

The status of care for persons with haemophilia registered within CNHP registry Annual Report 2018

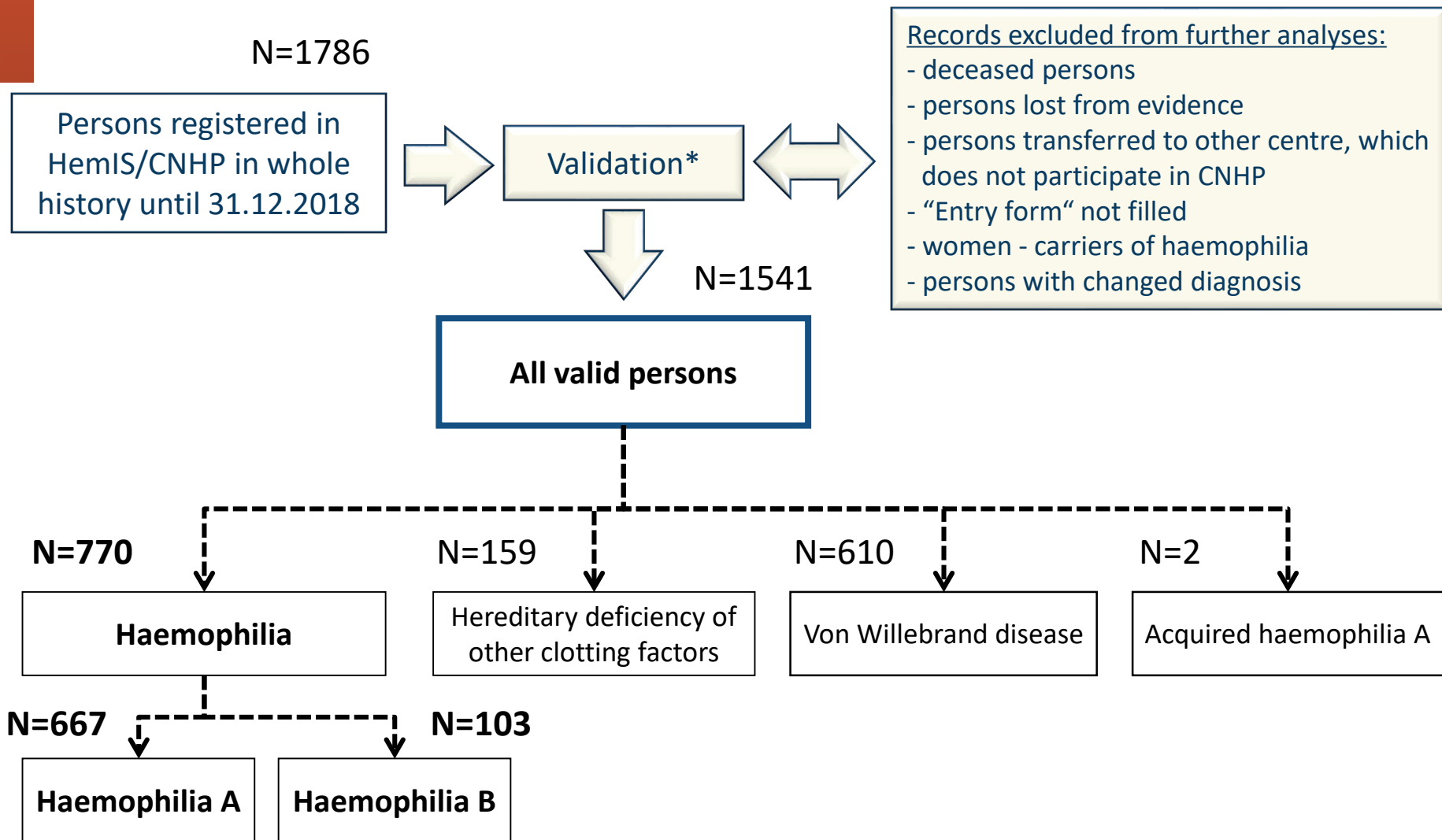
Jan Blatný, Petra Ovesná

on behalf of

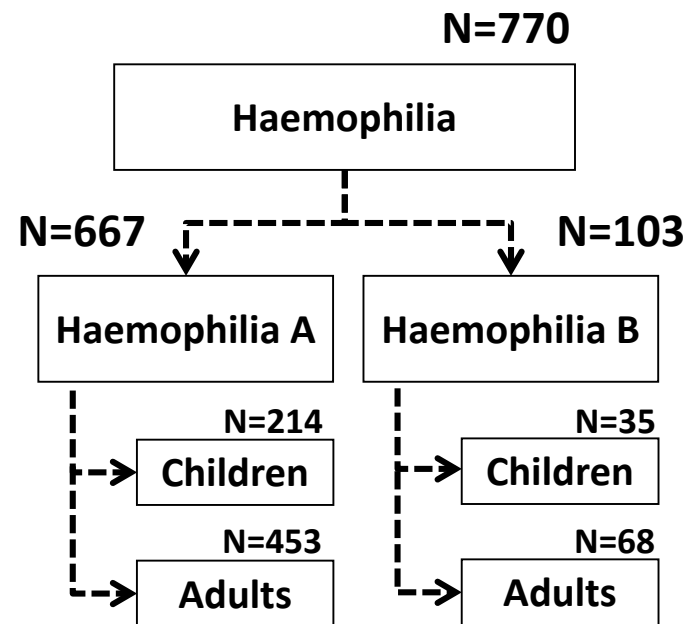
Centres contributing to CNHP registry
(Czech National Haemophilia Programme)

Export date: April 3, 2019

Sample size, valid records



Persons with haemophilia (PWH)



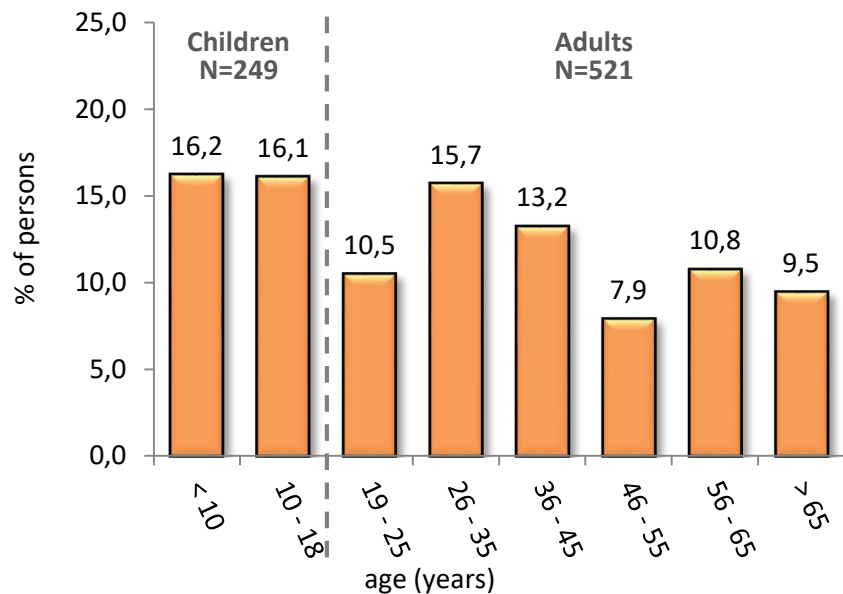
Centres participating in CNHP

Paediatric centres	Valid persons	
	N	%
Prague – Dpt. of Pediatric Haematology and Oncology, CUH Motol	89	11.6
Brno – Dpt. of Pediatric Haematology, CUH Brno	55	7.1
Ústí n.L. – Pediatric Dpt. – Haematology, Masaryk Hospital	28	3.6
Hradec Králové – Dpt. of Pediatric Medicine, UH HK	22	2.9
Ostrava – Dpt. of Pediatric Medicine, UH Ostrava	20	2.6
Olomouc – Dpt. of Pediatric Medicine, UH Olomouc	19	2.5
Pilsen – Pediatric Dpt., UH Pilsen	17	2.2
České Budejovice – Pediatric Dpt., Hospital CB	15	1.9

Adult centres	Valid persons	
	N	%
Brno – Dpt. Of Clin Hematol, UH Brno	152	19.7
Ostrava – Blood centre, UH Ostrava	76	9.9
Hradec Králové – IV. Internal and Hematology Dpt., UH HK	68	8.8
Olomouc – Haemato-Oncology Dpt., UH Olomouc	58	7.5
Pilsen – Dpt. of Biochemistry and Hematology, UH Pilsen	49	6.4
Liberec – Dpt. Of Clin Hematol, Hospital Liberec	37	4.8
Ústí n.L. – Dpt. Of Clin Hematol, Masaryk Hospital	29	3.8
České Budějovice – Dpt. Of Clin Hematol, Hospital CB	28	3.6
Pilsen - Hemacentrum	8	1.0

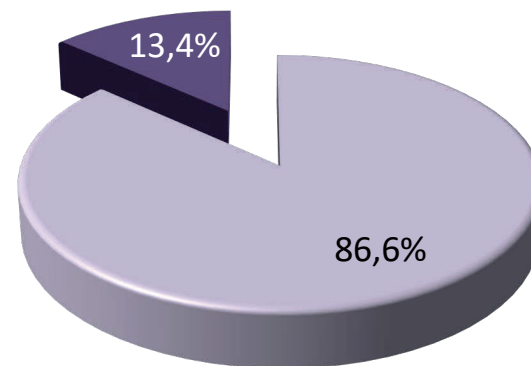
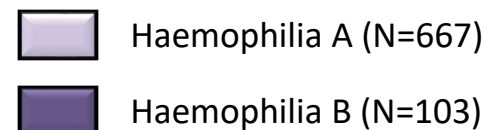
Basic demographics

	Actual age* (years)
N	770
Mean	32.8
Median (min - max)	29 (0 – 96)



* age reached in year 2018

Type of haemophilia



Twelve children with haemophilia were born in 2018.

Persons with haemophilia and inhibitors in 2018

Active inhibitors were recorded in 21 persons in the end of 2018 (+cca 5 in another centre, not reported here)

- 3 inhibitors in children with severe HA newly developed in 2018

PWH with inhibitors:

- 13 children and 8 adults
- 20 haemophilia A and 1 haemophilia B
- 17 in severe, 2 in moderate and 2 in mild haemophilia
- 17 high-titre and 4 low-titre (<5BU),
- 11 high response and 6 low response inhibitors; this information not available in 4 PWH with inhibitors
- 4 patients were treated with rFVIIa, 7 patients with aPCC and 3 patients both with rFVIIa and aPCC
 - 2 patients were treated with emicizumab
 - 5 patients were without any „by-pass“ therapy and 2 patients were without any recorded treatment at all

ITT:

- Seven of above mentioned 21 persons (six children, one adult) started ITT in 2018
 - Out of them three children developed inhibitors in 2018, three children and one adult earlier
- Another 6 patients (of them 1 adult) have already been on-going ITT in 2018 (started earlier)

Eradication of inhibitor:

- One child finished ITI successfully in the beginning of January 2018 and for 2018 is considered as inhibitor free.
- Another one child finished ITT unsuccessfully during 2018 (than commenced on emicizumab)
- None of the ITIs started in 2018 led to eradication in 2018. All of them are on-going also in 2019

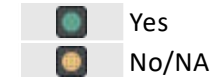
ABR and treatment regimens in patients with inhibitor

	Type	Year of birth	Severity	ITT	By-pass/emi prophylaxis	Titre	Responder	ABR	Joint / other
1	HA	2017	Severe	Yes	Temporary	Low	LR		3 0/3
2	HA	2017	Severe	Yes	Temporary	Low	LR		4 1/3
3	HA	2016	Severe	Yes	OD	High	NA		0 0/0
4	HA	2016	Severe	Yes	OD	High	LR		1 0/1
5	HA	2015	Severe	Yes	OD	High	NA		1 0/1
6	HA	2015	Severe	Yes	OD	Low	LR		1 0/1
7	HA	2015	Severe	Yes	Temporary	High	LR		8 3/5
8	HA	2014	Severe	Yes	OD	High	LR		1 0/1
9	HA	2011	Moderate	Yes	Temporary	High	LR		14 3/11
10	HA	2004	Severe	Yes	Temporary	High	LR		5 / 4
11	HA	2003	Severe	No/NA	Permanent	High	LR		14 8/6
12	HA	2001	Severe	Yes	Permanent	High	LR		4 2/2
13	HA	1988	Mild	No/NA	OD	Low	NA		0 0/0
14	HA	1977	Severe	No/NA	OD	High	LR		0 0/0
15	HA	1975	Severe	Yes	Permanent	High	LR		11 11/0
16	HA	1971	Severe	No/NA	OD	High	LR		1 0/1
17	HA	1971	Severe	No/NA	OD	High	LR		0 0/0
18	HA	1956	Severe	No/NA	Permanent	High	LR		0 0/0
19	HA	1949	Mild	No/NA	OD	High	NA		6 /
20	HA	1941	Moderate	Yes	Permanent	High	LR		1 1/0
21	HB	2007	Severe	No/NA	Temporary	High	LR		8 4/4

Severity



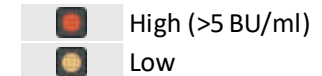
ITT



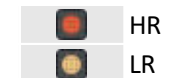
By-pass/emi prophylaxis



Titre



Responder



new in 2018

NA – not available

ABR according to treatment regimen in PWH with inhibitor

Diagnosis	ITT	By-pass/emi prophylaxis	N	ABR (mean)	ABR (median, min-max)	Joint / other bleeds (median)
Haemophilia A	Yes	Permanent	3	5.3	4 (1-11)	2 / 0
		Temporary	5	6.8	5 (3-14)	2 / 4
		OD	5	0.8	1 (0-1)	0 / 1
	No	Permanent	2	7.0	7 (0-14)	4 / 3
		OD	5	1.4	0 (0-6)	0 / 0
Haemophilia B	No	Temporary	1	8.0	8 (8-8)	4 / 4

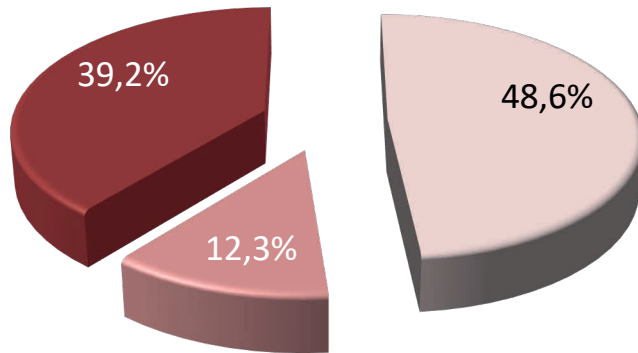
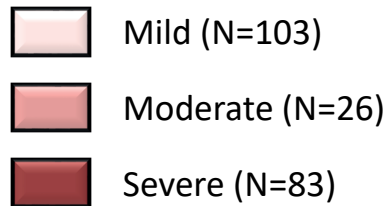
Demographic characteristics

Haemophilia A

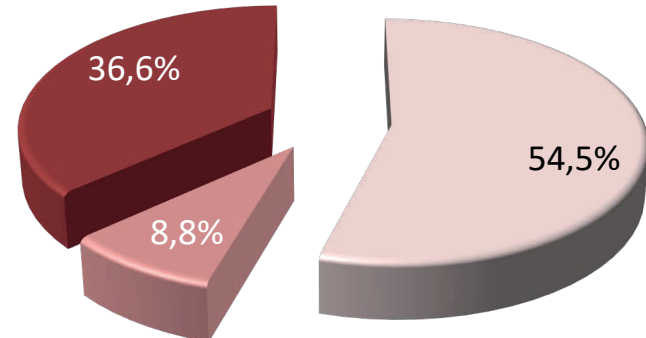
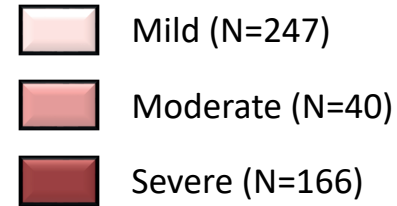


Severity of haemophilia A

Children (N=212*)

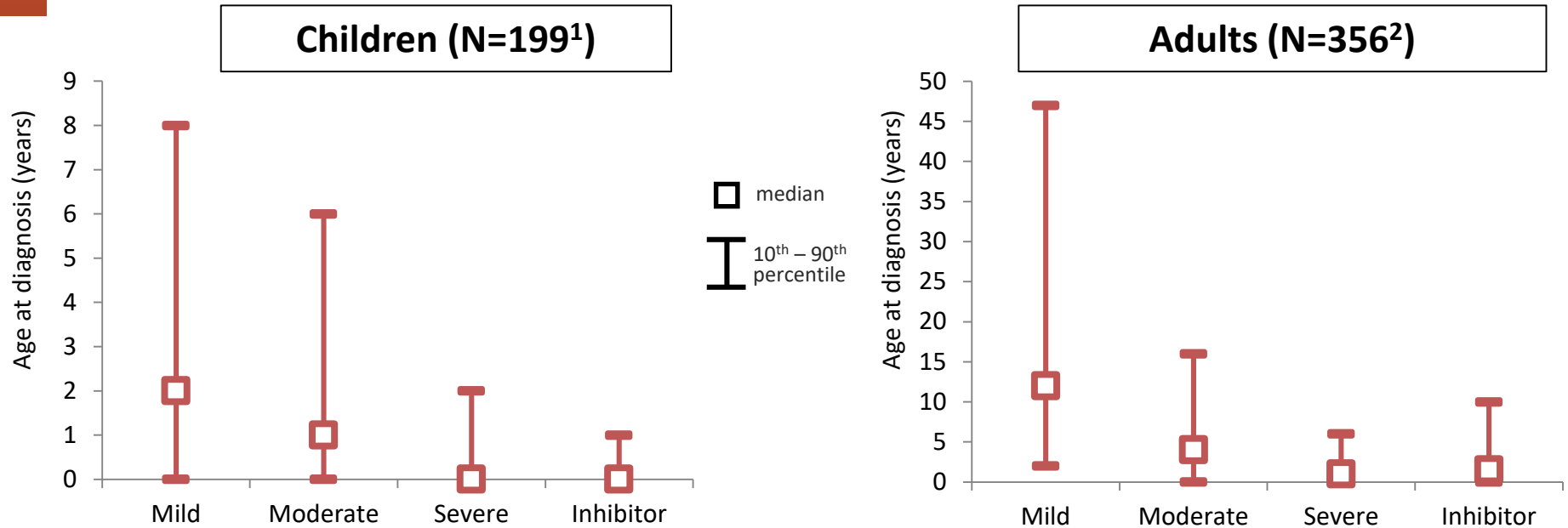


Adults (N=453)



* severity of haemophilia not known in 2 newly born children with haemophilia A

Age at diagnosis according to severity of haemophilia A



Mild*	Moderate*	Severe*	Inhibitor ⁺	Age at diagnosis (years)	Mild*	Moderate*	Severe*	Inhibitor ⁺
98	25	76	12	N valid	204	29	123	8
2.9	2.1	0.6	0.6	Mean	18.9	6.0	2.4	3.3
2 (0 – 11)	1 (0 – 11)	0 (0 – 7)	0 (0 – 4)	Median (min – max)	12 (0 – 67)	4 (0 – 32)	1 (0 – 38)	1.5 (0 – 10)

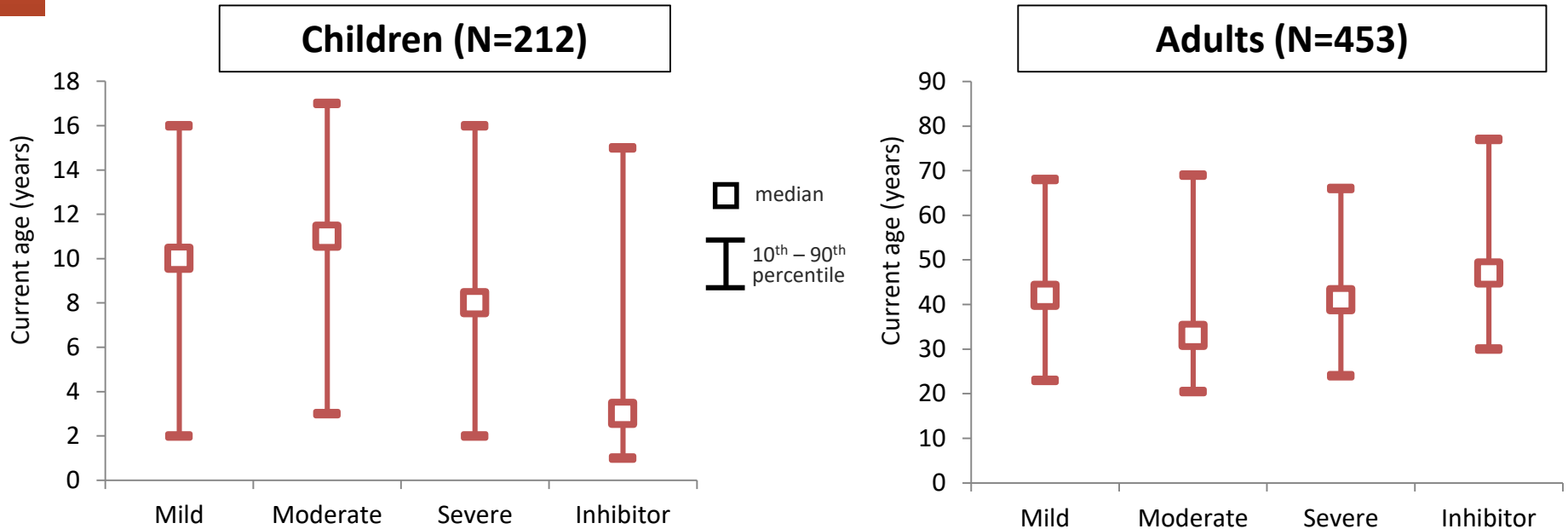
¹ Missing information on year of diagnosis in 13 children.

² Missing information on year of diagnosis in 97 adults.

