

# Health-Related Outcomes and Caregiver Burden in Pediatric Persons with Hemophilia A (PwHA) with Inhibitors: Prospective, Non-interventional Study (NIS) in a Real-world Setting

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## BACKGROUND

- Limited information has been published about the real-world experiences of persons with hemophilia A (PwHA), particularly children, who have developed alloantibodies (inhibitors) to factor VIII (FVIII) replacement therapies
- There is particularly little published information about the impact of the disease and its treatment on health-related quality of life and health status of pediatric PwHA with inhibitors and the associated caregiver burden
- A global, prospective, non-interventional study (NIS; NCT02476942) evaluated bleeding, adverse events, and health-related quality of life (HRQoL) in PwHA treated according to local routine clinical practice
- The NIS was a global, multicenter, prospective study that enrolled PwHA into 3 cohorts:
  - Cohort A: PwHA with FVIII inhibitors aged  $\geq 12$  years
  - Cohort B: PwHA with FVIII inhibitors aged  $< 12$  years
  - Cohort C: PwHA without inhibitors aged  $\geq 12$  years
- This poster will focus on Cohort B
  - Bleeding and treatment-related outcomes have been presented previously (59th American Society of Hematology Annual Meeting & Exposition; December 9–12, 2017; Atlanta, GA)

## OBJECTIVE

- To describe HRQoL outcomes and aspects related to caregiver burden for pediatric PwHA with inhibitors (Cohort B) evaluated in the NIS

## METHODS

- Participants aged  $< 12$  years were enrolled if they met the following criteria:
  - Congenital HA (any severity)
  - History of high-titer FVIII inhibitors ( $\geq 5$  Bethesda units/mL)
  - Received bypassing agents (BPAs) to treat or control bleeding for  $\geq 24$  weeks before study entry
  - $\geq 4$  bleeds in the last 6 months for those aged  $\geq 2$  and  $< 12$  years
  - $\geq 2$  bleeds in the last 3 months for those aged  $< 2$  years
- All treatments and assessments were conducted according to routine clinical practice; no protocol-specified interventions applied
- All outcomes, except hospitalizations, were reported by participants or their caregivers every 4 weeks (reflecting their experience in the past 4 weeks) using an electronic handheld device. Hospitalizations were recorded on the electronic case report form by the investigator
  - Haemophilia-Specific Quality of Life Assessment for Children Short Form (Haemo-QoL-SF)
    - Completed by participants aged 8–11 years
    - Consists of 35 items in 9 domains: 'Physical Health,' 'Feelings,' 'View of Yourself,' 'Family,' 'Friends,' 'Other People,' 'Sports & School,' 'Dealing with Haemophilia,' and 'Treatment'
  - Inhibitor-Specific Quality of Life with Aspects of Caregiver Burden (Adapted Inhib-QoL)
    - Completed by caregivers of all children
    - Consists of 34 items in 8 domains: 'Physical Health,' 'Treatment,' 'Perceive Condition,' 'Dealing with Inhibitor,' 'Perceive Treatment,' 'Family Life,' 'Siblings,' and 'Contact with Others'
  - Days missed from school/daycare and days hospitalized
  - Scales for both Haemo-QoL-SF and Adapted Inhib-QoL range from 0 (no impairment) to 100 (high impairment)

## RESULTS

### Participant population

- A total of 24 male participants (episodic BPAs, n=10; prophylactic BPAs, n=14) were enrolled
- Demographic and baseline characteristics are listed in **Table 1**
- Median (range) observation time
  - Episodic BPAs: 31.2 (21.3–44.1) weeks
  - Prophylactic BPAs: 17.9 (8.7–36.4) weeks

**Table 1: Demographics and clinical characteristics**

Characteristic	Episodic BPAs n=10	Prophylactic BPAs n=14	All N=24
Age			
Median (min–max) age, years	6.5 (2–11)	8.0 (3–11)	7.5 (2–11)
0 to $< 2$ , n (%)	0 (0.0)	0 (0.0)	0 (0.0)
2 to $< 8$ , n (%)	6 (60.0)	6 (42.9)	12 (50.0)
8 to $< 12$ , n (%)	4 (40.0)	8 (57.1)	12 (50.0)
Race, n (%)			
White	3 (30.0)	8 (57.1)	11 (45.8)
Asian	5 (50.0)	3 (21.4)	8 (33.3)
Black/African American	1 (10.0)	1 (7.1)	2 (8.3)
Multiple	0	1 (7.1)	1 (4.2)
Bleeds in previous 6 months*			
Participants, n	9	14	23
Mean (SD)	9.9 (4.6)	6.0 (2.9)	7.5 (4.1)
Median (range)	8.0 (4–17)	5.0 (4–15)	6.0 (4–17)
Previously treated with immune tolerance induction, n (%)	1 (10.0)	11 (78.6)	12 (50.0)

\*As reported by investigators based on medical records. One participant excluded from the episodic group because bleeds corresponded to previous 4 months, not 6 months

