

## INTRODUCTION

- Over the past two decades, treatment options for hemophilia have evolved significantly.
- The specific dosing regimens prescribed by the specialists who treat and care for people with hemophilia have not been widely studied.

## OBJECTIVES

- The study objective is to describe the trends observed in clinician prescribing practices for management of hemophilia A (HA) and B (HB) in the United States via three surveys taken in 1999, 2015 and 2021.

## METHODS

- We administered surveys to members of the Hemostasis & Thrombosis Research Society (HTRS) via an in-person paper survey at its annual symposia in 1999 and 2015, and an online survey in 2021.
- Forty-one clinicians completed the survey in 1999 and 2021, 53 in 2015.
- The survey participants included physicians, physician assistants, and nurse practitioners who manage the care of hemophilia patients at hemophilia treatment centers in the US.
- The surveys collected information regarding:
  - Characteristics of the clinician practices
  - Clotting factor products prescribed and dosages used for routine bleeds or major life-threatening bleeding, total joint replacement, and port placement,
  - Reasons for changing doses
  - Frequency of recommendation for prophylaxis and inhibitor treatment for associated factor and non-factor products, and
  - Gene therapy (only in 2021 survey)

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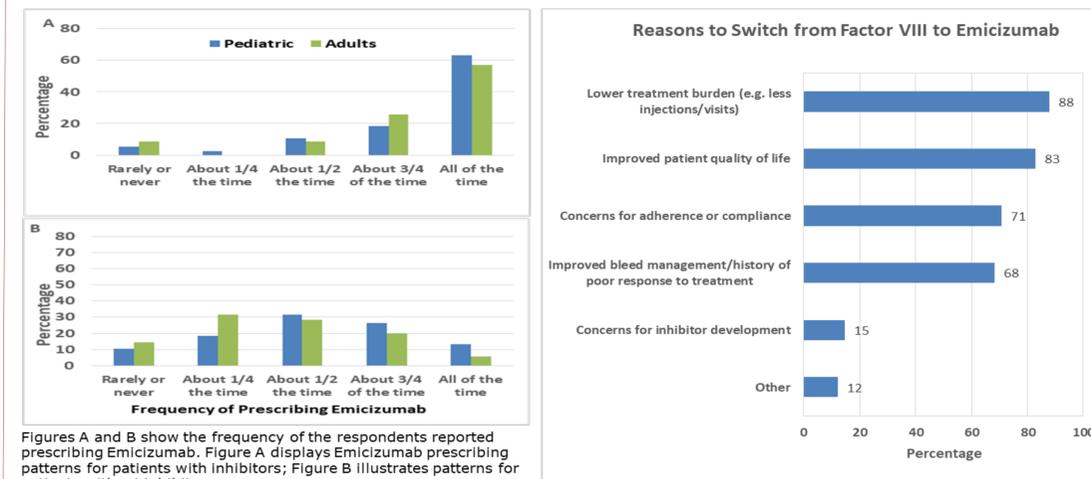
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## Table 1. Report Rates of Dose for Bleeding

Variable	Factor VIII				Factor IX			
	1999	2015	2021 SHL	2021 EHL†	1999	2015	2021 SHL	2021 EHL†
<b>Routine Bleed*</b>								
10 - 15 (IU/KG)	2.50	1.89	0.00	0.00	0.00	0.00	0.00	0.00
16 – 20 (IU/KG)	17.50	3.77	2.44	0.00	10.00	0.00	0.00	0.00
21 – 25 (IU/KG)	50.00	22.64	19.51	17.07	10.00	5.66	0.00	0.00
26 – 30 (IU/KG)	17.50	32.08	29.27	24.39	10.00	5.66	2.44	0.00
31 – 35 (IU/KG)	5.00	9.43	9.76	7.32	15.00	3.77	0.00	7.32
36 – 40 (IU/KG)	7.50	18.87	9.76	17.07	32.50	30.19	9.76	2.44
>40 (IU/KG)	0.00	11.32	29.26	31.71	22.50	50.95	87.80	85.36
Other	0.00	0.00	0.00	2.44	0.00	3.77	0.00	4.88
<b>Major life-threatening bleed*</b>								
36 – 40 (IU/KG)	5.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00
41 – 45 (IU/KG)	2.56	1.92	0.00	0.00	2.50	0.00	0.00	0.00
46 – 50 (IU/KG)	46.15	15.38	29.27	19.51	5.00	0.00	2.44	2.44
51 – 55 (IU/KG)	41.03	59.62	51.22	51.22	7.50	0.00	0.00	2.44
56 – 60 (IU/KG)	2.56	5.77	12.20	12.20	15.00	5.79	4.88	17.07
> 60 (IU/KG)	2.56	17.31	7.31	7.31	67.50	86.54	90.24	65.85
Other	0.00	0.00	0.00	9.76	2.50	7.69	2.44	12.20