* including persons with inhibitor

⁺ in 2018

Actual age according to severity of haemophilia A



Mild*	Moderate*	Severe*	Inhibitor ⁺	Current age ⁺⁺ (years)	Mild*	Moderate*	Severe*	Inhibitor ⁺
103	26	83	12	N valid	247	40	166	8
9.4	10.2	8.7	6.0	Mean	44.7	40.4	43.0	52.0
10 (0 – 18)	11 (3 – 17)	8 (0 – 18)	3 (1 – 17)	Median (min – max)	42 (19 – 96)	33 (19 – 77)	41 (19 – 79)	47 (30 – 77)

* including persons with inhibitor

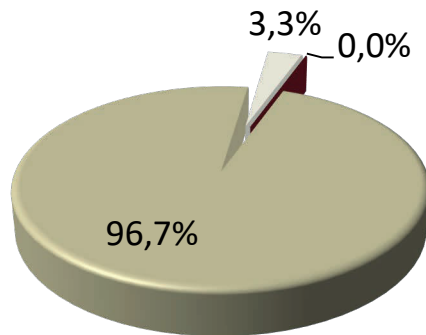
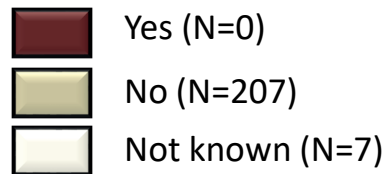
⁺ in 2018

⁺⁺ age reached in year 2018

Hepatitis (ever) experienced

Children
Haem A
N=214

Experienced hepatitis



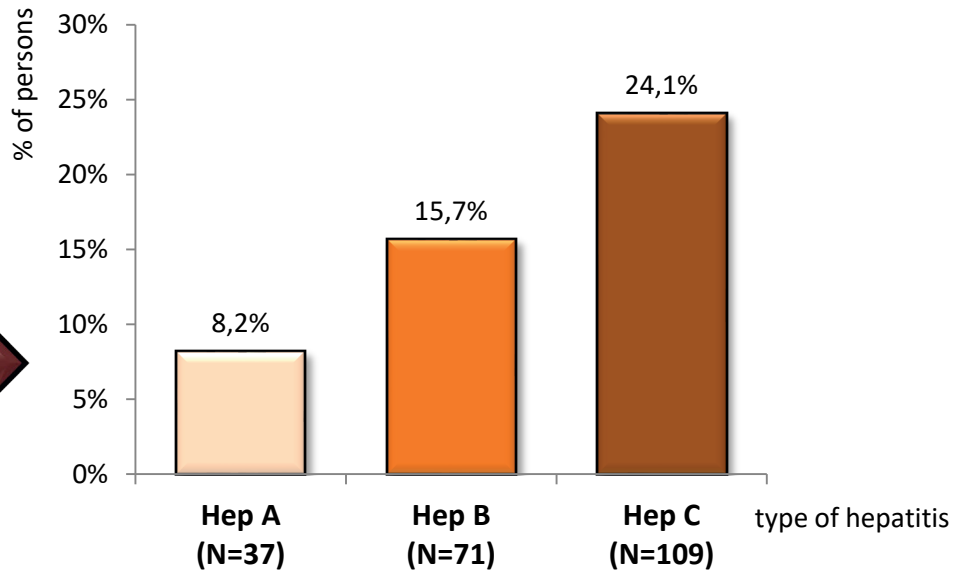
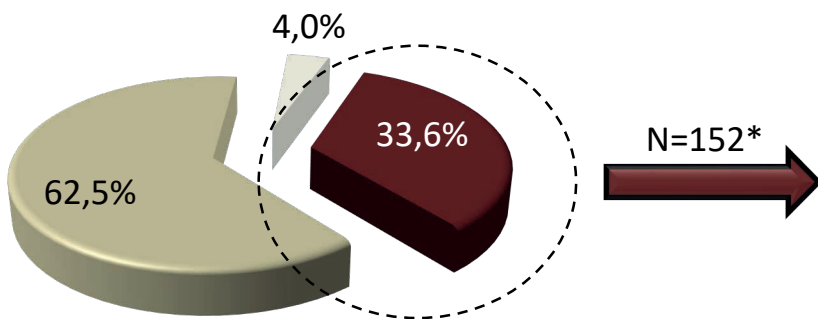
No child has hepatitis.

Data from last completed annual report of each person.

Hepatitis (ever) experienced

Experienced hepatitis

- Yes (N=152)
- No (N=283)
- Not known (N=18)



31 adults are HCV RNA positive




Data from last completed annual report of each person.

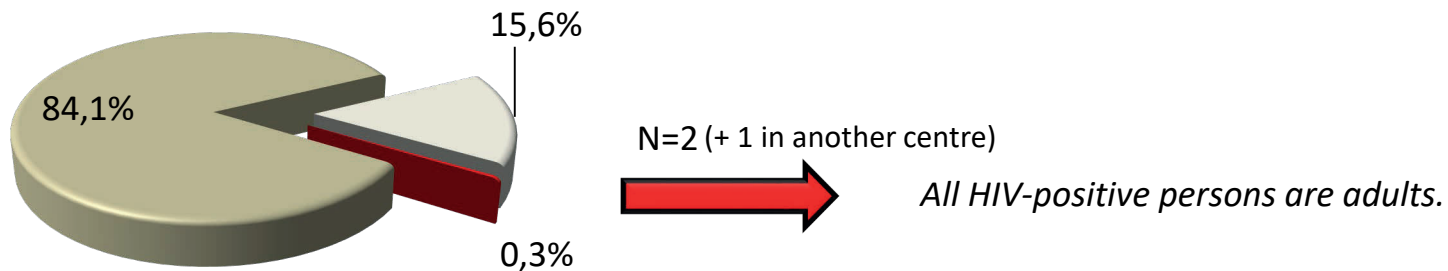
*Total of 217 cases of hepatitis in 152 persons. One person may have more types of hepatitis recorded.

HIV

All
Haem A
N=667

HIV

-  Positive (N=2)
-  Negative (N=561)
-  Not known / not available (N=104)



Data from last completed annual report of each person.

Treatment outcomes and bleeding frequency

Haemophilia A



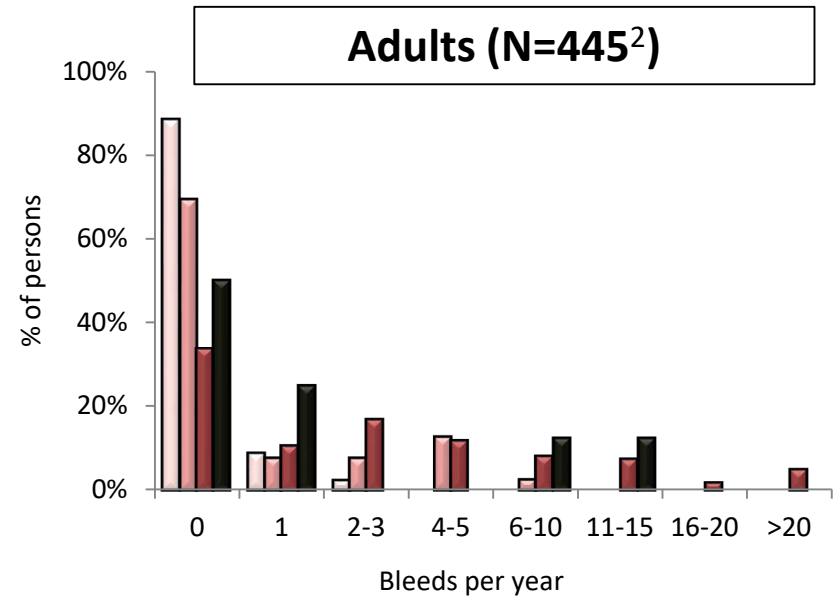
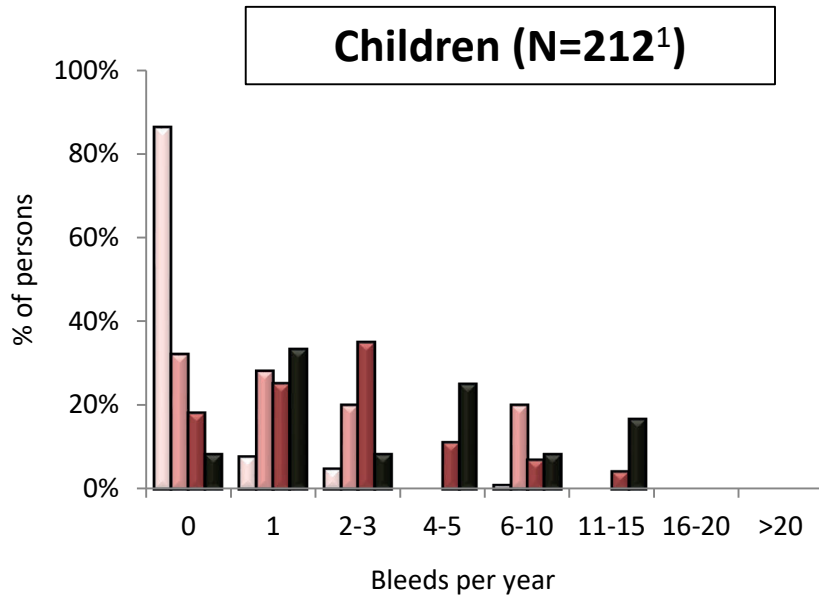
All
Haem A
N=667

Data from year 2018 – sample size

	Valid persons		→	Persons with <u>valid</u> annual report		→	Persons <u>examined</u>		→	Persons <u>treated</u>	
	N	%		N	%		N	%		N	%
All	667	100%	→	643	96.4%	→	508	76.2%	→	356	53.4%
of them with inhibitor	20			20			19			18	
Children	214	100%	→	208	97.2%	→	186	86.9%	→	122	57.0%
of them with inhibitor	12			12			12			12	
Adults	453	100%	→	435	96.0%	→	322	71.1%	→	234	51.7%
of them with inhibitor	8			8			7			6	



Frequency of bleeding requiring treatment in 2018



Mild*	Moderate*	Severe*	Inhibitor	Frequency of bleeding	Mild*	Moderate*	Severe*	Inhibitor
103	25	72	12	N valid	245	39	153	8
0.3	2.2	2.7	4.7	Mean	0.2	1.1	4.5	2.4
0 (0 – 7)	1 (0 – 9)	2 (0 – 15)	3.5 (0 – 14)	Median (min – max)	0 (0 – 3)	0 (0 – 10)	2 (0 – 39)	0.5 (0 – 11)
89 (86.4%)	8 (32%)	13 (18.1%)	1 (8.3%)	N (%) with no bleed	217 (88.6%)	27 (69.2%)	54 (33.5%)	4 (50%)

* without inhibitor

¹ Missing severity in 2 children.

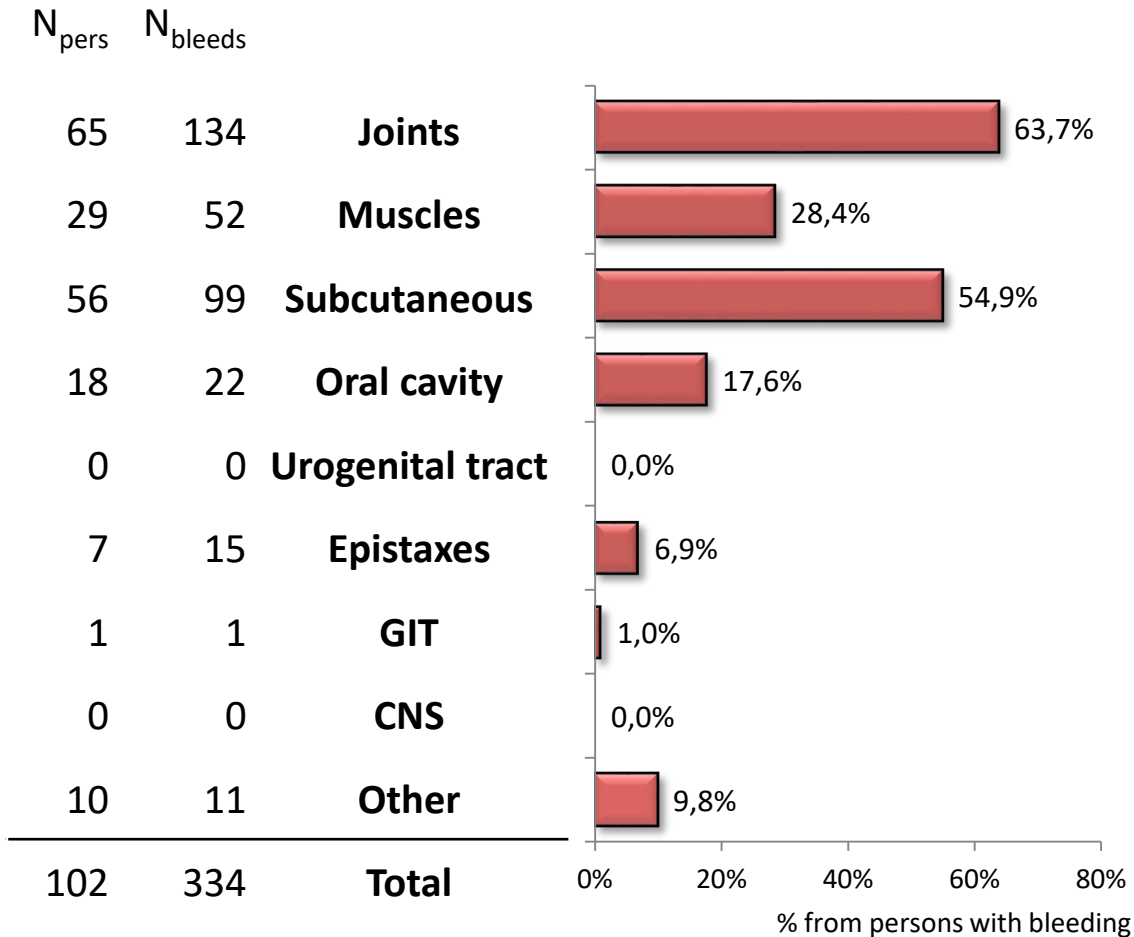
² Frequency of bleeding is missing in 8 adults.

Location of bleeds in 2018

102 (47.7%) children experienced bleeding requiring treatment at least once in year; 334 bleeds were recorded in total, 25 bleeds required hospitalization.

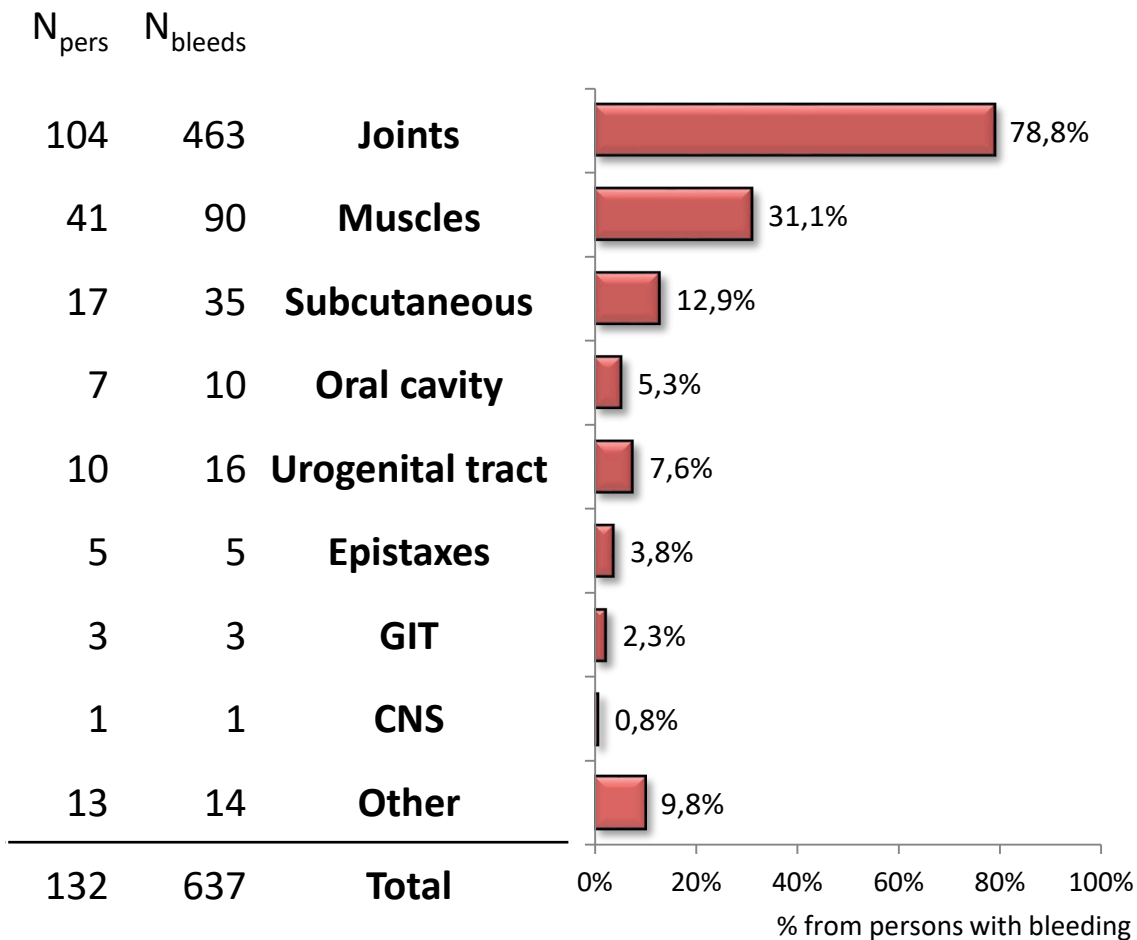
All of these 102 children have recorded location of their bleeds.

112 (52.3%) children recorded no bleed during year 2018.



Location of bleeds in 2018

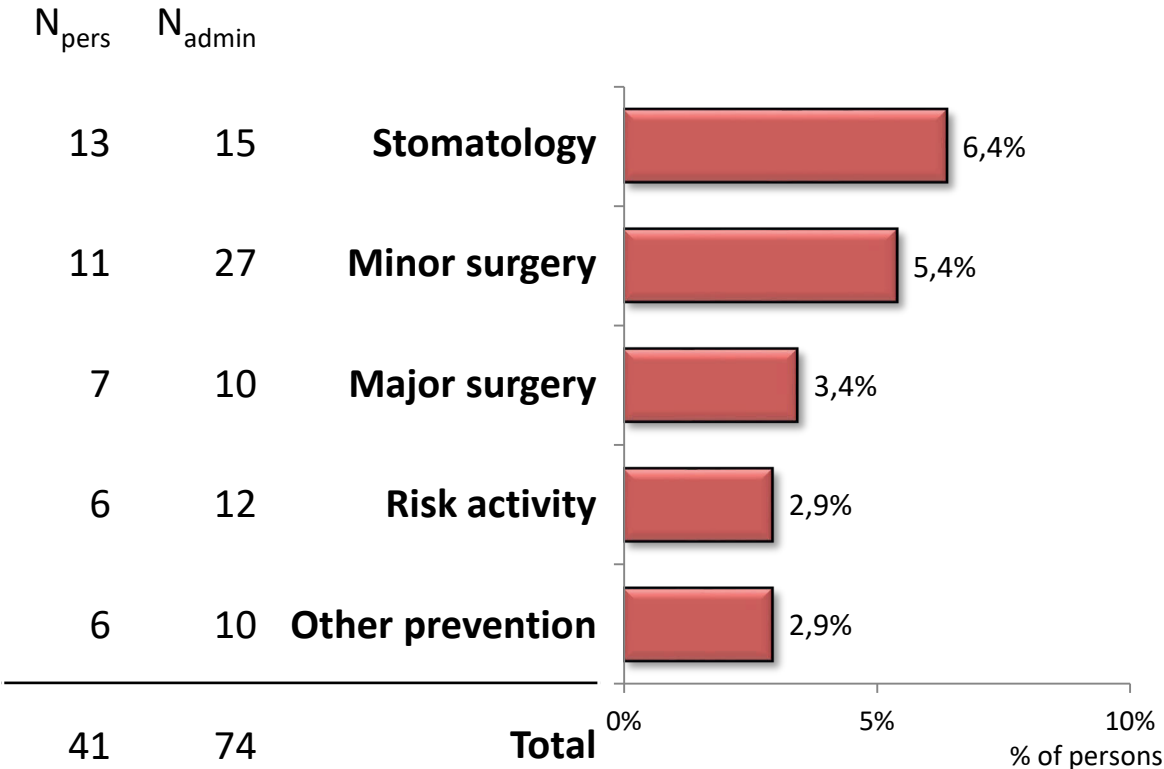
143 (32.1%) adults experienced bleeding requiring treatment at least once in year; 788 bleeds were recorded in total, 24 bleeds required hospitalization.
132 of these 143 adults have recorded location of their bleeds. Localization is not known in 11 adults. 302 (67.9%) adults have recorded no bleed during year 2018.



¹Frequency of bleeding is missing in 8 adults.

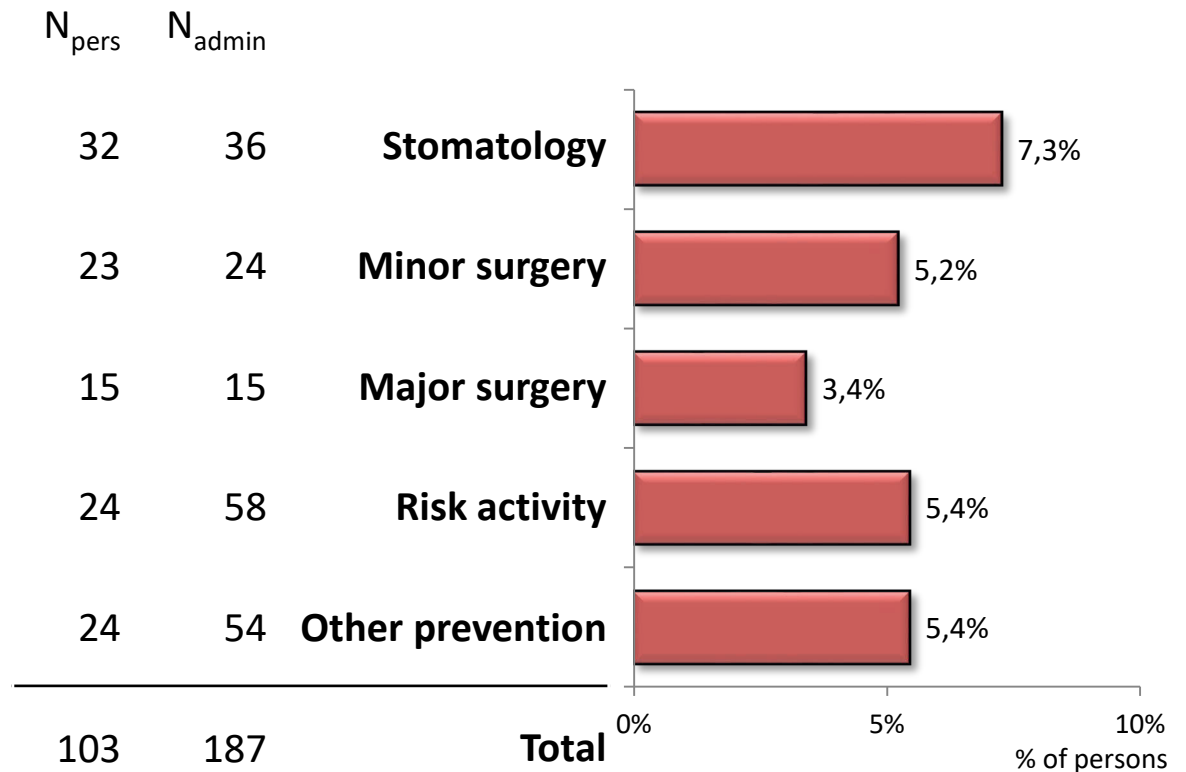
Preventive administration in 2018

41 (19.2%) children were given factor to prevent bleeding during/before risk situation.
74 preventive administrations were recorded in total.



Preventive administration in 2018

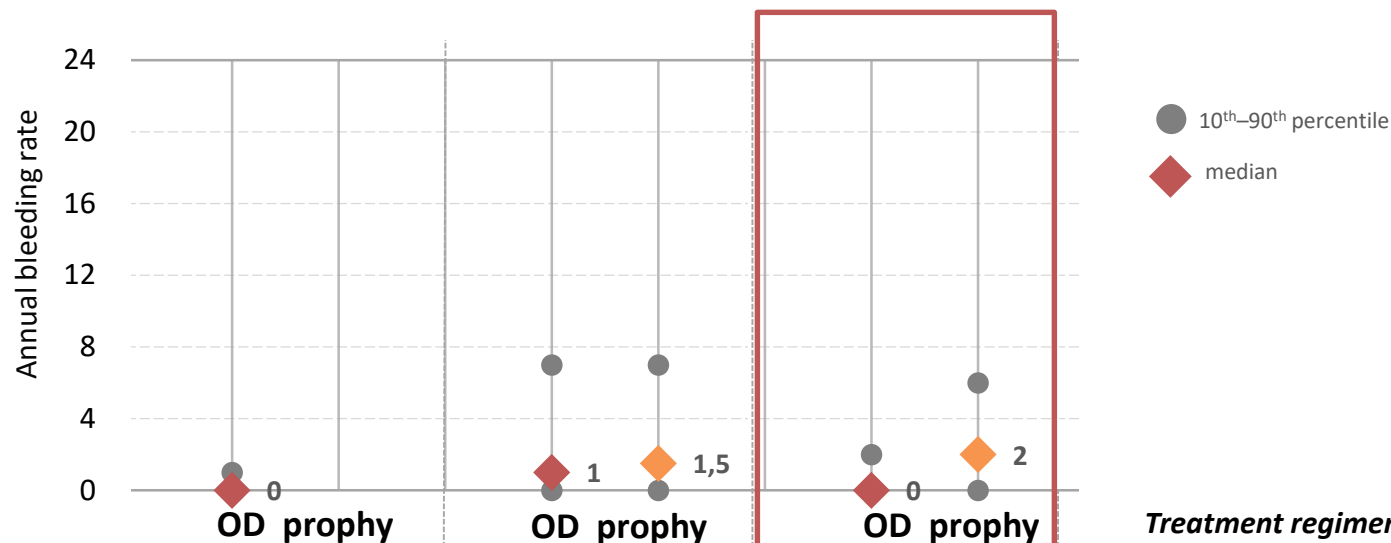
103 (22.7%) persons were given factor to prevent bleeding during/before risk situation.
187 preventive administrations were recorded in total.