### Haemophilia-Specific Quality of Life for Children Short Form (Haemo-QoL-SF)

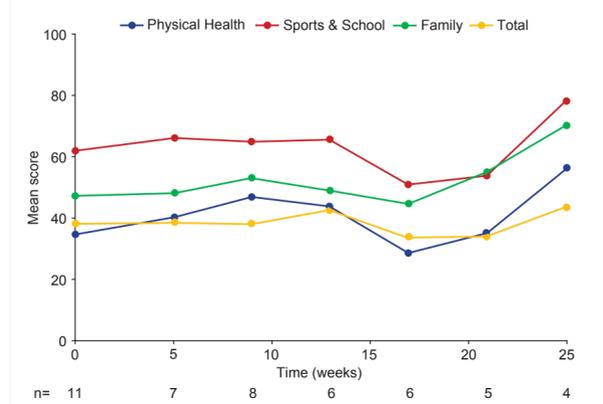
- The Haemo-QoL-SF was completed by 3 of 4 eligible participants (aged 8–11 years) in the episodic group and 8 of 8 in the prophylactic group
- Mean Haemo-QoL-SF 'Total' and domain scores at Week 1 are listed in **Table 2**
- Mean 'Total' and key domain scores over time are shown in **Figure 1**
  - Because so few participants completed the Haemo-QoL-SF in the episodic group, the episodic and prophylactic groups were combined in the graph
- The greatest impairments were seen in the 'Sports & School' and 'Family' domains
- Although mean scores for some domains differed between the episodic and prophylactic groups, there were no consistent differences between groups, and no systematic variations with time in any domain or the 'Total' score through Week 25

**Table 2: Haemo-QoL-SF domain and 'Total' scores\* at Week 1**

Domain	Episodic BPAs n=3 <sup>†</sup> Mean (SD)	Prophylactic BPAs n=8 <sup>†</sup> Mean (SD)
Physical Health	50 (13)	29 (26)
Feelings	23 (25)	38 (25)
View of Yourself	29 (19)	39 (18)
<b>Family</b>	<b>65 (13)</b>	<b>41 (22)</b>
Friends	50 (38)	31 (28)
Other People	38 (13)	23 (13)
<b>Sports &amp; School</b>	<b>71 (10)</b>	<b>59 (27)</b>
Dealing with Haemophilia	17 (24)	26 (21)
Treatment	40 (10)	43 (24)
<b>Total</b>	<b>42 (8)</b>	<b>37 (14)</b>

Domains with greatest impairment highlighted in bold  
 \*Scale ranges from 0 (no impairment) to 100 (high impairment)  
<sup>†</sup>Only participants aged 8–11 years eligible to complete questionnaire  
 BPA, bypassing agent; Haemo-QoL-SF, Haemophilia-Specific Quality of Life Assessment for Children Short Form

### Figure 1: Haemo-QoL-SF domain and 'Total' scores\* over time (all participants who completed the questionnaire)



\*Scale ranges from 0 (no impairment) to 100 (high impairment)  
<sup>†</sup>Only participants aged 8–11 years were eligible to complete this questionnaire  
 Haemo-QoL-SF, Haemophilia-Specific Quality of Life Assessment for Children Short Form

### Inhibitor-Specific Quality of Life with Aspects of Caregiver Burden (Adapted Inhib-QoL)

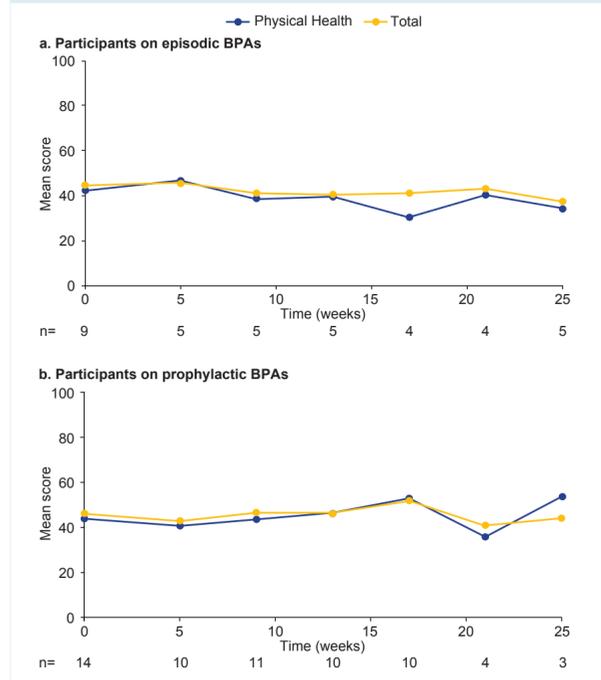
- Mean Adapted Inhib-QoL 'Total' and domain scores at Week 1 are listed in **Table 3**
- Mean 'Total' and 'Physical Health' domain scores over time are shown in **Figure 2**
- Mean scores over time for those domains particularly indicative of caregiver burden are shown in **Figure 3**
  - Types of questions covered by these domains
    - 'Dealing with Inhibitor': how worried/afraid caregiver is as a result of the child's hemophilia
    - 'Family Life': how the child's hemophilia impacts family life
    - 'Perceive Condition': how concerned caregiver is about child's hemophilia and impact on family
    - 'Perceive Treatment': how satisfied caregiver is with child's treatment
- The greatest impairments were seen in the 'Dealing with Inhibitor' domain
- Although mean scores for some domains differed between the episodic and prophylactic groups, there were no consistent differences between groups, and no systematic variations with time in any domain or the total score through Week 25