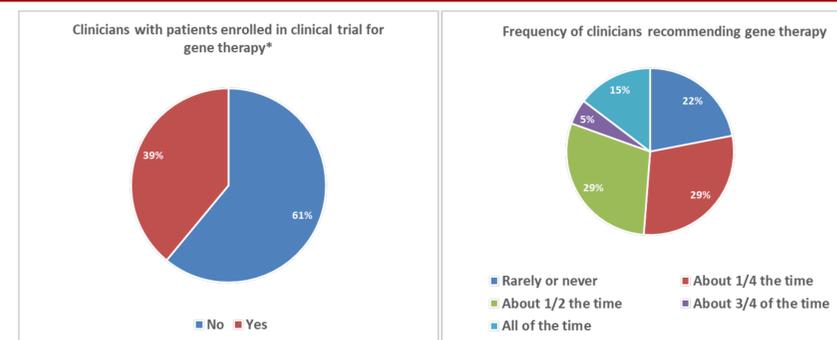
Note: Data was presented as proportion of respondents reported dose range that they prescribed for treating routine bleed or major life-threatening bleed. \*Clotting factor units were presented in units/kg body weight. †Only 2021 survey asked dosage of prescribing extended half life product. Abbreviations: SHL, standard half-life; EHL, extended half-life.

## Figure 1. Prescribing Practices for Emicizumab



Figures A and B show the frequency of the respondents reported prescribing Emicizumab. Figure A displays Emicizumab prescribing patterns for patients with inhibitors; Figure B illustrates patterns for patients without inhibitors.

## Figure 2. Gene Therapy in 2021 Survey



\* About 28% of clinicians reported that they have patients who have completed gene therapy.

## RESULTS

- The mean number of patients seen by respondents increased from 142 (range: 0-314) for children and 101 (0-480) for adults in 1999 to 202 (0-900) for children and 154 (0-500) for adults in 2021.
- The proportion of clinicians prescribing >40 units/kg of Standard Half Life (SHL) Factor IX concentrates for routine bleeding events in HB patients grew fourfold over time, increasing from 22.5% in 1999 to 50.9% in 2015, and 87.8% in 2021.
- The proportion of clinicians reporting SHL Factor VIII usage for routine bleeding at a dose of >40 units/kg in HA patients increased from none in 1999 to 11.3% in 2015 and 29.3% in 2021.
- The reported rates of prescribing an average >60 units/kg factor to treat major life-threatening bleeds increased from 67.5% in 1999 to 90.3% in 2021 for HB; for treating HA, rates were 2.5% in 1999, 17.3% in 2015 and 7.3% in 2021.
- For children <4 years of age, 22.2% of clinicians prescribed primary prophylaxis all of the time in 1999. This rose to 68.2% in 2015, and 86.5% in 2021. For adults, 12.5% of clinicians prescribed secondary prophylaxis all of the time in 1999, 27.3% in 2015 and 42.5% in 2021.
- For treatment of patients with HA or HB inhibitors, the proportions of clinicians who reported prescribing immune tolerance induction (ITI) therapy all of the time for pediatric patients were 50%, 75.0% and 63.2% respectively in the three surveys, but <25% for adult patients in all three surveys.
- In the 2021 survey, >91% of clinicians reported ever prescribing emicizumab to treat HA with inhibitors in patients of all ages, while >87% reported ever prescribing it to treat HA without inhibitor.
- Clinicians were more likely to prescribe emicizumab to treat HA patients with inhibitors all of the time (63.2% for children and 57.1% for adults), as compared to prescribing it for those without inhibitors (13.2% for children and 5.7% for adults).
- The most frequently reported method of treating a patient with a history of inhibitor on emicizumab who had breakthrough bleeds was rFVIIa: 85.4% for children, and 75.6% for adults.
- The most frequently reported reasons for switching from FVIII to emicizumab were fewer injections/visits (87.8%), and improved patient quality of life (82.9%).
- Thirty-nine percent of clinicians reported caring for patients currently in gene therapy trials; 27.5% had patients who had completed gene therapy.
- When asked about potential future prescribing practices for patients who successfully pass the screening tests, 14.6% reported that they would prescribe gene therapy “all the time”, 4.9% would prescribe it “about 3/4 of the time”, 29.3% “about 1/2 the time”, 29.3% “about 1/4 the time”, and 22.0% “rarely or never”.

## CONCLUSIONS

- Prescribing of high doses of factor (>40 units/kg) has increased, while ITI prescribing practices remained similar over time.
- In the 2021 survey, most clinicians frequently prescribed emicizumab for patients with HA inhibitors, but less frequently for those without inhibitors.
- In the 2021 survey, the expected uptake of gene therapy diverges widely among clinicians.