Poster No. 1793

Analysis of Hemophilia A Outcomes and Treatment Patterns Using Real-World Data From the Canadian Hemophilia Bleeding Disorder Registry

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Disclosures

AL: received honoraria from Takeda for consultancy and participation in a speaker bureau and honoraria from Bayer. **FG**: received research funding from F. Hoffmann-La Roche Ltd, Novo Nordisk, Takeda and Bayer. **MCP**: received honoraria from F. Hoffmann-La Roche Ltd, Bayer, Bioverativ/Sanofi, CSL Behring, Novo Nordisk, Pfizer and Takeda for participation in advisory board meetings, and research funding from Bayer and CSL Behring. **AS**, **OM** and **CSS:** employees and shareholders of F. Hoffmann-La Roche Ltd. **FN**: employee of F. Hoffmann-La Roche Ltd and has received research funding from Novartis and GSK. **DM**: received honoraria from Pfizer, Sobi, Bioverativ and Sigilon, and research funding from Pfizer. **AI**: received research funding from Bayer, BioMarin, CSL Behring, Freeline, Grifols, Novo Nordisk, Octapharma, Pfizer, F. Hoffmann-La Roche Ltd, Sanofi, Spark, Takeda and Uniqure. **AK** and **QI**: no disclosures to declare.

Key takeaways

- This study confirms the feasibility of using the Canadian Hemophilia Bleeding Disorder Registry (CBDR) to analyze characteristics of persons with hemophilia A
- CBDR data may have the potential to enable future comparison of treatment patterns and patient outcomes before and after emicizumab introduction

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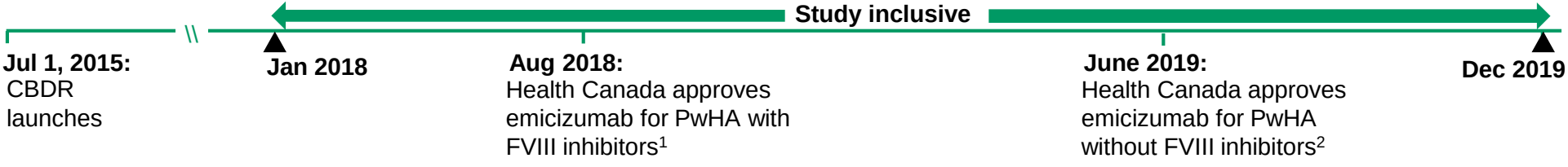
This analysis describes the demographics, treatment patterns, and outcomes among PwHA who registered in the CBDR and had not received emicizumab

Background

- The CBDR is a clinical database for people in Canada with hemophilia and other bleeding disorders, used by all Canadian hemophilia treatment centers
- It includes data on treatment, bleeding events, and PROs

Methods

- This study included all registered PwHA who had *not* received emicizumab from January 2018–December 2019
  - Although emicizumab was approved in August 2018, limited access was available beforehand through early access programs
- Data were de-identified and statistically analyzed to examine demographic patterns and outcomes
  - Treatment was classified as on-demand, prophylaxis, or ITI; these groups were not mutually exclusive, as individuals could have received more than one type of treatment
  - ABRs and AJBRs were calculated*



*ABRs and AJBRs were calculated by (total number of bleeds / duration of follow-up)*365.25 for each PwHA with at least 1 treated bleed.
ABR, annualized bleeding rate; AJBR, annualized joint bleeding rate; CBDR, Canadian Hemophilia Bleeding Disorders Registry; FVIII, factor VIII; ITI, immune tolerance induction; PRO, patient-reported outcome; PwHA, persons with hemophilia A.

1. Health Canada. Regulatory Decision Summary. Accessed Oct 27, 2020;
2. Reuters Press Release. Health Canada Approves Hemlibra For Hemophilia A Patients Without Factor VIII Inhibitors. Accessed Nov 12, 2020.