**Table 3: Adapted Inhib-QoL domain and 'Total' scores\* at Week 1**

Domain	Episodic BPAs n=9 <sup>†</sup> Mean (SD)	Prophylactic BPAs n=14 <sup>†</sup> Mean (SD)
Physical Health <sup>‡</sup>	42 (13)	44 (21)
Treatment	42 (34)	31 (29)
Perceive Condition <sup>§</sup>	42 (18)	40 (24)
<b>Dealing with Inhibitor<sup>§</sup></b>	<b>63 (14)</b>	<b>64 (20)</b>
Perceive Treatment <sup>§</sup>	37 (20)	53 (9)
Family Life <sup>§</sup>	41 (19)	42 (21)
Siblings	13 (25)	21 (22)
Contact with Others	35 (39)	24 (28)
<b>Total</b>	<b>44 (11)</b>	<b>46 (15)</b>

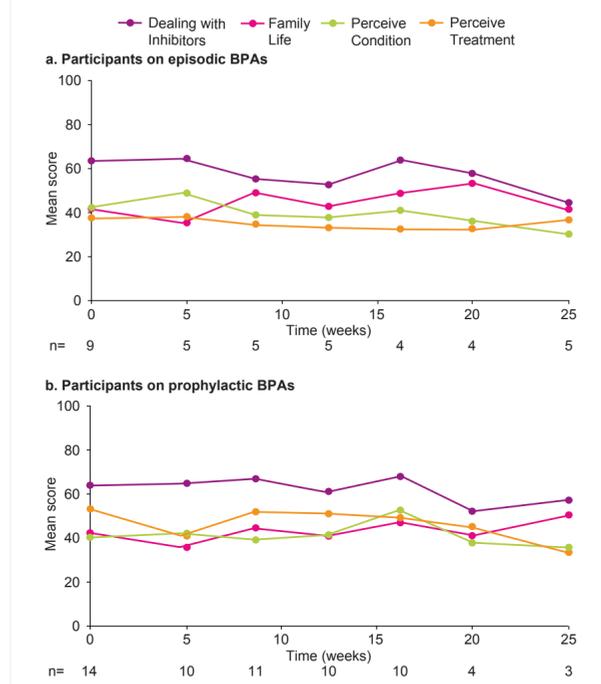
Domains with greatest impairment highlighted in bold  
 \*Scale ranges from 0–100 (0 indicates no impairment; higher values indicate greater impairment).  
<sup>†</sup>One caregiver did not complete the form at Week 1  
<sup>‡</sup>Reflects the caregiver's perception of the child's physical health  
<sup>§</sup>Domains most reflective of caregiver burden  
 Adapted Inhib-QoL, Inhibitor-Specific Quality of Life with Aspects of Caregiver Burden; BPA, bypassing agent

### Figure 2: Adapted Inhib-QoL 'Physical Health'\* domain and 'Total' scores<sup>†</sup> over time



\*Reflects the caregiver's perception of the child's physical health  
<sup>†</sup>Scale ranges from 0 (no impairment) to 100 (high impairment)  
 Adapted Inhib-QoL, Inhibitor-Specific Quality of Life with Aspects of Caregiver Burden; BPA, bypassing agent

### Figure 3: Adapted Inhib-QoL scores\* over time for domains particularly indicative of caregiver burden



\*Scale ranges from 0 (no impairment) to 100 (high impairment)  
 Adapted Inhib-QoL, Inhibitor-Specific Quality of Life with Aspects of Caregiver Burden; BPA, bypassing agent

### Hospitalizations and school/daycare absences

- Mean proportion of missed days (days missed/days expected) from school/daycare:
  - Episodic BPAs: 9%
  - Prophylactic BPAs: 25%
- Mean (SD) days hospitalized:
  - Episodic BPAs: 2.7 (4.9) during mean of 31.2 weeks' follow-up
  - Prophylactic BPAs: 10.1 (24.0) during mean of 17.9 weeks' follow-up
    - Driven by 2 patients with long hospitalizations (87 and 33 days) due to several serious bleeding events

## CONCLUSIONS

- In this real-world setting, HRQoL scores indicated moderate to severe impairment in several areas of function in pediatric PwHA with inhibitors regardless of BPA treatment regimen
- The burden on caregivers was also substantial, regardless of BPA treatment regimen, with the greatest impact due to dealing with the child's inhibitors
- This NIS suggests that the burden of disease and BPA treatment for pediatric PwHA with inhibitors has a substantial negative impact on the daily lives of the children affected and adds considerable burden to caregivers

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