ABR according to treatment regimen Haemophilia A without inhibitor



Annual bleeding rate according to treatment regimen



Frequency of bleeding	Mild*		Moderate*		Severe*	
N valid	103	0	17	8	6	66
Mean	0.3		1.8	3.0	0.5	2.9
Median (min – max)	0 (0 – 7)		1 (0 – 9)	1.5 (0 – 7)	0 (0 – 2)	2 (0 – 15)
Total no of recorded bleeds	27		31	24	3	192
children on permanent prophylaxis	0 (0%)		8 (32%)		66 (91.7%)	
% of factor (FVIII) consumed by children on permanent prophylaxis	-		89.3%		99.9%	

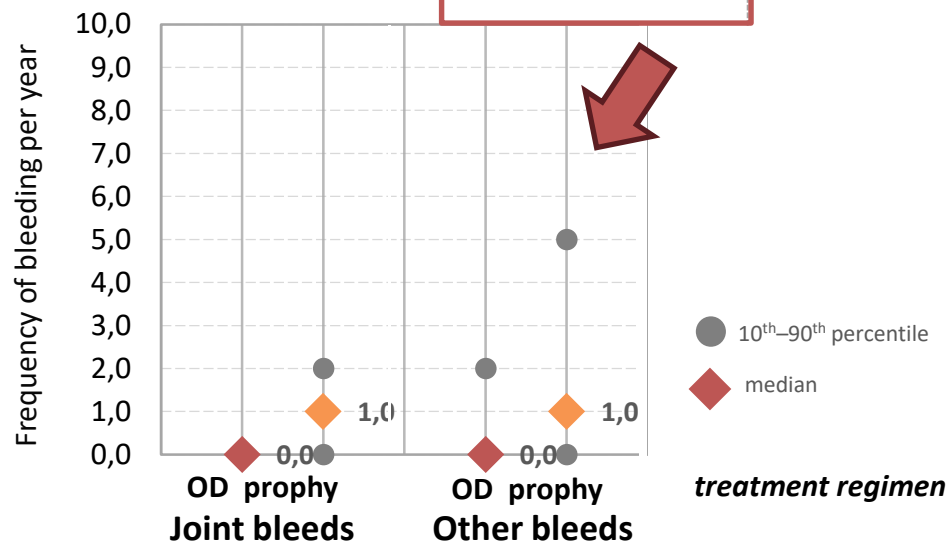
Treatment regimen:
OD = on demand and/or temporary prophylaxis
prophy = permanent prophylaxis

* without inhibitor,
missing severity in 2 children

Joint and other bleeds according to treatment regimen

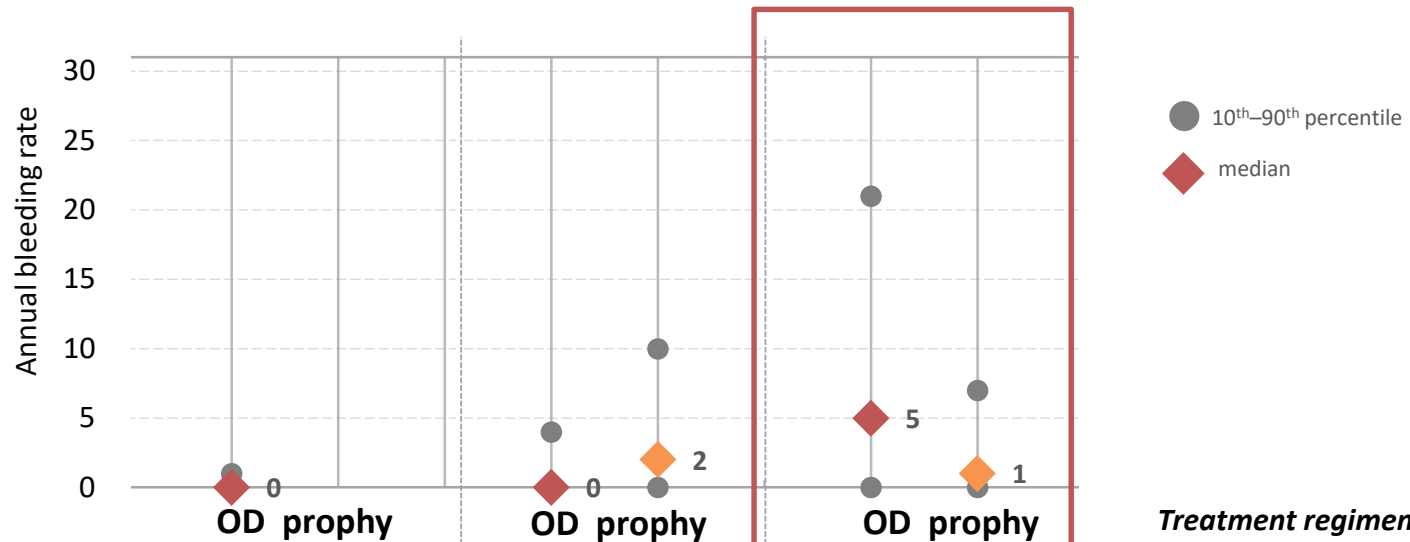
Frequency of bleeding	Mild*		Moderate*		Severe*	
	OD	prophy	OD	prophy	OD	prophy
Treatment regimen	OD	prophy	OD	prophy	OD	prophy
N valid	103	0	17	8	6	66
JOINT BLEEDS						
Mean	0.1		0.6	1.5	0.0	1.3
Median (range)	0 (0-3)		0 (0-3)	1 (0-6)	0 (0-0)	1 (0-10)
Total no of recorded bleeds	7		11	12	0	87
OTHER BLEEDS						
Mean	0.2		1.2	1.5	0.5	1.6
Median (range)	0 (0-6)		1 (0-7)	0.5 (0-5)	0 (0-2)	1 (0-8)
Total no of recorded bleeds	20		20	12	3	105

* without inhibitor,
missing severity in 2 children



Treatment regimen:
OD = on demand and/or temporary
prophylaxis
prophy = permanent prophylaxis

Annual bleeding rate according to treatment regimen



Frequency of bleeding	Mild*		Moderate*		Severe*	
N valid	245	0	33	6	57	96
Mean	0.2		0.7	3.2	7.3	2.9
Median (min – max)	0 (0 – 3)		0 (0 – 5)	2 (0 – 10)	5 (0 – 28)	1 (0 – 39)
Total no of recorded bleeds	37		22	19	416	275
adults on permanent prophylaxis	0 (0%)		6 (15.4%)		96 (59.6%)	
% of factor (FVIII) consumed by adults on permanent prophylaxis	-		73.5%		87.0%	

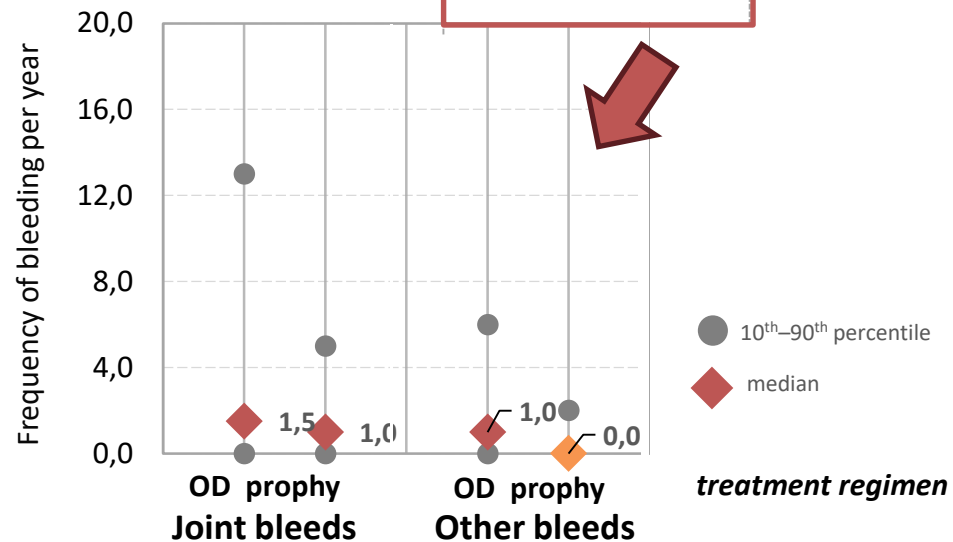
Treatment regimen:
OD = on demand and/or temporary prophylaxis
prophy = permanent prophylaxis

* without inhibitor;
 missing ABR in 8 adults

Joint and other bleeds according to treatment regimen

* without inhibitor; missing location of bleeds in 11 adults

Frequency of bleeding	Mild*		Moderate*		Severe*	
	OD	prophy	OD	prophy	OD	prophy
Treatment regimen	OD	prophy	OD	prophy	OD	prophy
N valid	245	0	33	6	49	93
JOINT BLEEDS						
Mean	0.0		0.5	2.5	4.2	2.2
Median (range)	0 (0-1)		0 (0-4)	1.5 (0-7)	1.5 (0-22)	1 (0-39)
Total no of recorded bleeds	12		17	15	203	204
OTHER BLEEDS						
Mean	0.1		0.2	0.7	1.6	0.7
Median (range)	0 (0-3)		0 (0-3)	0 (0-3)	1 (0-9)	0 (0-14)
Total no of recorded bleeds	25		5	4	77	62



Treatment regimen:
OD = on demand and/or temporary prophylaxis
prophy = permanent prophylaxis

Joint and other bleeds according to treatment regimen and age

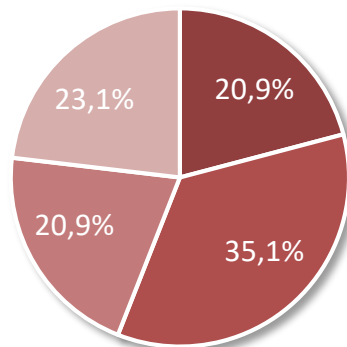
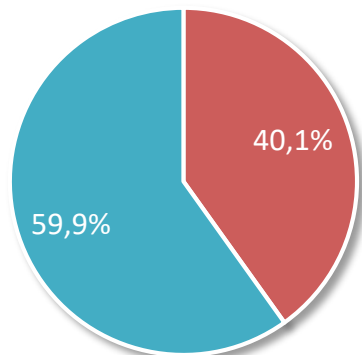
* without inhibitor; missing location of bleeds in 11 adults

Frequency of bleeding	Mild*		Moderate*		Severe*		
Treatment regimen	OD	prophy	OD	prophy	OD	prophy	
N valid	187	0	19	4	45	63	
JOINT BLEEDS							
Mean	0.0		0.4	3.3	4.5	2.5	Adults (haem A) born <u>before 1990</u> N=318
Median (range)	0 (0-1)		0 (0-4)	2.5 (1-7)	2.5 (0-22)	1 (0-39)	
Total no of recorded bleeds	9		8	13	200	156	
OTHER BLEEDS							
Mean	0.1		0.1	1.0	1.6	0.4	Adults (haem A) born in <u>1990 or later</u> N=108
Median (range)	0 (0-3)		0 (0-1)	0.5 (0-3)	1 (0-9)	0 (0-5)	
Total no of recorded bleeds	18		1	4	71	27	

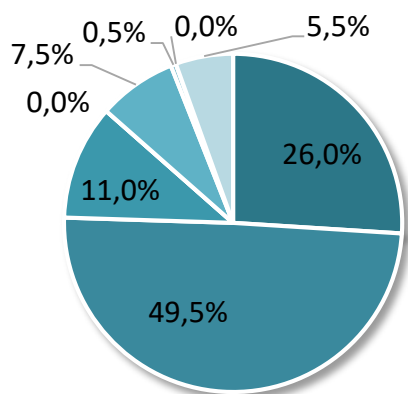
Frequency of bleeding	Mild*		Moderate*		Severe*		
Treatment regimen	OD	prophy	OD	prophy	OD	prophy	
N valid	58	0	14	2	4	30	
JOINT BLEEDS							
Mean	0.1		0.6	1.0	0.8	1.6	Adults (haem A) born in <u>1990 or later</u> N=108
Median (range)	0 (0-1)		0 (0-4)	1 (0-2)	0.5 (0-2)	0.5 (0-14)	
Total no of recorded bleeds	3		9	2	3	48	
OTHER BLEEDS							
Mean	0.1		0.3	0.0	1.5	1.2	Adults (haem A) born in <u>1990 or later</u> N=108
Median (range)	0 (0-2)		0 (0-3)	0 (0-0)	0 (0-6)	0 (0-14)	
Total no of recorded bleeds	7		4	0	6	35	

Location and etiology of bleeds

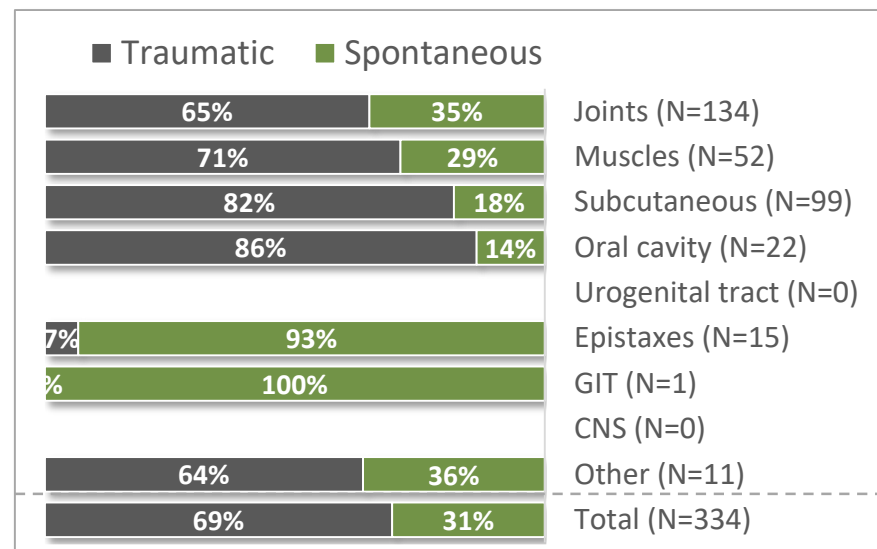
- Joints (N=134)
- Other (N=200)



- Knee (N=28)
- Ankle (N=47)
- Elbow (N=28)
- Other joint (N=31)



- Muscles (N=52)
- Subcutaneous (N=99)
- Oral cavity (N=22)
- Urogenital tract (N=0)
- Epistaxes (N=15)
- GIT (N=1)
- CNS (N=0)
- Other (N=11)



Detailed treatment of bleeds

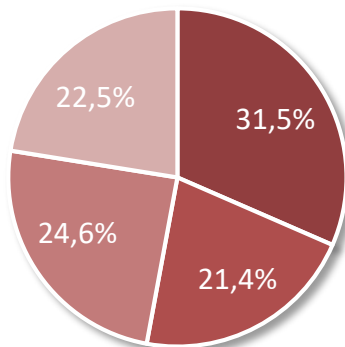
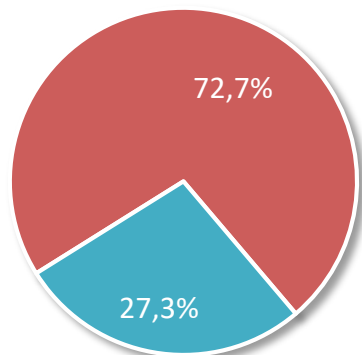
* number of bleeds

	Joints	Muscles	Subcutaneous	Oral cavity	Urogenital tract	Epistaxes	GIT	CNS	Other	Total
No. of bleeds	134	52	99	22	0	15	1	0	11	334
FVIII consumption per bleed (IU), valid N	122	45	83	22		15	1		10	298
geometric mean	1740.5	2457.6	1005.4	1046.0		815.4	3500.0		2800.8	1485.8
median	1500.0	2000.0	1000.0	875.0		1000.0	3500.0		2750.0	1375.0
min – max	250–25000	500–130500	500–12000	500–20500		500–2000	3500–3500		500–20000	250–130500
sum	336250	421250	126000	51000		13250	3500		55500	1006550
No. of doses per bleed										
geometric mean	1.7	2.4	1.5	1.8		1.0	7.0		4.4	1.8
median	1	2	1	1		1	7		4	1
min – max	1–112	1–60	1–44	1–20		1–1	7–7		1–56	1–112
Duration of therapy per bleed, days										
geometric mean	1.7	2.3	1.5	2.2		1.0	4.0		6.1	1.8
median	1	2	1	2		1	4		8	1
min – max	1–56	1–66	1–31	1–16		1–1	4–4		1–59	1–66
N (%) with hospitalization	3 (2.2%)	5 (9.6%)	7 (7.1%)	4 (18.2%)		0 (0%)	1 (100%)		5 (45.5%)	25 (7.5%)
N (%) with rebleeding	8 (6%)	0 (0%)	0 (0%)	4 (18.2%)		3 (20%)	0 (0%)		1 (9.1%)	16 (4.8%)

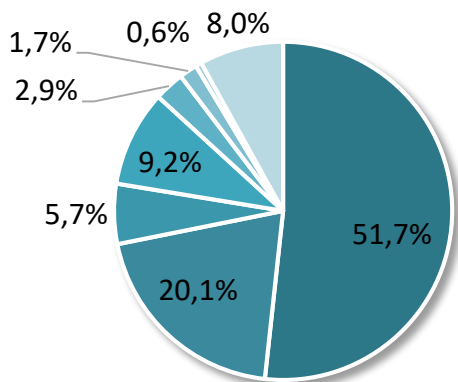
Location and etiology of bleeds

* number of bleeds

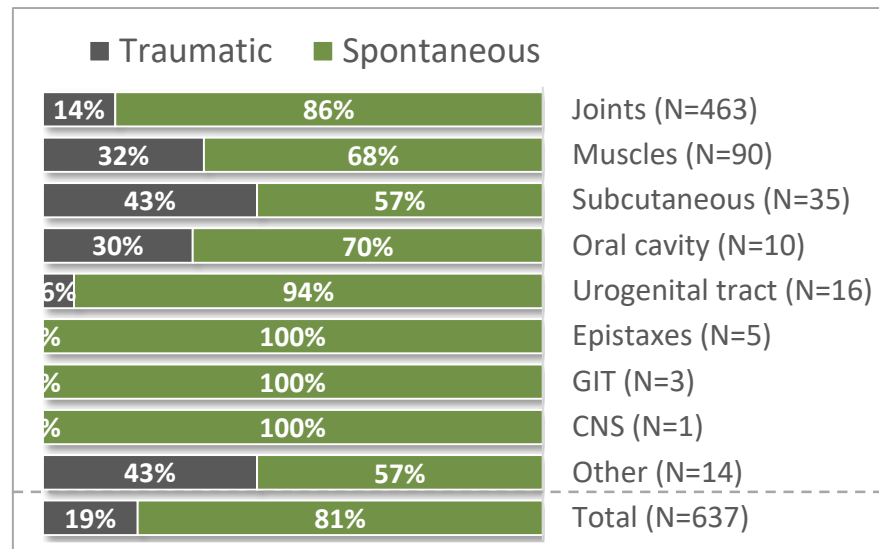
- Joints (N=463)
- Other (N=174)



- Knee (N=146)
- Ankle (N=99)
- Elbow (N=114)
- Other joint (N=104)



- Muscles (N=90)
- Subcutaneous (N=35)
- Oral cavity (N=10)
- Urogenital tract (N=16)
- Epistaxes (N=5)
- GIT (N=3)
- CNS (N=1)
- Other (N=14)



Detailed treatment of bleeds

* number of bleeds

	Joints	Muscles	Subcutaneous	Oral cavity	Urogenital tract	Epistaxes	GIT	CNS	Other	Total
No. of bleeds	463	90	35	10	16	5	3	1	14	637
FVIII consumption per bleed (IU), valid N	451	89	35	10	16	5	3	1	14	624
geometric mean	2004.6	3328.3	3307.6	1669.3	7838.4	2940.9	37755.6	467000.0	2997.0	2369.9
median	2000.0	3000.0	3000.0	1500.0	7750.0	2000.0	30000.0	467000.0	2000.0	2000.0
min – max	500–59000	500–44000	1000–23000	500–7000	500–140500	1000–10000	23000–78000		1000–13000	500–467000
sum	1522500	457000	167000	23500	358500	20500	131000	467000	57000	3204000
No. of doses per bleed										
geometric mean	1.7	2.5	1.7	1.2	5.2	2.4	27.3	226.0	1.9	1.9
median	1	2	1	1	4	2	20	226	2	1
min – max	1–55	1–30	1–20	1–3	1–95	1–10	13–78	226–226	1–7	1–226
Duration of therapy per bleed, days										
geometric mean	1.6	2.3	1.6	1.2	4.2	1.8	13.8	147.0	1.8	1.7
median	1	2	1	1	4	2	11	147	2	1
min – max	1–120	1–33	1–16	1–3	1–34	1–5	7–34	147–147	1–6	1–147
N (%) with hospitalization	11 (2.4%)	4 (4.4%)	0 (0%)	1 (10%)	4 (25%)	0 (0%)	3 (100%)	1 (100%)	0 (0%)	24 (3.8%)
N (%) with rebleeding	21 (4.5%)	2 (2.2%)	2 (5.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (7.1%)	26 (4.1%)

ABR according to centres Haemophilia A (PWHA)