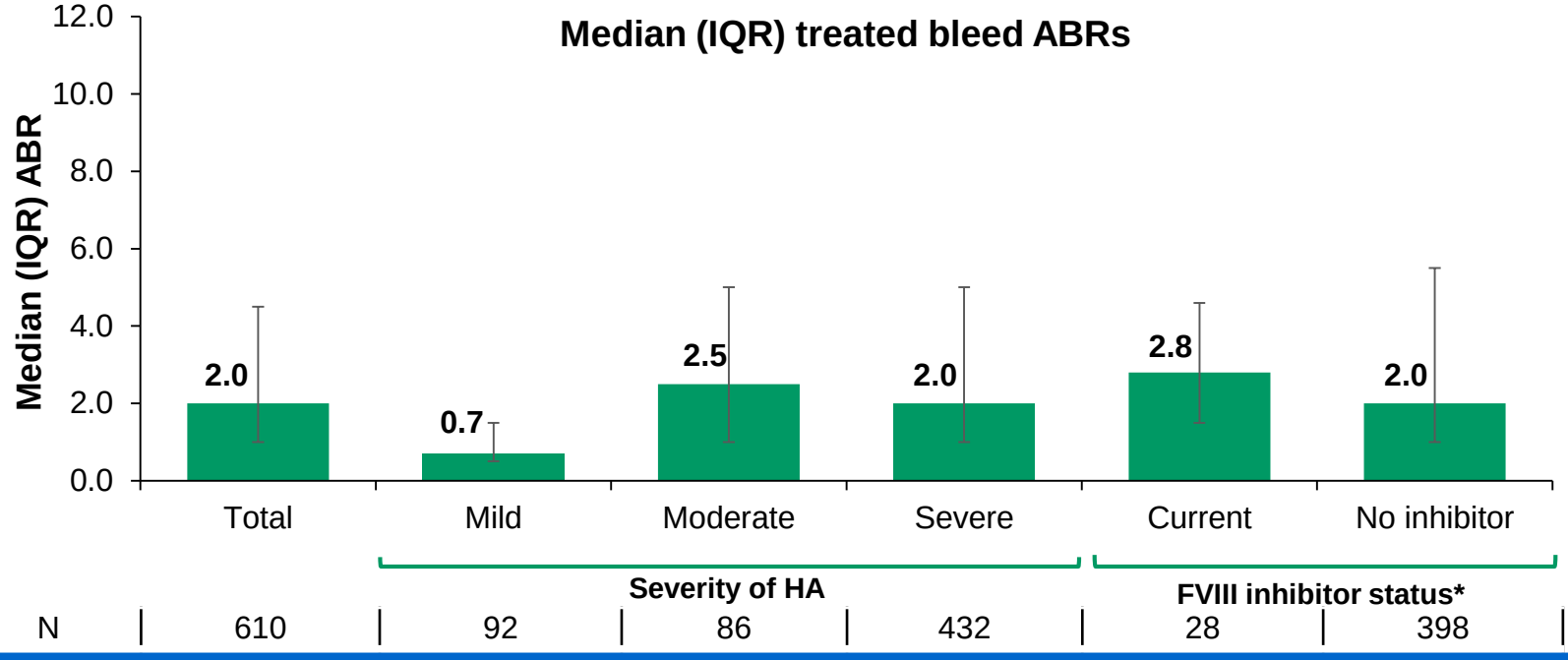
Participant demographics from the CBDR are representative of the current Canadian HA population

	Total population	Severity of HA*		
		Mild	Moderate	Severe
Participants included, N (%)	2525	1436 (56.9)	247 (9.8)	842 (33.3)
Male, n (%)	2433/2525 (96.4)	1348/1436 (93.9)	247/247 (100)	838/842 (99.5)
Age, years				
Mean ± SD	36.7 ± 21.5	42.9 ± 21.6	36.2 ± 21.3	26.2 ± 16.9
2–<18, n (%)	586/2523 (23.2)	201/1436 (14.0)	60/247 (24.3)	325/840 (38.7)
18–50, n (%)	1231/2523 (48.8)	685/1436 (47.7)	122/247 (49.4)	424/840 (50.5)
≥50, n (%)	706/2523 (28.0)	550/1436 (38.3)	65/247 (26.3)	91/840 (10.8)
Missing	2/2525 (0.1)	0/1436 (0.0)	0/247 (0.0)	2/842 (0.2)
FVIII inhibitor status,† n (%)				
History of FVIII inhibitors	236/1326 (17.8)	50/416 (12.0)	27/171 (15.8)	159/739 (21.5)
No FVIII inhibitor, n (%)	1040/1326 (78.4)	356/416 (85.6)	139/171 (81.3)	545/739 (73.7)
Current treatment,§ n (%)				
• On demand	417/1040 (40.1)	284/356 (79.8)	74/139 (53.2)	59/545 (10.8)
• Prophylaxis	608/1040 (58.5)	22/356 (6.2)	74/139 (53.2)	512/545 (93.9)
Current FVIII inhibitor and titer, n (%)	50/1326 (3.8)	10/416 (2.4)	5/171 (2.9)	35/739 (4.7)
• Low	33/50 (66.0)	6/10 (60.0)	4/5 (80.0)	23/35 (65.7)
• High	17/50 (34.0)	4/10 (40.0)	1/5 (20.0)	12/35 (34.3)
ITI	8/50 (16.0)	1/10 (10.0)	1/5 (20.0)	6/35 (17.1)

