

The current status of care for persons with haemophilia and von Willebrand's disease registered within CNHP registry

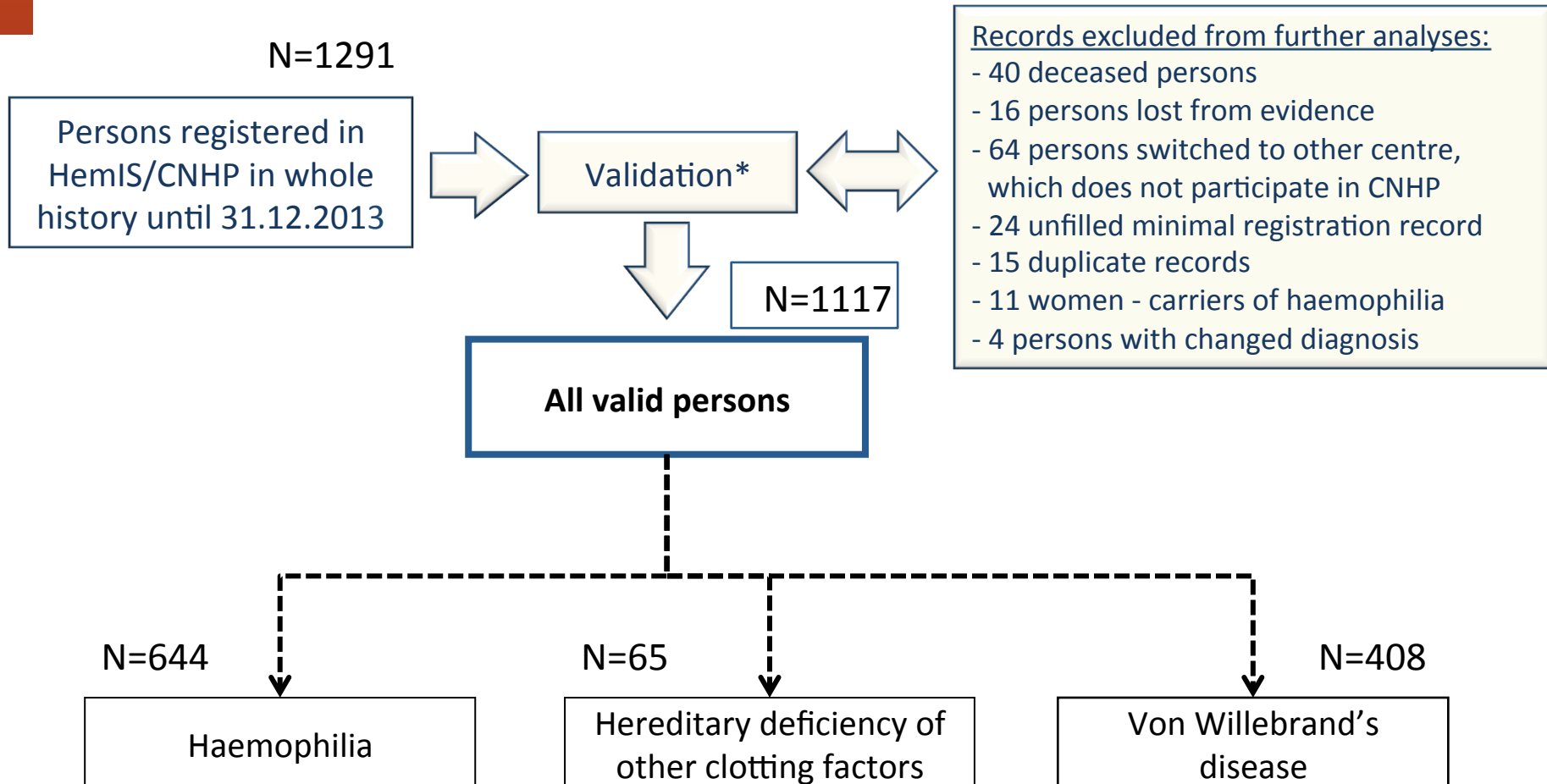
Jan Blatný, Petra Ovesná

on behalf of

Centres contributing to common database
of the CNHP (Czech National Haemophilia Programme)

April 2014

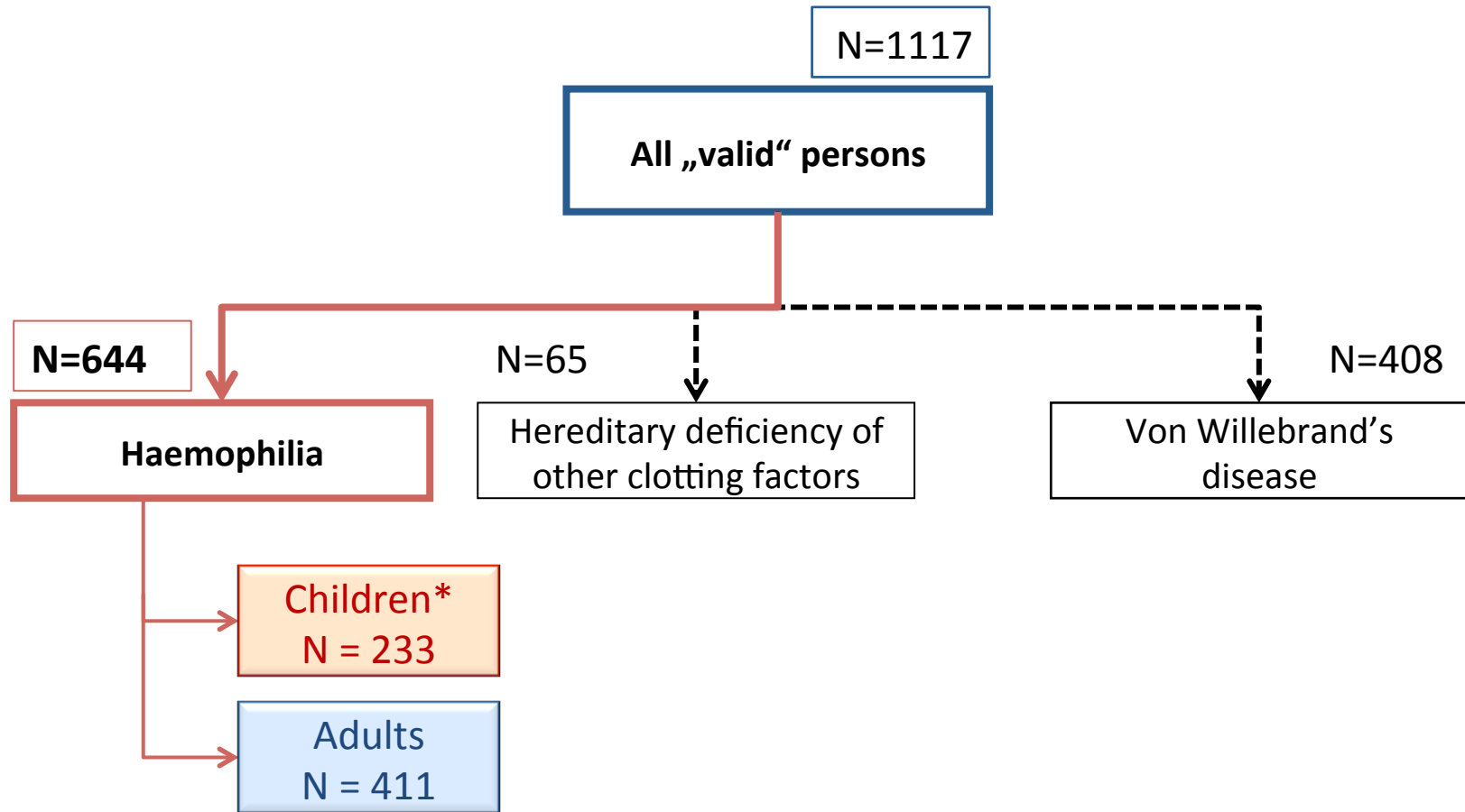
Sample size, valid records



Part A

Persons with haemophilia (PWH)

Sample size



* Persons under 19 years old in 2013

Participating centres in CNHP

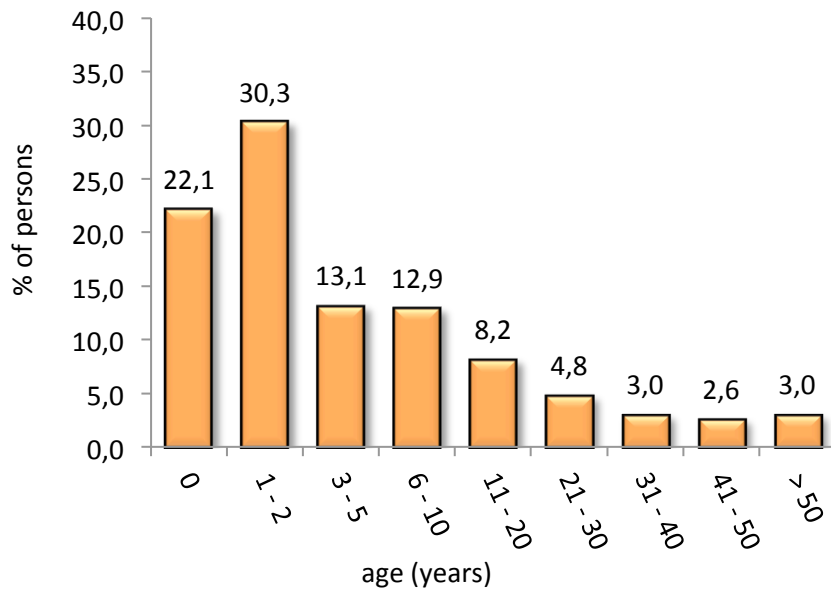
Paediatric centres	Valid persons	
	N	%
FN Motol – Dpt. of Pediatric Haematology and Oncology	78	12.1
FN Brno – DN – Dpt. of Pediatric Haematology	49	7.6
FNHK – Dpt. of Pediatric Medicine	31	4.8
FN Ostrava – Dpt. of Pediatric Medicine	31	4.8
UnL – Pediatric Dpt. – Haematology	30	4.7
CB – Pediatric Dpt.	13	2.0
FN Plzen – Pediatric Dpt.	11	1.7
FN Olomouc – Dpt. of Pediatric Medicine	9	1.4

Adult centres	Valid persons	
	N	%
FN Brno – OKH	132	20.5
FN Ostrava – Blood centre	67	10.4
FN Olomouc – Haemato-Oncology Dpt.	62	9.6
FN Plzen – UKBH	42	6.5
KN Liberec – OKH	34	5.3
CB – OKH	29	4.5
FN a LF HK – IV. IHK	26	4.0

Age

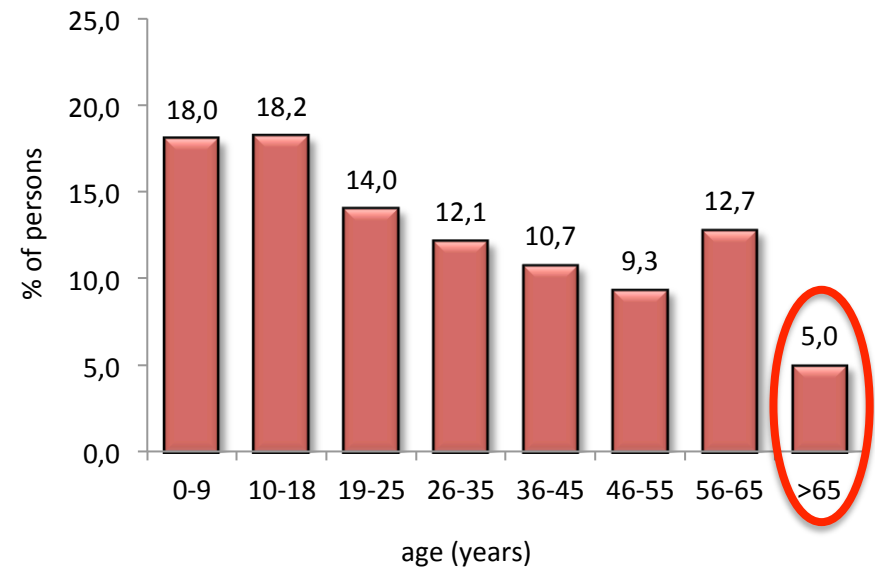
All
N=644

Age at diagnosis (years)	
N	502*
Mean	8.3
Median (min - max)	2 (0 – 81)



* Missing information on year of diagnosis in 142 persons.

