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Relationship Between Treatment Strategy and Impairment in Severe Haemophilia

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Key Highlights

- The aim of this study is to describe the relationship between treatment strategies and observed work & activity impairment in severeHaemophilia patients
- Analysis of observational data from 541 EU5 patients that completed a self-assessment survey, including the Work Productivity and Activity Impairment Questionnaire
- Consistent differences were observed between treatment strategies, with primary prophylaxis patients reporting the lowest impairment score on average
- Mean levels of impairment, both work and activity related, appear to show an association with the treatment strategy of the individual

Background

- Individuals with severe haemophilia (<1 IU/dL factor levels) represent approximately one-third of the haemophilia population in Europe[1,2] and can experience recurrent spontaneous bleeds often in the absence of any trauma event
- Acute symptoms of a bleed event include inflammation of the synovial fluid (synovitis), pain, and reduced mobility. Chronic synovitis arising from frequent bleed events leads to arthropathy and degeneration of the joint, with associated impact on mobility and chronic pain
- Impact of bleed frequency and joint status on an individual's health-related quality of life (HRQoL) is therefore not only physical but also observed in psychological and societal effects, including engagement in daily activities and work participation[3]
- Previous research[4] has indicated that an individual's treatment (Tx) strategy – namely, either on-demand (OD) treatment at the time of a bleed or preventative 'prophylaxis' therapy (PX), or some combination of the two – may influence the individual's clinical trajectory, and by proxy their level of life impairment due to haemophilia

Objective

- To describe the relationship between Tx strategy and work/activity impairment in severe haemophilia using real world observational data

Method

- Data were drawn from the 'Cost of Haemophilia across Europe – a Socioeconomic Survey' (CHESS),[5] a burden of disease assessment in severe haemophilia A and B across five European countries (France, Germany, Italy, Spain, and the UK) conducted in 2015
- Physicians provided clinical and sociodemographic information for 1,285 adult patients, 541 of whom completed corresponding questionnaires covering out-of-pocket expenditure and psychosocial impact
- The WPAI-general health version (WPAI-GH) was used to measure the patients' work and activity impairments. The WPAI-GH questionnaire is an instrument to measure impairments in both paid work and unpaid work.[6,7] It measures absenteeism, presenteeism as well as the impairments in unpaid activity because of health problems during the past seven days
- Four main outcomes can be generated from the WPAI-GH and expressed in percentages:
  1. Percent work time missed due to health for those who were currently employed;
  2. Percent impairment while working due to health for those who were currently employed and actually worked in the past seven days;
  3. Percent overall work impairment due to health for those who were currently employed;
  4. Percent activity impairment due to health for all respondents
- Tx strategy was stratified based on those who had received the strategy consistently since initiation ('primary' regimens) versus those who had switched strategies ('secondary' regimens) (PPX/SPX and POD/SOD)
- Mean WPAI-GH scores for all outcomes was compared by Tx strategy, calculating the proportion above and below the mean value. Results were contrasted with population norms derived from the National Health and Wellness Survey (NHWS) a US-based survey of a nationally representative sample of adults (N=71,141)[8]

Results

- Patterns of target joints (areas of chronic synovitis) were inconsistent between Tx strategies: for PX regimens, reporting of any target joint was less frequent in the employed cohort versus the whole reporting cohort; for OD regimens, either no difference (POD) or a higher incidence of target joints (SOD) was reported among the employed cohort
- Similar patterns were observed in reporting of chronic pain: for PX regimens, reporting of any pain was lower for employed patients, suggestive of a relationship between chronic pain and work participation. For OD regimens, however, either no difference (POD) or a higher level of chronic pain (SOD) was reported among the employed cohort

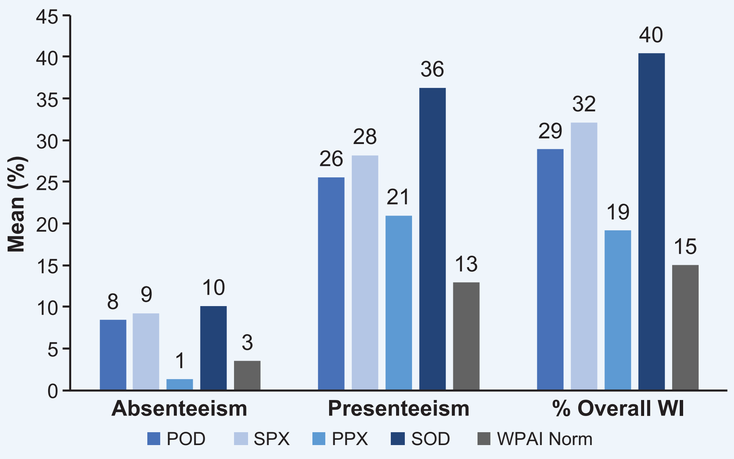
Table 1. Patient Demographics and Clinical Characteristics across Employed and Total Cohort, by Tx Strategy

