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Treatment regimens and outcomes in severe and moderate haemophilia A in the UK: The Thunder Study.

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1 **Abstract**

2 **Introduction:** The THUNDER study provides an analysis of treatment patterns and outcomes in UK
3 patients with severe or moderate Haemophilia A (SHA/ MHA) in 2015.

4 **Methods:** Patients with SHA or MHA registered with the UK National Haemophilia Database (NHD)
5 were segregated by severity, inhibitor status and age. Haemophilia joint health score (HJHS) was
6 derived from NHD records and treatment regimen and annualised bleed/ joint-bleed rate (ABR/
7 AJBR) from Haemtrack (HT) in HT-compliant patients.

8 **Results:** We report 1810 patients with SHA and 864 with MHA. Prophylaxis was used in 94.9%
9 (n=130/137) of HT-compliant children <12 years with SHA, falling to 74.1% (n=123/166) aged ≥40
10 years. Median ABR increased with age (1.0, IQR 0.0 – 5.0, <12 years; 3.0 IQR, 1.0 - 8.0, ≥40 years).
11 Inhibitors were present in 159 (8.8%) SHA and 34 (3.9%) MHA. Median ABR increased from 2.0 (<12
12 years) to 21.0 (≥40 years) in SHA inhibitor patients using prophylaxis. Prophylaxis was used by 68.8%
13 of HT-compliant MHA patients (n=106) (median FVIII baseline 0.01 IU/mL) associated with a median
14 (IQR) ABR of 3.0 (1.0 – 7.0).

15 Median HJHS (n=453) increased with age in SHA and MHA. Median (IQR) HJHS was higher in SHA
16 inhibitor (17.0, 0.0 - 64.5) than non- or past-inhibitor patients (7.0, 0.0 – 23.0).

17 **Conclusions:** Increasing ABR with age persists despite current prophylaxis regimens. SHA and MHA
18 had similar ABR/ AJBR and HJHS, leading to a suspicion that a subgroup of MHA may be relatively
19 undertreated. More intensive prophylaxis may improve outcomes, but this requires further study.

20

1 **Introduction**

2 Although the severity of Haemophilia A (HA) is defined by the baseline factor VIII (FVIII)
3 level, there is considerable overlap in bleeding phenotype between severe (SHA; <0.01
4 IU/mL) and moderate HA (MHA; 0.01-0.05 IU/mL) [1] and many patients with MHA have a
5 severe bleeding phenotype [2].

6 The standard of care for SHA is prophylactic FVIII replacement therapy to elevate the
7 patient's trough FVIII to a level adequate to prevent joint bleeding. Primary prophylaxis,
8 usually initiated pre-emptively before the second birthday [3,4], minimises or prevents
9 spontaneous bleeding events and arthropathy [5,6]. The role of FVIII prophylaxis in MHA is
10 less clear, given that these patients already have a baseline FVIII level of ≥ 0.01 IU/mL and a
11 variable bleeding phenotype. However, a subgroup of these patients suffer frequent
12 haemarthroses and are therefore managed with FVIII prophylaxis [7].

13 Although FVIII prophylaxis effectively reduces the frequency of bleeding events,
14 individualisation of treatment is required to achieve the best bleed control [8,9]. Although it
15 is often advised to maintain a trough FVIII level ≥ 0.01 IU/mL, complete bleed-avoidance
16 commonly requires a higher level [10,11]. Prophylaxis is also demanding, prone to poor
17 compliance and, as currently practiced, does not completely prevent arthropathy [12,13].
18 Consequently, many patients are still treated with sub-optimal prophylaxis or on-demand
19 treatment, resulting in a continuing unmet need.

20 Bypass therapy administered on-demand or as prophylaxis in patients with persistent
21 inhibitors is only partially effective in treating or preventing haemarthroses [14–16].
22 Consequently, these patients experience a higher annualised bleed-rate and reduced life
23 expectancy than patients lacking inhibitors [17]. The extent to which this morbidity may be
24 minimised or prevented by early inhibitor eradication through immune tolerance induction
25 is unknown.

26 Treatment and disease outcome of HA by age, disease severity and inhibitor status in
27 complete national haemophilia cohorts are not well documented. The THUNDER study
28 (Treatment of Haemophilia, Unmet Need and Disease Epidemiology in the Real world) was
29 established to provide an analysis of real-world treatment of HA in the UK, derived
30 prospectively from data collected by the UK National Haemophilia Database (NHD) and the
31 Haemtrack (HT) patient-reported treatment diary [18]. Treatment practice and patterns
32 were analysed in relation to patient-reported and objectively measured outcomes in the UK
33 cohort of patients with SHA or MHA treated during 2015, to evaluate continued unmet need
34 in this patient-group.

1 **Materials and methods**

2 ***Study objectives***

3 The objective of this study was to describe the current standard of care and to evaluate
4 unmet need in UK patients with SHA and MHA, by age and inhibitor status in the whole UK
5 HT population. We evaluated the treatment regimen and outcome as reflected by patient
6 reported annualised bleed/ joint bleed rates (ABR/ABJR); bleed-related pain and
7 interruption of daily function, in patients fulfilling pre-set HT-compliance criteria only.
8 Haemophilia Joint Health Score (HJHS) was analysed where available.

