The Relationship Between Bleeding Frequency and EQ-5D in Severe Haemophilia

Charlotte Camp,[1] Jamie O'Hara,[1] David Hughes,[1] Shaun Walsh,[1] Jason Booth,[2]

[1]HCD Economics, United Kingdom; [2]*Shire, Cambridge, United States

INTRODUCTION

- Joint bleeding (haemarthrosis) is a distinctive characteristic of haemophilia with physical, psychological and societal effects. It has an immediate impact resulting in pain, swelling, inability to follow daily activities, as well as long-term severe consequences for patients' mobility and general well-being.[1] A single joint bleed may cause permanent damage. Two or three bleeds into the same joint can result in increased bodily pain, reduced physical functioning or disability.[2]
- Recurrent haemorrhage in the same joint may result in irreversible intra-articular damage, chronic pain, impaired mobility, and inability to do certain jobs culminating in haemophilic arthropathy. This along with the psychological consequences for the patients and their social functioning can negatively impact their health-related quality of life (HRQoL).[3]
- Haemophilia treatment depends on the severity of the condition and the patient's preferences. There are two main approaches to treating haemophilia patients; preventative (prophylaxis) and on-demand (OD) treatment.
- Optimal HRQoL outcomes can be supported by maintaining low or zero ABR among haemophilia patients through prophylactic treatment.[2]

OBJECTIVE

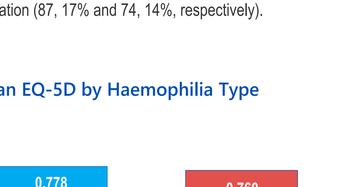
- The purpose of this abstract is to investigate, using descriptive analysis, the association between annual bleeding rates (ABR) and HRQoL of patients with severe haemophilia A or B.

METHODS

- Data were taken from the 'Cost of Haemophilia across Europe: Socioeconomic Survey (CHESS) – A cross-section of 139 haemophilia specialists (surveyed between January and April 2015) providing demographic and clinical information and 12-month ambulatory and secondary care activity for 1,285 patients via an online survey. In turn, 551 of those patients provided corresponding direct and indirect non-medical cost information, including work loss and out-of-pocket expenses. A cost database was developed for each country using publically-available information. Study ethics was governed and approved by the University of Chester Ethics Committee.
- The inclusion criteria for the study were that patients have a factor level of < 1%, are over 18 years old and are diagnosed with hereditary haemophilia A or B
- The EQ-5D-3L instrument was the patient-reported outcome measure (PROM) used to assess the HRQoL of participants in CHESS.
- Physician-recorded monthly bleeding rates were annualized to generate ABRs. Patients were grouped into one of five cohorts (ABR = 0, 12, 24, 36, or 48). Standard t-tests were conducted to test for between-group differences.
- Patients with inhibitors were excluded from this analysis
- Treatment strategies in this analysis have been categorized as: primary prophylaxis (on prophylaxis from diagnosis), secondary prophylaxis (on prophylaxis, previously on-demand at any point), primary on-demand (always been on-demand), and secondary on-demand (previously on prophylaxis and moved to on-demand regimen).

RESULTS

Figure 1. Haemophilia Subtype of Study Population



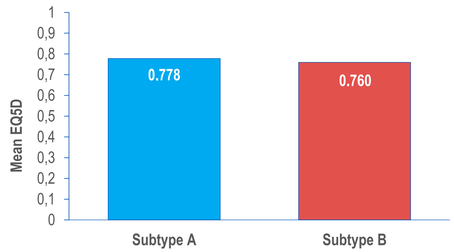
- Of the available population of 1,227 (excludes current inhibitor patients), 515 patients completed information for EQ-5D scores; these patients were the focus of this analysis.
- The majority of the study population (n=400, 78%) had haemophilia A, with the remaining (n = 115, 22%) patients, haemophilia B.
- The average age of patients was 38 years (SD 15yrs), with a mean age at start of treatment of 17 years (SD 15.84).
- Patients examined in the analysis had a mean number of target joints of 1.3 (SD 1.42).
- A breakdown of treatment strategies for the study population is presented in Table 1.

Table 1: Breakdown of Treatment Strategies of Study Population

Treatment Strategy	Frequency	Percent	Cumulative Frequency	Cumulative Percent
Primary OD	113	22.03	113	22.03
Secondary OD	87	16.96	513	38.99
Primary prophylaxis	74	14.42	426	53.41
Secondary prophylaxis	239	46.59	352	100

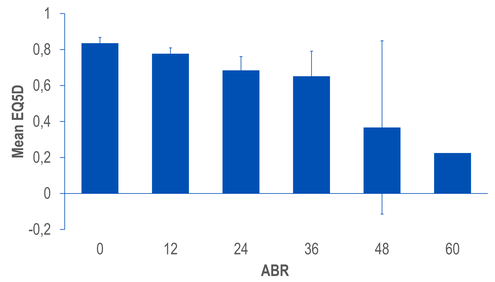
- The majority of patients were using secondary prophylaxis (n=239, 47%).
- Primary on demand was the second most common treatment regimen (113, 22%); secondary on demand and primary prophylaxis accounted for the remaining population (87, 17% and 74, 14%, respectively).