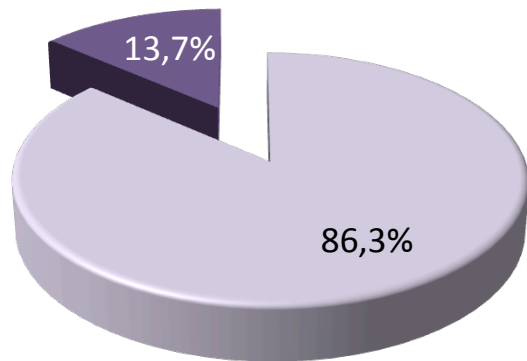
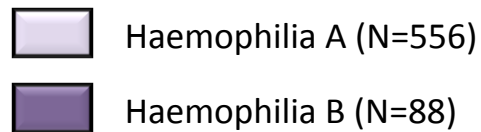
Current age (years)	
N	644
Mean	30.6
Median (min - max)	25 (0 – 91)



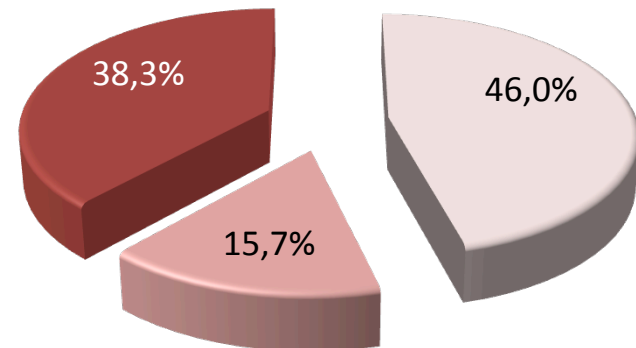
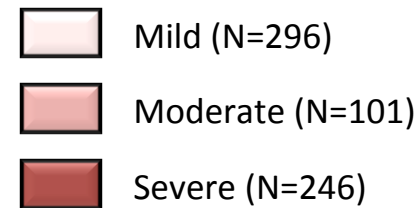
Type and severity of haemophilia I

All
N=644

Type of haemophilia



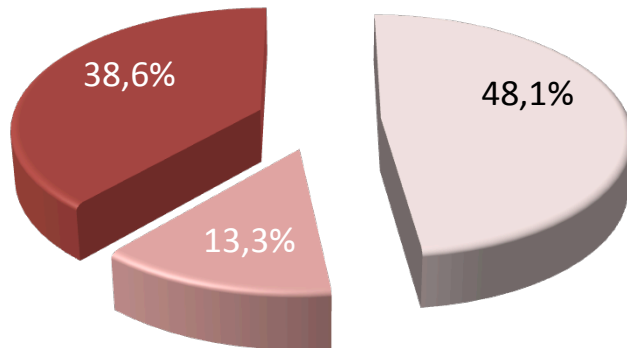
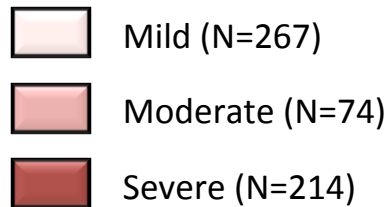
Severity of haemophilia (N=643*)



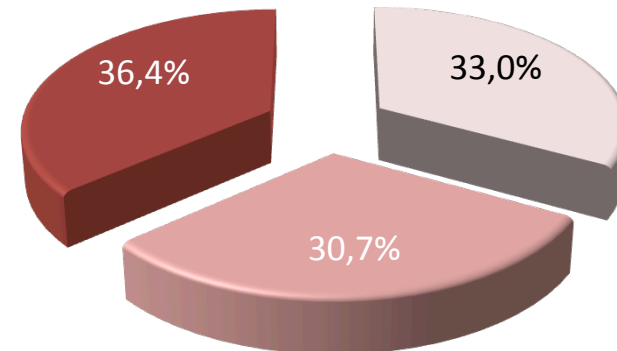
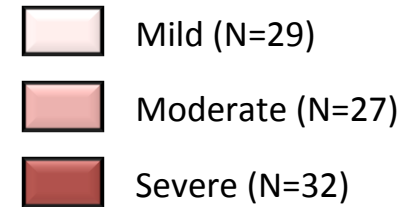
* Severity of haemophilia not known in 1 person.

Type and severity of haemophilia II

Haemophilia A (N=555¹⁾)



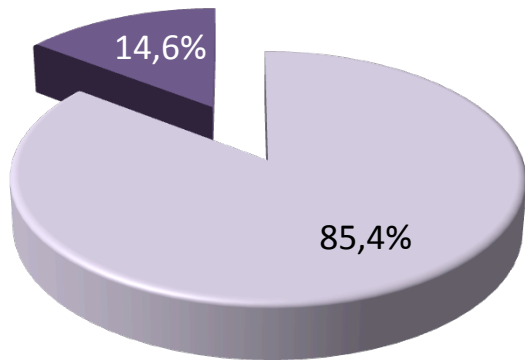
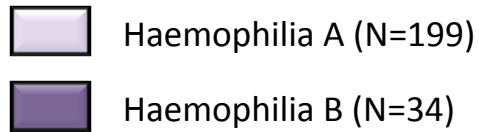
Haemophilia B (N=88)



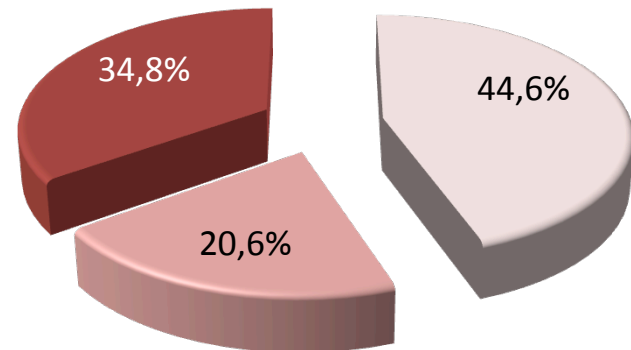
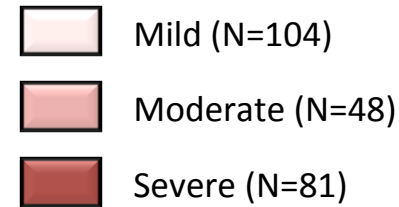
¹⁾ Severity not known in 1 person with haemophilia A.

Type and severity of haemophilia I

Type of haemophilia



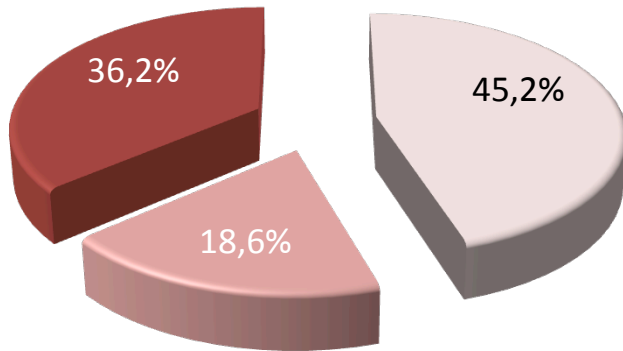
Severity of haemophilia



Type and severity of haemophilia II

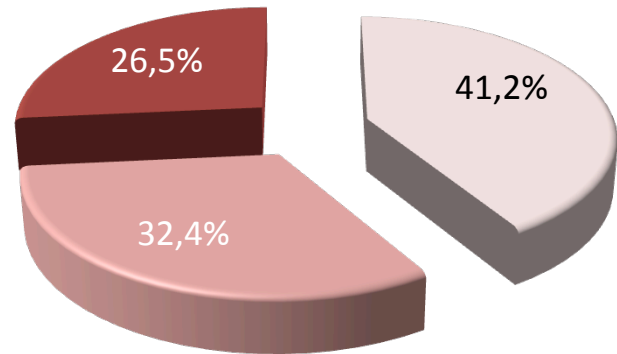
Haemophilia A (N=199)

- Mild (N=90)
- Moderate (N=37)
- Severe (N=72)



Haemophilia B (N=34)

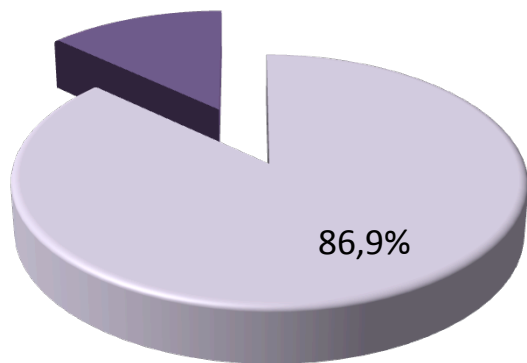
- Mild (N=14)
- Moderate (N=11)
- Severe (N=9)



Type and severity of haemophilia I

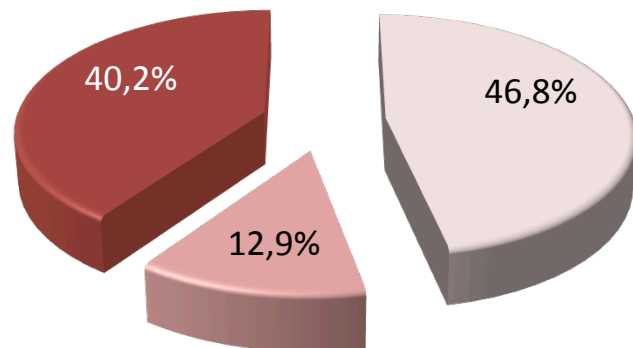
Type of haemophilia

- Haemophilia A (N=357)
- Haemophilia B (N=54)



Severity of haemophilia (N=410*)

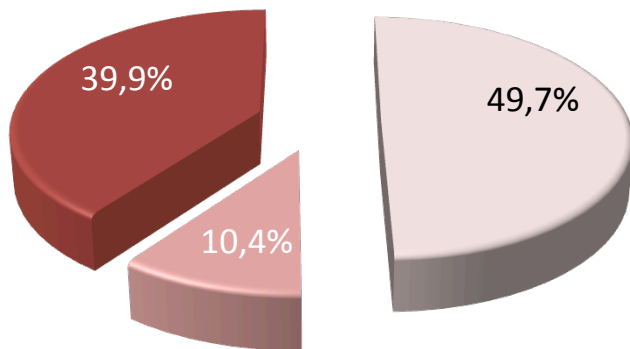
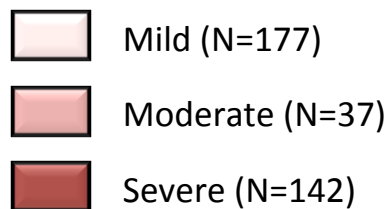
- Mild (N=192)
- Moderate (N=53)
- Severe (N=65)



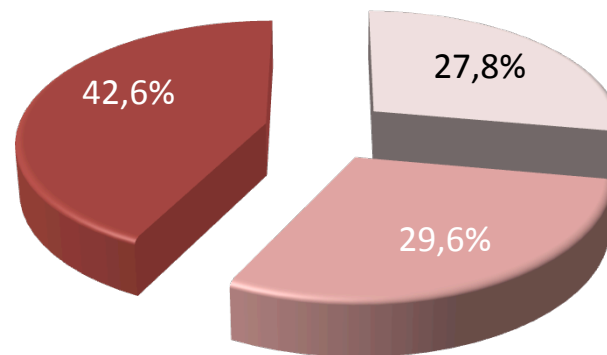
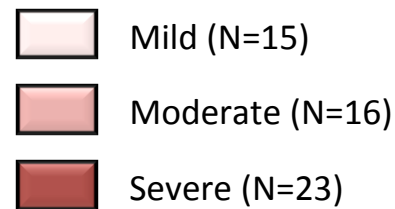
* Severity of haemophilia not known in 1 adult.