9 ***Data source and patient population***

10 The UK NHD prospectively collects data for all UK patients registered as having a bleeding
11 disorder. Diagnoses, adverse events and mortality are updated electronically in real time
12 and treatment data is reported quarterly, including individual patient product and volume.

13 The HT system is a primarily electronic, home-therapy patient-reporting diary, which
14 integrates with NHD systems [18]. Patients report treatment-related infusions, including
15 product and dose administered and the reason for infusion. For treatments, patients also
16 report severity of the bleed, cause (spontaneous or traumatic), location, associated pain and
17 disruption of planned activities.

18 Patients with SHA and MHA are recommended to have a HJHS every 6-12 months.
19 Workshops have been conducted in the UK to decrease inter-centre variability in HJHS
20 scoring. Where HJHS is recorded electronically by the local haemophilia centre, it is available
21 to the NHD to analyse. Patients with MHA using HT and those who have had a HJHS
22 performed are predominantly phenotypically at the severe end of the moderate FVIII range
23 (median (IQR) FVIII baseline of 0.01 (0.01-0.02) IU/mL). This means they are a selected
24 subset of people with MHA.

25 All patients with SHA (FVIII < 0.01 IU/mL) or MHA (FVIII = 0.01 – ≤ 0.05 IU/mL) registered
26 with the NHD during 2015 were included. The study duration was calendar year, 2015, this
27 being the first period when we had sufficient patients compliant with HT reporting and with
28 HJHS to permit meaningful analysis. HT data analysis (treatment administered and bleeding
29 outcomes) was restricted to a group who fulfilled pre-set compliance criteria, reporting
30 usage of >75% of FVIII or bypassing agent issued to them per year. Regular prophylaxis was
31 defined as ≥2.5 infusions/week for >45 weeks/year (extended half-life FVIII had not been
32 introduced at that time).

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1 ***Study design and statistics***

2 All statistical analyses are descriptive in nature. Continuous data are summarised as
3 medians and interquartile range (IQR, 25th – 75th percentile). Categorical data are presented
4 as counts and percentages. All statistical analyses were performed using Stata/SE 11.2
5 (StataCorp LLC, College Station, Tx, USA) and R (R Foundation for Statistical Computing,
6 Vienna, Austria).

7 **Results**

8 **Patient demographics**

9 During the study period, 1810 individuals with SHA and 864 with MHA were registered with
10 the NHD with 1150 and 273, respectively, registered to use HT. Of these, 607 (52.8%) with
11 SHA and 163 (59.7%) with MHA fulfilled the HT-compliance criteria and were included in the
12 bleeding outcomes analysis. In MHA, HT use was largely confined to more severely affected
13 patients who had a median (IQR) FVIII baseline 0.01 (0.01-0.02) IU/mL. A current inhibitor
14 was reported in 159 (8.8%) of individuals with SHA and 34 (3.9%) with MHA. Disposal of
15 these patients is summarised in table 1 and figure 1.

16

17 **Haemtrack reported treatment practices and bleeding outcomes in SHA and MHA.**

18 During the study period, there were a total of 1620 bleeds reported amongst the 770
19 individuals meeting the HT compliance criteria; 52.8% of these were reported to be
20 traumatic. The cause of bleeding events varied with age; 63.0% of bleeds in individuals aged
21 0 – 11 years were reported as traumatic, compared with 48.2% in patients \geq 40 years.

22 **Non-inhibitor patients**

23 Of 717 non-inhibitor patients with SHA or MHA reporting HT-compliant data during the
24 study period, 563 (78.5%) had SHA and 154 (21.5%) MHA. Of these, 465 (82.5%) with SHA
25 and 106 (68.8%) with MHA reported using regular prophylaxis. The proportion of patients
26 using prophylaxis was highest in younger patients and fell progressively with increasing age.
27 The distribution by age, treatment regimen, ABR and AJBR of the group with SHA reporting
28 prophylaxis is summarised in table 2 and figure 2. The median (IQR) ABR in patients with
29 SHA on prophylaxis was 2.0 (0.0 – 7.0) and 6.5 (2.0 – 17.8) on-demand. The median (IQR)
30 AJBR was 1.0 (0.0 - 4.0) and 3.5 (0.0 – 12.8), respectively. In the SHA group using
31 prophylaxis, 29% were bleed-free; 38% were joint-bleed-free. In the on-demand group, 19%
32 were bleed-free and 28% reported no joint bleeding. ABR and AJBR increased with age in
33 both the prophylaxis and on-demand groups (table 2, figure 2 & 3).