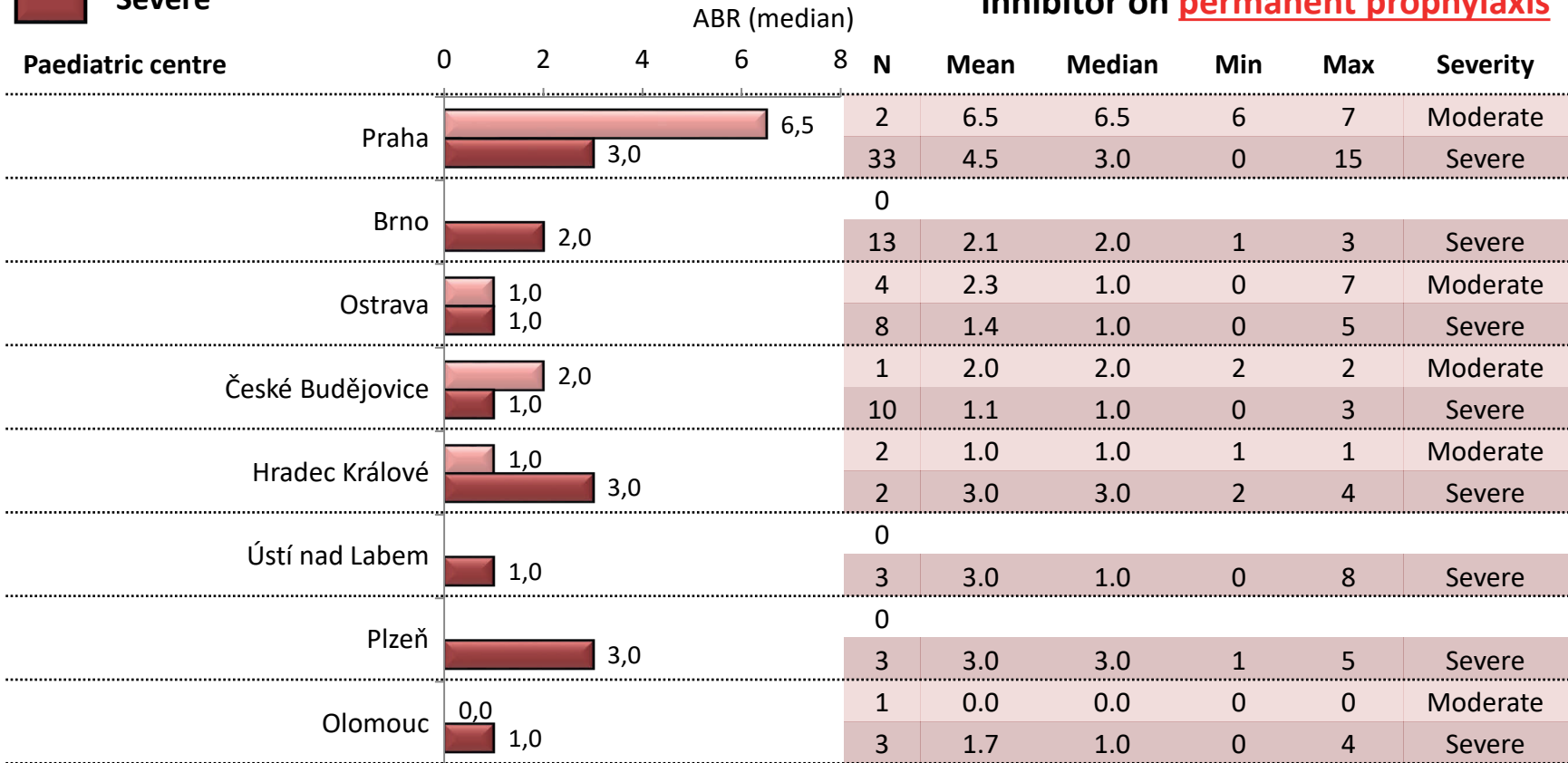


Annual bleeding rate on permanent prophylaxis

HaemA on prophylaxis
Paed. centres
N=85



Frequency of bleeding in PWhA without inhibitor on **permanent prophylaxis**

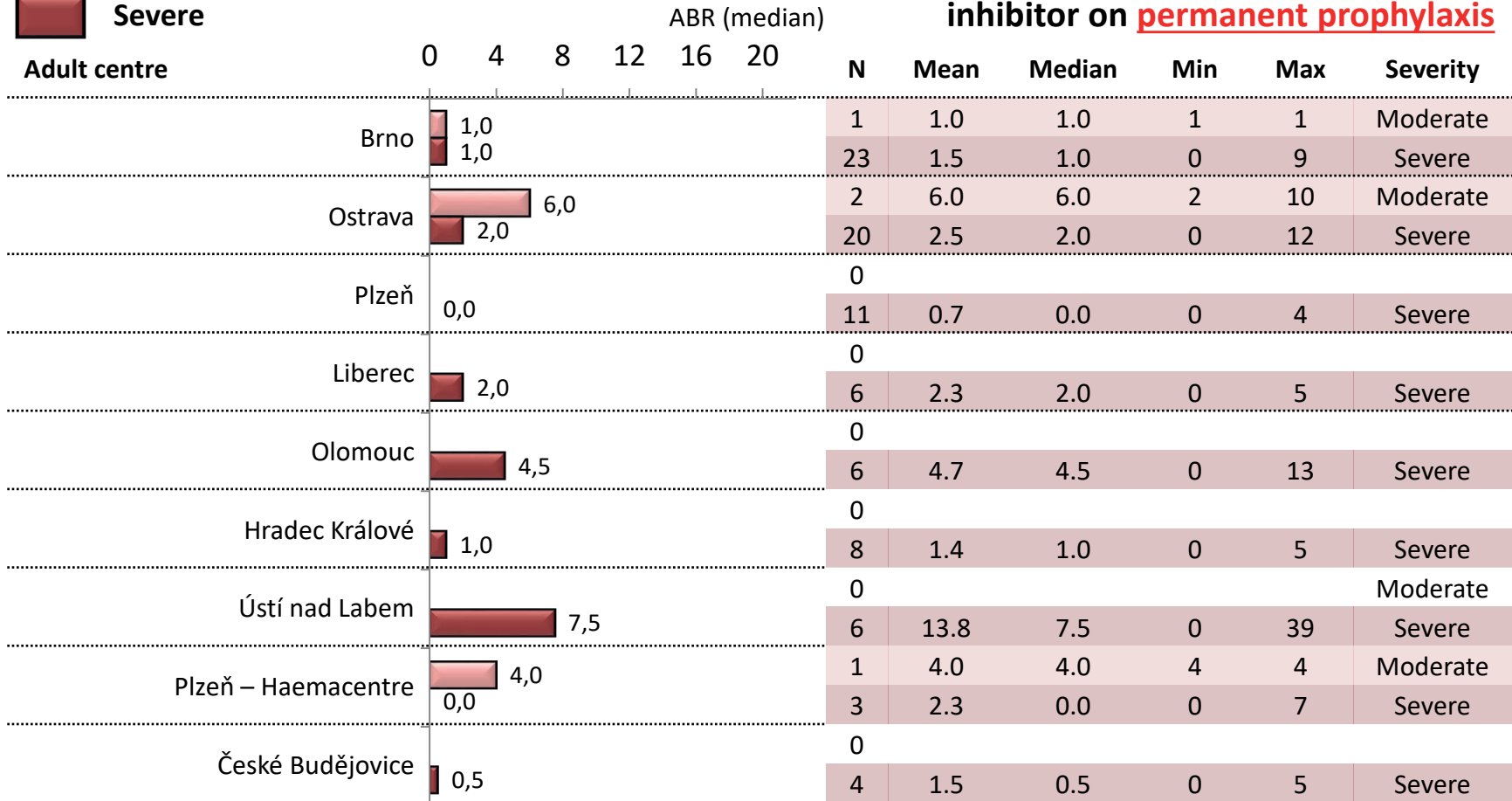


Annual bleeding rate on permanent prophylaxis

HaemA on prophylaxis
Adult centres
N=91



Frequency of bleeding in PWhA without inhibitor on **permanent prophylaxis**

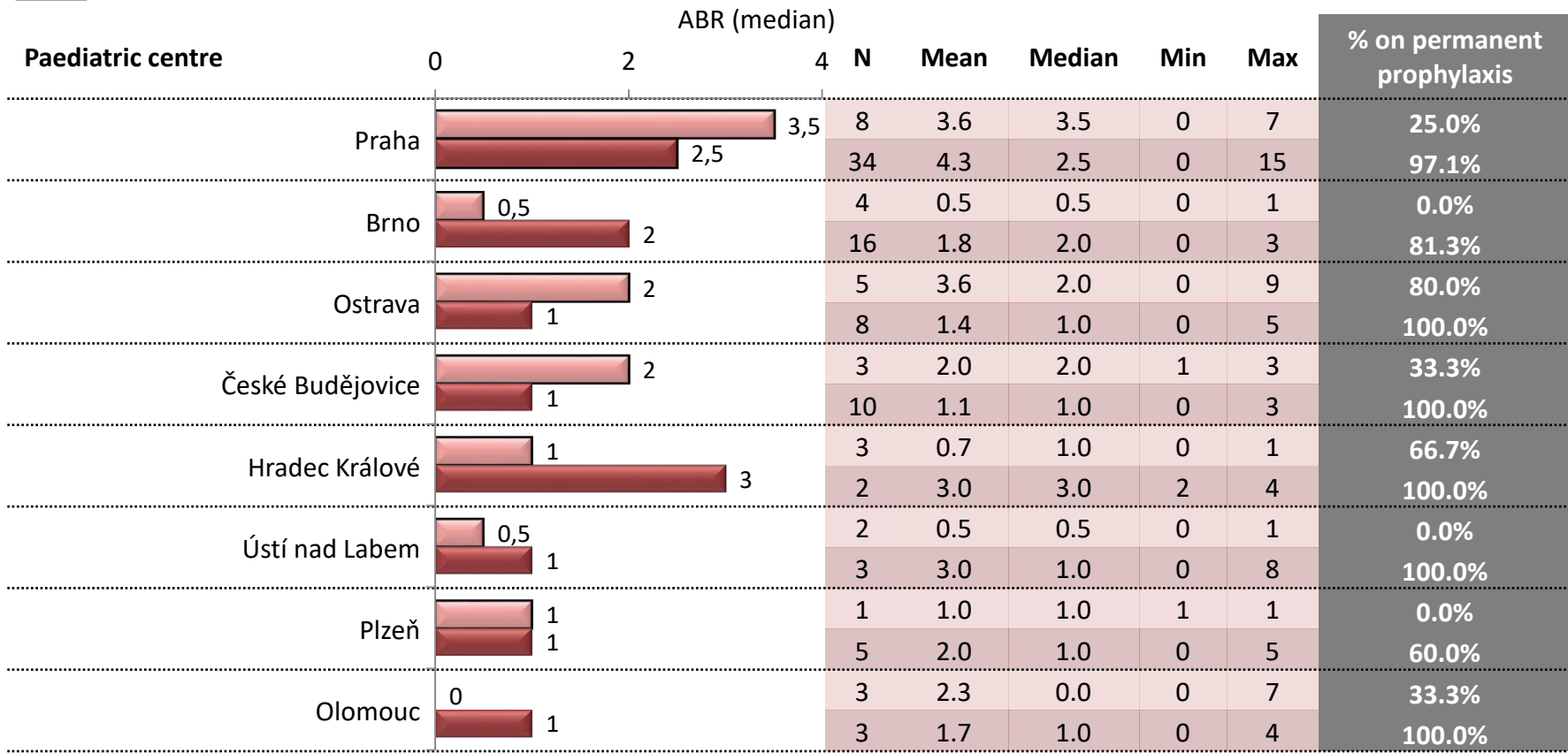


Annual bleeding rate regardless prophylaxis

HaemA
Paed. centres
N=110



Frequency of bleeding in PWhA without inhibitor **regardless of prophylaxis**



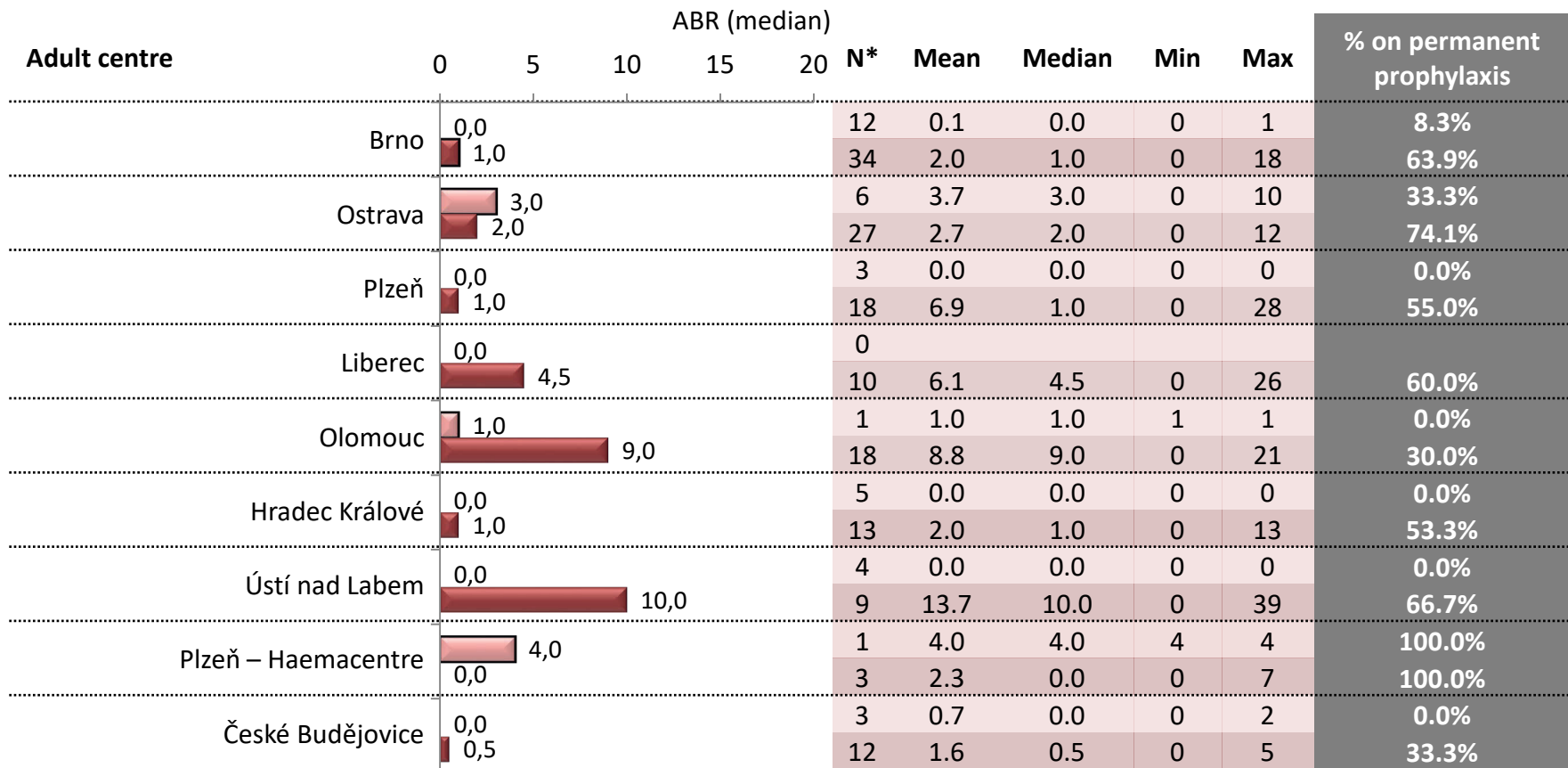
Annual bleeding rate regardless prophylaxis

HaemA
Adult centres
N=179*

* missing ABR in 8 adults



Frequency of bleeding in PWHA without inhibitor regardless of prophylaxis



Prophylactic regimens and treatment outcomes

HaemA
Paed. centres
N=110

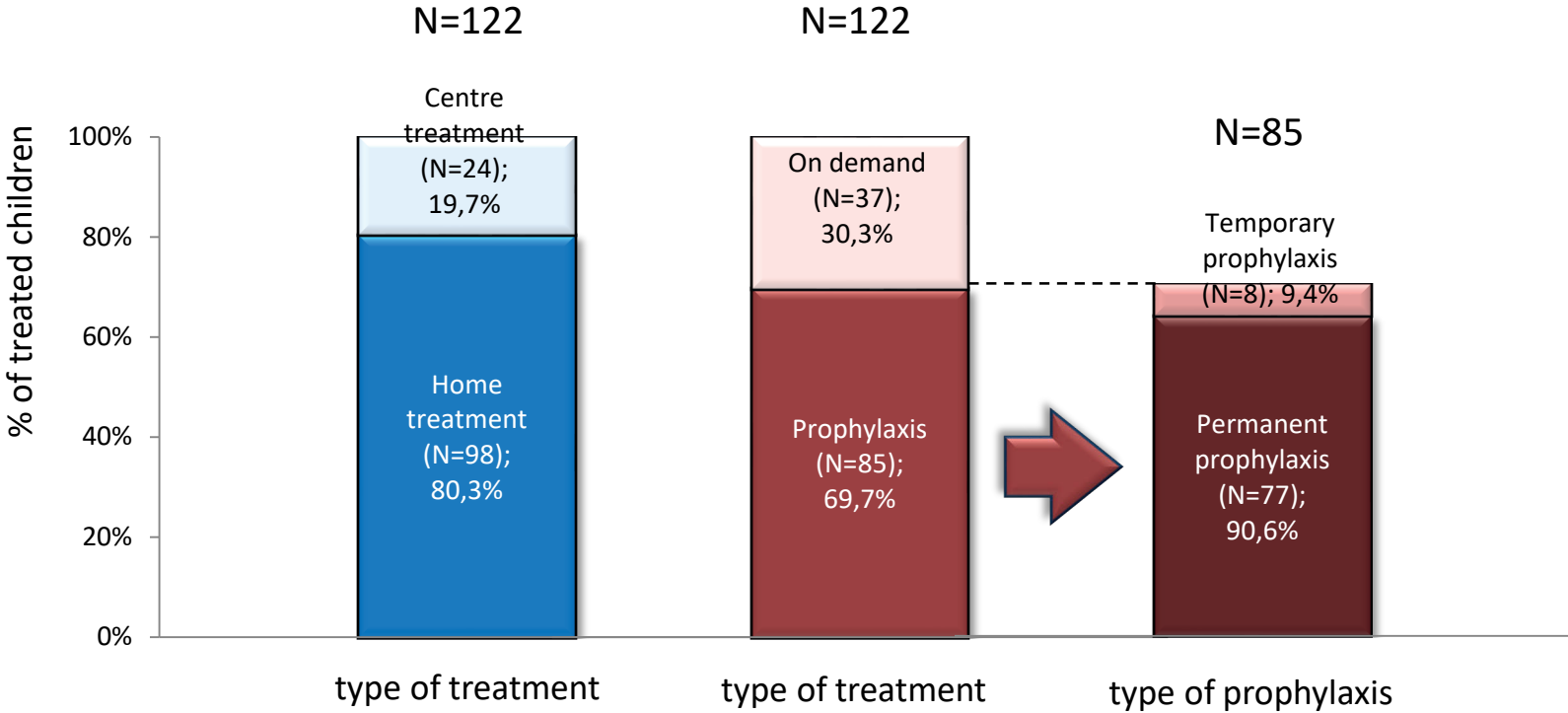
Paediatric centre	Severity	Total N	PERMANENT PROPHYLAXIS								ON-DEMAND / TEMPORARY PROPHY		
			% of patients	N	Dosing of prophylaxis (IU/kg per week)				ABR		N	ABR	
					Mean	Median	Min	Max	Mean	Median		Mean	Median
Praha	Moderate	8	25.0%	2	49.7	49.7	49.4	50.0	96.8	96.8	6	6.0	8.0
	Severe	34	97.1%	33	79.1	78.5	22.8	121.5	0.0	0.0	1	1.0	3.0
Brno	Moderate	4	0.0%	0							4	4.0	1.0
	Severe	16	81.3%	13	92.9	83.3	65.2	140.0	17.9	17.9	3	3.0	2.0
Ostrava	Moderate	5	80.0%	4	68.5	65.9	52.6	89.7	0.0	0.0	1	1.0	0.0
	Severe	8	100.0%	8	90.4	98.6	52.6	115.6	0.0	0.0	0	0.0	3.0
Č. Budějovice	Moderate	3	33.3%	1	34.3	34.3	34.3	34.3	58.8	58.8	2	2.0	1.0
	Severe	10	100.0%	10	55.5	50.1	20.8	109.6	0.0	0.0	0	0.0	0.0
Hradec Králové	Moderate	3	66.7%	2	54.8	54.8	12.9	96.8	0.0	0.0	1	1.0	1.0
	Severe	2	100.0%	2	76.9	76.9	70.1	83.7	0.0	0.0	0	0.0	0.0
Ústí nad Labem	Moderate	2	0.0%	0							2	2.0	0.0
	Severe	3	100.0%	3	57.4	61.6	46.6	64.0	0.0	0.0	0	0.0	1.0
Plzeň	Moderate	1	0.0%	0							1	1.0	1.0
	Severe	5	60.0%	3	60.1	58.1	55.2	66.8	0.0	0.0	2	2.0	1.0
Olomouc	Moderate	3	33.3%	1	26.3	26.3	26.3	26.3	0.0	0.0	2	2.0	1.0
	Severe	3	100.0%	3	28.4	26.3	19.2	39.7	0.0	0.0	0	0.0	0.0

Prophylactic regimens and treatment outcomes

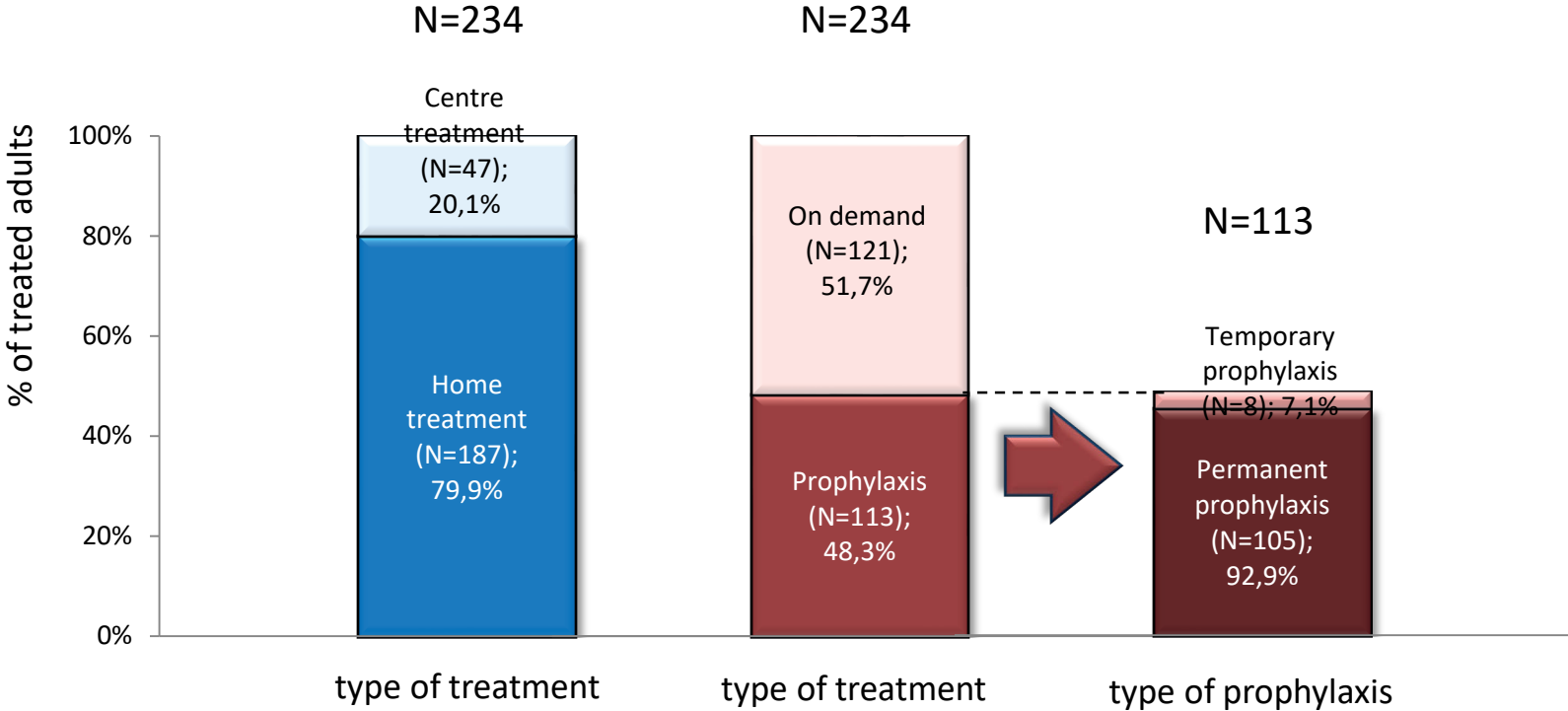
Adult centre	Severity	Total N	PERMANENT PROPHYLAXIS									ON-DEMAND / TEMPORARY PROPHY				
			% of patients	N	Dosing of prophylaxis (IU/kg per week)				ABR*		Age	N	ABR*		Age	
					Mean	Median	Min	Max	Mean	Median	Median		Mean	Median	Median	
Brno	Moderate	12	8.3%	1	42.9	42.9	42.9	42.9	42.9	1.0	1.0	29	11	0.0	0.0	47
	Severe	36	63.9%	23	54.8	44.9	19.0	100.0	100.0	1.5	1.0	37	13	3.0	1.0	46
Ostrava	Moderate	6	33.3%	2	71.8	71.8	52.7	90.9	90.9	6.0	6.0	68	4	2.5	2.5	53
	Severe	27	74.1%	20	58.6	53.8	35.1	96.8	96.8	2.5	2.0	39	7	3.1	3.0	61
Plzeň	Moderate	3	0.0%	0									3	0.0	0.0	42
	Severe	20	55.0%	11	42.2	39.5	14.3	107.4	107.4	0.7	0.0	44	9	16.6	20.0	51
Liberec	Moderate	0														
	Severe	10	60.0%	6	63.1	61.0	40.9	96.2	96.2	2.3	2.0	37	4	11.8	8.0	64
Olomouc	Moderate	1	0.0%	0									1	1.0	1.0	23
	Severe	20	30.0%	6	37.8	36.3	20.0	62.5	62.5	4.7	4.5	29	14	10.8	11.0	52
Hradec Králové	Moderate	5	0.0%	0									5	0.0	0.0	23
	Severe	15	53.3%	8	63.5	63.0	45.5	90.0	90.0	1.4	1.0	29	7	3.0	1.0	32
Ústí n. Labem	Moderate	4	0.0%	0									4	0.0	0.0	24
	Severe	9	66.7%	6	47.6	32.5	13.9	100.5	100.5	13.8	7.5	31	3	13.3	10.0	43
Plzeň - Haemacentre	Moderate	1	100.0%	1	24.9	24.9	24.9	24.9	24.9	4.0	4.0	49	0			
	Severe	3	100.0%	3	62.8	73.2	31.0	84.3	84.3	2.3	0.0	45	0			
Č. Budějovice	Moderate	3	0.0%	0									3	0.7	0.0	72
	Severe	12	33.3%	4	51.8	52.1	33.3	69.8	69.8	1.5	0.5	51	8	1.6	0.5	52