Type and severity of haemophilia II

Haemophilia A (N=356¹⁾)

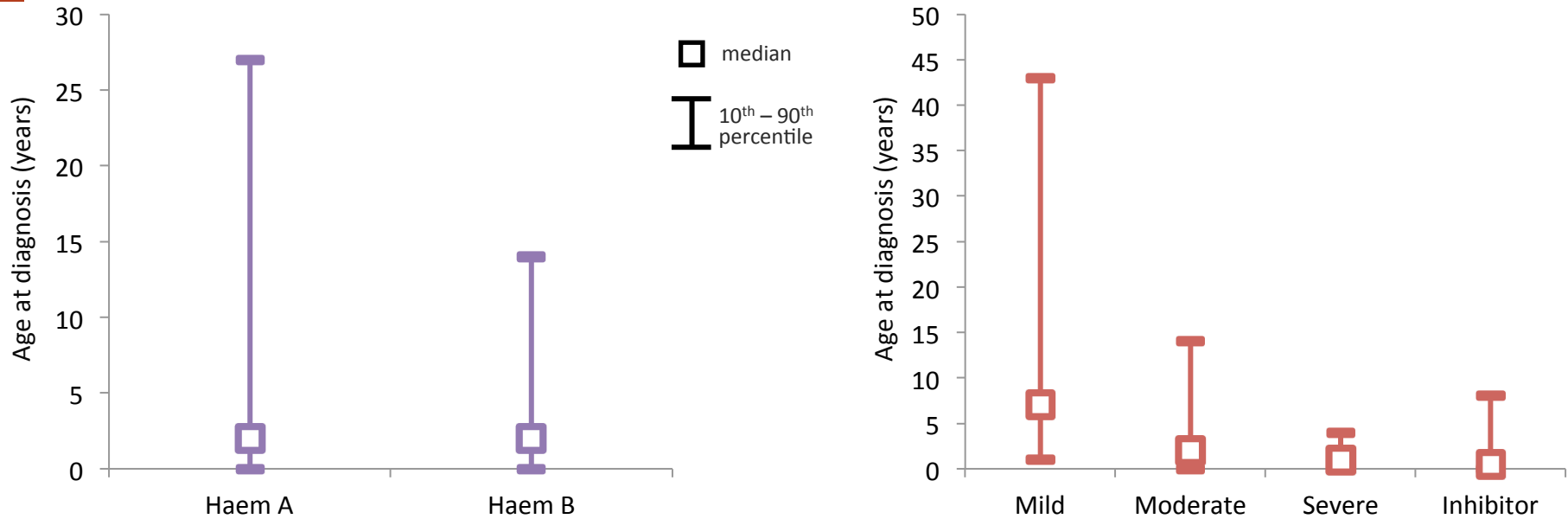


Haemophilia B (N=54)



¹⁾ Severity not known in 1 adult with haemophilia A.

Age at diagnosis according to type and severity of haemophilia



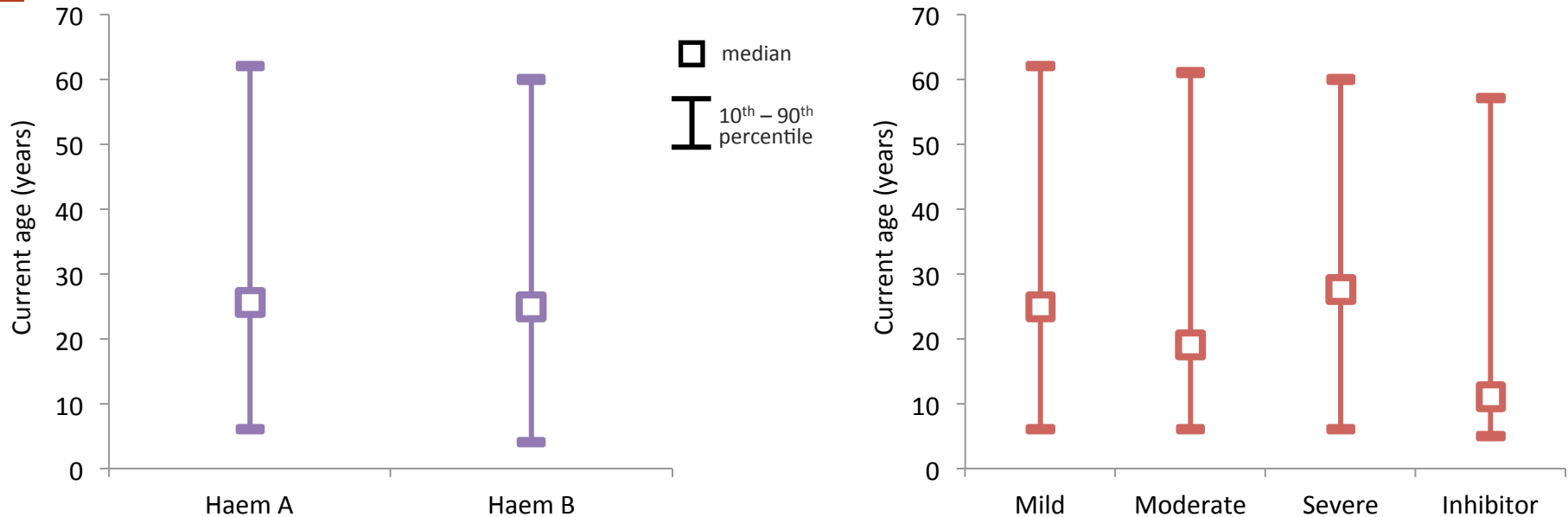
Haemophilia A	Haemophilia B	Age at diagnosis (years)	Mild*	Moderate*	Severe*	Inhibitor ⁺
556	88	N	296	101	246	12
8.5	7.2	Mean	14.2	5.2	2.0	2.2
2 (0 – 81)	2 (0 – 63)	Median (min – max)	7 (0 – 81)	2 (0 – 61)	1 (0 – 48)	0.5 (0 – 10)

* including persons with inhibitor

+ in 2013

All
N=644

Current age according to type and severity of haemophilia

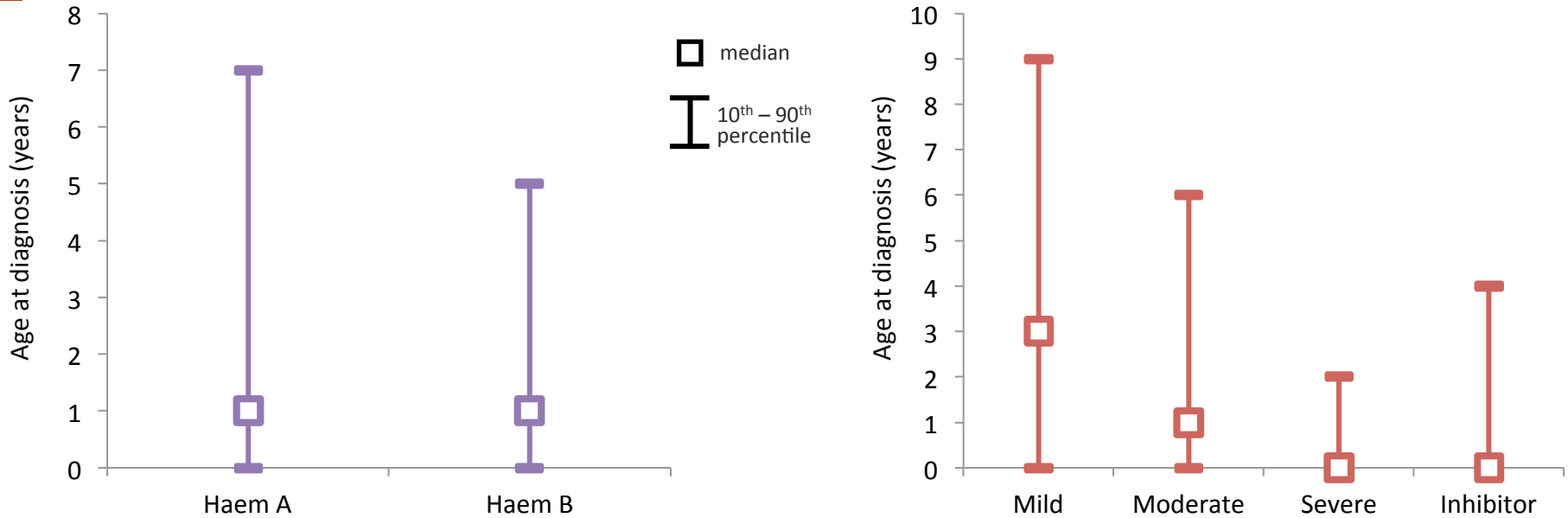


Haemophilia A	Haemophilia B	Current age [†] (years)	Mild*	Moderate*	Severe*	Inhibitor [†]
556	88	N	296	101	246	12
30.7	29.9	Mean	31.4	27.7	30.8	23.6
25.5 (0 – 91)	25 (0 – 68)	Median (min – max)	25 (0 – 91)	19 (0 – 72)	27.5 (0 – 74)	11 (2 – 72)

[†]Current age = age reached in year 2013

* including persons with inhibitor
 † in 2013

Age at diagnosis according to type and severity of haemophilia

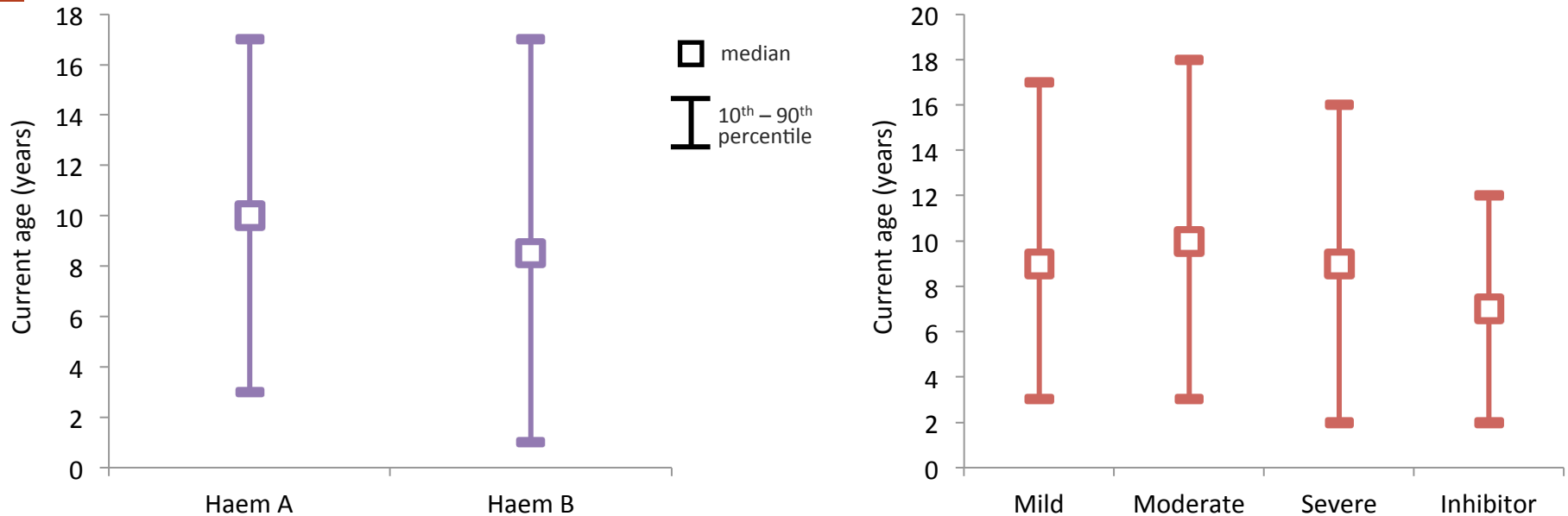


Haemophilia A	Haemophilia B	Age at diagnosis (years)	Mild*	Moderate*	Severe*	Inhibitor ⁺
199	34	N	104	48	81	7
2.5	2.2	Mean	3.9	2.2	0.7	1
1 (0 – 16)	1 (0 – 13)	Median (min – max)	3 (0 – 13)	1 (0 – 16)	0 (0 – 6)	0 (0 – 4)