34 The ABR in the subgroup of MHA patients who met the HT compliance criteria was higher
35 than SHA: median (IQR) ABR/ AJBR was 3.0 (1.0 – 7.0)/ 2.0 (0.0 – 5.0) in those reporting

1 prophylaxis and 11.0 (4.8 – 20.3)/ 5.0 (2.0 – 15.3) in those treated on-demand. For patients
2 with MHA reporting prophylaxis, 24% and 30% were bleed-free or joint-bleed-free,
3 respectively. In the on-demand group, this was 10% and 15%, respectively.

4

5 ***Inhibitor patients***

6 A total of 53 patients with SHA or MHA *and* an inhibitor reported HT-compliant treatment in
7 2015; 44 (83.0%) with SHA and 9 (16.9%) MHA. Of these, 40 (90.9%) with SHA and 8 (88.8%)
8 with MHA reported treatment consistent with regular FVIII or bypass-therapy prophylaxis.

9 For patients with SHA and an inhibitor using FVIII prophylaxis (n=27), the median (IQR) ABR
10 was 1.0 (0.0 – 3.0) and for those with inhibitors using bypass-agent prophylaxis (n=8), the
11 median (IQR) ABR was 14.5 (4.0 – 22.0). Five patients with SHA reported prophylaxis with
12 both FVIII and bypass-agents during the study period, with a median (IQR) ABR of 10 (8.0 –
13 11.0).

14 Seven inhibitor patients with MHA and compliant with HT used FVIII prophylaxis, reporting a
15 median (IQR) ABR of 2.0 (0.5 – 4.5).

16 ***Haemophilia joint health score in patients with severe and moderate haemophilia A***

17 A HJHS (range 0 – 124) measured during the study period was available for 453 individuals
18 (331 (18.3%) with SHA; 122 (14.1%) with MHA). The median (IQR) baseline FVIII level of the
19 patients with MHA and a reported HJHS was 0.02 (0.01 – 0.03) IU/mL. Median HJHS
20 increased incrementally with age in SHA and MHA, both in patients using prophylaxis and
21 those using on-demand treatment.

22 The median (IQR) HJHS of patients with SHA using prophylaxis was 0.0 (0.0 – 1.0) at age 0 –
23 18 years and 65.0 (37.0 – 67.0) at age ≥ 60 years. The median (IQR) HJHS in patients treated
24 on-demand was 0.0 (0.0 – 0.0), 0-18 years and 56.5 (53.0 – 60.0), aged >60 years (figure 4).

25 HJHS appeared higher in SHA patients with a current inhibitor compared to patients with no
26 inhibitor history or a past inhibitor history, at all ages. Median (IQR) HJHS for patients with
27 SHA and a current inhibitor (n=22) was 17.0 (0.0 - 64.5); for those with an inhibitor history,
28 but no current inhibitor (n=45), it was 1.0 (0.0 – 15.5); and for those with no inhibitor
29 history (n=264), it was 8.0 (0.0 – 26.0) (p=0.015). The distribution of HJHS in the people with
30 MHA who had a HJHS performed suggests a similar pattern to SHA, although patient
31 numbers were too low to confirm this definitively (figure 5).

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1 **Pain associated with bleeding events**

2 Pain associated with bleeding events is reported to HT on a scale of one to six, six being the
3 highest level of pain. Patients are also requested to define bleeding episodes as minor or
4 major/ life threatening. The median pain score reported for all minor bleeds (n=1181) was
5 3.0. For major bleeding (n=458), the median pain score was 5.0, although the number of
6 episodes was substantially less than the number of minor bleeding events. There was no
7 difference in reported pain according to the nature of the bleed (spontaneous, surgery/
8 dental or trauma/activity).

9

10 **Disruption to planned activities associated with bleeding events and time from bleed-**
11 **onset to treatment**

12 During the study period, 51.0 % of bleeding episodes were reported to disrupt a planned
13 activity. There appeared to be no relationship between the frequency of disruption and the
14 age of the patient. The median (IQR) time elapsed from bleed onset to treatment was 2.0
15 (1.0 – 4.0) hours.

16

1 **Discussion:**

2 We report a prospective study of treatment practices and associated outcomes in a national cohort
3 of 2674 UK patients with SHA and MHA during 2015. Around 53% of this population used HT, 55% of
4 whom fulfilled compliance criteria, permitting analysis of treatment regimen and outcome. The SHA
5 HT cohort are a representative sample of UK patients with SHA lacking inhibitors [18], but HT-using
6 patients with MHA have a predominantly severe bleeding phenotype.

7 The proportion of children using prophylaxis was high (94%), decreasing to 74% of older adults.
8 Prophylaxis has been the standard of care in children for many years [6,19]. The gradual uptake of
9 prophylaxis in adult patients has been less consistent, despite good evidence to support its use [20].
10 There is considerable national variation, from zero to 100%, in the use of prophylaxis amongst adult
11 patients, even in countries with similar healthcare systems and wealth [21,22]. The proportion of
12 adults using prophylaxis in the UK has increased substantially over the past 10 years. Although we
13 found relatively low ABRs in patients treated on-demand, this probably reflects treatment selection
14 bias, since on-demand regimens are generally used in patients with a relatively mild bleeding
15 phenotype in countries where prophylaxis is the standard of care.

