

Association of Hemophilia A Inhibitor Status and Patient-Reported Outcomes with Work Productivity and Health-Related Quality of Life

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Introduction

- ❑ Persons with hemophilia A (PwHA) suffer from recurrent bleeds, especially hemarthrosis, resulting in joint damage
- ❑ Hemophilia inhibitor status impacts bleeding, which is associated with acute and chronic pain
- ❑ It is important to understand how inhibitors impact health-related quality of life (HRQoL), work productivity and activity impairment in PwHA
- ❑ Our study objectives:
 - Compare patient-reported outcomes including bleed rate, pain, joint health, HRQoL, work productivity and activity impairment (WPAI) by inhibitor status
 - Investigate the correlation of patient-reported outcomes with WPAI and HRQoL

Methods

- ❑ Enrolled PwHA (FVIII activity level <5%) aged ≥ 2 years with and without inhibitors at a 1:2 ratio, 2019-2021
- ❑ Participants from 4 geographically diverse U.S. Hemophilia Treatment Centers (HTCs) classified into 3 groups
 - Active inhibitor: FVIII inhibitor titer >1.0 BU 6 months prior to enrollment
 - Tolerized inhibitor: history of inhibitor titer >1.0 BU plus past Immune Tolerance Induction (ITI), and/or use of factor VIII for prophylaxis at enrollment
 - No inhibitor
- ❑ Parents/adult participants completed a survey at enrollment to collect sociodemographic and clinical data, patient-reported outcomes (pain, bleeding, joint stiffness, WPAI, and HRQoL measured by the EQ-5D-3L)
- ❑ Clinical chart review documented hemophilic severity, inhibitor titer level and treatment regimen

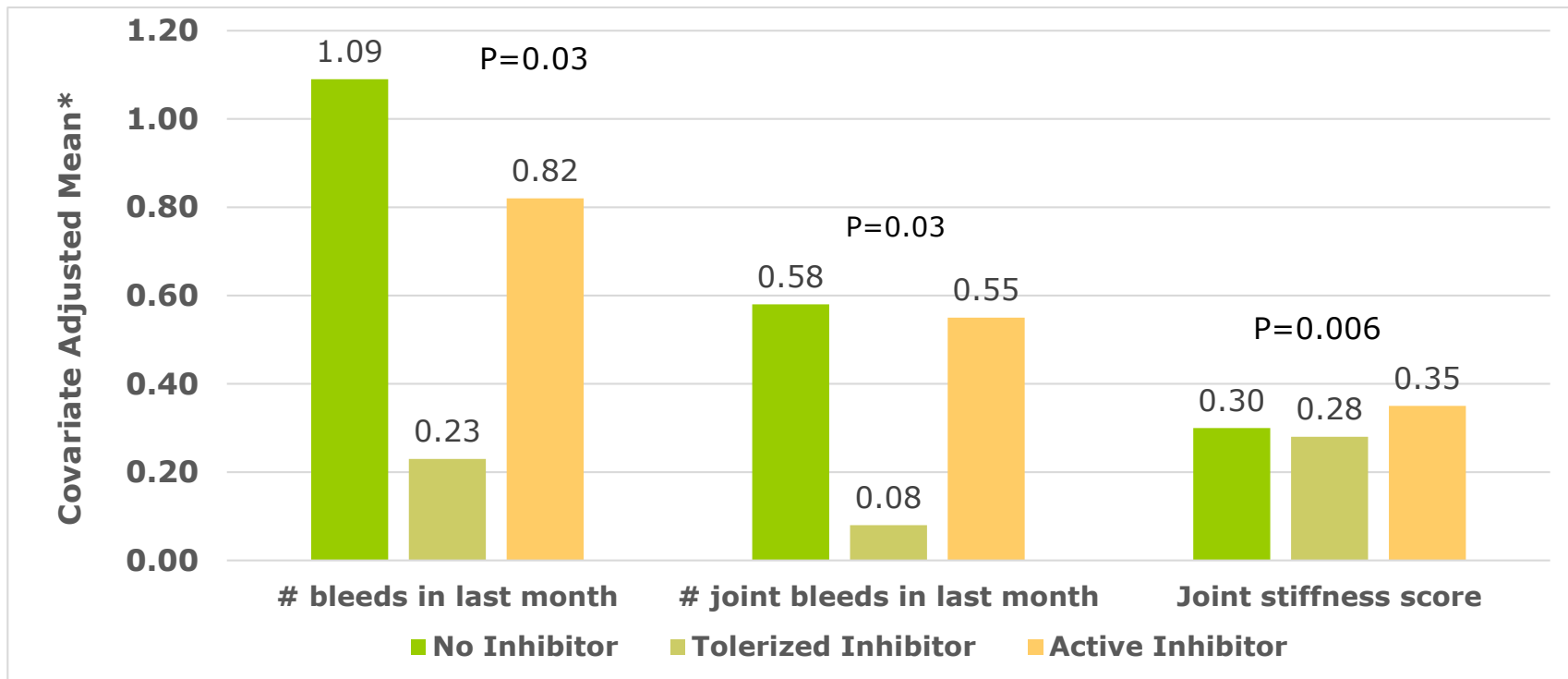
Results: Participant Characteristics by Inhibitor Status