		Tx Strategy			
Employed Cohort (N=239)		**POD**	**SPX**	**PPX**	**SOD**
N (%)		50 (21%)	121 (51%)	27 (11%)	41 (17%)
Age (years)	<30	30%	17%	85%	17%
	30-50	60%	72%	15%	59%
	>50	10%	11%	0%	24%
Number of Target Joints[a]	0	32%	26%	48%	10%
	1	40%	30%	22%	39%
	2	20%	29%	26%	32%
	>2	8%	15%	4%	20%
Chronic Pain[b]	No Pain	52%	36%	63%	27%
	Mild	46%	61%	37%	73%
	Moderate	2%	3%	0%	0%
Whole Cohort (N=541)		**POD**	**SPX**	**PPX**	**SOD**
N (%)		126 (23%)	247 (46%)	72 (13%)	96 (18%)
Age (years)	<30	33%	21%	94%	30%
	30-50	43%	58%	6%	41%
	>50	24%	21%	0%	29%
Number of Target Joints[a]	0	32%	23%	43%	28%
	1	37%	28%	32%	30%
	2	18%	29%	24%	26%
	>2	13%	20%	1%	16%
Chronic Pain[b]	No pain	52%	28%	60%	35%
	Mild	46%	66%	40%	61%
	Moderate	2%	6%	0%	3%

Work Impairment (WI)

- Mean absenteeism, presenteeism and WI were highest among the SOD cohort **(Figure 1)**; with the exception of absenteeism in PPX regimens, work impairment scores were consistently above population norms
- While patients on PPX experienced little to no absenteeism, there was notably higher presenteeism versus population norms (21% versus 13%) and, as a result, overall WI (19% versus 15%)

Figure 1. Absenteeism, Presenteeism, and Work Impairment Scores for Employed Cohort, by Tx Strategy and Normative Population[5] (%)

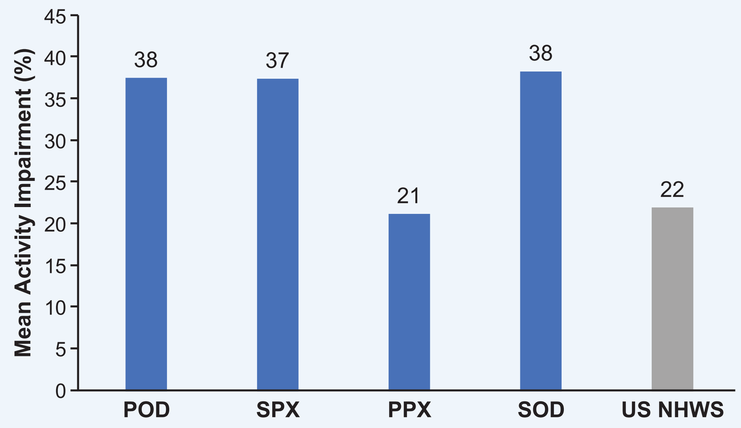


Tx: treatment; POD: primary on-demand; SOD: secondary on-demand; PPX: primary prophylaxis; SPX: secondary prophylaxis
[a]Target joints are defined as locations of chronic synovitis[5]
[b]Physician-reported pain of the patient, scored on a 0–3 scale ('No pain' – 'Severe pain') (N.B. 'Severe pain' N=0 in all cohorts)

Activity Impairment (AI)

- AI was lowest in the PPX cohort (mean 21%) **(Figure 2)**, less than normative levels (22%)
- In all other Tx strategies, AI was broadly uniform (range 37-38%) and higher than normative levels

Figure 2. Mean Activity Impairment by Treatment Strategy and Normative Population[5] (%)



POD: primary on-demand; SOD: secondary on-demand; PPX: primary prophylaxis; SPX: secondary prophylaxis

Study Limitations

- Levels of impairment may be influenced by the demographic characteristics of each treatment group, including a notably younger average age in the PPX cohort
- In addition, Tx strategy decisions may be driven by pre-existing morbidity of an individual
- Normative WPAI was available only in a US cohort and may not be directly comparable to a European cohort

Discussion

- The results are suggestive of differential work productivity and activity impairment between Tx strategies in severe haemophilia
- In particular, patients moving to OD regimens following a period of PX report consistently higher levels of impairment compared to other Tx strategies
- Patients receiving PPX regimens experience minimal absenteeism versus other Tx cohorts, but report greater levels of impairment while working relative to population norms
- Across all Tx strategies, impairment while working, and overall impairment, is higher than would be expected in an 'average' adult population
- The relationship between clinical outcomes and employment status is inconsistent between treatment strategy, and warrants further study
- Further research into the driving factors of impairment will assist in qualifying the relationship between Tx strategy and life impairment for persons with haemophilia

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