* missing ABR in 8 adults

Type of treatment (subgroup of treated patients)



Type of treatment (subgroup of treated patients)



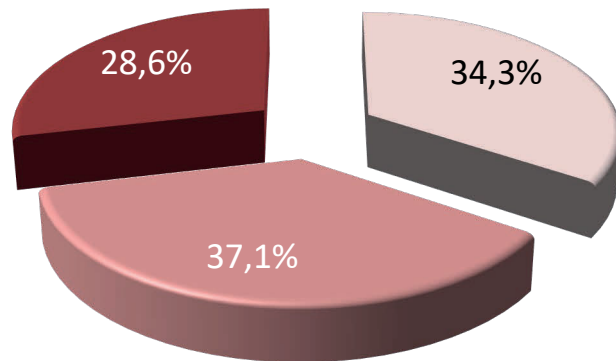
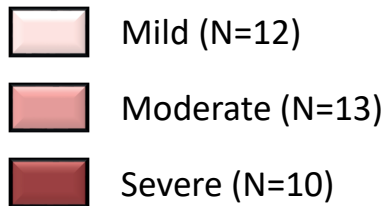
Demographic characteristics

Haemophilia B

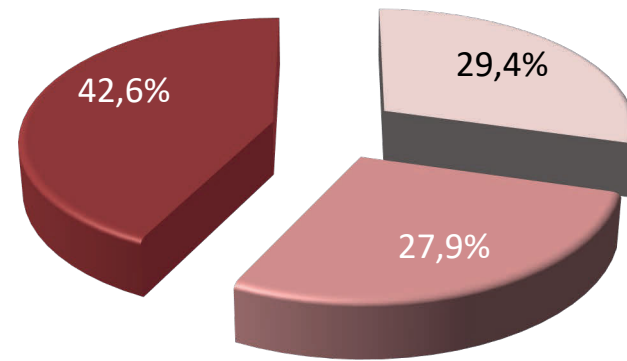
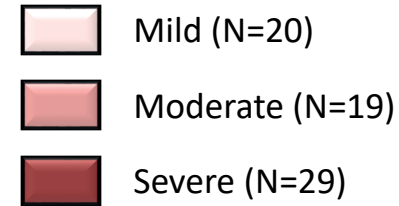


Severity of haemophilia B

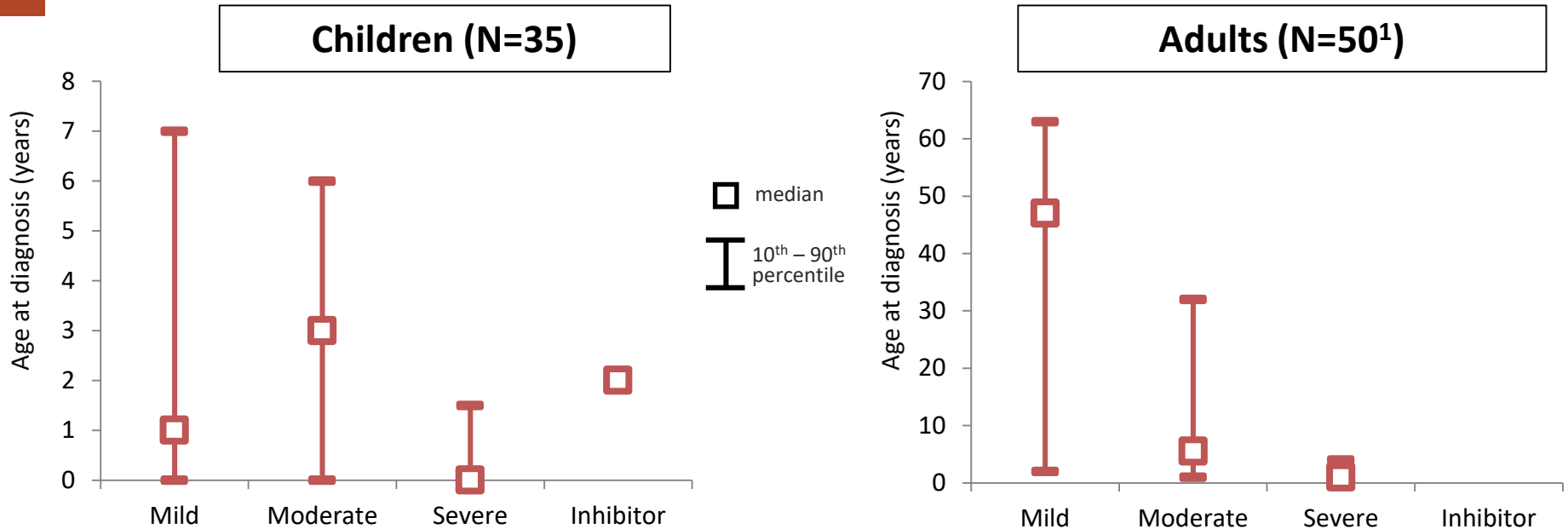
Children (N=35)



Adults (N=68)



Age at diagnosis according to severity of haemophilia B

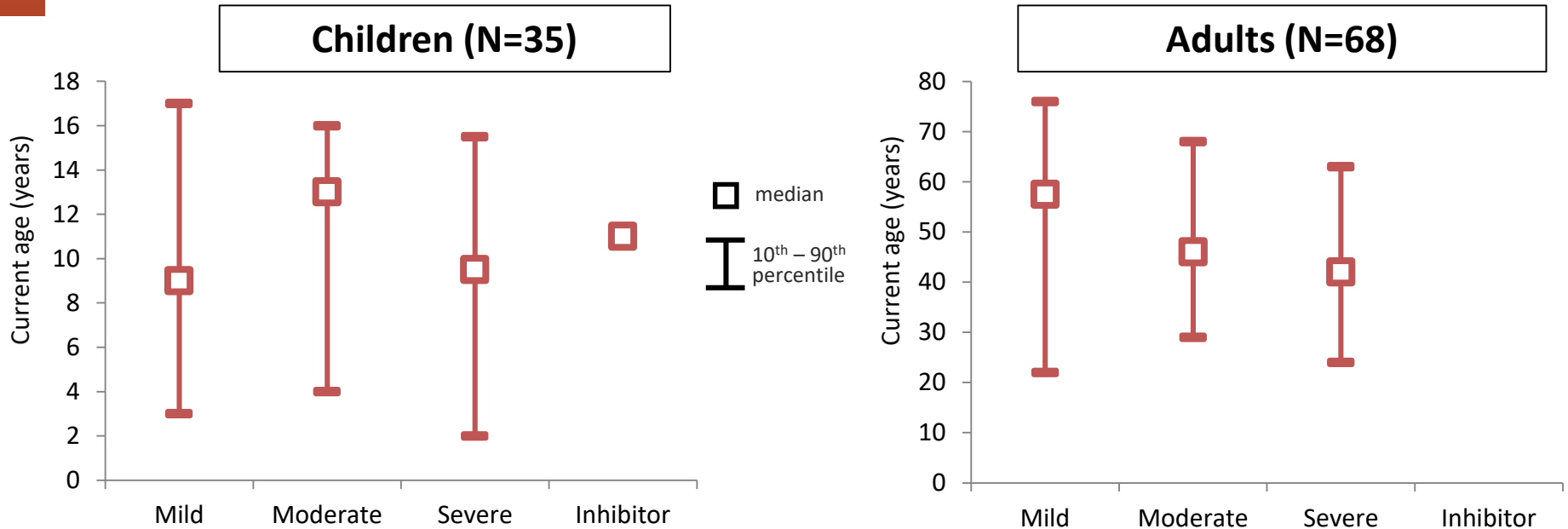


Mild*	Moderate*	Severe*	Inhibitor ⁺	Age at diagnosis (years)	Mild*	Moderate*	Severe*	Inhibitor ⁺
12	13	10	1	N valid	13	14	23	0
2.3	2.7	0.5	2.0	Mean	33.5	10.5	1.7	
1 (0 – 11)	3 (0 – 8)	0 (0 – 2)	2 (2 – 2)	Median (min – max)	47 (0 – 67)	5.5 (0 – 61)	1 (0 – 8)	

¹ Missing information on year of diagnosis in 18 adults.

* including persons with inhibitor
+ in 2018

Actual age according to severity of haemophilia B



Mild*	Moderate*	Severe*	Inhibitor ⁺	Current age ⁺⁺ (years)	Mild*	Moderate*	Severe*	Inhibitor ⁺
12	13	10	1	N valid	20	19	29	0
8.7	10.2	8.8	11.0	Mean	51.8	47.8	43.1	
9 (1 – 18)	13 (1 – 17)	9.5 (1 – 16)	11 (11 – 11)	Median (min – max)	57.5 (20 – 93)	46 (19 – 69)	42 (20 – 67)	

* including persons with inhibitor

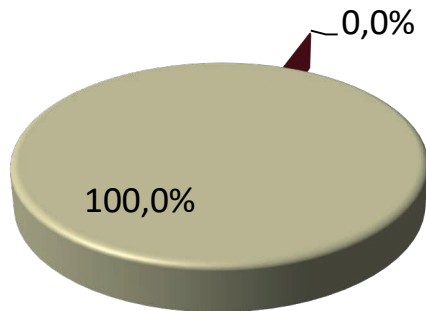
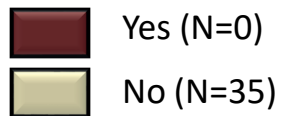
⁺ in 2018

⁺⁺ age reached in year 2018

Hepatitis (ever) experienced

Children
Haem B
N=35

Experienced hepatitis



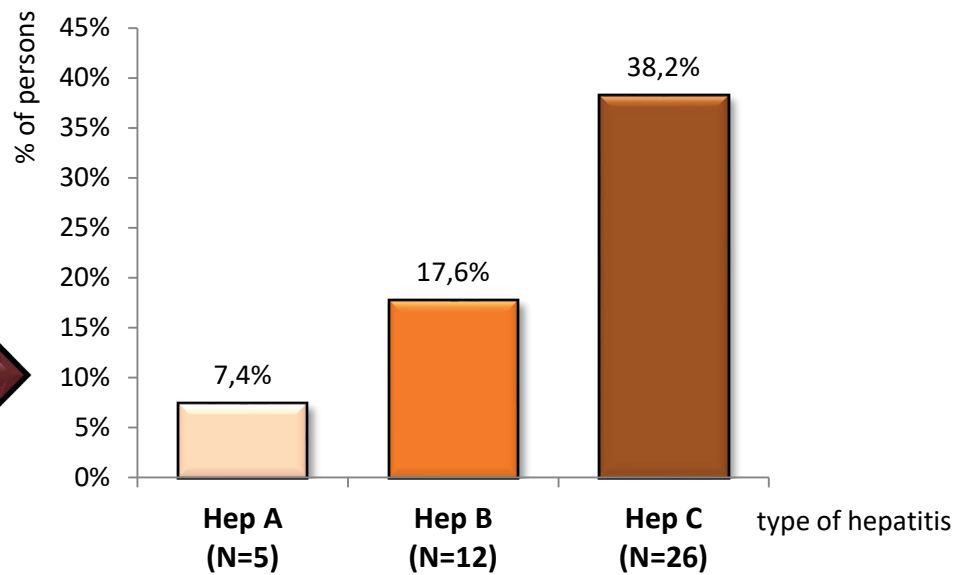
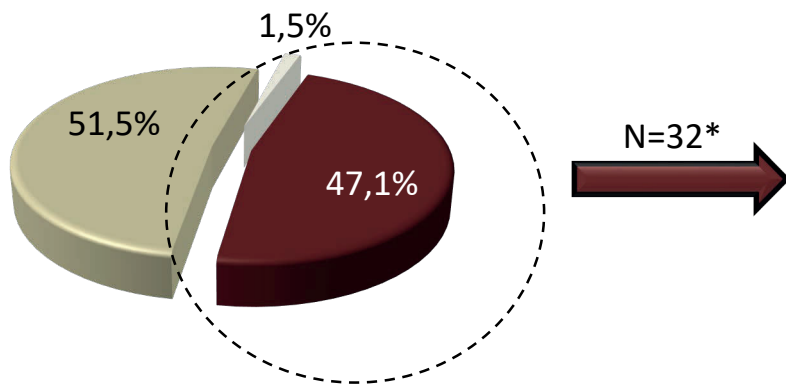
No child has hepatitis C.

Data from last completed annual report of each person.

Hepatitis (ever) experienced

Experienced hepatitis

- Yes (N=32)
- No (N=35)
- Not known (N=1)



Data from last completed annual report of each person.

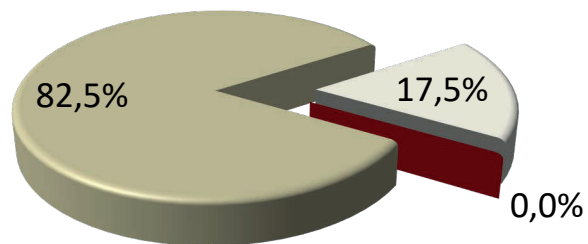
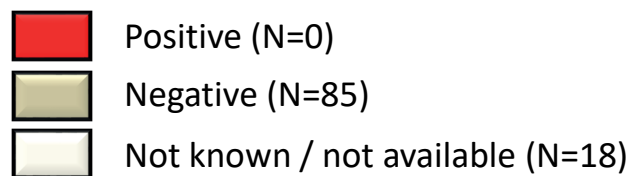
*Total of 43 cases of hepatitis in 32 persons. One person may have more types of hepatitis recorded.

11 adults are HCV RNA positive

HIV

All
Haem B
N=103

HIV



No HIV-positive person.

Data from last completed annual report of each person.

Treatment outcomes and bleeding frequency

Haemophilia B



All
Haem B
N=103

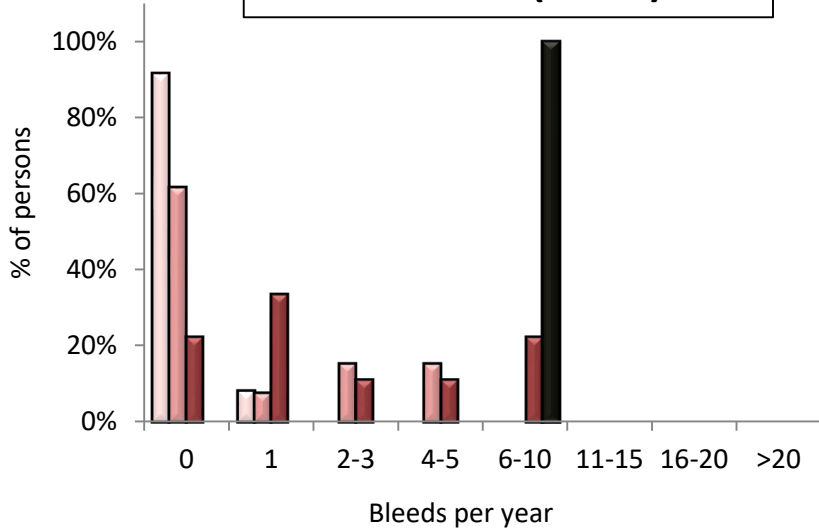
Data from year 2018 – sample size

	Valid persons			Persons with <u>valid</u> annual report			Persons <u>examined</u>			Persons <u>treated</u>	
	N	%		N	%		N	%		N	%
All	103	100%	→	100	97.1%	→	83	80.6%	→	63	61.2%
of them with inhibitor	1			1			1			1	
Children	35	100%	→	35	100.0%	→	29	82.9%	→	17	48.6%
of them with inhibitor	1			1			1			1	
Adults	68	100%	→	65	95.6%	→	54	79.4%	→	46	67.6%
of them with inhibitor	0			0			0			0	

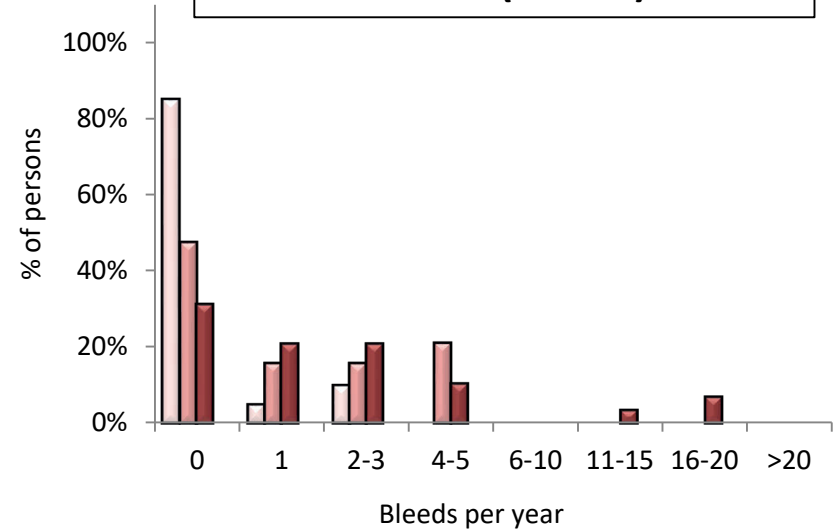


Frequency of bleeding requiring treatment in 2018

Children (N=35)



Adults (N=66¹)



Mild*	Moderate*	Severe*	Inhibitor	Frequency of bleeding	Mild*	Moderate*	Severe*	Inhibitor
12	13	9	1	N valid	20	19	27	0
0.1	1.1	3.3	8.0	Mean	0.3	1.4	3.0	
0 (0 – 1)	0 (0 – 5)	1 (0 – 10)	8 (8 – 8)	Median (min – max)	0 (0 – 2)	1 (0 – 4)	1 (0 – 18)	
11 (91.7%)	8 (61.5%)	2 (22.2%)	0 (0%)	N (%) with no bleed	17 (85%)	9 (47.4%)	9 (31%)	

* without inhibitor

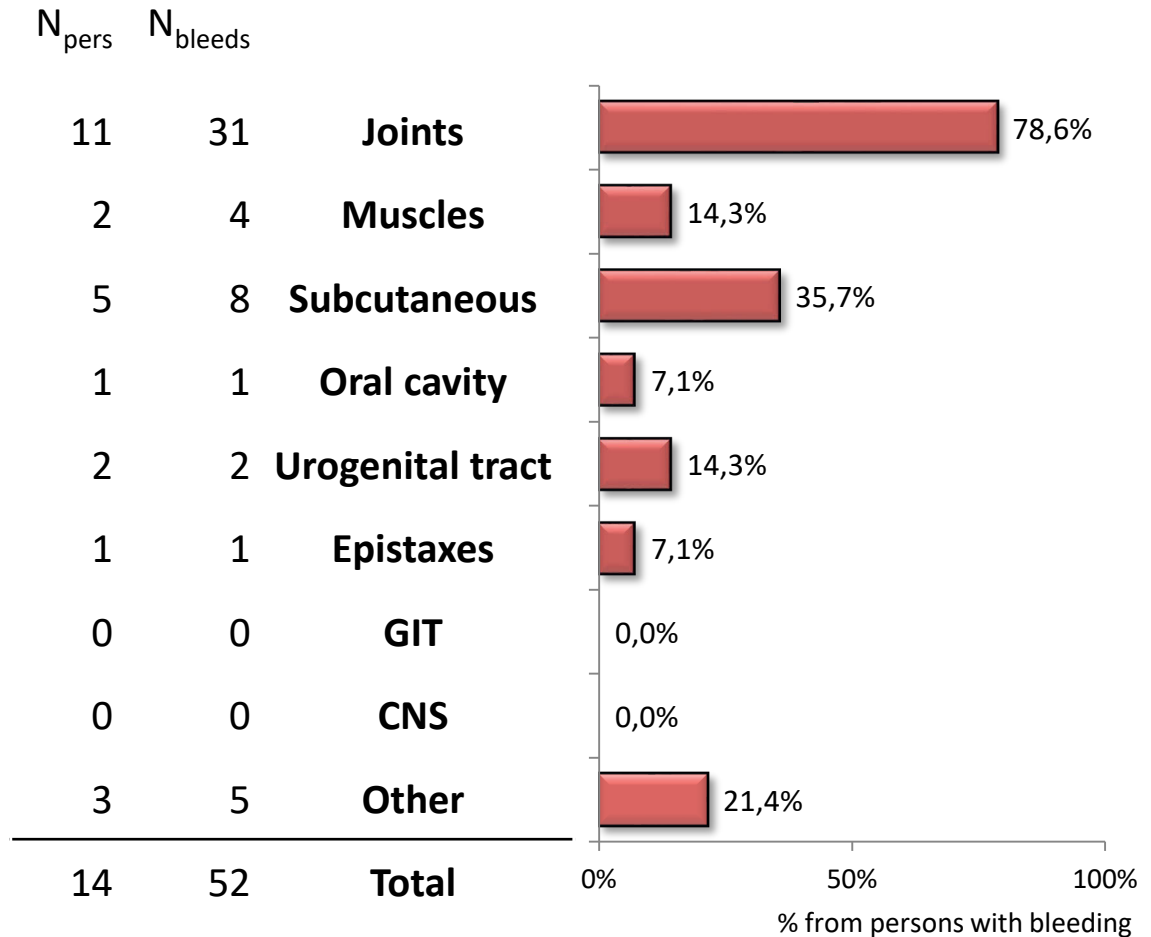
¹Frequency of bleeding is missing in 2 adults.

Location of bleeds in 2018

14 (40%) children experienced bleeding requiring treatment at least once in year; 53 bleeds were recorded in total, 4 bleeds required hospitalization.

All of these children have recorded location of their bleeds except of one bleed.

21 (60%) children recorded no bleed during year 2018.