FVIII inhibitor status was missing for 47.5% of the total population; of those with status available, 17.8% had history of FVIII inhibitors and 3.8% had current FVIII inhibitors

*Severe (FVIII <0.01 IU/mL), moderate (0.01 ≤FVIII ≤0.05 IU/mL) and mild (0.05 <FVIII ≤0.40 IU/mL);
†Current inhibitor detected in 2018 or 2019; low titer <5 BU, high titer ≥5 BU; history of FVIII inhibitor – detected prior 2018 but no current inhibitor; §During 2018 and 2019.
BU, Bethesda units; CBDR, Canadian Hemophilia Bleeding Disorders Registry; FVIII, factor VIII; HA, hemophilia A; ITI, immune tolerance induction; SD, standard deviation

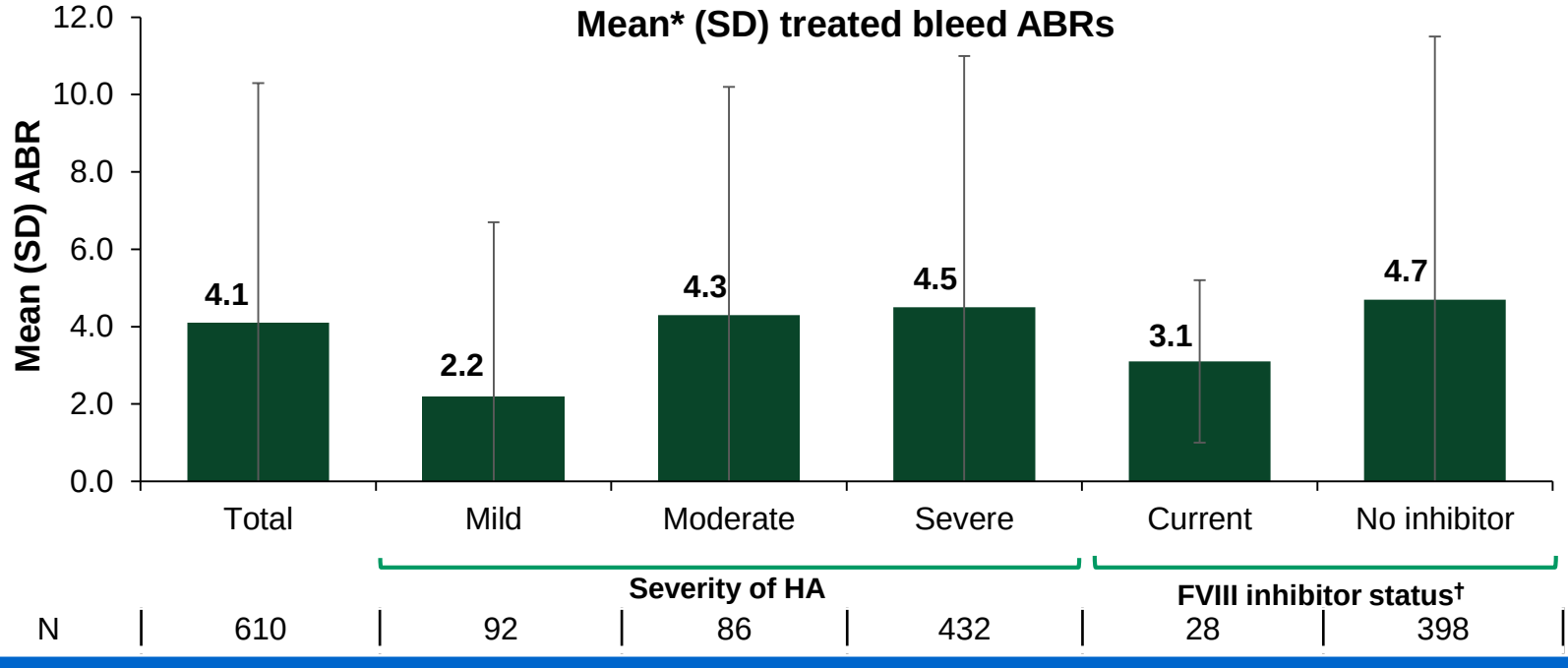
Treated bleed ABRs were similar in individuals with moderate and severe HA