* including persons with inhibitor

+ in 2013

Actual age according to type and severity of haemophilia

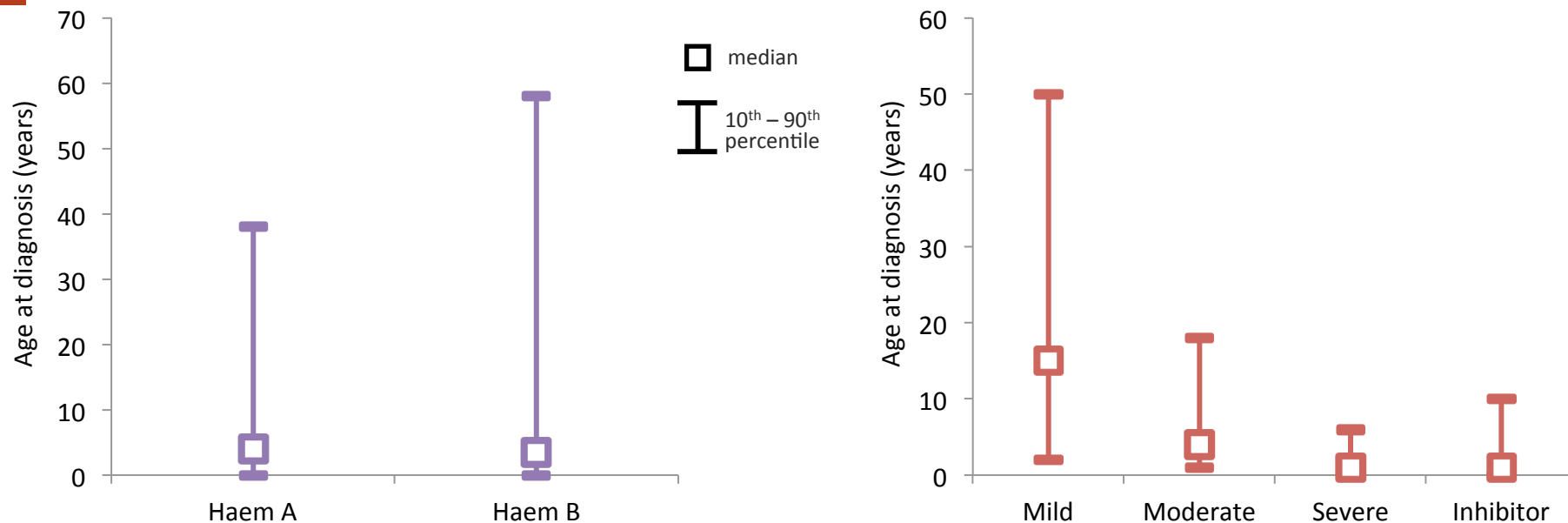


Haemophilia A	Haemophilia B	Current age* (years)	Mild*	Moderate*	Severe*	Inhibitor ⁺
199	34	N	104	48	81	7
10.0	8.9	Mean	9.8	10.4	9.5	7.3
10 (0 – 18)	8.5 (0 – 18)	Median (min – max)	9 (0 – 18)	10 (0 – 18)	9 (0 – 18)	7 (2 – 12)

*Current age = age reached in year 2013

* including persons with inhibitor
+ in 2013

Age at diagnosis according to type and severity of haemophilia

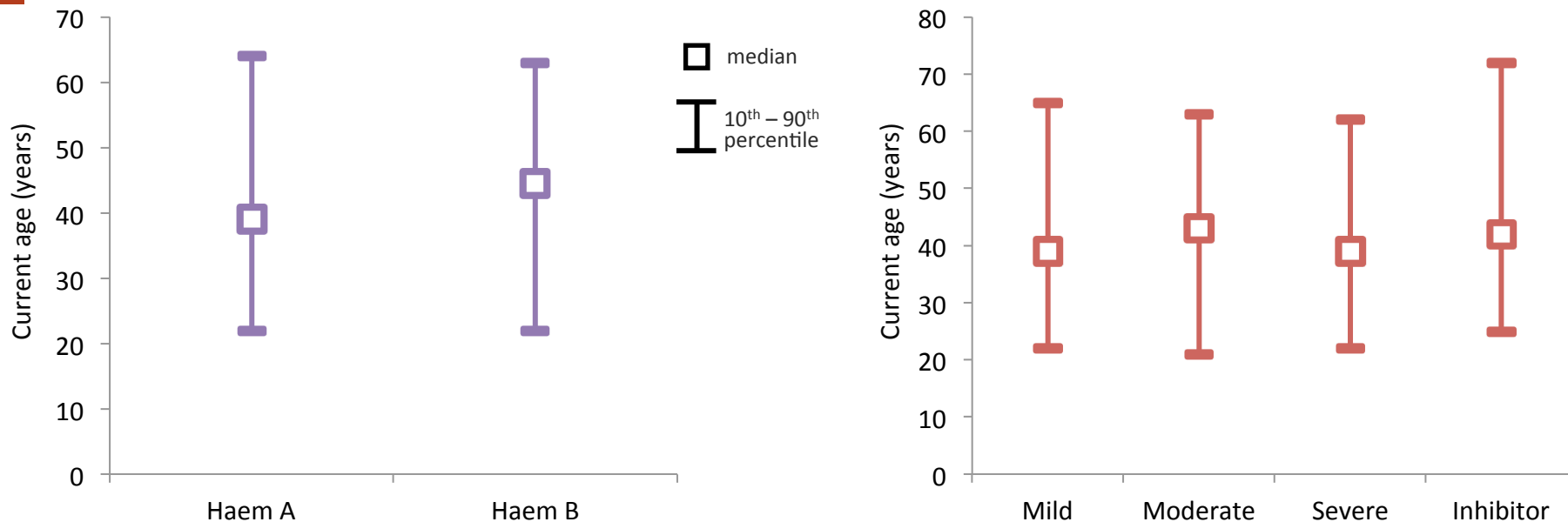


Haemophilia A	Haemophilia B	Age at diagnosis (years)	Mild*	Moderate*	Severe*	Inhibitor ⁺
357	54	N	192	53	165	5
12.1	11.6	Mean	20.4	8.0	2.7	3.8
4 (0 – 81)	3.5 (0 – 63)	Median (min – max)	15 (0 – 81)	4 (0 – 61)	1 (0 – 48)	1 (0 – 10)

* including persons with inhibitor

+ in 2013

Actual age according to type and severity of haemophilia



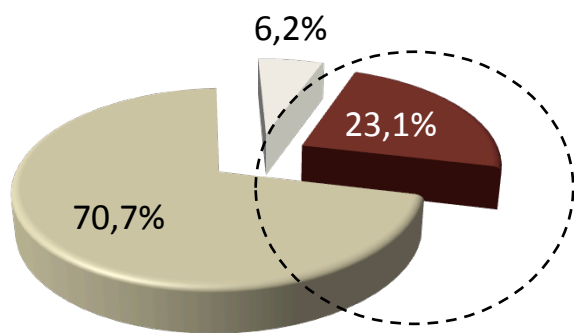
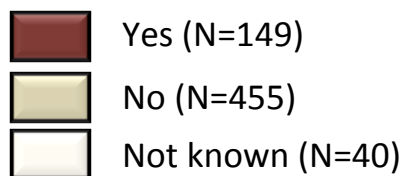
Haemophilia A	Haemophilia B	Current age* (years)	Mild*	Moderate*	Severe*	Inhibitor ⁺
357	54	N	192	53	165	5
42.3	43.0	Mean	43.1	43.4	41.2	46.4
39 (19 – 91)	44.5 (19 – 68)	Median (min – max)	39 (19 – 91)	43 (19 – 72)	39 (19 – 74)	42 (25 – 72)

*Current age = age reached in year 2013

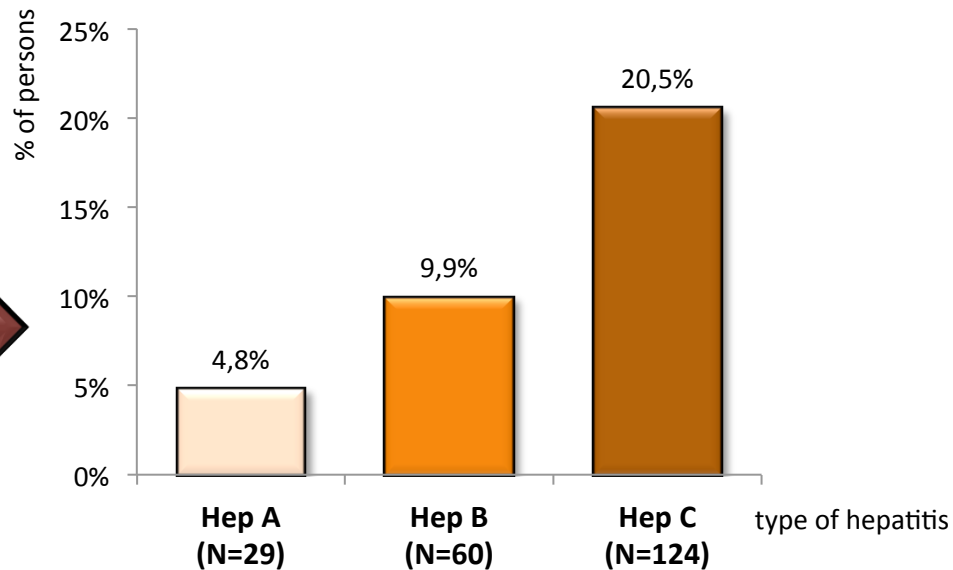
* including persons with inhibitor
+ in 2013

Hepatitis experienced

Experienced hepatitis



N=149



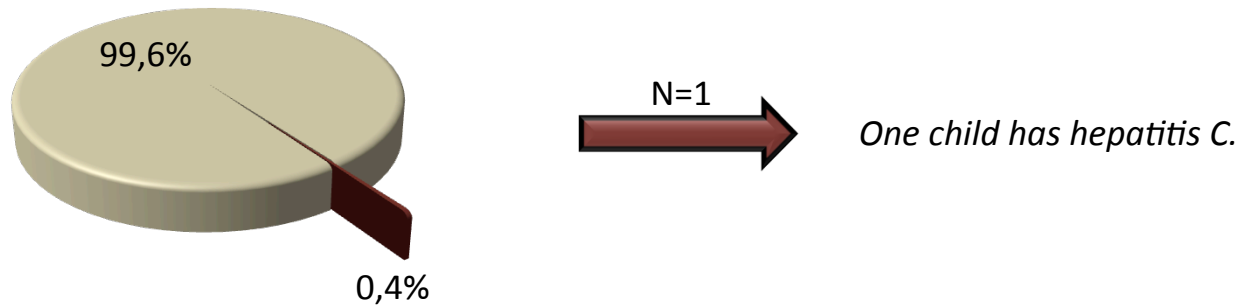
Data from last annual report of each person.

Type of hepatitis not specified in 2 persons. One person may have recorded more types of hepatitis.

Hepatitis experienced

Experienced hepatitis

- Yes (N=1)
- No (N=232)

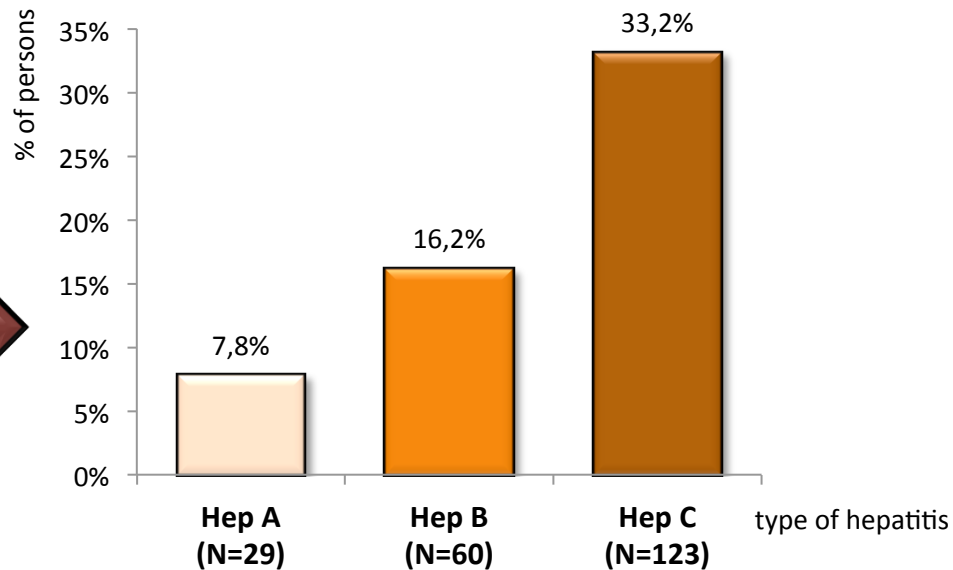
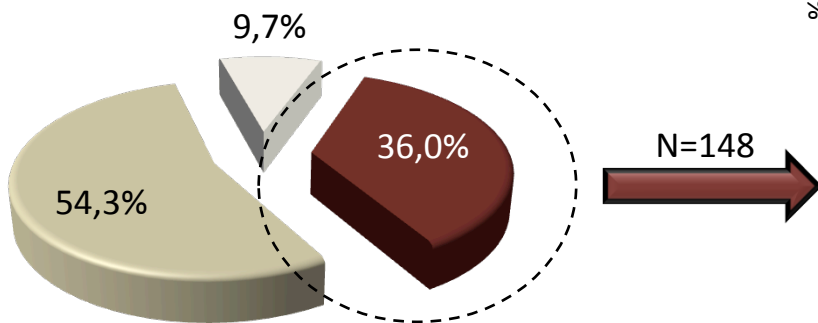


Data from last annual report of each person.