Figure 2: Mean EQ-5D by Haemophilia Type



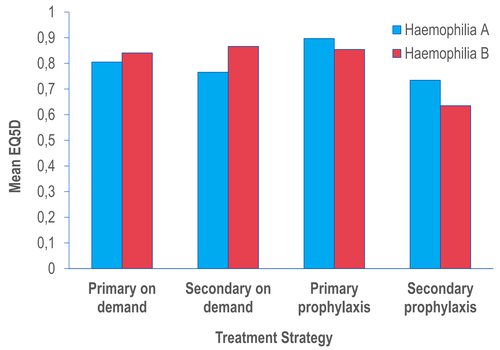
- A higher HRQoL was reported for patients with haemophilia A (n = 400) compared to patients with haemophilia B (n=115) (0.778 vs 0.760), however this difference was not found to be statistically significant.

Figure 3: EQ-5D by ABR



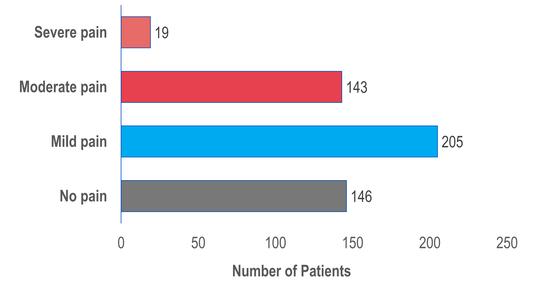
- Patients with no recorded bleeding (n = 172) reported the highest mean EQ-5D score, 0.84 (standard deviation (SD) 0.21).
- ABRs inversely correlated with EQ-5D: individuals with one recorded bleed per month (ABR = 12; n = 251) reported mean EQ-5D of 0.78 (SD 0.26); in the ABR = 24 cohort (n = 68), mean reported EQ-5D decreased to 0.68 (SD 0.31); for ABR = 36 (n = 15), mean reported EQ-5D is similar, 0.65 (SD 0.25); in the ABR = 48 cohort (n = 7), mean EQ-5D almost halves versus the ABR = 36 cohort (mean 0.37; SD 0.52). With the exception of ABR = 24 versus ABR = 36, cohort differences between groups were found to be statistically significant (P < 0.05).
- Patients with zero bleeds (N = 172) had higher EQ-5D compared to non-zero bleeds (0.84 vs 0.74), which was statistically significant (< 0.0001) and clinically meaningful.[4]

Figure 4: EQ-5D by Treatment Strategy and Haemophilia Type



- Patients receiving primary prophylaxis recorded the highest average EQ-5D across the sample, with haemophilia A patients reporting the greatest EQ-5D (0.90, 0.85). Secondary prophylaxis patients reported the lowest mean EQ-5D in the study with (0.734) for haemophila A and (0.635) for haemophilia B.
- Haemophilia A patients receiving prophylaxis recorded a higher EQ-5D than did those with haemophilia B. This was the reverse for on demand patients, with mean EQ-5D scores of (0.805, 0.841) for primary on demand and (0.765, 0.866) for secondary on demand.

Figure 4: Chronic Pain Ratings



- Chronic pain scores were examined across the study population as this is another important indicator of HRQoL.
- The majority of patients reported some level of existing chronic pain (n=367, 72%)
- 40% reported mild pain (n = 205); 28% (n = 143) moderate pain; 28% (n = 146) experienced no pain; 4% (n = 19) of patients reported that they experienced severe pain.

CONCLUSION

- The analysis conducted on the chosen sample suggests an inverse relationship between patient bleeding rate and reported HRQoL, with patients with zero bleeding reporting the highest HRQoL.
- Further investigation is needed to better understand the impact of underlying confounding factors (including age, previous incidence of inhibitor, comorbidities and country effects).
- This descriptive analysis supports care pathways and treatment strategies which are geared toward lower ABR among haemophilia patients, as this is positively related to better HRQoL.

REFERENCES

1. Roosendaal G, Lafeber FP. Pathogenesis of haemophilic arthropathy. *Haemophilia* 2006;12(Suppl 3):117-121.
2. Gringeri A, Ewenstein B, Reininger A. The burden of bleeding in Haemophilia: is one bleed too many? *Haemophilia.* 2014;20(4):459-463.
3. Epstein J, Xiong Y, Ito D, et al. Patient characteristics and health outcomes of severe Haemophilia A children reporting zero annual bleeds. *Haemophilia.* 2013;19(Suppl 2):20.
4. Walters SJ, Brazier JE. Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D. *Qual Life Res.* 2005 Aug;14(6):1523-32. (Highlights importance/patient impact of zero bleeds.)

DISCLOSURES

The original CHESS study was supported by unrestricted research grants from Swedish Orphan Biovitrum AB (Sobi) and Novo Nordisk. The study was approved by the University of Chester Ethics Committee. The wider project was conducted in collaboration with the UK Haemophilia Society (UKHS) and governed by a steering committee chaired by Liz Carrol, Chief Executive of the UKHS.
*Jason Booth is an employee of Baxalta (Baxalta US, Inc, Cambridge, MA USA), now part of Shire.
The studies were sponsored by Baxalta US, Inc., now part of Shire. The sub analysis presented in this poster was supported by Baxalta