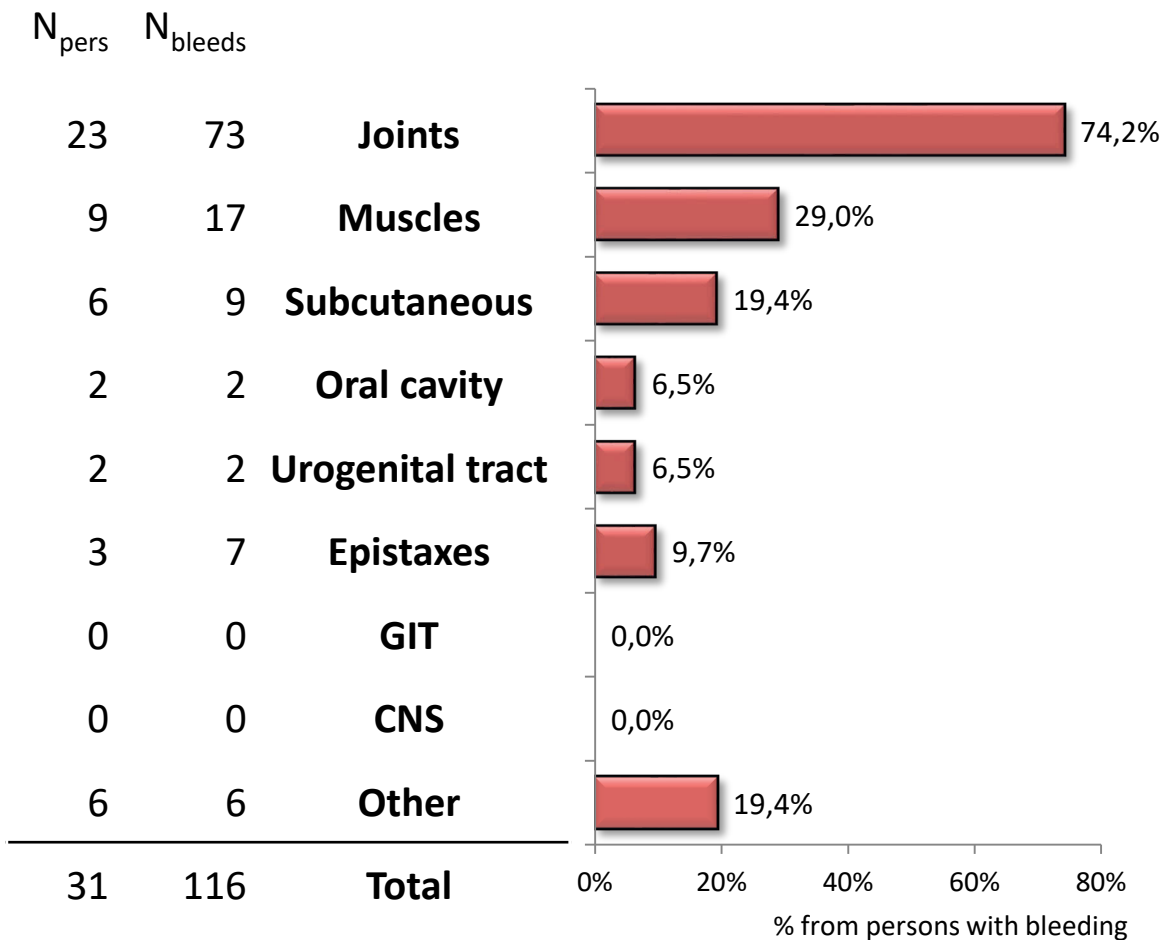


Location of bleeds in 2018

31 (47%) adults experienced bleeding requiring treatment at least once in year; 116 bleeds were recorded in total, 6 bleeds required hospitalization.

All of these 33 adults have recorded location of their bleeds.

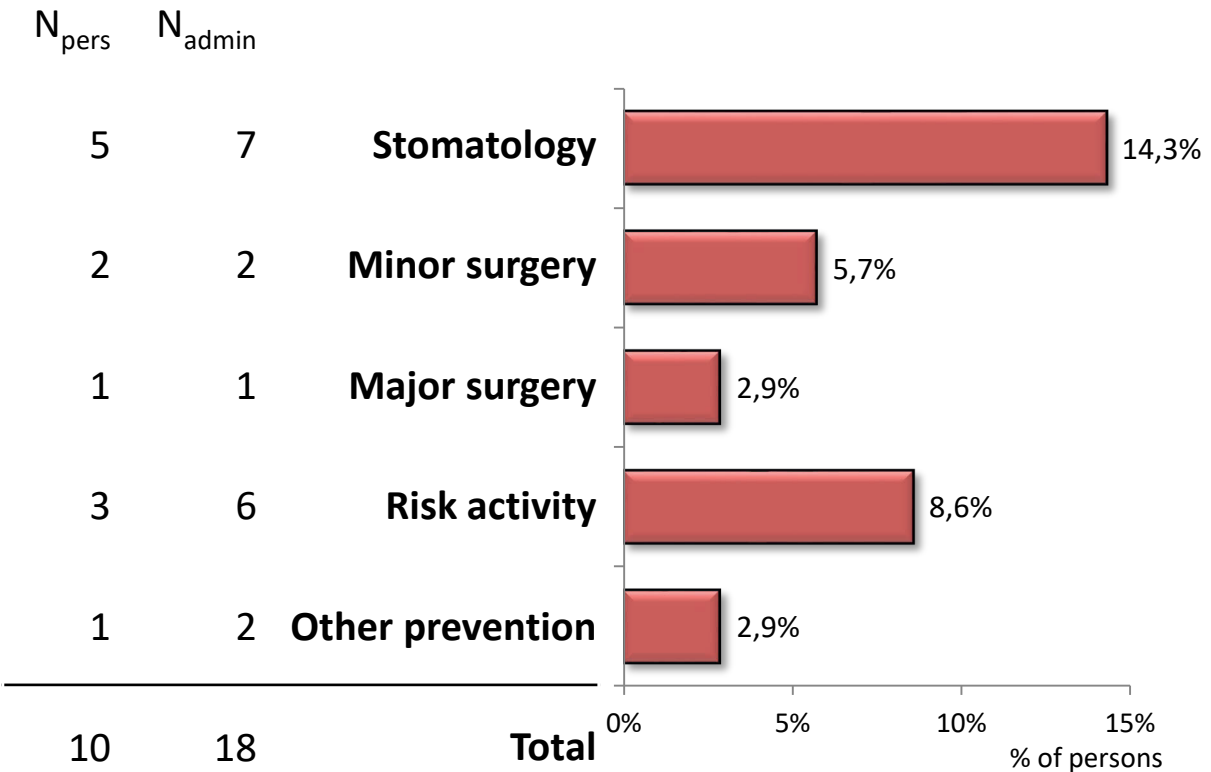
35 (53%) adults have recorded no bleed during year 2018.



¹Frequency of bleeding is missing in 2 adults.

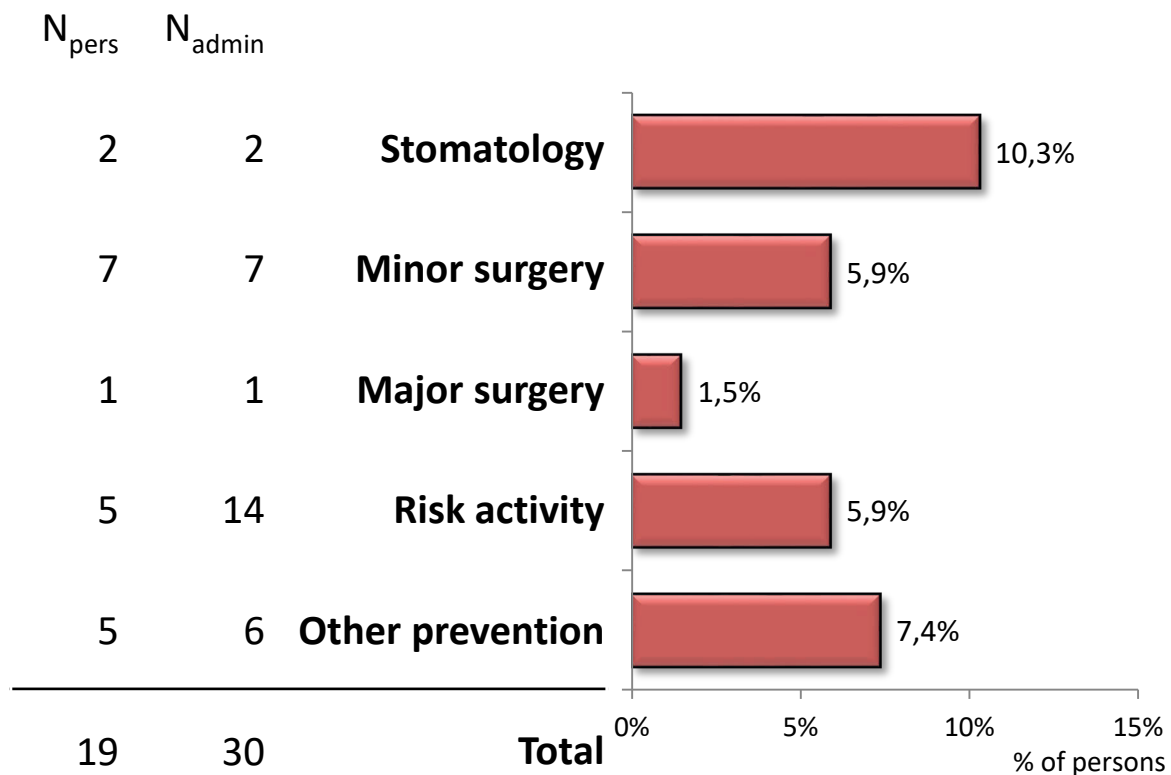
Preventive administration in 2018

10 (28.6%) children were given factor to prevent bleeding during/before risk situation.
18 preventive administrations were recorded in total.



Preventive administration in 2018

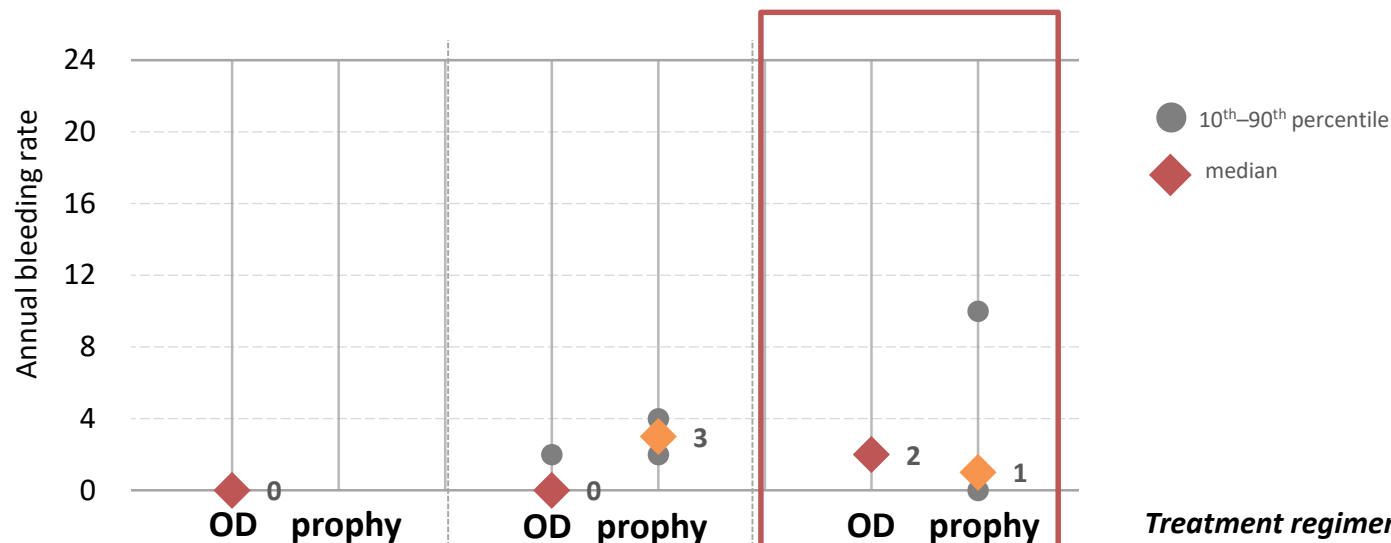
19 (27.9%) persons were given factor to prevent bleeding during/before risk situation.
30 preventive administrations were recorded in total.



ABR according to treatment regimen Haemophilia B without inhibitor



Annual bleeding rate according to treatment regimen



Frequency of bleeding	Mild*		Moderate*		Severe*	
N valid	12	0	11	2	1	8
Mean	0.1		0.7	3.0	2.0	3.5
Median (min – max)	0 (0 – 1)		0 (0 – 5)	3 (2 – 4)	2 (2 – 2)	1 (0 – 10)
Total no of recorded bleeds	1		8	6	2	28
children on permanent prophylaxis	0 (0%)		2 (15.4%)		8 (88.9%)	
% of factor (FIX) consumed by children on permanent prophylaxis	-		90.5%		99.8%	

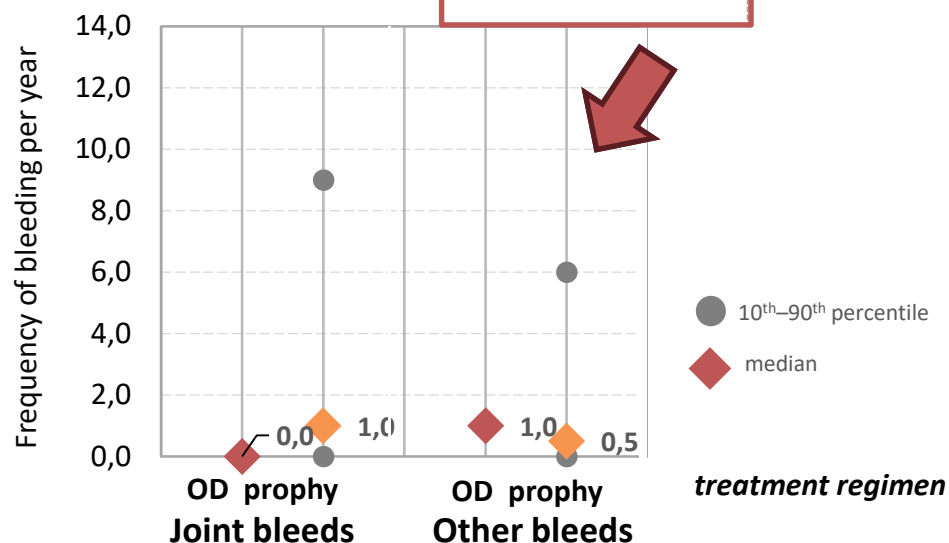
Treatment regimen:
OD = on demand and/or temporary prophylaxis
prophy = permanent prophylaxis

* without inhibitor

Joint and other bleeds according to treatment regimen

* without inhibitor

Frequency of bleeding	Mild*		Moderate*		Severe*	
	OD	prophy	OD	prophy	OD	prophy
Treatment regimen	OD	prophy	OD	prophy	OD	prophy
N valid	12	0	11	2	1	8
JOINT BLEEDS						
Mean	0.0		0.4	3.0	0.0	2.1
Median (range)	0 (0-0)		0 (0-2)	3 (2-4)	0 (0-0)	1 (0-9)
Total no of recorded bleeds	0		4	6	0	17
OTHER BLEEDS						
Mean	0.1		0.4	0.0	1.0	1.4
Median (range)	0 (0-1)		0 (0-3)	0 (0-0)	1 (1-1)	0.5 (0-6)
Total no of recorded bleeds	1		4	0	1	11

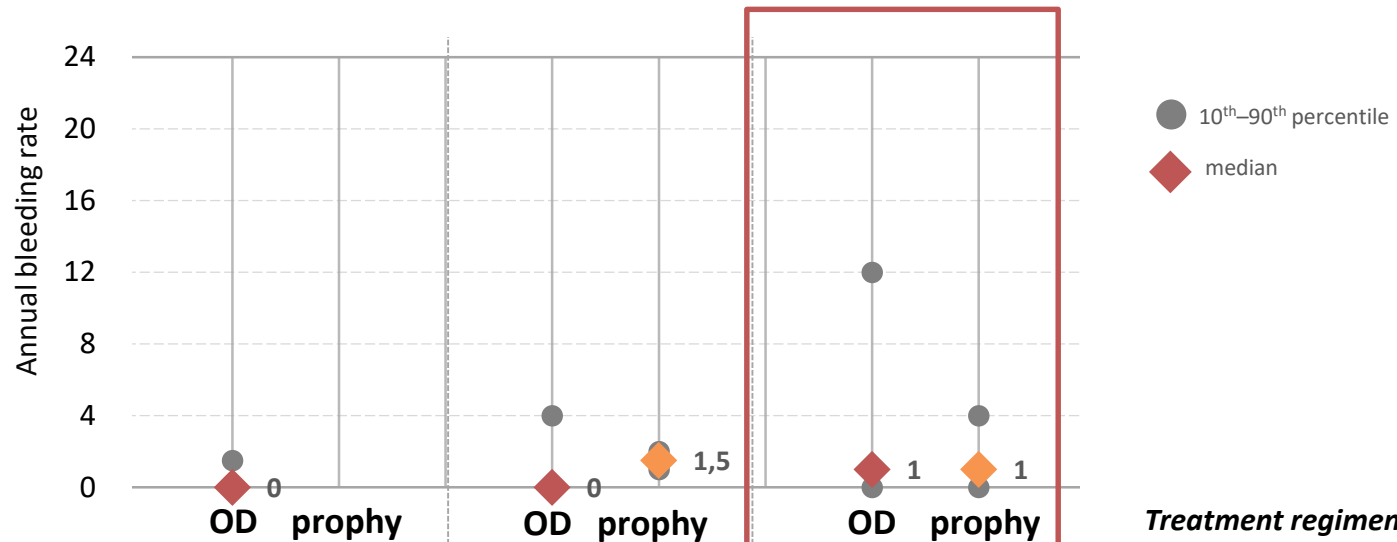


Treatment regimen:

OD = on demand and/or temporary prophylaxis

prophy = permanent prophylaxis

Annual bleeding rate according to treatment regimen



Frequency of bleeding	Mild*		Moderate*		Severe*	
N total	20	0	17	2	12	15
Mean	0.3		1.4	1.5	3.6	2.5
Median (min – max)	0 (0 – 2)		0 (0 – 4)	1.5 (1 – 2)	1 (0 – 18)	1 (0 – 17)
Total no of recorded bleeds	5		23	3	43	37
adults on permanent prophylaxis	0 (0%)		2 (10.5%)		16 (55.2%)	
% of factor (FIX) consumed by adults on permanent prophylaxis	-		23.7%		91.0%	

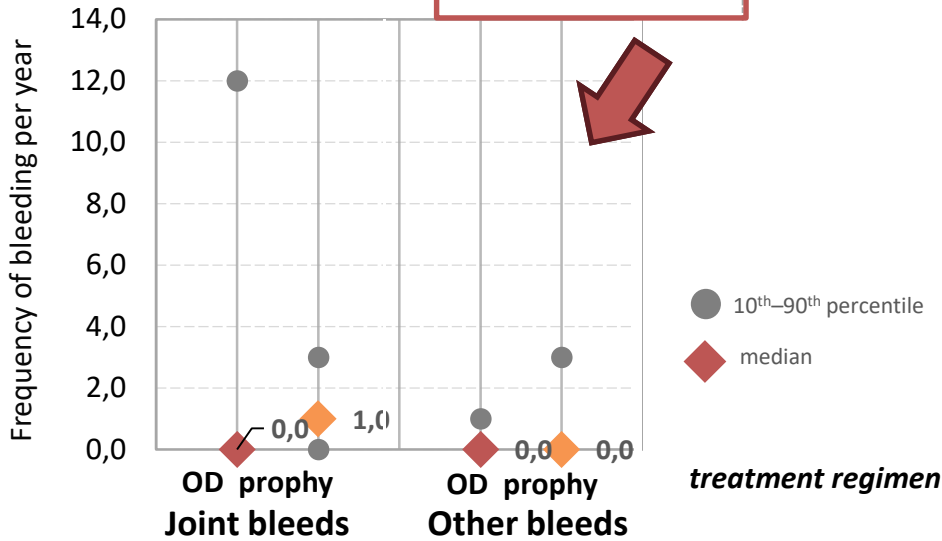
Treatment regimen:
OD = on demand and/or temporary prophylaxis
prophy = permanent prophylaxis

* without inhibitor;
 missing ABR in 2 adults

Joint and other bleeds according to treatment regimen

Frequency of bleeding	Mild*		Moderate*		Severe*	
	OD	prophy	OD	prophy	OD	prophy
Treatment regimen	OD	prophy	OD	prophy	OD	prophy
N valid	20	0	17	2	12	15
JOINT BLEEDS						
Mean	0.1	0	0.6	1.5	2.8	1.3
Median (range)	0 (0-1)	(-)	0 (0-4)	1.5 (1-2)	0 (0-13)	1 (0-7)
Total no of recorded bleeds	2	0	11	3	34	19
OTHER BLEEDS						
Mean	0.2	0	0.7	0.0	0.8	1.3
Median (range)	0 (0-2)	(-)	0 (0-4)	0 (0-0)	0 (0-5)	0 (0-10)
Total no of recorded bleeds	3	0	12	0	9	19

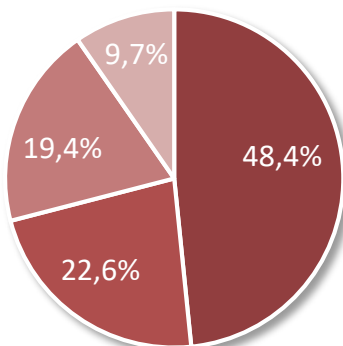
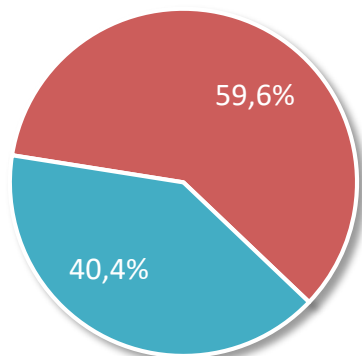
* without inhibitor; missing location of bleeds in 2 adults



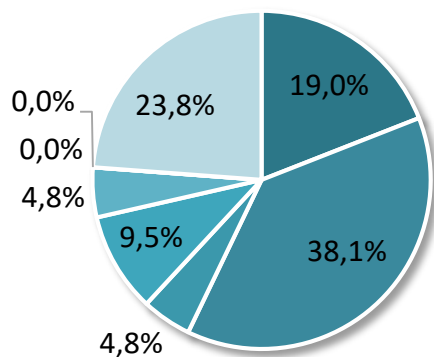
Treatment regimen:
OD = on demand and/or temporary prophylaxis
prophy = permanent prophylaxis

Location and etiology of bleeds

- Joints (N=31)
- Other (N=21)



- Knee (N=15)
- Ankle (N=7)
- Elbow (N=6)
- Other joint (N=3)



- Muscles (N=4)
- Subcutaneous (N=8)
- Oral cavity (N=1)
- Urogenital tract (N=2)
- Epistaxes (N=1)
- GIT (N=0)
- CNS (N=0)
- Other (N=5)

	Traumatic	Spontaneous	
	65%	35%	Joints (N=31)
	50%	50%	Muscles (N=4)
	100%	0%	Subcutaneous (N=8)
	100%	0%	Oral cavity (N=1)
	0%	100%	Urogenital tract (N=2)
	100%	0%	Epistaxes (N=1)
	0%	0%	GIT (N=0)
	0%	0%	CNS (N=0)
	100%	0%	Other (N=5)
	71%	29%	Total (N=52)

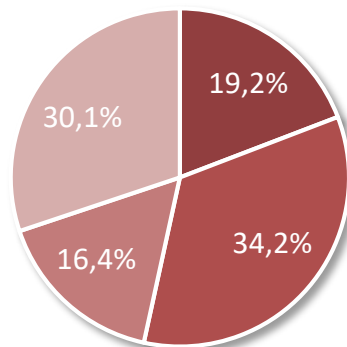
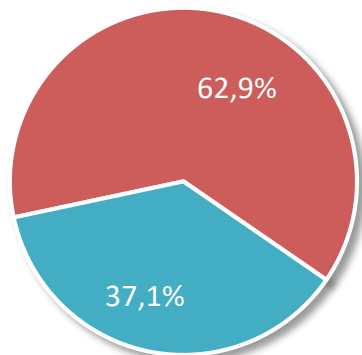
Detailed treatment of bleeds