Hepatitis experienced

Experienced hepatitis

- Yes (N=148)
- No (N=223)
- Not known (N=40)

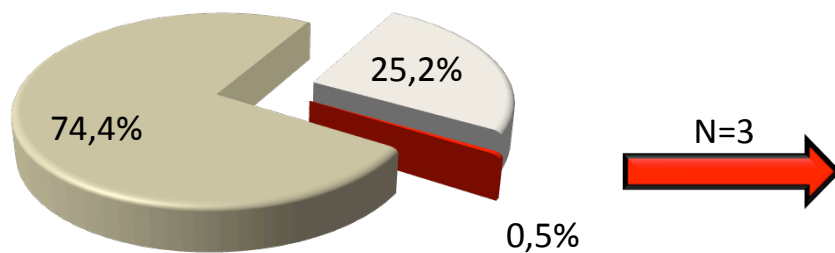
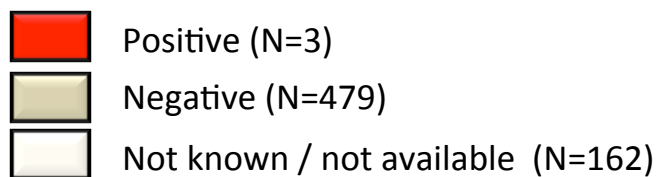


Data from last annual report of each person.

Type of hepatitis not specified in 2 adults. One person may have recorded more types of hepatitis.

HIV

HIV



All HIV-positive persons are adults.

Data from last annual report of each person.

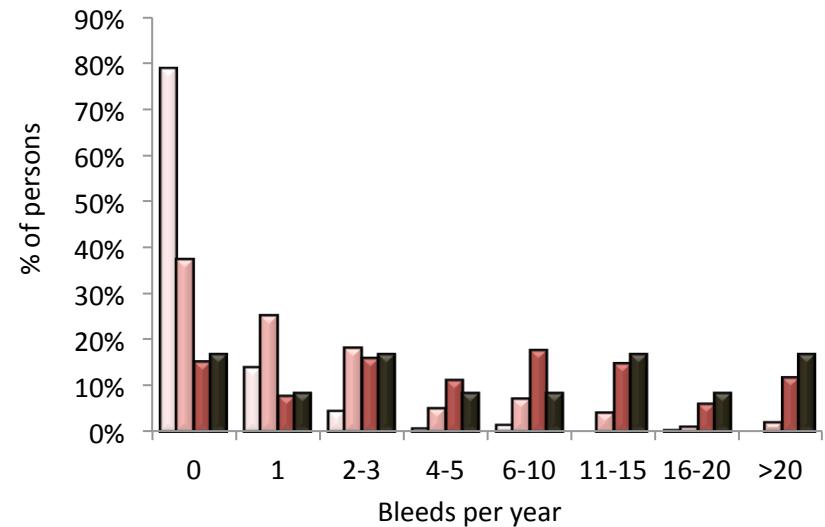
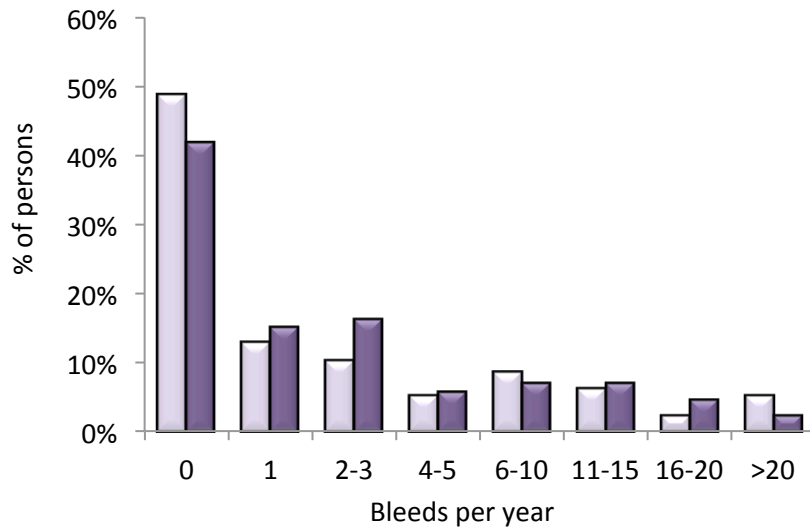
Data from year 2013 – sample size

	Valid persons		→	Persons with annual report in 2013		→	Persons examined in 2013		→	Persons treated in 2013	
	N	%		N	%		N	%		N	%
All	644	100%	→	634	98.4%	→	533	82.8%	→	370	57.5%
of them with inhibitor				12			12			10	
Children	233	100%	→	229	98.3%	→	213	91.4%	→	139	59.7%
of them with inhibitor				7			7			7	
Adults	411	100%	→	405	98.5%	→	320	77.9%	→	231	56.2%
of them with inhibitor				5			5			3	

Persons with haemophilia with inhibitors

- inhibitor was recorded in **12 persons** in year 2013
 - 7 children and 5 adults
 - 11 haemophilia A and 1 haemophilia B
 - 10 severe, 1 moderate and 1 mild haemophilia
 - 8 HR and 2 LR (other two patients had in 2013 low level of inhibitor due to by-pass therapy only)
 - 3 patients were treated with rFVIIa, 1 patient with aPCC, other 2 patients both with rFVIIa and aPCC
 - ITT was started in 3 children
 - 2 patients were without any recorded treatment

Frequency of bleeding requiring treatment in 2013



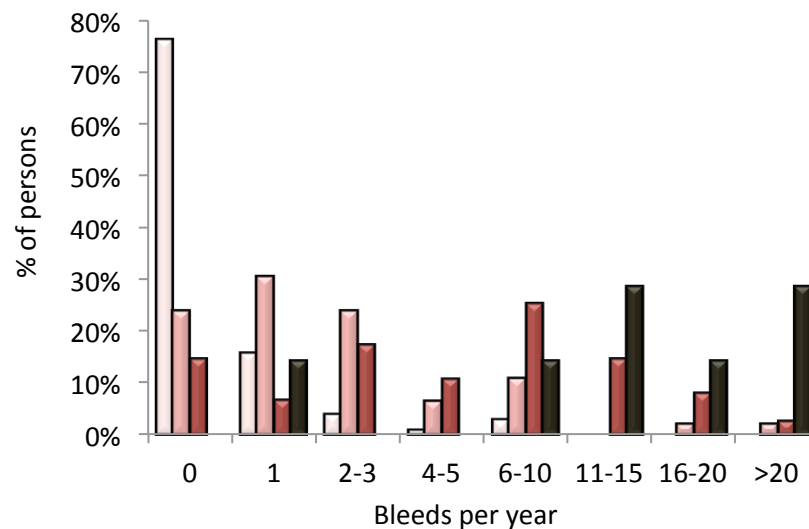
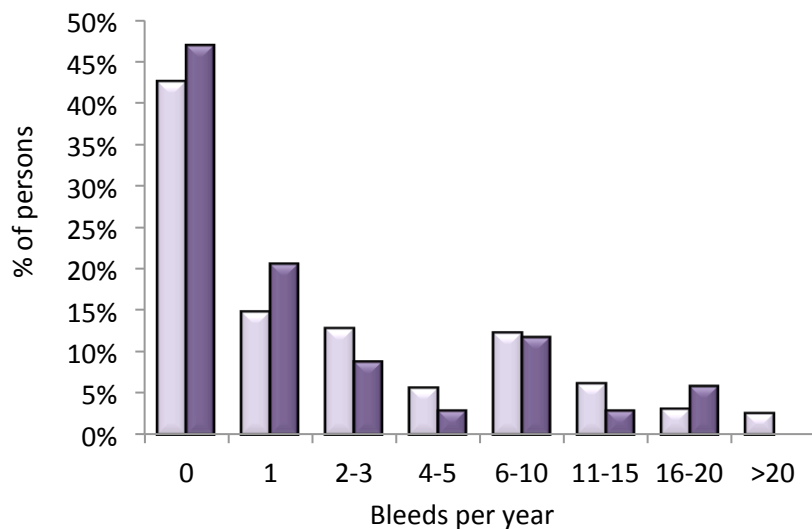
Haemophilia A	Haemophilia B	Frequency of bleeding	Mild*	Moderate*	Severe*	Inhibitor
547	87	N total	286	100	234	12
545	86	N valid	286	99	232	12
4.6	4.0	Mean	0.4	2.7	10 / 6.6[†]	9.7
1 (0 – 124)	1 (0 – 53)	Median (min – max)	0 (0 – 17)	1 (0 – 30)	5.5 / 4 (0 – 124)	6 (0 – 30)

* without inhibitor

[†] mean and median of frequency of bleeding in persons with severe haemophilia without inhibitor on permanent prophylaxis

Frequency of bleeding is missing in 207 persons.

Frequency of bleeding requiring treatment in 2013



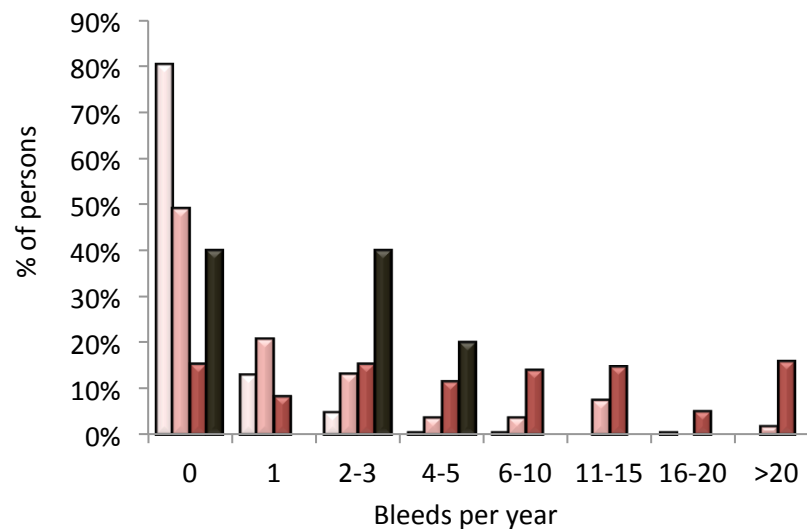
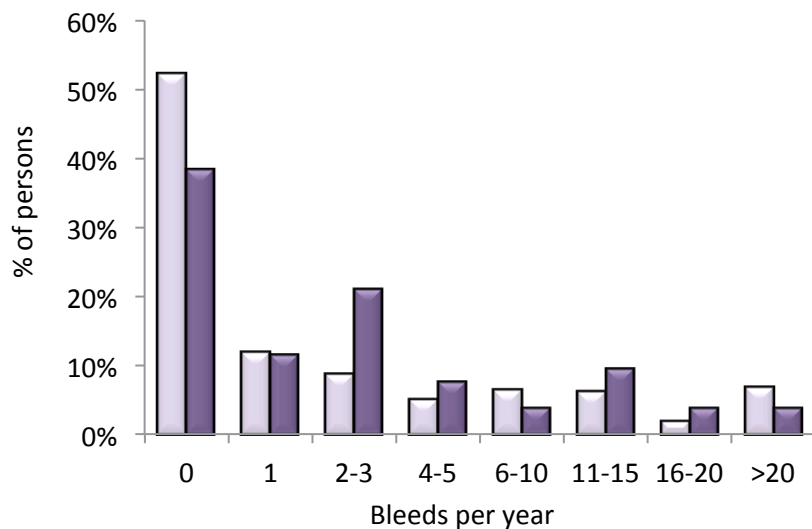
Haemophilia A	Haemophilia B	Frequency of bleeding	Mild*	Moderate*	Severe*	Inhibitor
195	34	N total	101	46	75	7
195	34	N valid	101	46	75	7
3.9	2.7	Mean	0.5	2.9	7.6 / 7.0[†]	15.3
1 (0 – 59)	1 (0 – 17)	Median (min – max)	0 (0 – 7)	1 (0 – 22)	6 / 6 (0 – 59)	12 (1 – 30)

* without inhibitor

[†] mean and median of frequency of bleeding in children with severe haemophilia without inhibitor on permanent prophylaxis

Frequency of bleeding is missing in 19 children.