- Missing FVIII inhibitor status and incomplete treatment records in CBDR may contribute to the small sample size and selection bias of current FVIII inhibitors. ABR results must be interpreted with caution
- These data were not sufficiently powered to meet statistical significance, emphasizing the value of up-to-date and complete data collection

*Current FVIII inhibitor: detected in 2018 or 2019; no FVIII inhibitor: no inhibitor detected or observed yet.
ABR, annualized bleeding rate; FVIII, factor VIII; HA, hemophilia A; IQR, interquartile range; PwHA, persons with hemophilia A.

Treated bleed ABRs were similar in individuals with moderate and severe HA



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*The mean ABR was calculated as the total number of bleeds/duration of follow-up for each patient with at least 1 treated bleed in their follow-up, without using a regression model; therefore, the mean can be influenced by the outlying observations; †Current FVIII inhibitor: detected in 2018 or 2019; no FVIII inhibitor: no inhibitor detected or observed yet.
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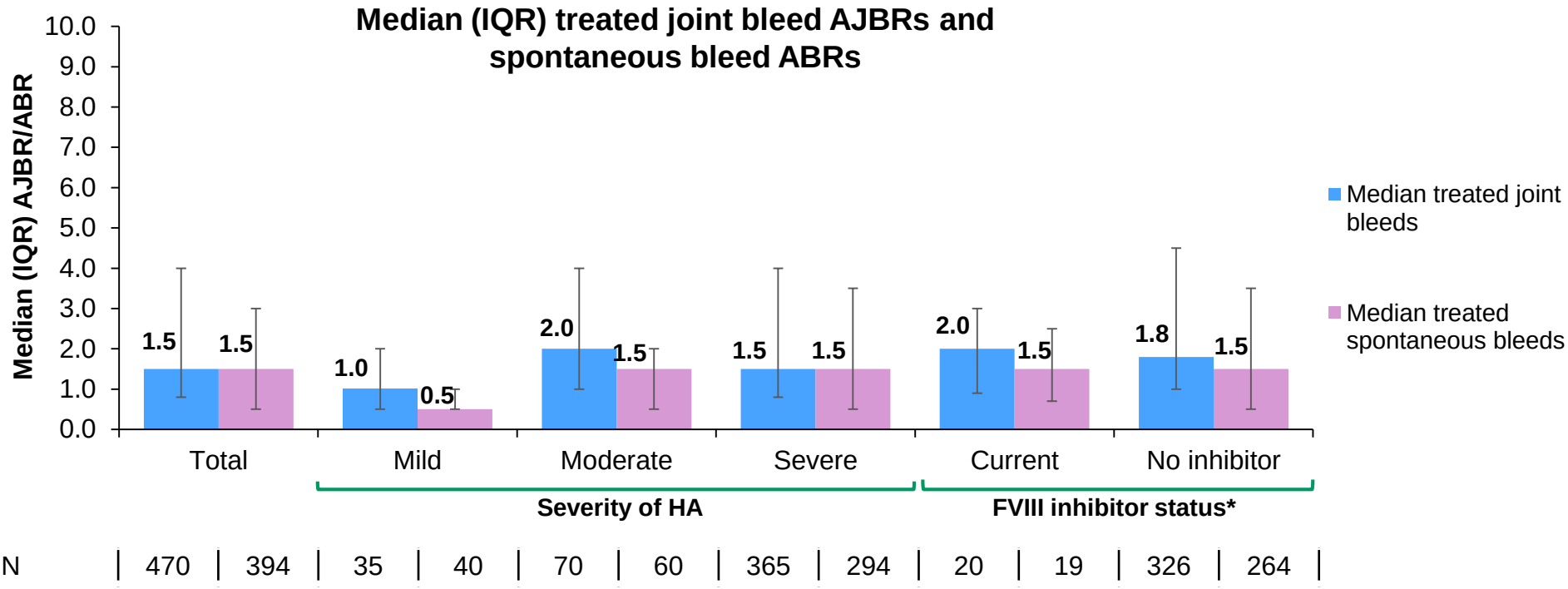
Treated joint and spontaneous bleeds were similar in individuals with moderate and severe HA



