	50 [13%]	23 [13%]
Secondary on-demand	50 [13%]	16 [9%]
Secondary prophylaxis	112 [28%]	62 [34%]
Annual bleed rate, ABR (mean ± SD)	3.31 ± 7.38	3.15 ± 3.08
Target joints (mean ± SD)	0.48 ± 0.86	0.54 ± 0.95
'Problem' joints (mean ± SD)	0.61 ± 0.94	0.66 ± 1.01

Abbreviations: HA, haemophilia A; SD, standard deviation.

Table 2. EQ-5D-5L anxiety/depression dimension responses

Patient-report of anxiety or depression (n [% of patients]) – EQ-5D-5L	**Haematologist-report** of anxiety and/or depression comorbidity		
	Yes	No	Total
1 Not anxious or depressed	16 [36%]	110 [52%]	126 [49%]
2 Slightly anxious or depressed	19 [42%]	79 [37%]	98 [38%]
3 Moderately anxious or depressed	5 [11%]	19 [9%]	24 [9%]
4 Severely anxious or depressed	4 [9%]	4 [2%]	8 [3%]
5 Extremely anxious or depressed	1 [2%]	1 [<1%]	2 [1%]
Total	**45**	**213**	**258**
EQ-5D-5L level ≥2 ("Slight" – "Extreme")	29 [64%]	103 [48%]	132 [51%]
EQ-5D-5L level ≥3 ("Moderate" – "Extreme")	10 [22%]	24 [11%]	34 [13%]

Fig 2. Patient and haematologist reports of anxiety/depression



EQ-5D-5L level: 1= Not [anxious or depressed]; *2*= Slightly; *3*= Moderately; *4*= Severely; *5*= Extremely

Table 3. Congruence in reporting of anxiety/depression

	Haematologist-report of anxiety and/or depression comorbidity		
	Yes	No	Total
EQ-5D-5L level ≥2 ("Slight" – "Extreme")			
Yes	**29 [64%]**	103 [48%]	
No	16 [36%]	**110 [52%]**	
Level of reporting congruence			**139 [54%]**
EQ-5D-5L level ≥3 ("Moderate" – "Extreme")			
Yes	**10 [22%]**	24 [11%]	
No	35 [78%]	**189 [89%]**	
Level of reporting congruence			**199 [77%]**

Conclusions

- Among patients in this study reporting some level of anxiety or depression, a corresponding comorbidity was generally reported by their haematologist. Congruence in reporting was greater when the level of patient-reported impairment was more severe (EQ-5D-5L dimension level ≥3).
- Nevertheless, a minority of patients reported significant levels of anxiety and depression that were unreported by their haematologist in this study.
- EQ-5D responses may be sensitive to short-term changes in mental health state resulting from acute events, such as a hospital admission or bleeding event.[9,10] The timing of any such events prior to EQ-5D completion was not captured in this study.
- A limitation of the haematologist-reporting in this study is a lack of determination of a formal diagnosis of anxiety or depression. Cross-disciplinary recognition and management of psychiatric challenges in people with haemophilia A is likely to be influenced by treatment guidelines of the respective countries and by broader cultural and health system perspectives on mental health.
- Future research should explore the reasons for disconnects in reporting and the impact of psychosocial awareness (of both clinician and patient) on clinical management and outcomes in haemophilia A.

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