Frequency of bleeding requiring treatment in 2013



Haemophilia A	Haemophilia B	Frequency of bleeding	Mild*	Moderate*	Severe*	Inhibitor
352	53	N total	185	54	159	5
350	52	N valid	185	53	157	5
4.9	4.8	Mean	0.4	2.5	11.2 / 6.3[†]	1.8
0 (0 – 124)	1.5 (0 – 53)	Median (min – max)	0 (0 – 17)	1 (0 – 30)	5 / 3 (0 – 124)	2 (0 – 5)

Frequency of bleeding is missing in 188 adults.

* without inhibitor

[†] mean and median of frequency of bleeding in adults with severe haemophilia without inhibitor on permanent prophylaxis

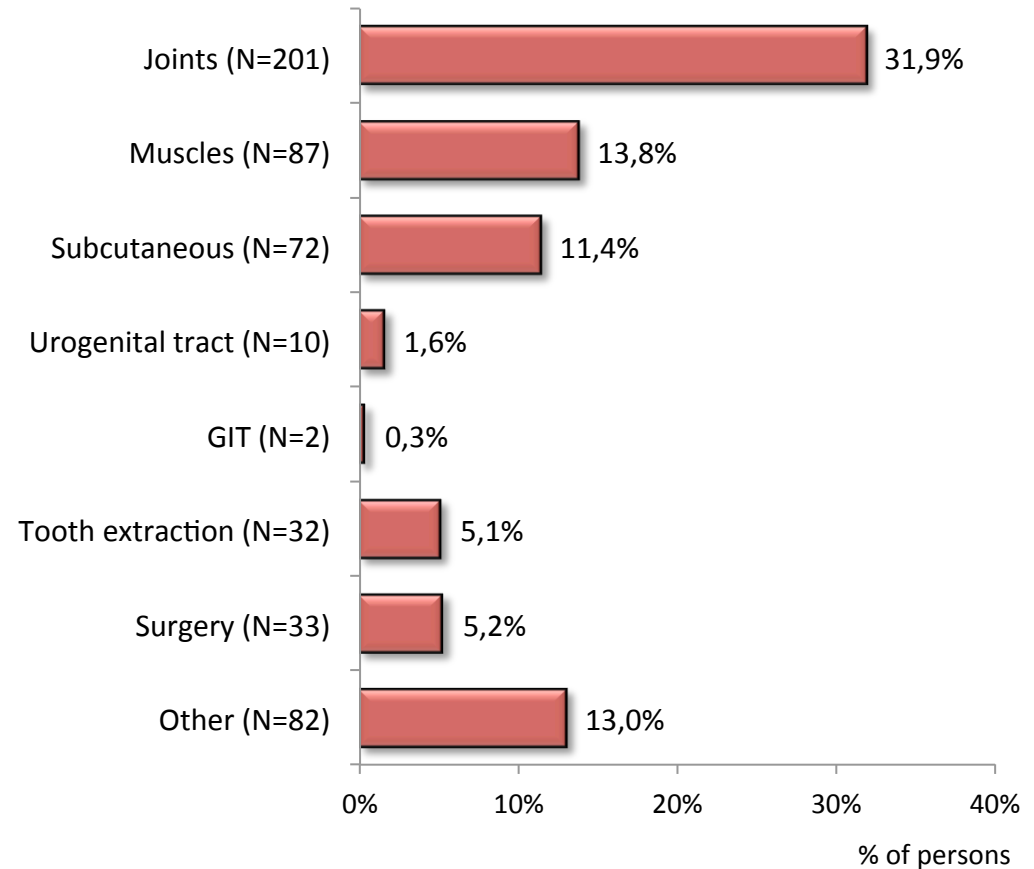
Location of (any) bleeds in 2013

329 (52.1%) persons experienced bleeding requiring treatment at least once per year; 2831 bleeds were recorded in total, 90 bleeds required hospitalization.

302 (47.9%) persons recorded no bleed during year 2013.

Information on frequency of bleeding is missing in 3 examined persons.

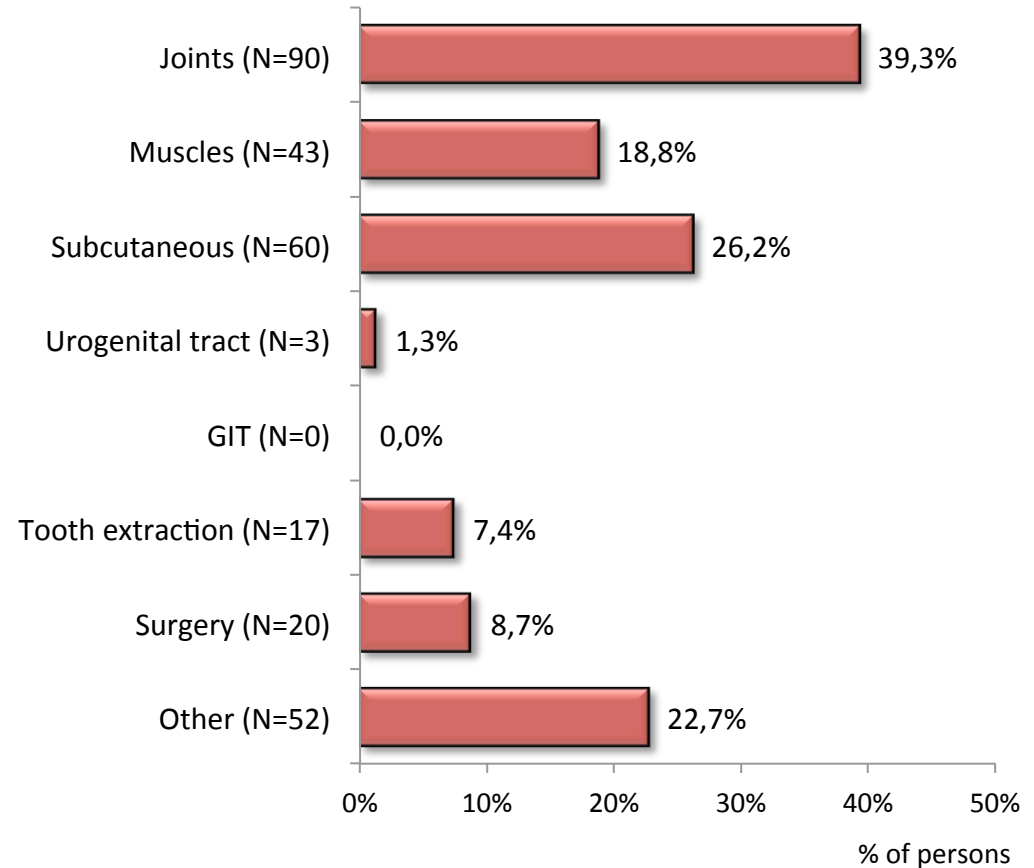
In total 271 persons recorded bleeds of any location *.



* all recorded bleeds, regardless of requirement of treatment

Location of (any) bleeds in 2013

130 (56.8%) children experienced bleeding requiring treatment at least once in year; 856 bleeds were recorded in total, 48 bleeds required hospitalization. 99 (43.2%) children recorded no bleed during year 2013. In total 133 persons recorded bleeds of any location*.



* all recorded bleeds, regardless of requirement of treatment

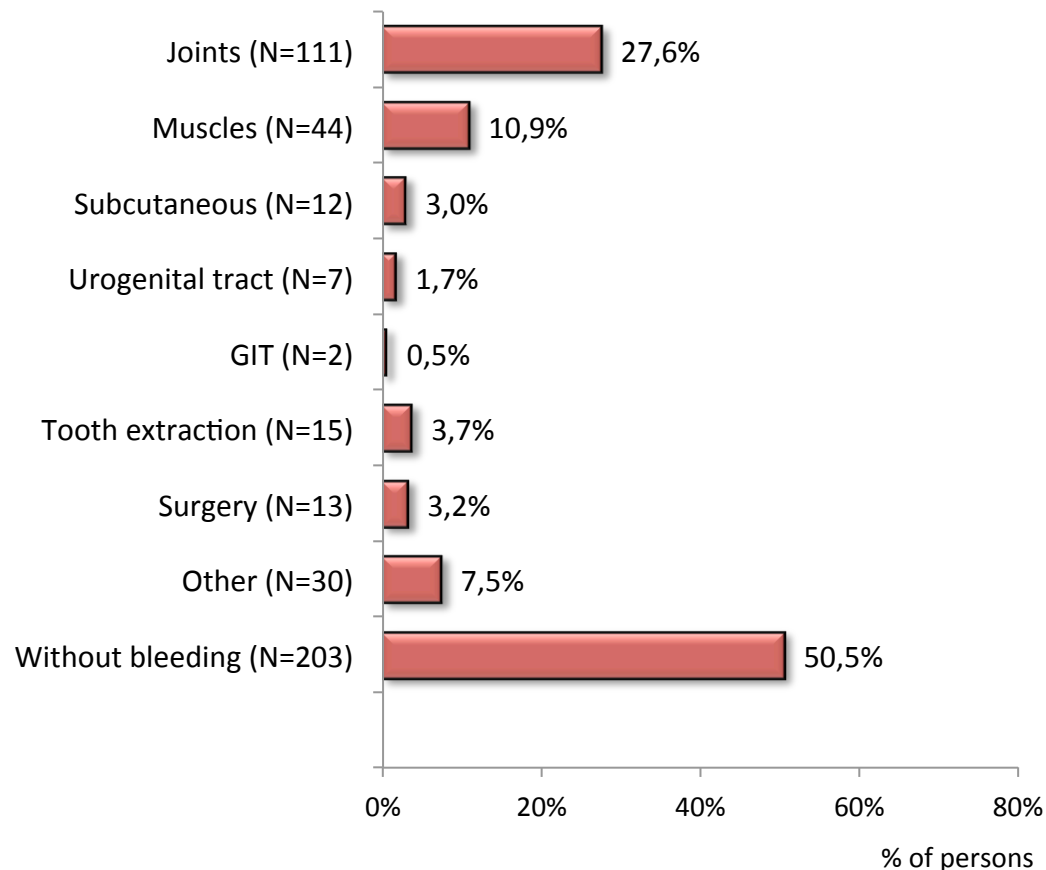
Location of (any) bleeds in 2013

199 (49.5%) adults experienced bleeding requiring treatment at least once in year; 1975 bleeds were recorded in total, 42 bleeds required hospitalization.

203 (50.5%) adults have recorded no bleed during year 2013.