	Joints	Muscles	Subcutaneous	Oral cavity	Urogenital tract	Epistaxes	GIT	CNS	Other	Total
No. of bleeds	31	4	8	1	2	1	0	0	5	52
FIX consumption per bleed (IU), valid N	27	3	6	1	1	1			5	44
geometric mean	2712.7	2381.1	1505.4	4000.0	1500.0	500.0			1745.4	2260.5
median	2500.0	2000.0	1578.0	4000.0	1500.0	500.0			1500.0	1828.0
min – max	500–52000	1500–4500	500–2500	4000–4000	1500–1500	500–500			1000–7200	500–52000
sum	140483	8000	10155	4000	1500	500			12200	176838
No. of doses per bleed										
geometric mean	1.9	1.6	1.1	4.0	3.7	1.0			1.2	1.7
median	2	2	1	4	8	1			1	1
min – max	1–14	1–3	1–2	4–4	1–14	1–1			1–3	1–14
Duration of therapy per bleed, days										
geometric mean	2.2	1.6	1.2	4.0	3.6	1.0			1.8	2.0
median	2	2	1	4	7	1			1	1
min – max	1–36	1–3	1–2	4–4	1–13	1–1			1–20	1–36
N (%) with hospitalization	2 (6.5%)	0 (0%)	1 (12.5%)	0 (0%)	1 (50%)	0 (0%)			0 (0%)	4 (7.7%)
N (%) with rebleeding	3 (9.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)			0 (0%)	3 (5.8%)

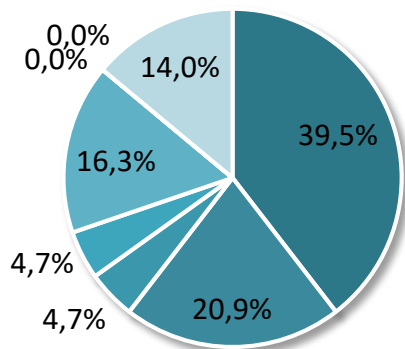
Location and etiology of bleeds

* number of bleeds

- Joints (N=73)
- Other (N=43)



- Knee (N=14)
- Ankle (N=25)
- Elbow (N=12)
- Other joint (N=22)



- Muscles (N=17)
- Subcutaneous (N=9)
- Oral cavity (N=2)
- Urogenital tract (N=2)
- Epistaxes (N=7)
- GIT (N=0)
- CNS (N=0)
- Other (N=6)

	Traumatic	Spontaneous	
Joints (N=73)	42%	58%	
Muscles (N=17)	18%	82%	
Subcutaneous (N=9)	67%	33%	
Oral cavity (N=2)	0%	100%	
Urogenital tract (N=2)	0%	100%	
Epistaxes (N=7)	14%	86%	
GIT (N=0)			
CNS (N=0)			
Other (N=6)	33%	67%	
Total (N=116)	37%	63%	

Adults
Haem B
N=116*

Detailed treatment of bleeds

* number of bleeds

	Joints	Muscles	Subcutaneous	Oral cavity	Urogenital tract	Epistaxes	GIT	CNS	Other	Total
No. of bleeds	73	17	9	2	2	7	0	0	6	116
FIX consumption per bleed (IU), valid N	73	17	9	2	2	7			6	116
geometric mean	3430.9	4257.3	5163.2	9219.5	4024.9	5858.2			3911.8	3876.9
median	3000.0	3600.0	3000.0	11000.0	5400.0	4200.0			5100.0	3550.0
min – max	1000–81000	1200–31000	1500–45000	5000–17000	1800–9000	1800–68500			1200–8000	1000–81000
sum	425200	98600	95800	22000	10800	93100			27800	773300
No. of doses per bleed										
geometric mean	1.9	2.4	2.5	12.2	2.8	3.3			1.8	2.1
median	2	2	1	13	3	3			2	2
min – max	1–43	1–15	1–15	10–15	2–4	1–26			1–6	1–43
Duration of therapy per bleed, days										
geometric mean	1.6	2.0	2.3	8.4	2.0	2.5			1.5	1.8
median	1	2	1	10	2	2			1	2
min – max	1–31	1–11	1–14	5–14	2–2	1–19			1–5	1–31
N (%) with hospitalization	1 (1.4%)	1 (5.9%)	1 (11.1%)	1 (50%)	0 (0%)	1 (14.3%)			1 (16.7%)	6 (5.2%)
N (%) with rebleeding	3 (4.1%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)	0 (0%)			0 (0%)	4 (3.4%)

ABR according to centres Haemophilia B (PWHB)

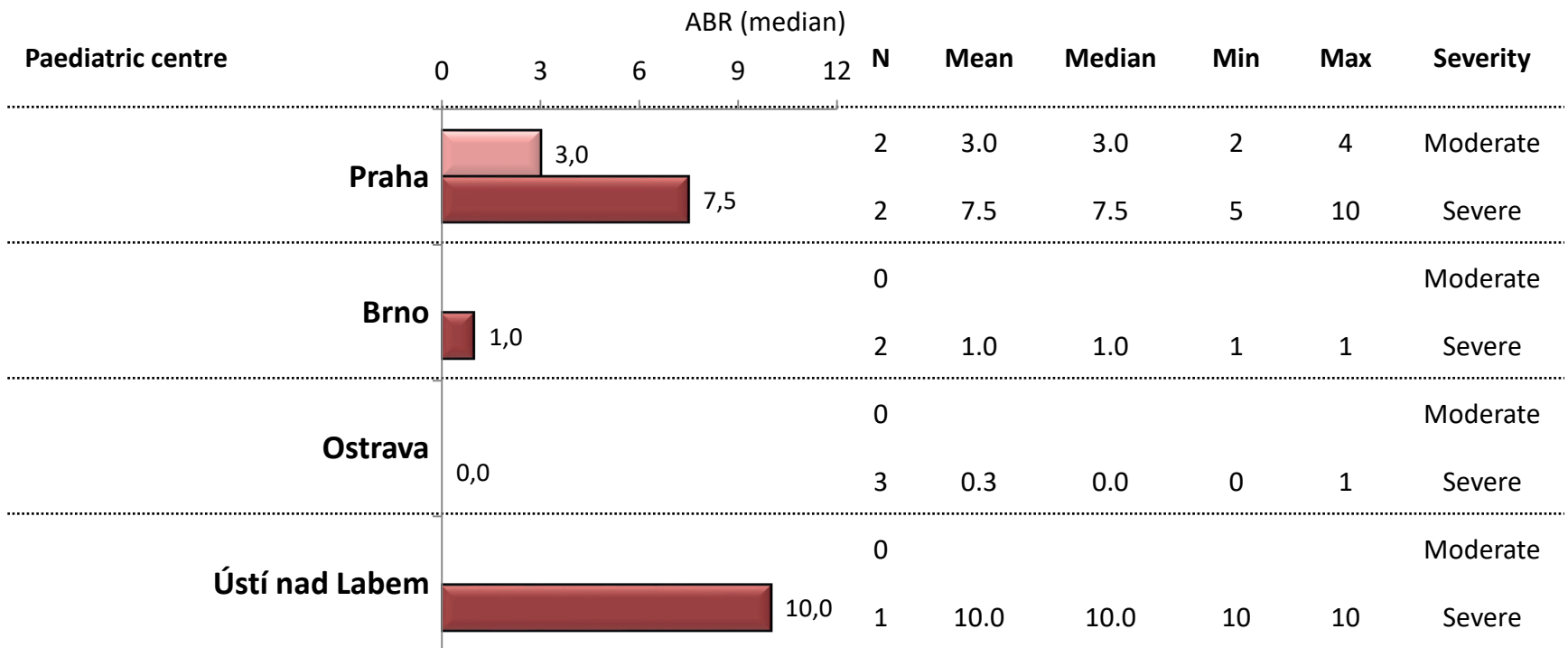


Annual bleeding rate on permanent prophylaxis

HaemB on prophylaxis
Paed. centres
N=10



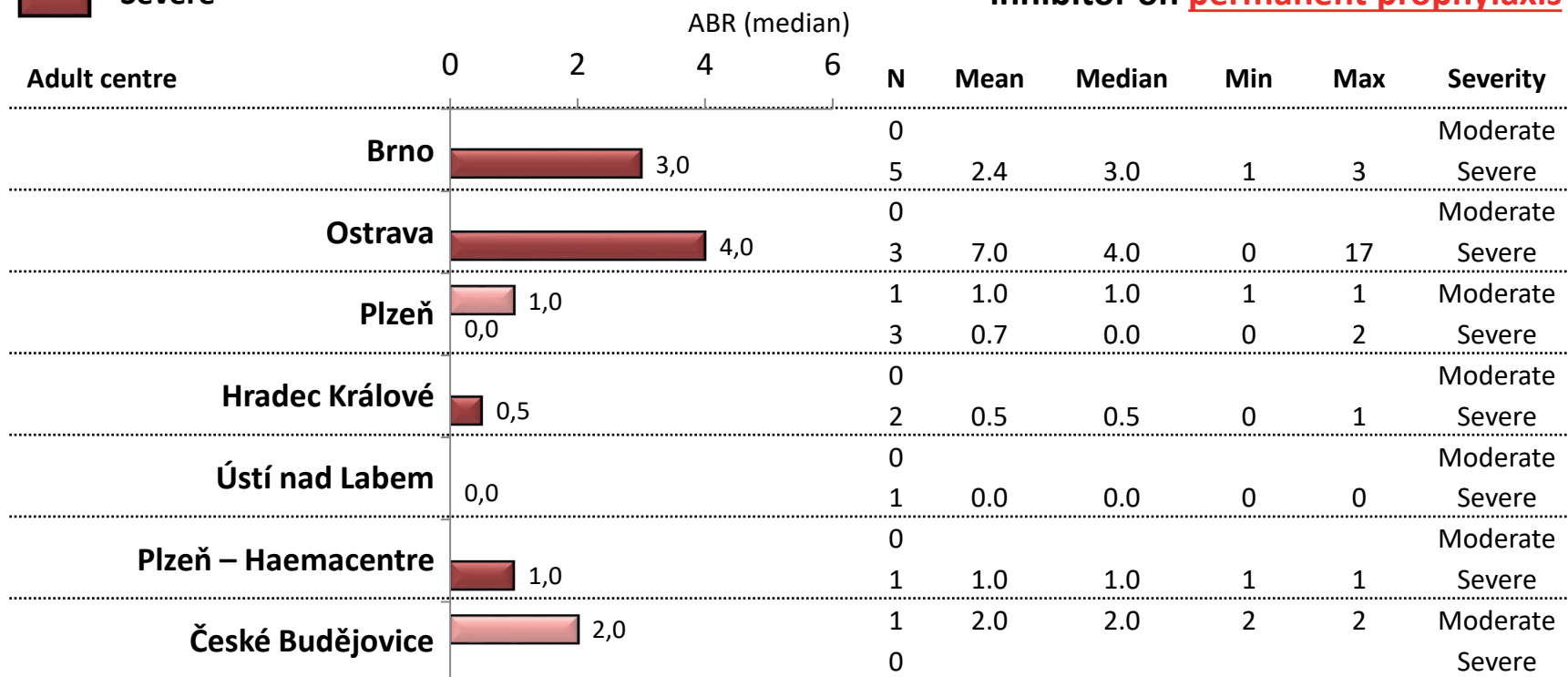
Frequency of bleeding in PWHB without inhibitor on **permanent prophylaxis**



Annual bleeding rate on permanent prophylaxis



Frequency of bleeding in PWHB without inhibitor on **permanent prophylaxis**



Annual bleeding rate regardless prophylaxis

HaemB
Paed. centres
N=23



Frequency of bleeding in PWHB without inhibitor **regardless of prophylaxis**

Paediatric centre	ABR (median)				N	Mean	Median	Min	Max	% on permanent prophylaxis
	0	5	10	15						
Praha	0,5				8	1.5	0.5	0	5	25.0%
		5,0			3	5.3	5.0	1	10	66.7%
Brno	0,0				1	0.0	0.0	0	0	0.0%
		1,0			2	1.0	1.0	1	1	100.0%
Ostrava					0					
	0,0				3	0.3	0.0	0	1	100.0%
České Budějovice	0,0				1	0.0	0.0	0	0	0.0%
					0					
Hradec Králové		2,0			1	2.0	2.0	2	2	0.0%
					0					
Ústí nad Labem					0					
			10,0		1	10.0	10.0	10	10	100.0%
Plzeň	0,0				1	0.0	0.0	0	0	0.0%
		2,0			1	2.0	2.0	2	2	0.0%
Olomouc	0,0				1	0.0	0.0	0	0	0.0%
					0					

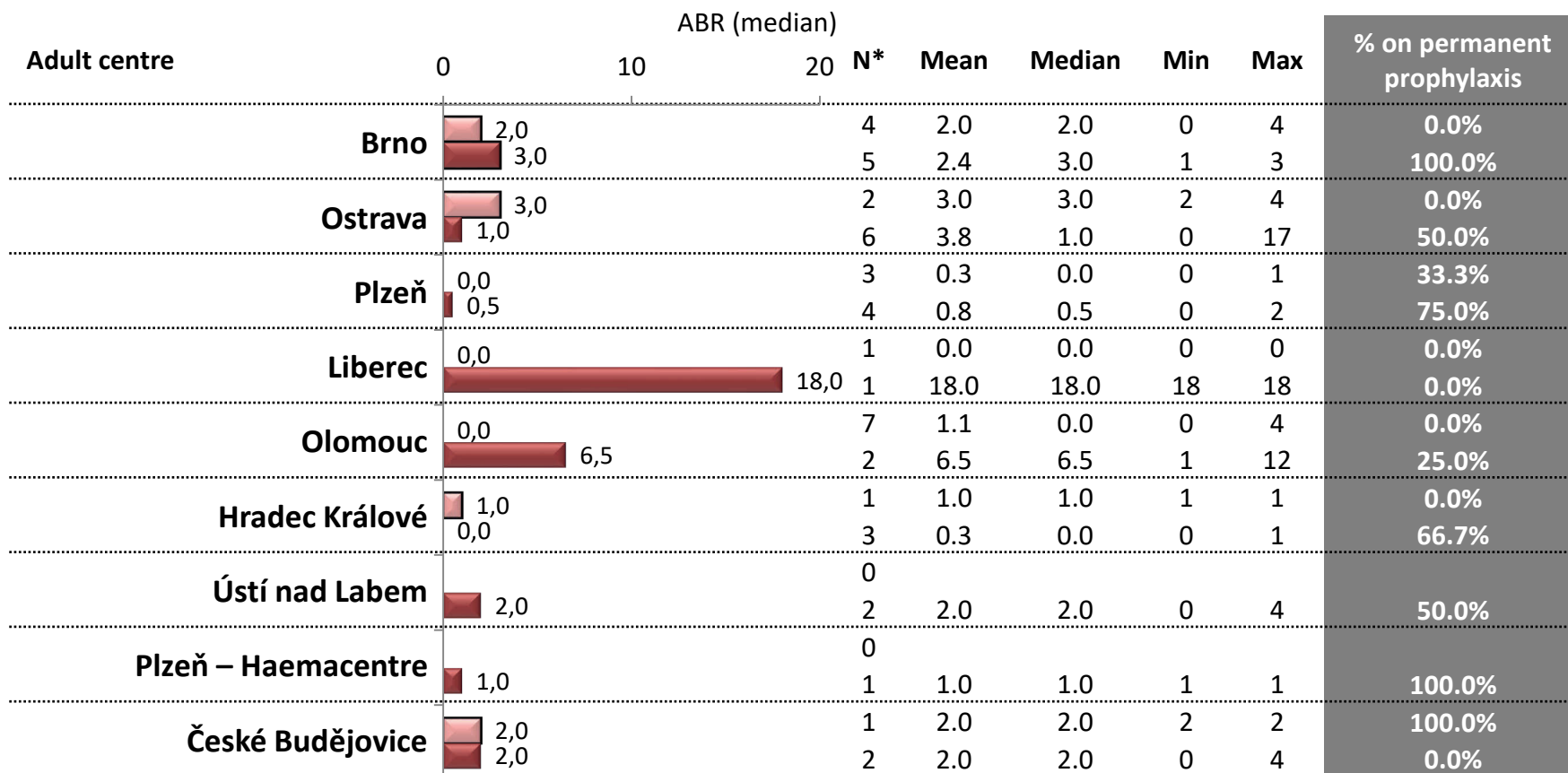
Annual bleeding rate regardless prophylaxis

HaemB
Adult centres
N=45

* missing ABR in 2 adults



Frequency of bleeding in PWHB without inhibitor **regardless of prophylaxis**



Prophylactic regimens and treatment outcomes

HaemB
Paed. centres
N=23

Paediatric centre	Severity	Total N	PERMANENT PROPHYLAXIS								ON-DEMAND / TEMPORARY PROPHY		
			% of patients	N	Dosing of prophylaxis (IU/kg per week)				ABR		N	ABR	
					Mean	Median	Min	Max	Mean	Median		Mean	Median
Praha	Moderate	8	25.0%	2	75.6	75.6	71.4	79.8	0.0	0.0	6	6.0	16.0
	Severe	3	66.7%	2	31.1	31.1	30.3	31.9	115.4	115.4	1	1.0	37.0
Brno	Moderate	1	0.0%	0							1	1.0	5.0
	Severe	2	100.0%	2	34.8	34.8	33.9	35.7	0.0	0.0	0		
Ostrava	Moderate	0	0.0%	0							0		
	Severe	3	100.0%	3	48.2	46.9	29.6	68.2	0.0	0.0	0		
Č. Budějovice	Moderate	1	0.0%	0							1	1.0	4.0
	Severe	0	0.0%	0							0		
Hradec Králové	Moderate	1	0.0%	0							1	1.0	4.0
	Severe	0	0.0%	0							0		
Ústí nad Labem	Moderate	0	0.0%	0							0		
	Severe	1	100.0%	1	62.7	62.7	62.7	62.7	0.0	0.0	0		
Plzeň	Moderate	1	0.0%	0							1	1.0	2.0
	Severe	1	0.0%	0							1	1.0	6.0
Olomouc	Moderate	1	0.0%	0							1	1.0	4.0
	Severe	0											

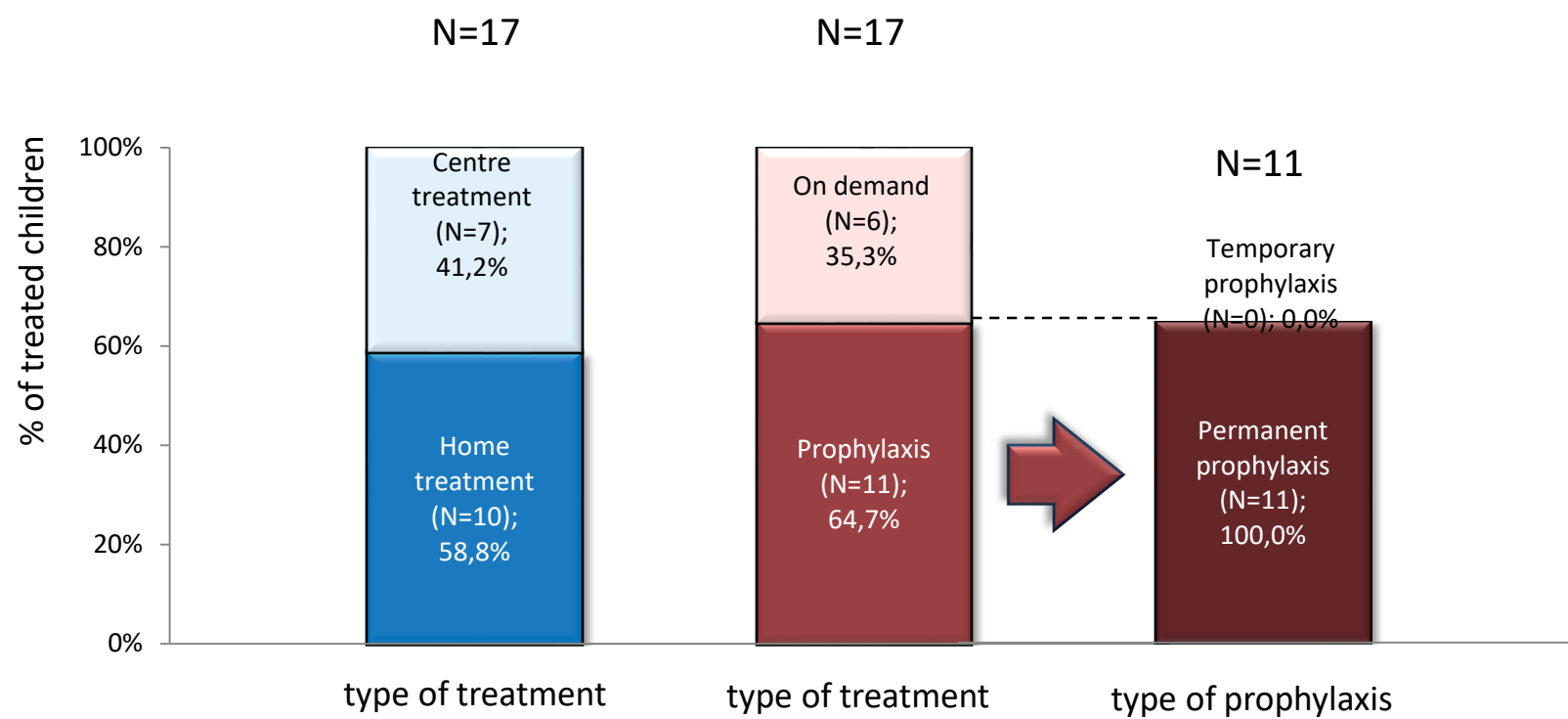
Prophylactic regimens and treatment outcomes