Individuals with moderate HA had similar numbers of treated joint bleeds and spontaneous bleeds to those with severe HA; this may reflect an unmet need in the moderate HA population

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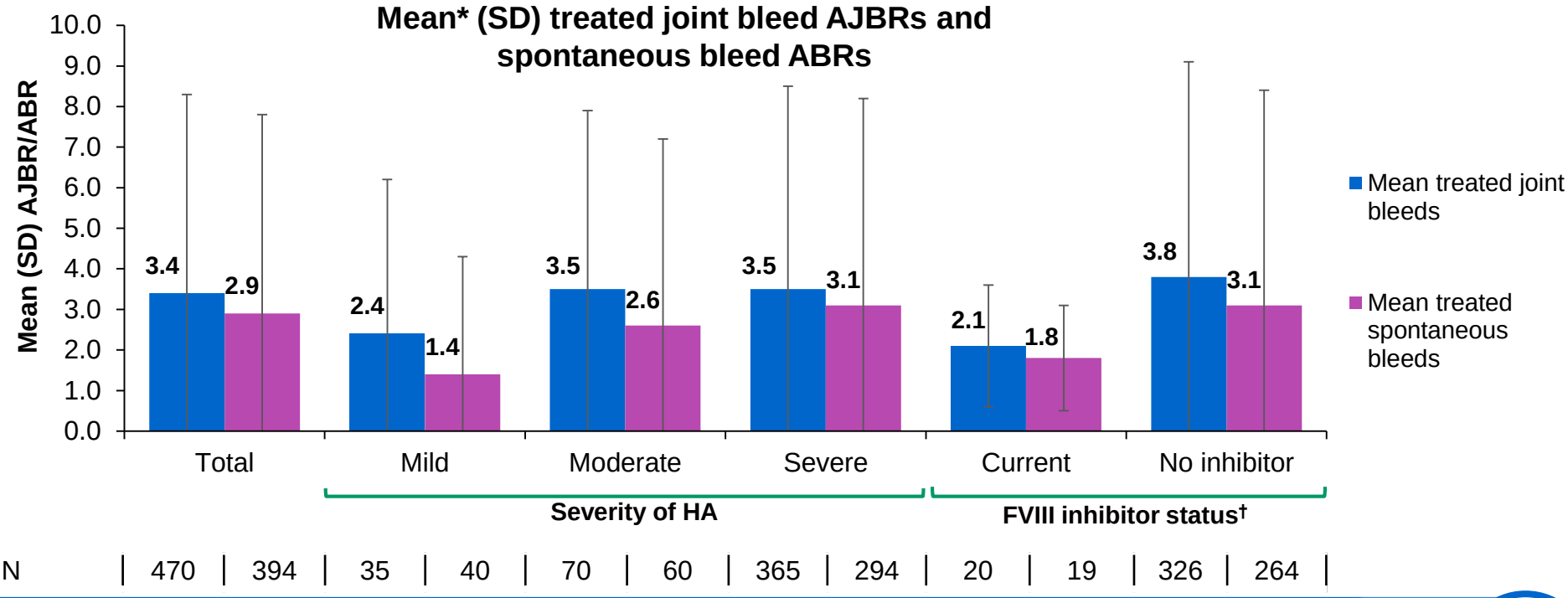