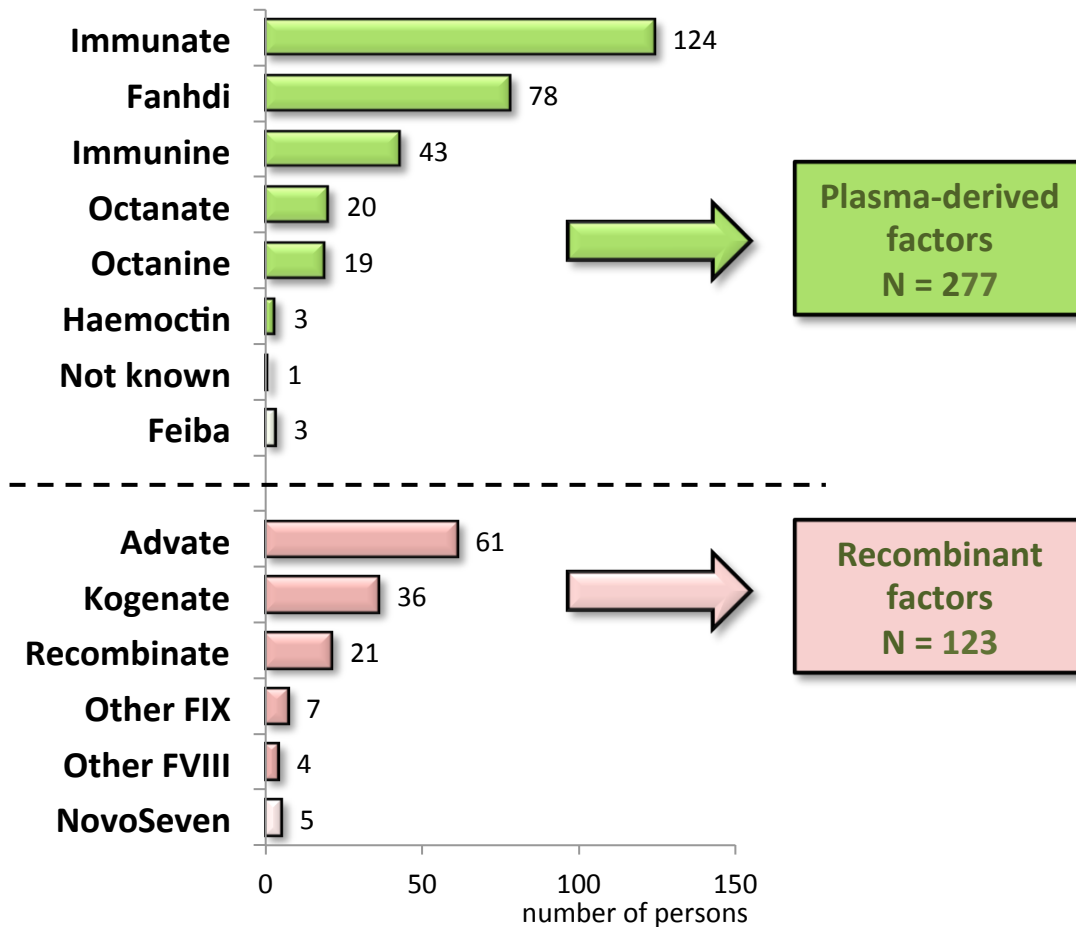
Information on frequency of bleeding is missing in 3 examined adults.

In total 138 persons recorded bleeds of any location*.



* all recorded bleeds, regardless of requirement of treatment

Treatment

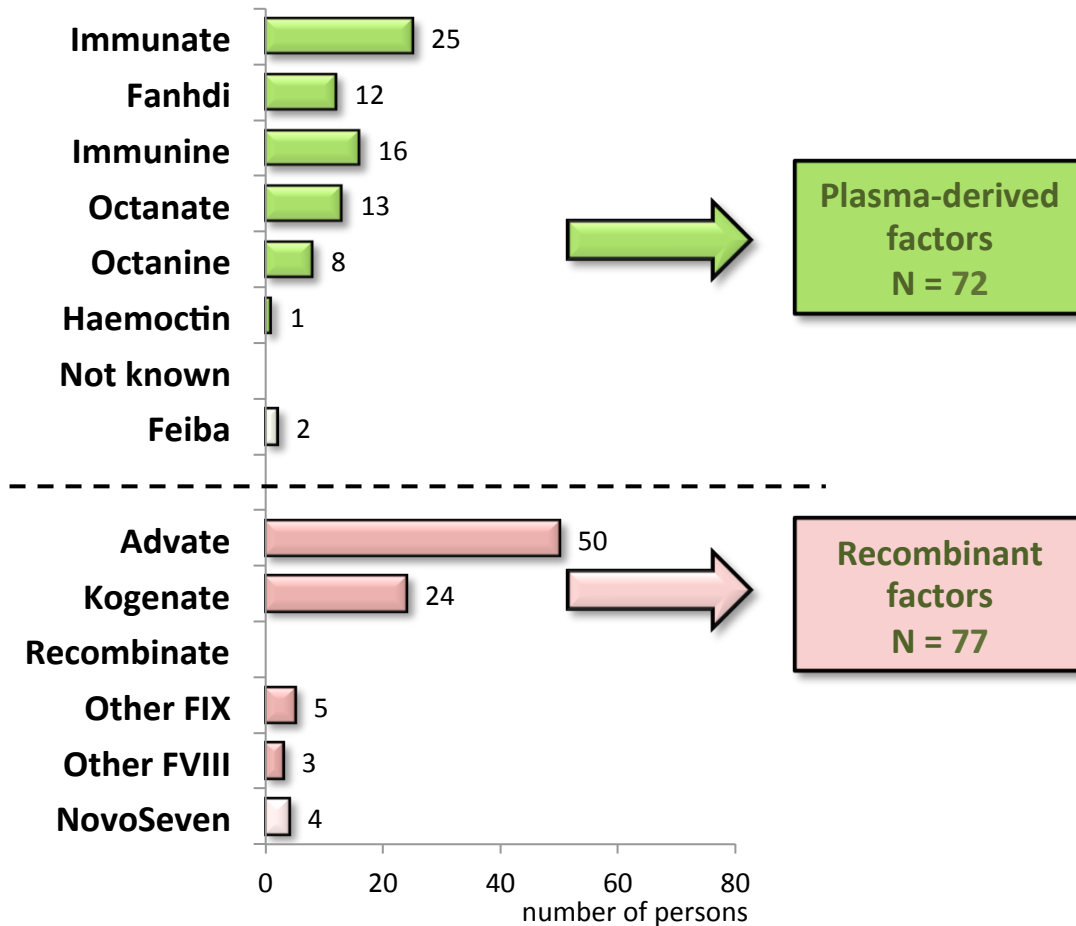


383 (60.4%) persons received factor concentrates in 2013 (39 of them received more than one type/make of concentrate).

Plasma-derived factors were administered more frequently – in 277 (43.7% of all PWHs) persons, whereas recombinant factors in 123 (19.4% of all PWHs) persons.

Twenty persons were treated with both plasma-derived and recombinant factor.

Treatment

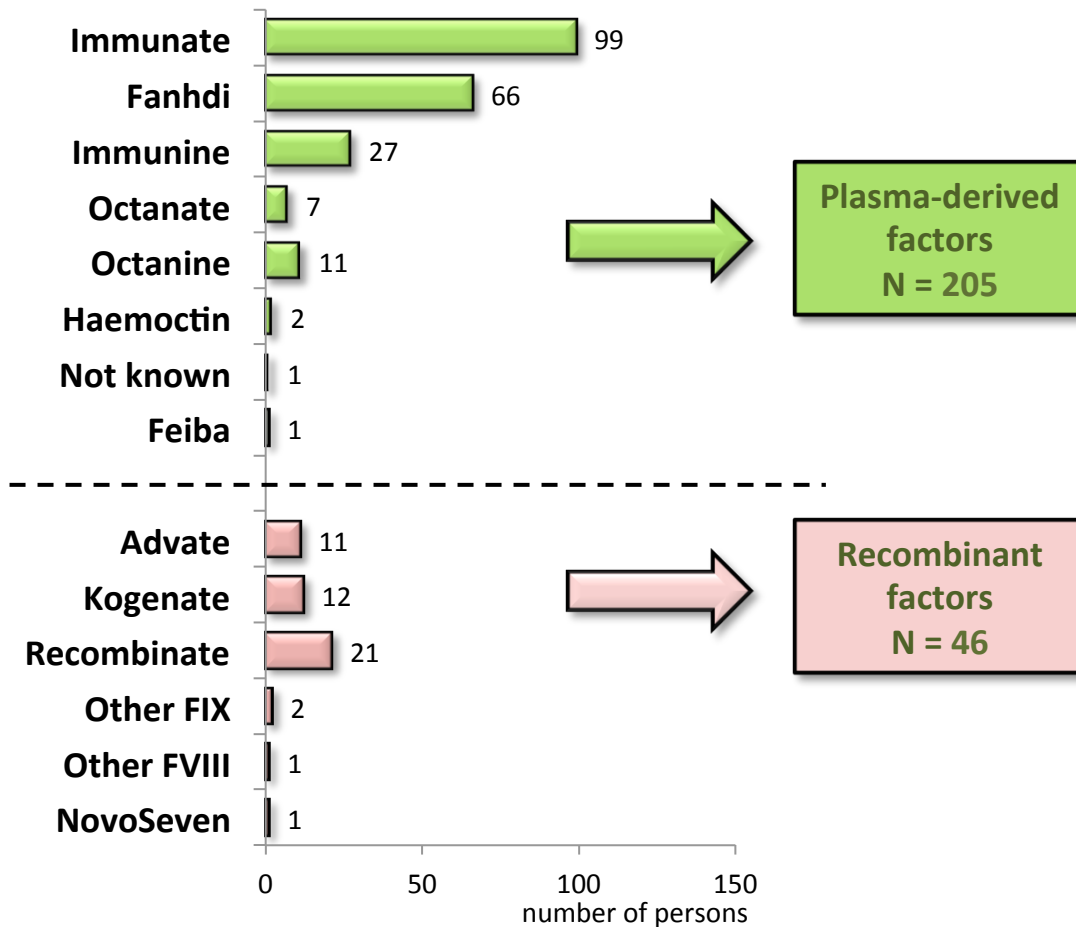


139 (60.7%) children received factor concentrates in 2013 (22 of them received more than one type/make of concentrate).

Plasma-derived factors were administered in 72 (31.4% of all) children, recombinant factors in 77 (33.6% of all) children.

Twelve children were treated with both plasma-derived and recombinant factor.

Treatment



244 (60.2%) adults received factor concentrates in 2013 (17 of them received more than one type/make of concentrate).

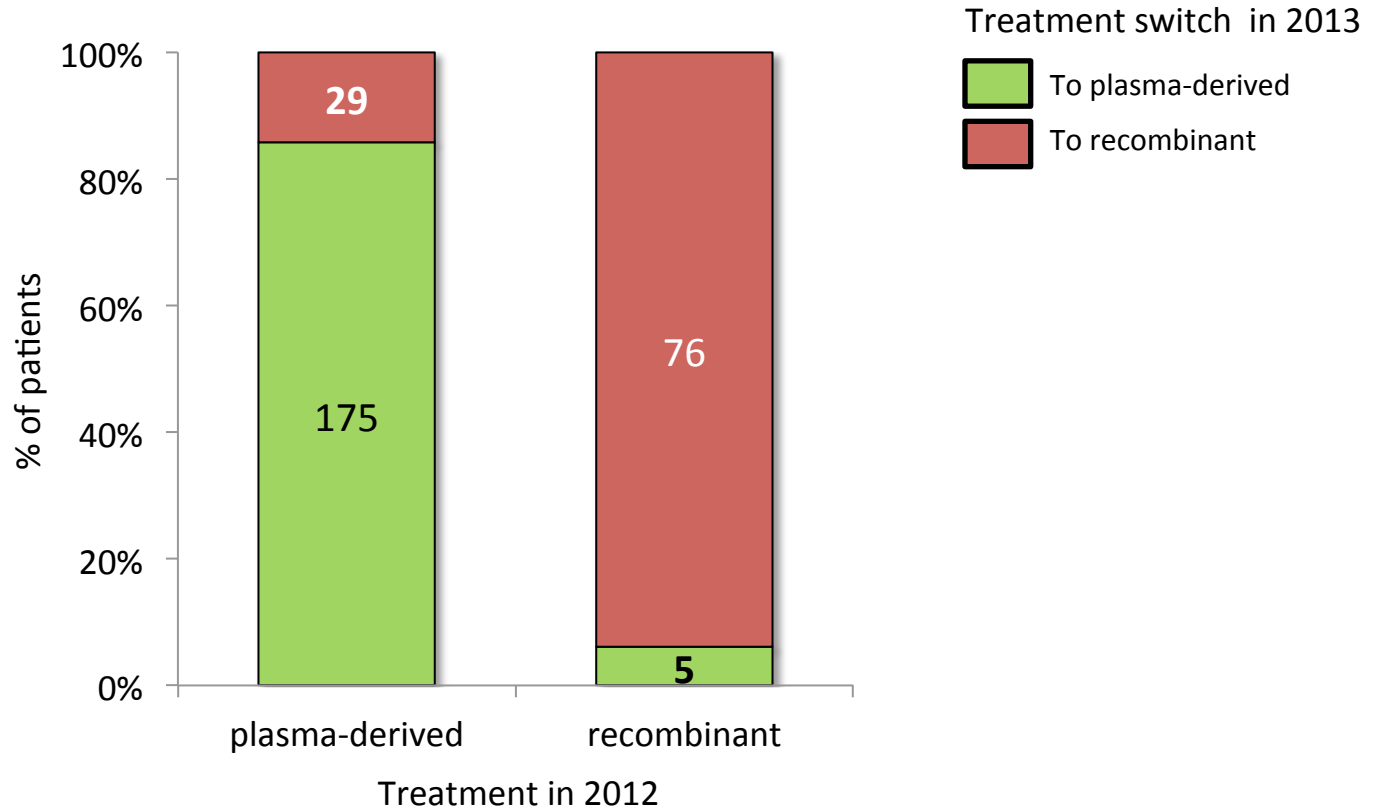
Plasma-derived factors were administered more frequently – in 205 (50.6% of all) adults, whereas recombinant factors in 46 (11.4% of all) adults.