HaemB
Adult centres
N=47

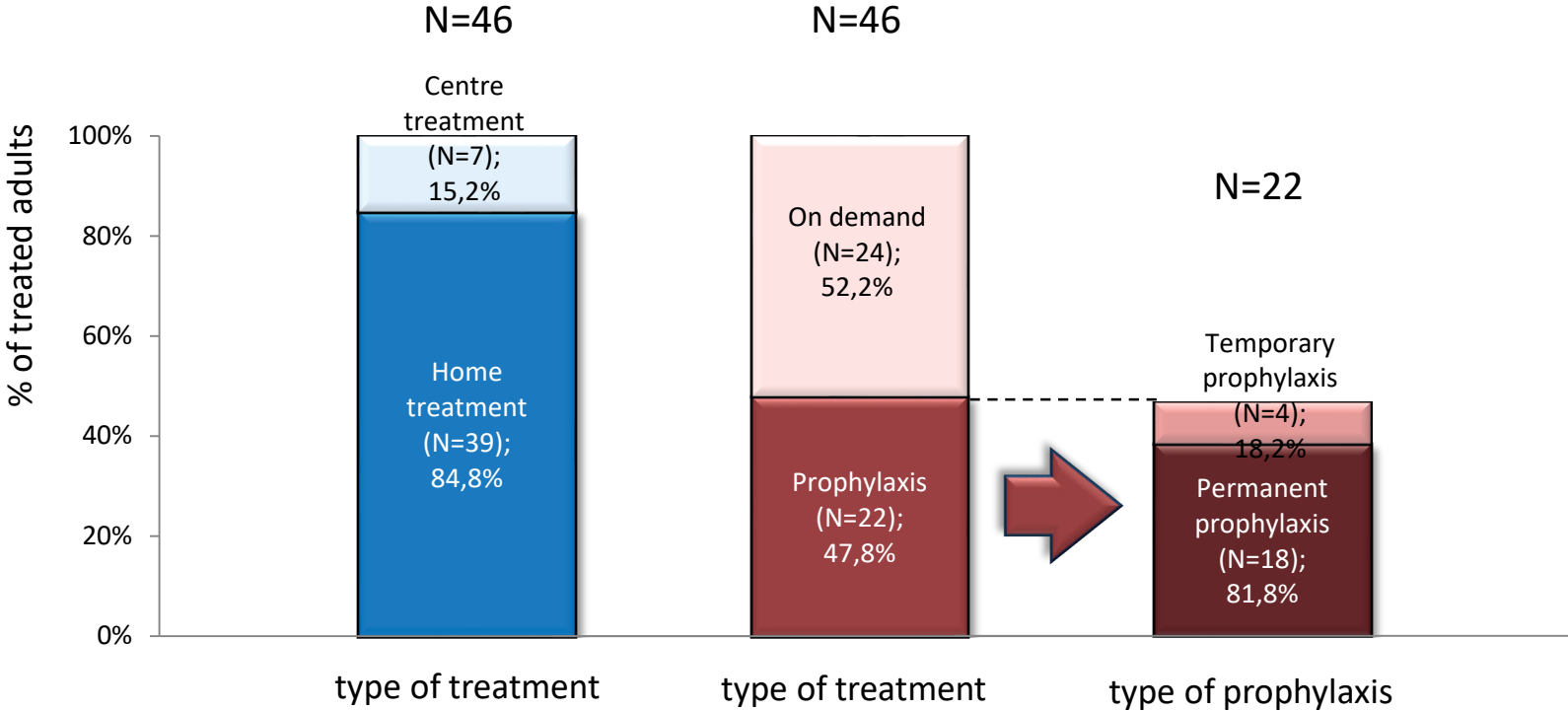
Adult centre	Severity	Total N	PERMANENT PROPHYLAXIS									ON-DEMAND / TEMPORARY PROPHY			
			% of patients	N	Dosing of prophylaxis (IU/kg per week)				ABR*		Age	N	ABR*		Age
					Mean	Median	Min	Max	Mean	Median	Median		Mean	Median	Median
Brno	Moderate	4	0.0%	0								4	2.0	2.0	49
	Severe	5	100.0%	5	54.3	54.5	43.8	73.2	2.4	3.0	31	0			
Ostrava	Moderate	2	0.0%	0								2	3.0	3.0	27
	Severe	6	50.0%	3	44.9	46.2	38.6	50.0	7.0	4.0	51	3	0.7	0.0	59
Plzeň	Moderate	3	33.3%	1	6.1	6.1	6.1	6.1	1.0	1.0	35	2	0.0	0.0	62
	Severe	4	75.0%	3	11.6	11.8	10.5	12.6	0.7	0.0	42	1	1.0	1.0	36
Liberec	Moderate	1	0.0%	0								1	0.0	0.0	45
	Severe	1	0.0%	0								1	18.0	18.0	26
Olomouc	Moderate	7	0.0%	0								7	1.1	0.0	45
	Severe	4	25.0%	1	26.7	26.7	26.7	26.7	0.0	0.0	52	3	6.5	6.5	49
Hradec Králové	Moderate	1	0.0%	0								1	1.0	1.0	64
	Severe	3	66.7%	2	36.4	36.4	21.1	51.7	0.5	0.5	40	1	0.0	0.0	62
Ústí n. Labem	Moderate	0													
	Severe	2	50.0%	1	52.5	52.5	52.5	52.5	0.0	0.0	23	1	4.0	4.0	47
Plzeň - Haemacentre	Moderate	0													
	Severe	1	100.0%	1	46.9	46.9	46.9	46.9	1.0	1.0	37	0			
Č. Budějovice	Moderate	1	100.0%	1	22.1	22.1	22.1	22.1	2.0	2.0	52	0			
	Severe	2	0.0%	0								2	2.0	2.0	50

* missing ABR in 2 adults

Type of treatment (subgroup of treated patients)



Type of treatment (subgroup of treated patients)



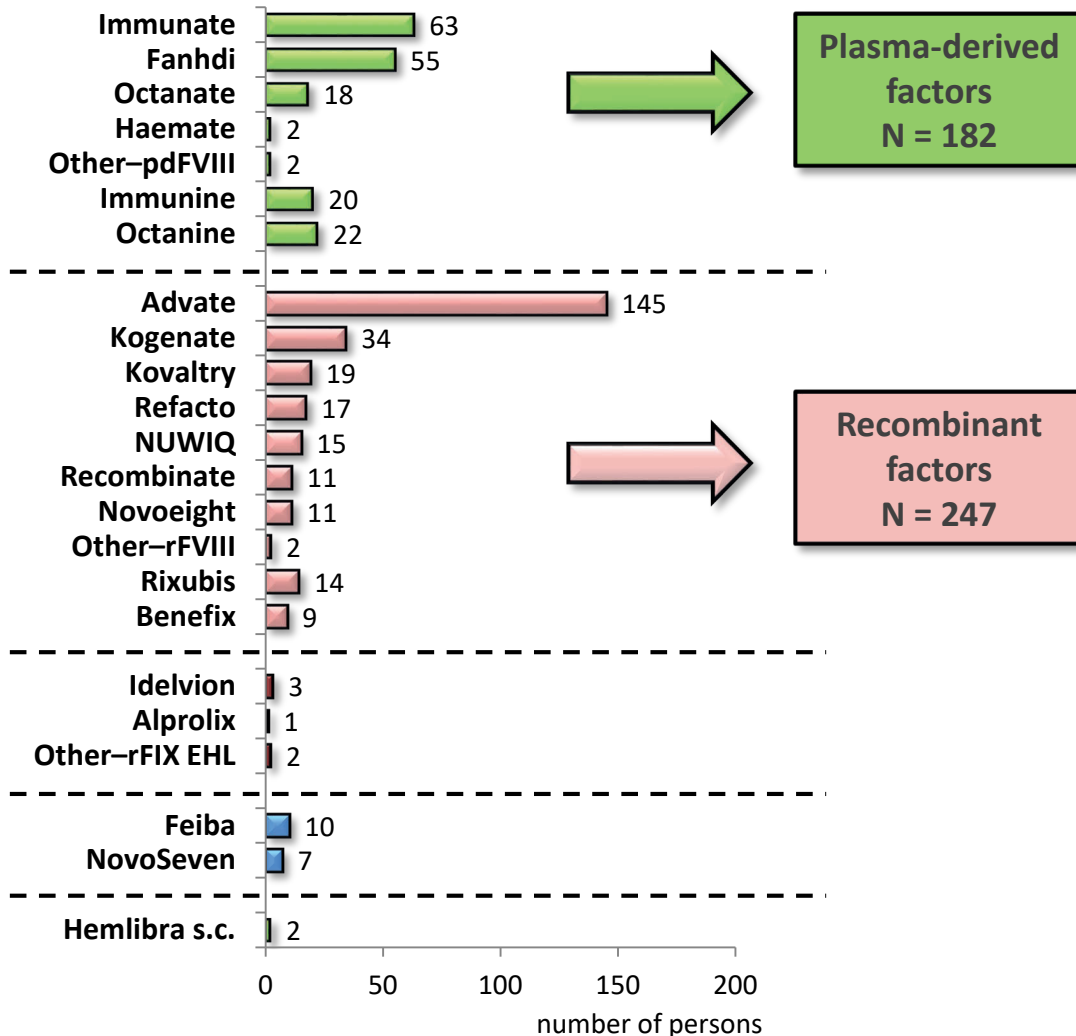
Treatment data and factor consumption

Haemophilia A and B



Treatment

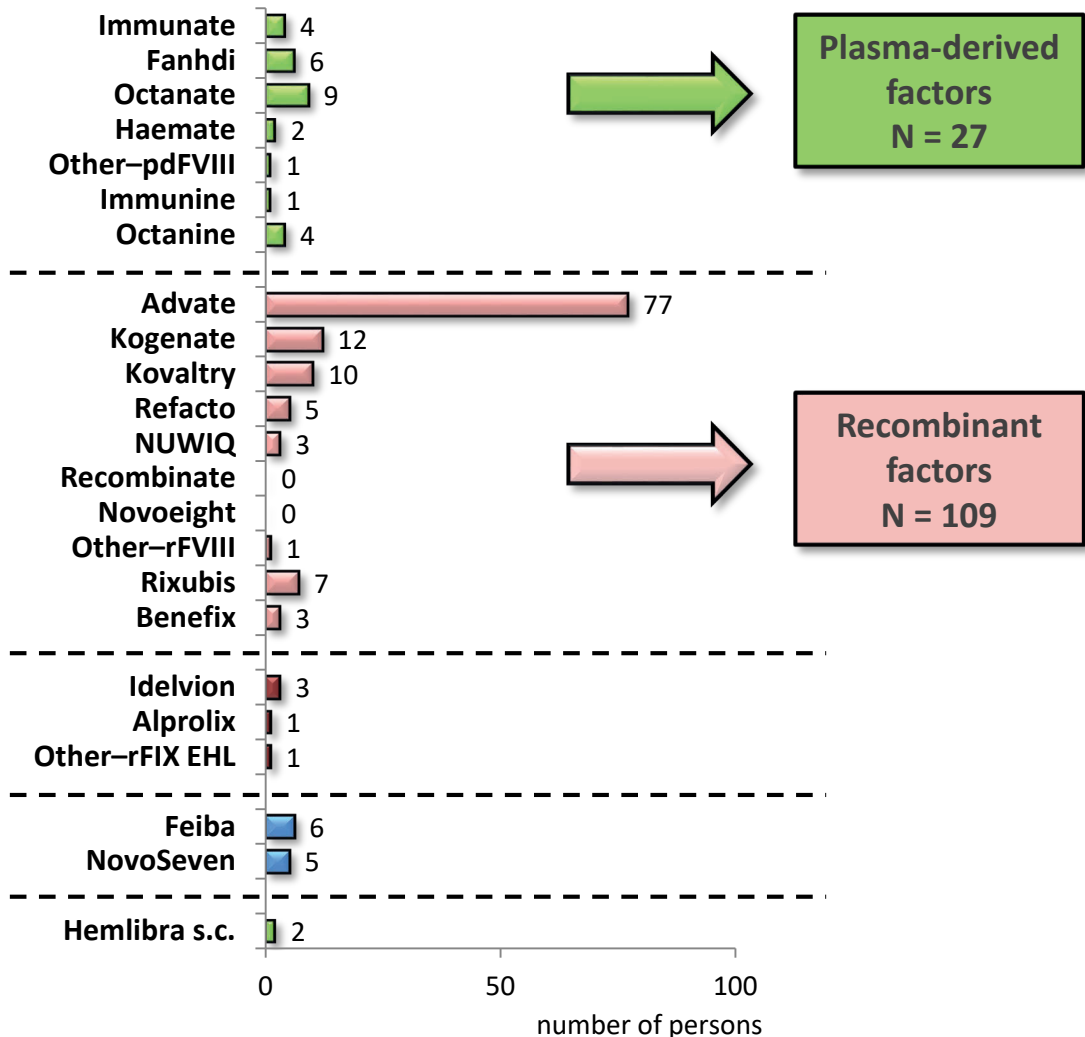
All
N=413¹



419 persons (54.4% of all PWH) were treated in 2018 (**404 persons received standard factor concentrates**, another 9 persons EHL factors, by-pass therapy or emicizumab and in 6 data are not available; 34 persons received more than one type/brand of concentrate). Plasma-derived factors were administered in 182 persons (23.6% of all PWH, 45% of 404 PHWs treated with factor), whereas recombinant factors in 247 persons (32.1% of all PWH, 61.1% of 404 factor treated PHWs). 25 persons were treated with both plasma-derived and recombinant factor.

¹ missing type of treatment in 5 adults and 1 child

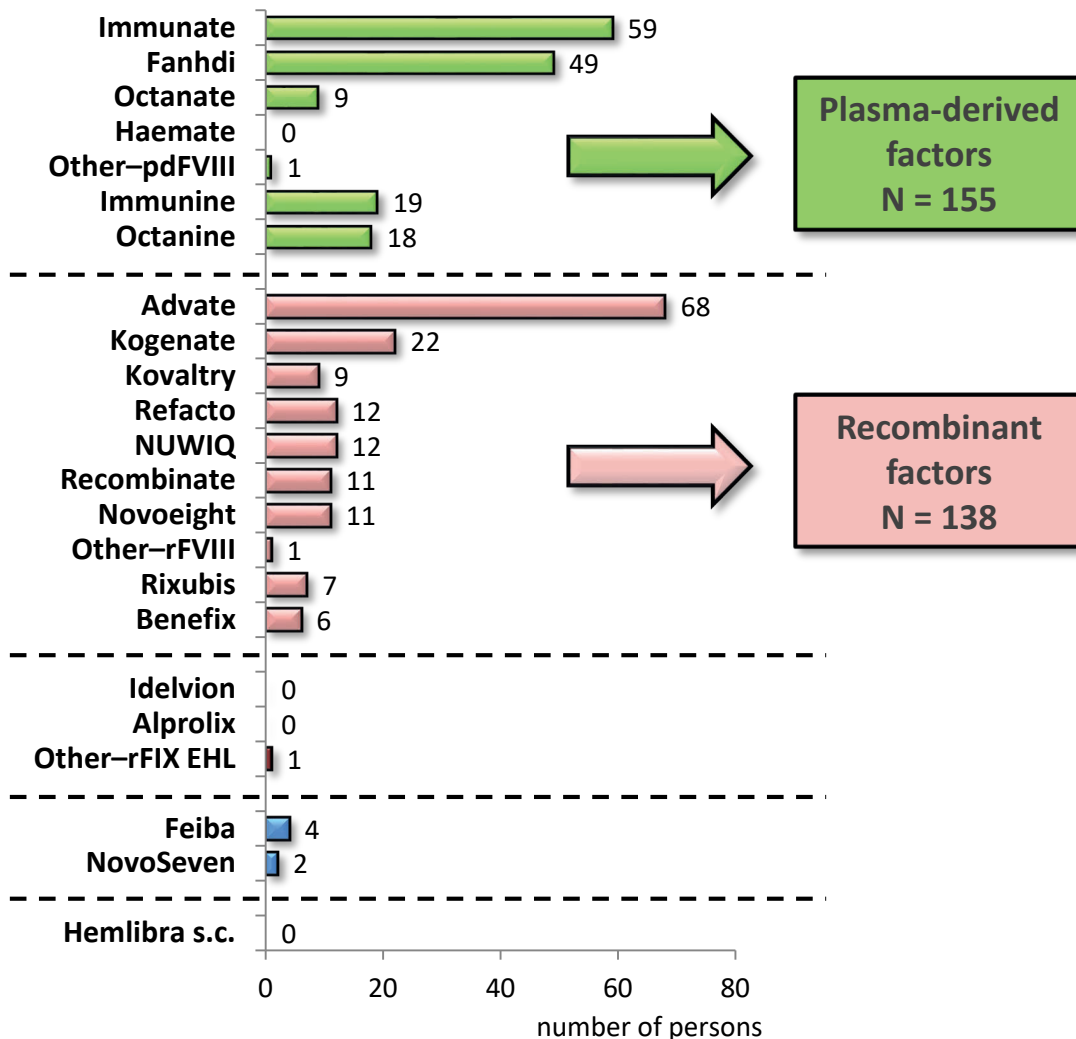
Treatment



139 children (55.8% of all PWH) were treated in 2018 (**133 children received standard factor concentrates**, another 5 children EHL factors, by-pass therapy or emicizumab and in 1 data are not available; 11 persons received more than one type/brand of concentrate). Plasma-derived factors were administered in 27 children (10.8% of all PWH, 20.3% of 133 PHWs treated with factor), whereas recombinant factors in 109 children (43.8% of all PWH, 82% of 133 factor treated PHWs). Three children were treated with both plasma-derived and recombinant factor.

¹ missing type of treatment in 1 child

Treatment



280 adults (53.7% of all PWH) were treated in 2018 (**271 adults received standard factor concentrates**, another 4 adults EHL factors or by-pass therapy only and in 5 data are not available; 23 adults received more than one type/brand of concentrate). Plasma-derived factors were administered in 155 adults (29.8% of all PWH, 57.2% of 271 PHWs treated with factor), whereas recombinant factors in 138 adults (26.5% of all PWH, 50.9% of 271 factor treated PHWs). 22 adults were treated with both plasma-derived and recombinant factor.

¹ missing type of treatment in 5 adults

Comparison of treatment in years 2018 and 2017

	2018			2017		
	N	% of all PWH	% treated PWH	N	% of all PWH	% treated PWH
All persons treated with factor concentrates	404	52.5	100.0	404	54.4	100.0
<i>Plasma-derived factor</i>	157	20.4	38.9	204	27.5	50.5
<i>Recombinant factor</i>	247	32.1	61.1	200	26.9	49.5
Without treatment	366	47.5	-	339	45.6	-
Total	770	100.0	-	743	100.0	-

Comparison of treatment in years 2018 and 2017

	2018			2017		
	N	% of all PWH	% treated PWH	N	% of all PWH	% treated PWH
All children treated with factor concentrates	133	53.4	100.0	134	56.5	100.0
<i>Plasma-derived factor</i>	24	9.6	18.0	28	11.8	20.9
<i>Recombinant factor</i>	109	43.8	82.0	106	44.7	79.1
Without treatment	116	46.6	-	103	43.5	-
Total	249	100.0	-	237	100.0	-



Comparison of treatment in years 2018 and 2017

	2018			2017		
	N	% of all PWH	% treated PWH	N	% of all PWH	% treated PWH
All adults treated with factor concentrates	271	52.0	100.0	270	53.4	100.0
<i>Plasma-derived factor</i>	133	25.5	49.1	176	34.8	65.2
<i>Recombinant factor</i>	138	26.5	50.9	94	18.6	34.8
Without treatment	250	48.0	-	236	46.6	-
Total	521	100.0	-	506	100.0	-



Consumption of drugs

All

	Drug (IU)	Total annual consumption	Number of treated persons	Average annual consumption per treated person	Number of valid persons	Average annual consumption per valid person
FVIII (IU)	<i>Immunate</i>	5 423 500	63	86 087.3		
	<i>Fanhdi</i>	8 648 000	55	157 236.4		
	<i>Octanate</i>	1 874 500	18	104 138.9		
	<i>Haemate P</i>	1 798 500	2	899 250.0		
	<i>Other plasma-derived</i>	307 000	2	153 500.0		
	FVIII PD total	18 051 500	140	128 939.3		
	<i>Advate</i>	21 264 650	145	146 652.8		
	<i>Kogenate</i>	5 123 250	34	150 683.8		
	<i>Kovaltry</i>	1 128 250	19	59 381.6		
	<i>Refacto</i>	1 363 000	17	80 176.5		
	<i>NUWIQ</i>	1 137 500	15	75 833.3		
	<i>Recombinate</i>	1 119 000	11	101 727.3		
	<i>Novoeight</i>	993 000	11	90 272.7		
	<i>Other recombinant</i>	421 500	2	210 750.0		
	FVIII REC total	32 550 150	225	144 667.3		
	FVIII total	50 601 650	347	145 826.1	667	75 864.5
FIX (IU)	<i>Immunine</i>	1 140 800	20	57 040.0		
	<i>Octanine</i>	1 126 500	22	51 204.5		
	FIX PD total	2 267 300	42	53 983.3		
	<i>Rixubis</i>	2 026 250	14	144 732.1		
	<i>Benefix</i>	666 500	9	74 055.6		
	FIX REC total	2 692 750	22	122 397.7		
	FIX total	4 960 050	57	87 018.4	103	48 155.8
EHL (IU)	<i>Idelvion</i>	443 850	3	147 950.0		
	<i>Alprolix</i>	10 200	1	10 200.0		
	<i>Other FIX EHL</i>	5 466	1	5 466.0		
by-pass	<i>Feiba (U)</i>	3 440 750	10	344 075.0		
	<i>NovoSeven (mg)</i>	5 180.0	7	740.0		
emicizumab	<i>Hemlibra s.c. (mg)</i>	1 620	2	810.0		

Consumption of drugs

Children

	Drug (IU)	Total annual consumption	Number of treated persons	Average annual consumption per treated person	Number of valid persons	Average annual consumption per valid person
FVIII (IU)	<i>Immunate</i>	202 000	4	50 500.0		
	<i>Fanhdi</i>	1 586 500	6	264 416.7		
	<i>Octanate</i>	1 169 000	9	129 888.9		
	<i>Haemate P</i>	1 798 500	2	899 250.0		
	<i>Other plasma-derived</i>	298 000	1	298 000.0		
	FVIII PD total	5 054 000	22	229 727.3		
	<i>Advate</i>	11 133 150	77	144 586.4		
	<i>Kogenate</i>	1 574 250	12	131 187.5		
	<i>Kovaltry</i>	547 750	10	54 775.0		
	<i>Refacto</i>	491 000	5	98 200.0		
	<i>NUWIQ</i>	322 000	3	107 333.3		
	<i>Recombinate</i>	0	0	-		
	<i>Novoeight</i>	0	0	-		
	<i>Other recombinant</i>	262 500	1	262 500.0		
	FVIII REC total	14 330 650	100	143 306.5		
	FVIII total	19 384 650	120	161 538.8	214	90 582.5
FIX (IU)	<i>Immunine</i>	7 200	1	7 200.0		
	<i>Octanine</i>	88 000	4	22 000.0		
	FIX PD total	95 200	5	19 040.0		
	<i>Rixubis</i>	643 250	7	91 892.9		
	<i>Benefix</i>	82 000	3	27 333.3		
	FIX REC total	725 250	9	80 583.3		
		FIX total	820 450	13	63 111.5	35
EHL (IU)	<i>Idelvion</i>	443 850	3	147 950.0		
	<i>Alprolix</i>	10 200	1	10 200.0		
	<i>Other FIX EHL</i>	5 466	1	5 466.0		
by-pass	<i>Feiba (U)</i>	1 952 750	6	325 458.3		
	<i>NovoSeven (mg)</i>	1 955.0	5	391.0		
emicizumab	<i>Hemlibra s.c. (mg)</i>	1 620	2	810.0		

Consumption of drugs

Adults

	Drug (IU)	Total annual consumption	Number of treated persons	Average annual consumption per treated person	Number of valid persons	Average annual consumption per valid person
FVIII (IU)	<i>Immunate</i>	5 221 500	59	88 500.0		
	<i>Fanhdi</i>	7 061 500	49	144 112.2		
	<i>Octanate</i>	705 500	9	78 388.9		
	<i>Haemate P</i>	0	0	-		
	<i>Other plasma-derived</i>	9 000	1	9 000.0		
	FVIII PD total	12 997 500	118	110 148.3		
	<i>Advate</i>	10 131 500	68	148 992.6		
	<i>Kogenate</i>	3 549 000	22	161 318.2		
	<i>Kovaltry</i>	580 500	9	64 500.0		
	<i>Refacto</i>	872 000	12	72 666.7		
	<i>NUWIQ</i>	815 500	12	67 958.3		
	<i>Recombinate</i>	1 119 000	11	101 727.3		
	<i>Novoeight</i>	993 000	11	90 272.7		
	<i>Other recombinant</i>	159 000	1	159 000.0		
	FVIII REC total	18 219 500	125	145 756.0		
	FVIII total	31 217 000	227	137 519.8	453	68 911.7
FIX (IU)	<i>Immunine</i>	1 133 600	19	59 663.2		
	<i>Octanine</i>	1 038 500	18	57 694.4		
	FIX PD total	2 172 100	37	58 705.4		
	<i>Rixubis</i>	1 383 000	7	197 571.4		
	<i>Benefix</i>	584 500	6	97 416.7		
	FIX REC total	1 967 500	13	151 346.2		
	FIX total	4 139 600	44	94 081.8	68	60 876.5
EHL (IU)	<i>Idelvion</i>	0	0	-		
	<i>Alprolix</i>	0	0	-		
	<i>Other FIX EHL</i>	0	0	-		
by-pass	<i>Feiba (U)</i>	1 488 000	4	372 000.0		
	<i>NovoSeven (mg)</i>	3 225.0	2	1 612.5		
emicizumab	<i>Hemlibra s.c. (mg)</i>	0	0	-		