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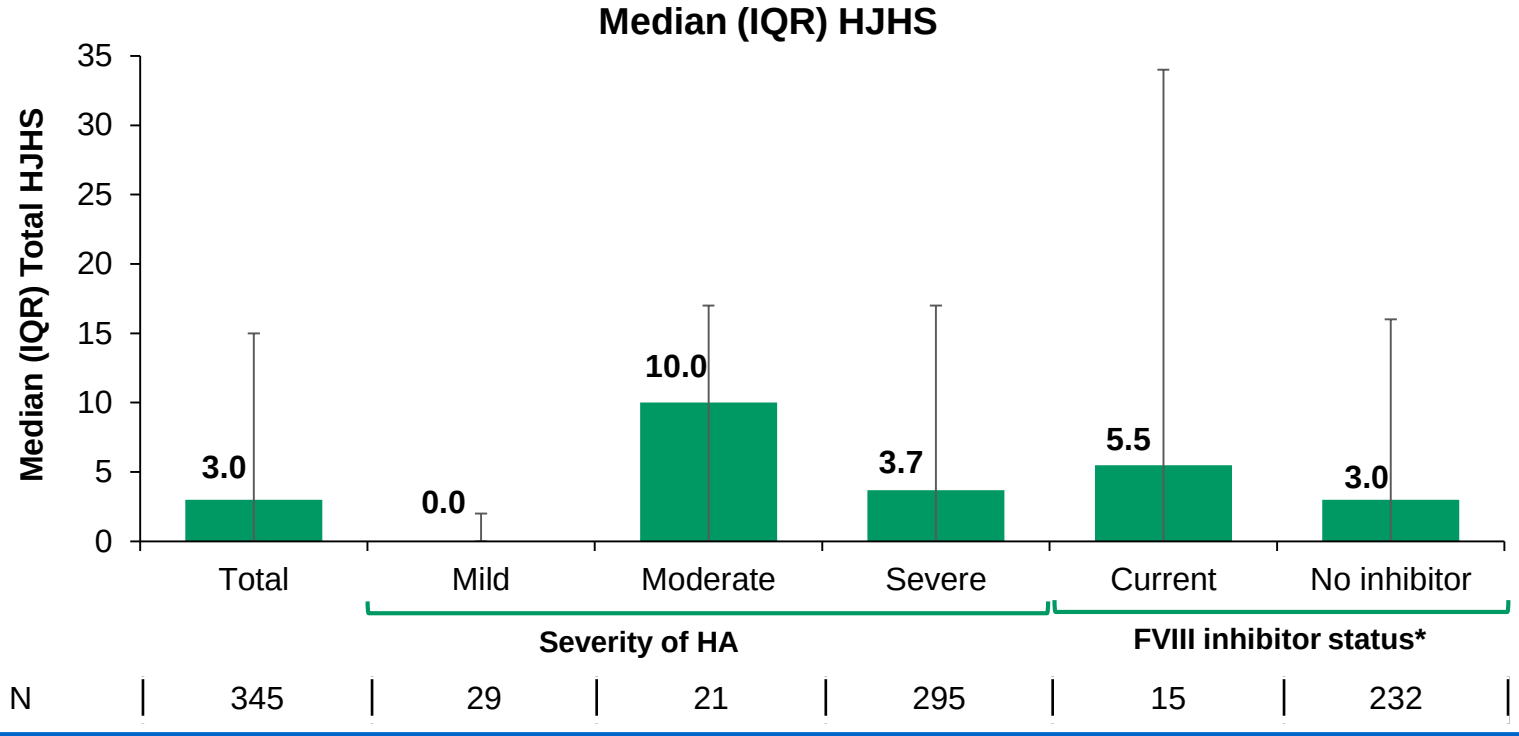
*The mean AJBR and spontaneous bleed ABR were calculated as the total number of bleeds/duration of follow-up for each patient with at least 1 treated bleed in their follow-up, without using a regression model; therefore, the mean can be influenced by the outlying observations; †Current FVIII inhibitor: detected in 2018 or 2019; no FVIII inhibitor: no inhibitor detected or observed yet.
ABR, annualized bleeding rate; AJBR, annualized joint bleeding rate; FVIII, factor VIII; HA, hemophilia A; PwHA, persons with hemophilia A; SD, standard deviation.

HJHS were highly variable as many responses were missing, highlighting the need for up-to-date, complete record keeping



The HJHS measures joint health of those most commonly affected by hemophilia: the knees, ankles, and elbows; a higher score indicates worse health[1]

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1. WFH Network. Hemophilia Joint Health Score (HJHS). Available at: https://elearning.wfh.org/resource/hemophilia-joint-health-score-hjhs/. Accessed Nov 12, 2020.