Variable	Total (N=80)	Active inhibitor (n=9, 11.3%)	Tolerized inhibitor (n=22, 27.5%)	No inhibitor (n=49, 61.3%)	P Value*
Mean (SD) age	24.9 (14.3)	21.9 (19.1)	16.3 (9.5)	29.3 (13.5)	0.001
Age group: Adults (%)	53 (66.3)	5 (55.6)	9 (40.9)	39 (79.6)	<0.01
Hemophilic severity (%)					0.13
Moderate	10 (12.5)	0 (0.0)	1 (4.5)	9 (18.4)	
Severe	70 (87.5)	9 (100.0)	21 (95.5)	40 (81.6)	
Prophylactic treatment (%)	70 (87.5)	9 (100.0)	21 (95.5)	40 (81.6)	0.13
Had bleeds in last month (%)	39 (48.8)	6 (66.7)	5 (22.7)	28 (57.1)	0.01
Chronic pain level (SE) ^{†,‡}		2.02 (0.88)	1.13 (0.64)	2.34 (0.44)	>0.06
EQ VAS (SE) ^{†,§}		71.32 (5.50)a	84.96 (3.99)b	86.49 (2.77)b	<0.02
EQ-5D index score (SE) ^{†,§}		0.79 (0.07)a	0.96 (0.05)b	0.90 (0.04)a,b	0.03

Note: Data are presented as number (column percentage) for categorical variables, or mean (SD or SE) for continuous variables. *P values were calculated from chi-square tests for categorical variables and analysis of variances for continuous variables to test the variables' association with inhibitor status. †Covariates included age, hemophilia severity, prophylactic treatment. a, b For each row, covariates adjusted mean with different symbols (a,b) across the inhibitor status categories statistically significantly differ from one another (P<0.05). The P value for each row is the maximum for all significant comparisons or the minimum across all nonsignificant comparisons. ‡Chronic pain was measured by a question: During the past month, how would you describe your chronic pain level in general on a scale of 0 (no pain) to 10 (worst possible pain)? §EQ VAS is a visual analog scale in which respondents indicate their overall health at the time of the survey. On the VAS, 0 indicates the worst imaginable health and 100 indicates the best imaginable health. The EQ-5D index score was derived from weighted values that represent the U.S. societal perspective, and ranged from 0 (a health state equivalent to death) to 1 (perfect health). Abbreviation: SD, standard deviation; SE, standard error.

Results: Bleeds and Joint Stiffness by Inhibitor Status



Note: Joint stiffness was measured using 5-item instrument of stiffness impact short form from the HealthMeasures Measurement Systems. Joint stiffness score was standardized to have a mean of 50 and standard deviation of 10. In order to present the data on the same scale, the scores were divided by 100. *Covariates included age, hemophilic severity, and prophylactic treatment.

Results: Correlation of PRO with WPAI and HRQoL

Pearson Correlation Coefficients*							
Prob > r under H0: Rho=0							
Number of Observations							
	EQ VAS	EQ index	Work time missed	Impairment while working	Overall work impairment	Activity impairment due to hemophilia	
Number of bleeds	-0.35	-0.46	0.40	0.26	0.40	0.18	
	0.001	<.0001	0.0005	0.03	0.0005	0.11	
	78	79	72	74	72	79	
Number of joint bleeds	-0.43	-0.51	0.28	0.34	0.39	0.33	
	<.0001	<.0001	0.02	0.003	0.0007	0.003	
	79	80	73	75	73	80	
Number of non-joint bleeds	-0.16	-0.25	0.40	0.08	0.28	-0.03	
	0.16	0.03	0.0005	0.49	0.02	0.81	
	78	79	72	74	72	79	
Bleeding related pain	-0.30	-0.51	0.18	0.20	0.25	0.39	
	0.07	0.001	0.32	0.25	0.15	0.02	
	37	37	34	35	34	37	
Chronic pain	-0.61	-0.69	0.21	0.22	0.28	0.51	
	<.0001	<.0001	0.07	0.05	0.02	<.0001	
	79	80	73	75	73	80	
Joint stiffness score	-0.67	-0.77	0.40	0.38	0.45	0.52	
	<.0001	<.0001	0.0005	0.0009	<.0001	<.0001	
	79	80	73	75	73	80	

Note: The WPAI measure includes 4 scores presented as percentage: work time missed, impairment while working, overall work impairment, and activity impairment due to hemophilia. *Correlation coefficients range from -1.0 (a perfect negative correlation) to positive 1.0 (a perfect positive correlation), where 0 indicates that there is no association, and absolute value of 1 indicates the strongest association between two variables. Abbreviations: PRO, patient reported outcome; WPAI, work productivity and activity impairment; HRQoL, health-related quality of life; EQ VAS, EuroQol Visual Analogue Scale.

Limitations

- ❑ The study sample was skewed toward a younger age in the tolerized inhibitor group, making age a possible confounding factor
- ❑ Better outcomes observed in the tolerized group might be due to younger age rather than inhibitor status

Conclusion

- ❑ PwHA in the active and no inhibitor groups experienced greater clinical burden as measured by bleeds compared to the tolerized group
 - This may be due to more consistent adherence to treatment regimens among tolerized PwHA so as to prevent inhibitor recurrence
- ❑ Those with active inhibitor displayed lower HRQoL scores than the tolerized inhibitor group
- ❑ Bleeds, chronic pain and joint stiffness were inversely correlated with HRQoL, resulting in lower work productivity and activity

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Conflict of Interest Disclosure

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