16 The median ABR and AJBR was low in non-inhibitor patients with SHA treated prophylactically,
17 especially in children < 12 years. However, large interpersonal variation was observed and a
18 significant proportion of adult patients with SHA still have an unacceptably high ABR. This may relate
19 to established arthropathy and the difficulty older patients experience distinguishing early bleeding
20 from arthropathic discomfort or to inadequate prophylaxis.

21 We show that prophylaxis is only partially effective in preventing self-reported bleeding; only 29% of
22 patients with SHA and 24% of patients with MHA using prophylaxis reported that they were bleed
23 free. This suggests that individual tailoring of prophylaxis could be improved. Current UK guidelines
24 recommend maintaining a trough FVIII level of > 0.01 IU/mL [3], However, patients with MHA and a
25 median (IQR) FVIII baseline 0.01 (0.01 - 0.02) IU/mL were found to have a an ABR of median 3.0 on
26 prophylaxis and 11.0 treated on-demand, both higher than observed in SHA. Since many patients
27 with a FVIII baseline of ≤ 0.02 IU/mL have a severe haemophilia phenotype [7,11], a trough level as
28 low as 0.01 IU/mL for FVIII prophylaxis is likely to be inadequate to render most patients bleed-free.
29 Many patients may require a significantly higher trough level of at least 0.03 – 0.05 IU/mL.

30 Despite this, prophylaxis was used in a lower proportion of HT-using patients with MHA than in SHA
31 (68.8% vs. 82.5). Patients with MHA were relatively undertreated, as previously reported [7]. Higher
32 baseline FVIII levels in MHA may provide false-reassurance of bleed protection and prophylaxis not
33 being started pre-emptively, as it is in SHA. Consequently, arthropathy may already be established
34 before prophylaxis is instigated. We found similar HJHS in both SHA and MHA regardless of
35 treatment regimen. It is important to recognise, however, that the patients with MHA included in
36 this report are a selected subgroup, because patients with minimal bleeding are less likely to require
37 Home therapy, Haemtrack or regular HJHS assessments.

38 HJHS increased progressively with age in both SHA and MHA. This reflects progression of
39 haemophilic arthropathy and the relative inadequacy of treatment regimens in past decades. Almost
40 all UK patients with SHA under the age of 19 years will have received prophylaxis from the early
41 infancy and consequently have a low HJHS. Those over the age of 40 years will have been treated

1 on-demand for much of their life and, therefore, have a high HJHS, whether currently treated on-
2 demand or with prophylaxis.

3 Although determining inhibitor epidemiology was not a primary objective of this analysis, our data
4 allows us to calculate an overall inhibitor prevalence of 7.2%; consistent with previous estimations in
5 unselected HA populations [23–25]. It is interesting to note that in the HT subgroup the prevalence
6 of inhibitors is remarkably similar (6.9%).

7 Patients with persistent inhibitors to FVIII, have significantly higher ABR and HJHS than non-inhibitor
8 patients with a similar factor VIII level, especially amongst the older patients, where pre-existing
9 arthropathy probably increases an individual's propensity to bleed. Surprisingly, although one might
10 expect some arthropathy to develop in the period before successful inhibitor eradication, we found
11 patients with a past inhibitor history to have a similar HJHS to patients who had never had an
12 inhibitor. This reinforces the importance of prompt, active inhibitor eradication [17].

13 Many historic investigations of treatment practices have relied on survey data, an approach limited
14 by reporting bias [25–29]. The HT system used by most UK haemophilia treatment centres, avoids
15 this by prospectively reporting actual patient practice, rather than the expected or prescribed
16 treatment. Although patient reported outcomes (PROs) and “real-world” data sources are
17 susceptible to other forms of reporting bias, such as poor reporting compliance [30], our compliance
18 checks are robust enough to eliminate many of these issues. Although PROs are relatively subjective
19 and cannot be completely verified, by analysing only patients who fulfil pre-set reporting compliance
20 criteria, cross-checked with NHD product issues data, we have a high degree of confidence that the
21 outcome data presented is compliantly reported. Our selection criteria minimise reporting
22 inaccuracies. Subjectivity in bleed reporting is reduced further by reporting only joint bleeding,
23 which is less susceptible to misclassification.

24 The NHD does not report bleed level data on patients that do not use HT, limiting analysis of non-HT
25 users to a comparison of overall FVIII usage. This may introduce some reporting bias. However, the
26 HT-data shows the outcome and limitations of treatment when it is used as intended by treatment
27 centres. It will be interesting to see, as our HJHS data becomes more complete, whether HT-
28 uncompliant patients have a poorer joint-outcome. Although this is the largest reported dataset of
29 HJHS, only a small number of older patients are reported and there is likely to be a degree of inter-
30 and intra-centre joint-scoring variability [31]. Furthermore, we are unable to confirm the presence of
31 co-morbid musculoskeletal conditions that may contribute to HJHS. Although we have drawn only
32 broad and general conclusions from our HJHS data, as the electronic reporting of HJHS to the NHD
33 becomes more routine and the dataset expands, we will be able link HJHS to treatment frequency
34 and intensity in addition to disease severity and other co-morbid conditions.