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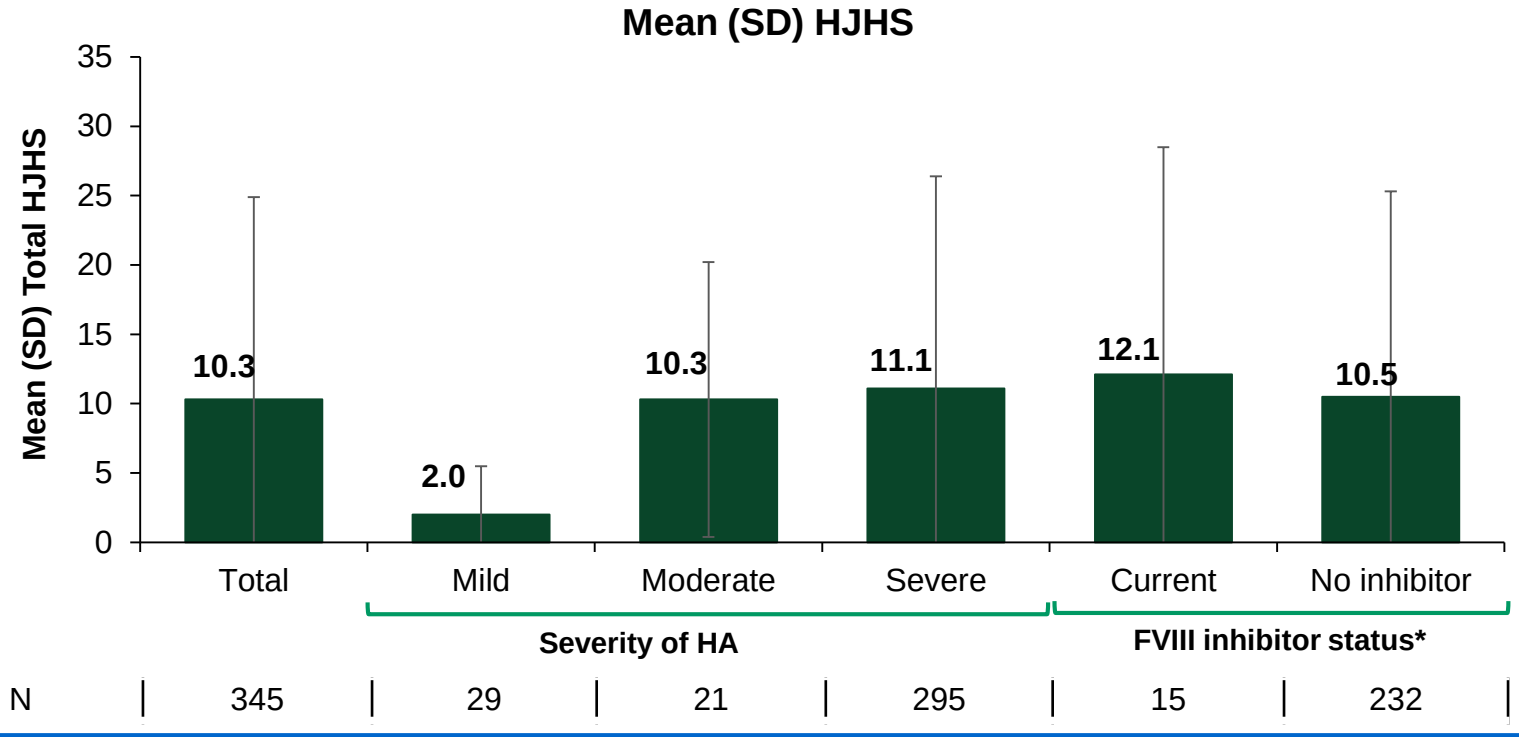

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Conclusions

- This analysis confirms the feasibility of using the CBDR database to provide a snapshot of demographics, treatments, bleeding, and joint status outcomes in PwHA
- CBDR data may have the potential to enable comparison of treatment patterns and patient outcomes before and after introducing emicizumab
- Caution is required when interpreting incomplete data (e.g. with respect to FVIII inhibitor status and HJHS score)
- Encouraging complete and up-to-date data entry will be important for maintaining data quality and accuracy

CBDR, Canadian Hemophilia Bleeding Disorders Registry; FVIII, factor VIII; HJHS, Hemophilia Joint Health Score; PwHA, persons with hemophilia A.

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