35 This is the first large-scale study using data derived from the HT system, demonstrating the great
36 potential for this tool to generate treatment-level data in large cohorts of patients. Uptake and
37 compliance with the system continues to increase. The dataset will evolve and there is potential to
38 link with other large National Databases and information systems, expanding the number of non-
39 traditional outcome measures available for analysis.

40 The THUNDER study demonstrates the limitations of prophylaxis as recently practiced in the UK.
41 Whilst outcomes in children appear excellent, prophylaxis has not succeeded in attaining the desired

1 bleed-free status in many children and most adults. Arthropathy is observed from early adulthood
2 onwards. Haemarthroses, when they occur, have a significant impact on daily life. Strategies to
3 improve these outcomes should be targeted to reduce bleeding in patients with high ABRs. This
4 should include more intense individualisation of prophylaxis, potentially requiring trough FVIII levels
5 beyond 0.01 – 0.02 IU/mL, optimised pharmacokinetically in some patients. Prophylaxis should be
6 started early in patients with MHA if spontaneous bleeding episodes occur. We should aim for our
7 patients to be bleed-free and, as newer agents become increasingly available for routine clinical use,
8 this may soon become a realistic aspiration.

9

10

11

1 **Author contributions:**

2 The analysis was conducted by BP, HX and MS in the UK NHD, with advisory input from CRMH, CS
3 and the other co-authors. The first draft of the manuscript was written by CRMH and MS.
4 Subsequent drafts were edited by CRMH, MS, DPH, CS, HX, BP and PWC and DS.

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11 staff at the National Haemophilia Database are also thanked for their contribution to data collection.

12

13 **Conflicts of Interest:**

14 MS is a Bayer Haemophilia Clinical Research Fellow and has received sponsorship to attend meetings
15 from Bayer, Pfizer, Shire and Sobi.

16 CRMH has participated in Roche advisory panels and has received research support from Novo,
17 Pfizer, Shire Bayer and Sobi and acted as speaker in sponsored symposia for Pfizer, Shire, Bayer,
18 Sobi and Biotest.

19 HX and BP have no competing interests to declare

20 DPH – Has received research support from Shire, Octapharma and Bayer and has worked as a paid
21 consultant or speaker for Pfizer, Shire, Sobi, Octapharma, Novo Nordisk, UniQure, Roche, Biotest
22 and Bayer

23 PWC – Has worked as a paid consultant to Roche; has received research support and support to
24 attend meetings from CSL Behring, NovoNordisk and Bayer.

25 CSS is employed by Roche/ Genentech and holds stock in the company.

26 DS – Has received research support from Pfizer and Novo Nordisk and has worked as paid speaker
27 at sponsored educational meetings for Pfizer, Bayer and Shire

28

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1 **Tables and Figures:**

2 **Figure 1:** Distribution of study population

3 **Figure 2:** Median annualised bleed rates for Haemtrack-compliant patients with severe
4 haemophilia A using prophylaxis and on-demand treatment, categorised according to age
5 and inhibitor status

6 **Figure 3:** Median annualised joint bleed rates for Haemtrack-compliant patients with severe
7 haemophilia A using prophylaxis and on-demand treatment, categorised according to age
8 and inhibitor status

9 **Figure 4:** Median Haemophilia Joint Health Score for patients with severe haemophilia A and
10 moderate haemophilia A, categorised according to treatment type and age. The line
11 represents the median value; the box interquartile range and the whiskers the lowest data
12 still within 1.5 IQR of the lower quartile, and the highest data still within 1.5 IQR of the upper
13 quartile.

14 **Figure 5:** Mean Haemophilia Joint Health Score for patients with severe haemophilia A and
15 moderate haemophilia A categorised according to inhibitor status

16 **Table 1:** Study population categorised according to age at study mid-point and compliance
17 with Haemtrack (HT) reporting for **(a)** severe haemophilia A, and **(b)** moderate haemophilia
18 A.

19 **Table 2:** Number of non-inhibitor Haemtrack-compliant patients with SHA, categorised
20 according to age, treatment type and associated annual bleed rate (ABR)/ annual joint bleed
21 rate (AJBR)

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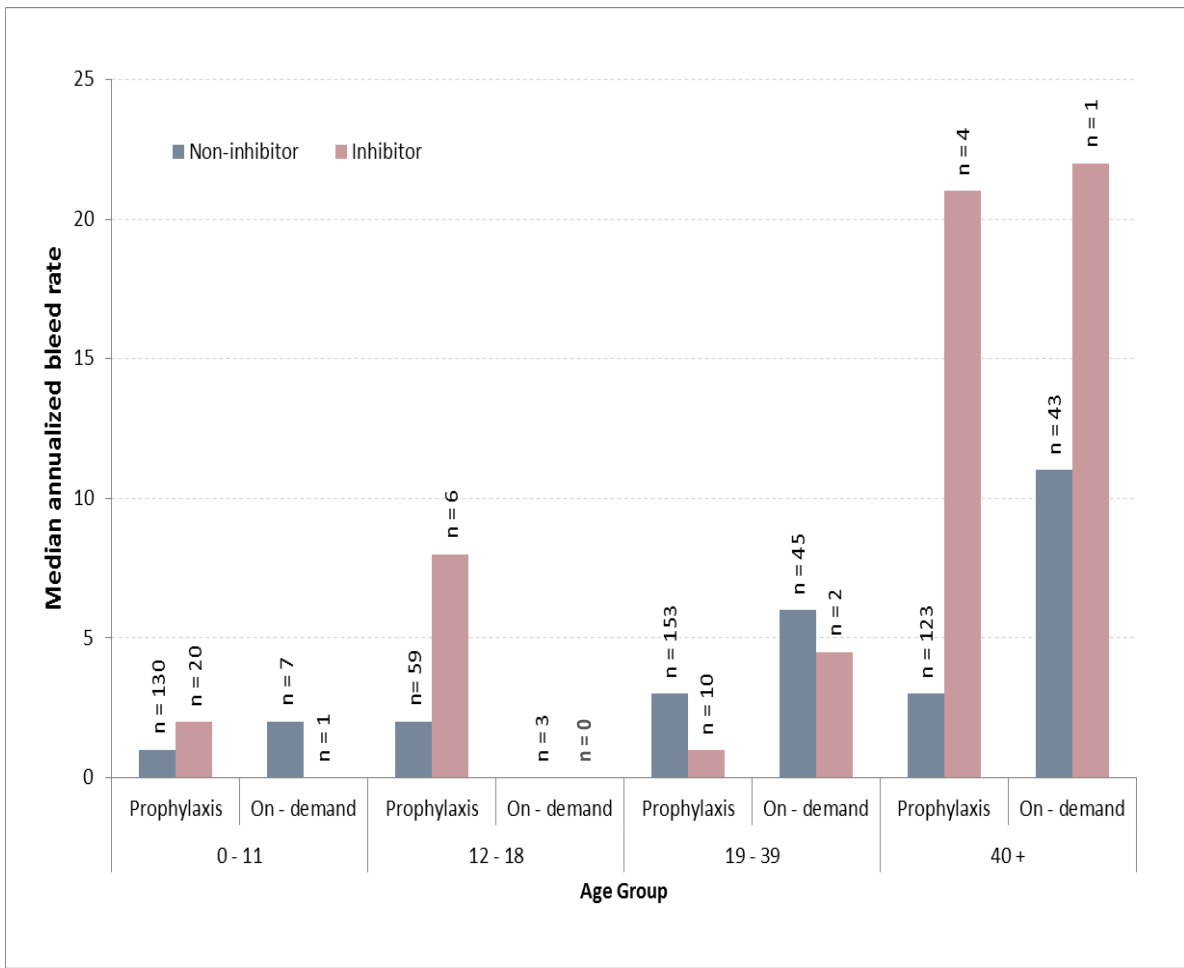
1 **Figure 1:**

			Severe	Moderate	Total
Study population	NHD Registration of Haemophilia A (2015)	All Patients	1810	864	2674
		Current Inhibitor	159	34	193
Haemtrack Subgroup	Haemtrack Registered		1150	273	1423
	Haemtrack Compliant	Inhibitor Negative	563	154	717
		Current Inhibitor	44	9	53
HJHS Subgroup	HJHS Available		331	122	453
	Current Inhibitor		22	9	31
	Previous Inhibitor		45	11	56
	No Inhibitor History		264	102	366

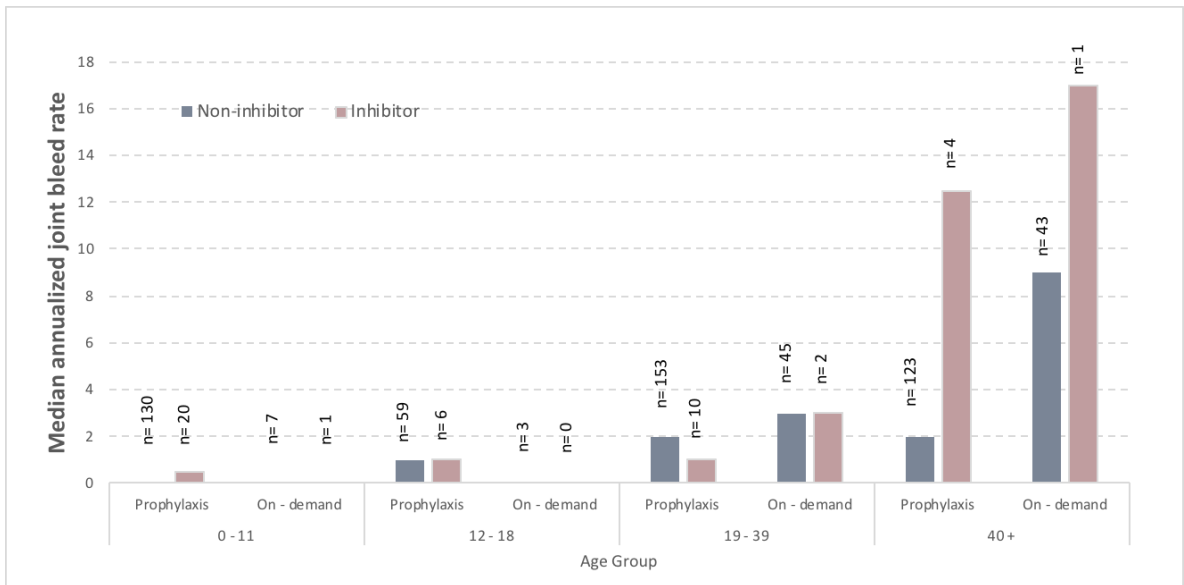
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1 **Figure 2**



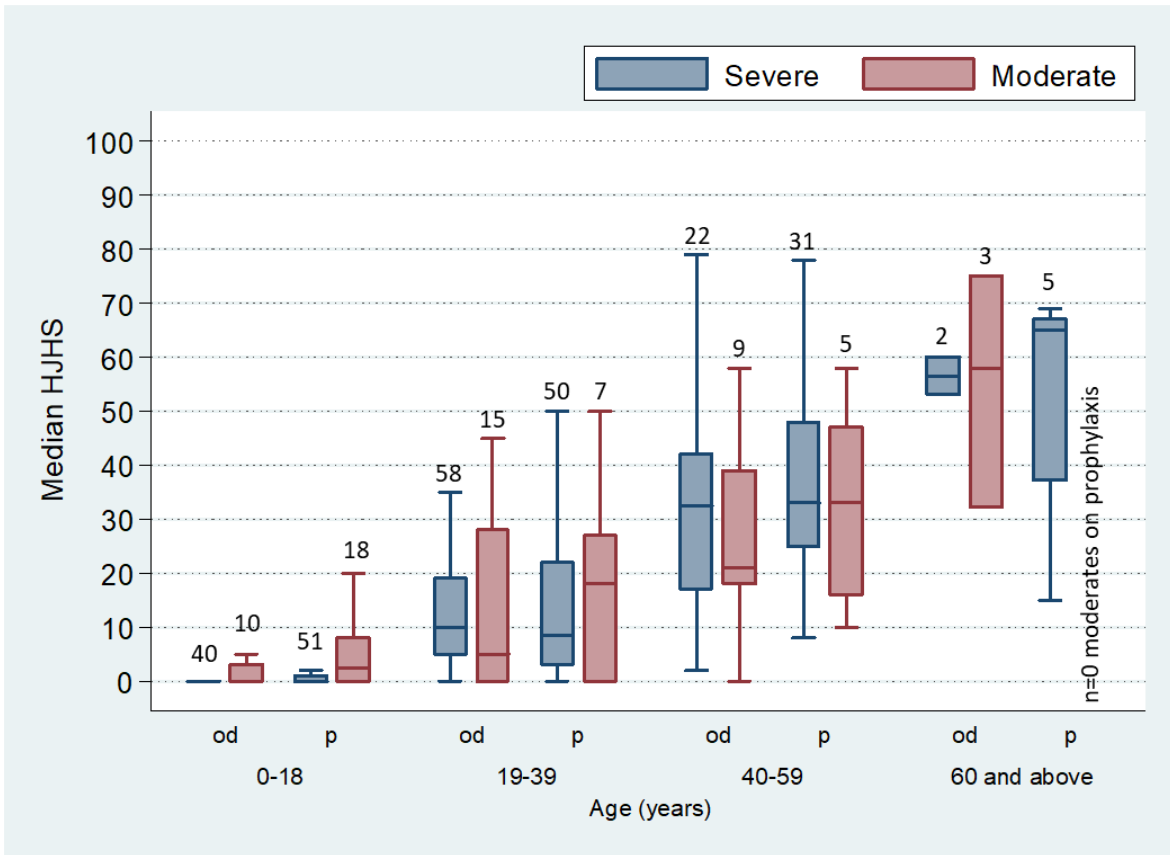
16 **Figure 3**



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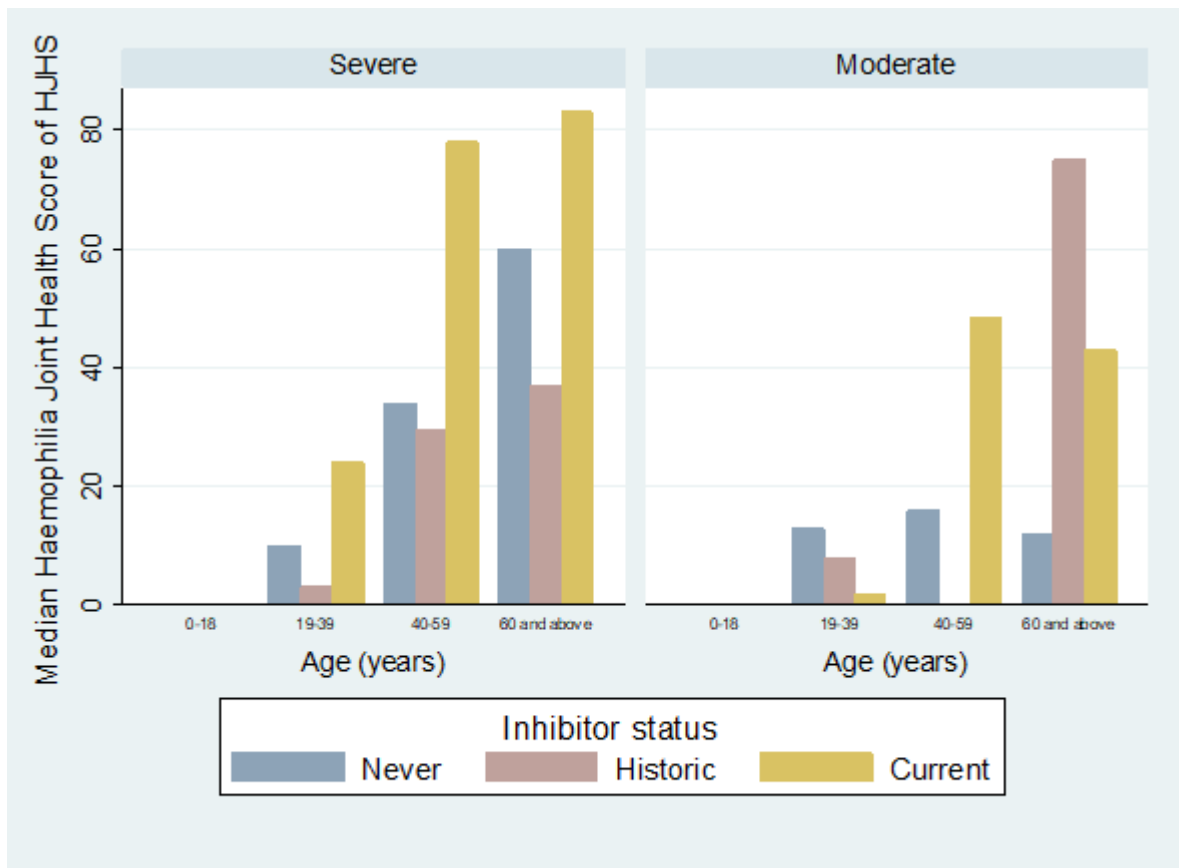
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1 **Figure 4**



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1 **Figure 5**



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3 **Table 1 (a)**

	Severe			
Age/ years	Total, n (%)	HT Compliant, n (%)	HT Non-compliant, n (%)	Not HT registered, n (%)
0 - 12	491 (27.1)	178 (36.3)	121 (24.6)	192 (39.1)
13 - 24	446 (24.6)	118 (26.5)	158 (35.4)	170 (38.1)
25 - 36	395 (21.8)	124 (31.4)	133 (33.7)	138 (34.9)
37 - 49	258 (14.3)	105 (40.7)	71 (27.5)	82 (31.8)
≥ 50	220 (12.2)	91 (41.4)	51 (23.2)	78 (35.5)

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1 **Table 1 (b)**

	Moderate			
Age/ years	Total, n (%)	HT Compliant, n (%)	HT Non-compliant, n (%)	Not HT registered, n (%)
0 - 12	147 (17.0)	20 (13.6)	28 (19.0)	99 (67.3)
13 – 24	160 (18.5)	35 (21.9)	27 (16.9)	98 (61.3)
25 – 36	182 (21.1)	32 (17.6)	32 (17.6)	118 (64.8)
37 – 49	152 (17.6)	29 (19.1)	25 (16.4)	98 (64.5)
≥ 50	223 (25.8)	25 (11.2)	20 (9.0)	178 (79.8)

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3 **Table 2.**

Age (yrs)	Prophylaxis			On-demand		
	n (%)	ABR (IQR)	AJBR (IQR)	n (%)	ABR (IQR)	AJBR (IQR)
0-11	130 (95)	1.0 (0.0-5.0)	0.0 (0.0 – 1.0)	7 (5)	2.0 (1.5-4.0)	0 (0 – 0.5)
12-18	59 (95)	2.0 (0.0 -7.0)	1.0 (0.0 – 3.0)	3 (5)	0.0 (0.0 -1.0)	0.0 (0.0 – 1.0)
19-39	153 (77)	3.0 (1.0 -8.0)	2.0 (0.0 – 6.0)	45 (23)	6.0 (0.0 13.0)	3.0 (0.0 – 7.0)
>-40	123 (74)	3.0 (1.0 – 8.0)	2 (0 – 6.5)	43 (26)	11 (2.5 - 27.0)	9.0 (1.5 – 18.0)

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