Eight adults were treated with both plasma-derived and recombinant factor.

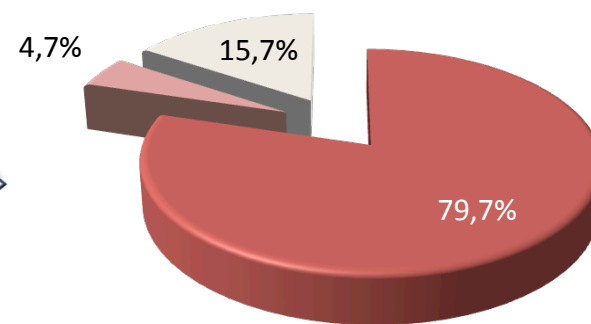
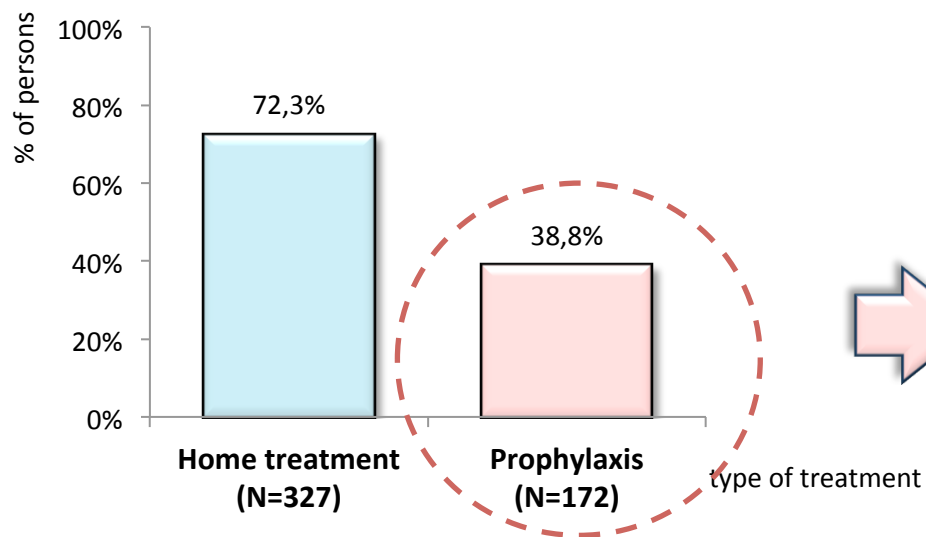
Comparison of treatment in years 2012 and 2013

		Treatment in 2013				
	Number of persons treated with:	Plasma-derived factor	Recombinant factor	All with treatment	Without treatment	Total
Treatment in 2012	Plasma-derived factor	175	<u>29</u>	188	40	228
		27.6%	4.6%	29.7%	6.3%	36.0%
	Recombinant factor	<u>5</u>	76	79	10	89
		0.8%	12.0%	12.5%	1.6%	14.0%
	All persons with treatment	177	99	260	51	311
		27.9%	15.6%	41.0%	8.0%	49.1%
	Without treatment	88	22	109	214	323
		13.9%	3.5%	17.2%	33.8%	50.9%
Total	265	121	369	265	634	
	41.8%	19.1%	58.2%	41.8%	100.0%	

Change of treatment in years 2012 and 2013



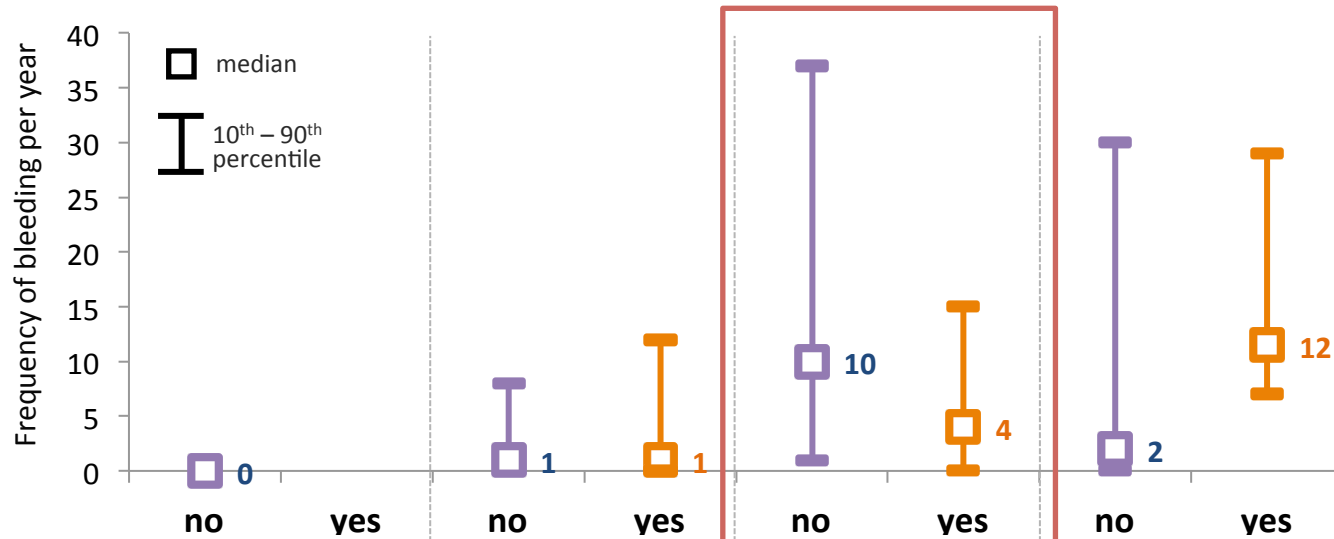
Type of treatment



Type of prophylaxis (N=172)

- Permanent (N=137)
- Temporary ≥12 weeks (N=8)
- Temporary <12 weeks (N=27)

Bleeding requiring treatment according to prophylaxis



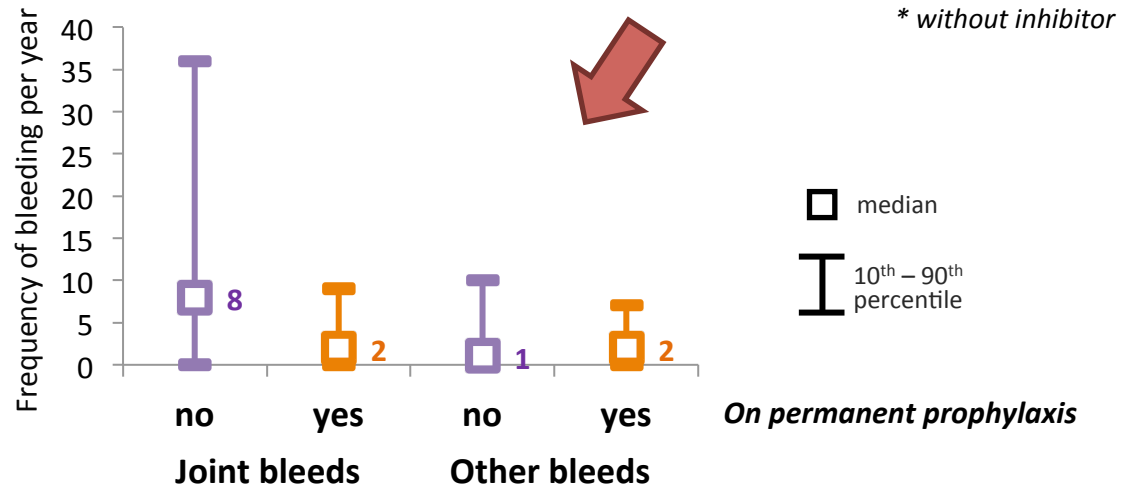
permanent prophylaxis

Frequency of bleeding	Mild*		Moderate*		Severe*		Inhibitor	
N	210	0	72	14	101	119	8	4
Mean	0.5		2.9	3.3	15.1	6.6	7.1	14.8
Median (min – max)	0 (0 – 7)		1 (0 – 30)	1 (0 – 16)	10 (0 – 124)	4 (0 – 45)	2 (0 – 30)	11.5 (7 – 29)
persons on permanent prophylaxis	0		14 (16.1%)		119 (53.6%)		4 (33.3%)	
% of drugs (FVIII and FIX) consumed by persons on permanent prophylaxis	-		4.8 %		63.5 %		3.9 %	

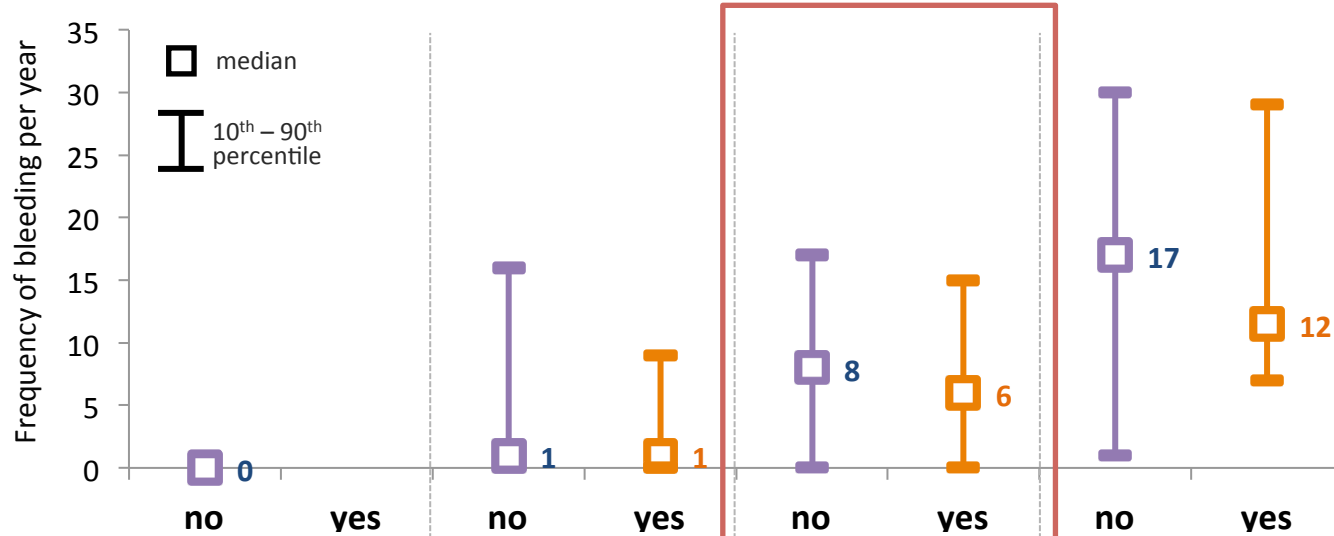
* without inhibitor

Joint and other bleeds according to prophylaxis

Frequency of bleeding	Mild*		Moderate*		Severe*		Inhibitor	
N total	210	0	72	14	101	119	8	4
N valid	193	0	63	13	71	96	6	4
JOINT BLEEDS								
Mean	0.1		1.4	2.7	13.7	3.7	4.5	6.3
Median (range)	0 (0-5)		0 (0-17)	1 (0-12)	8 (0-124)	2 (0-30)	0 (0-18)	6 (4-9)
Total bleeding rate	23		91	35	975	355	27	25
OTHER BLEEDS								
Mean	0.3		1.4	0.8	3.2	2.8	3.8	8.5
Median (range)	0 (0-5)		0 (0-13)	0 (0-6)	1 (0-36)	2 (0-16)	1.5 (0-12)	5.5 (3-20)
Total bleeding rate	52		88	10	226	264	23	34



Bleeding requiring treatment according to prophylaxis



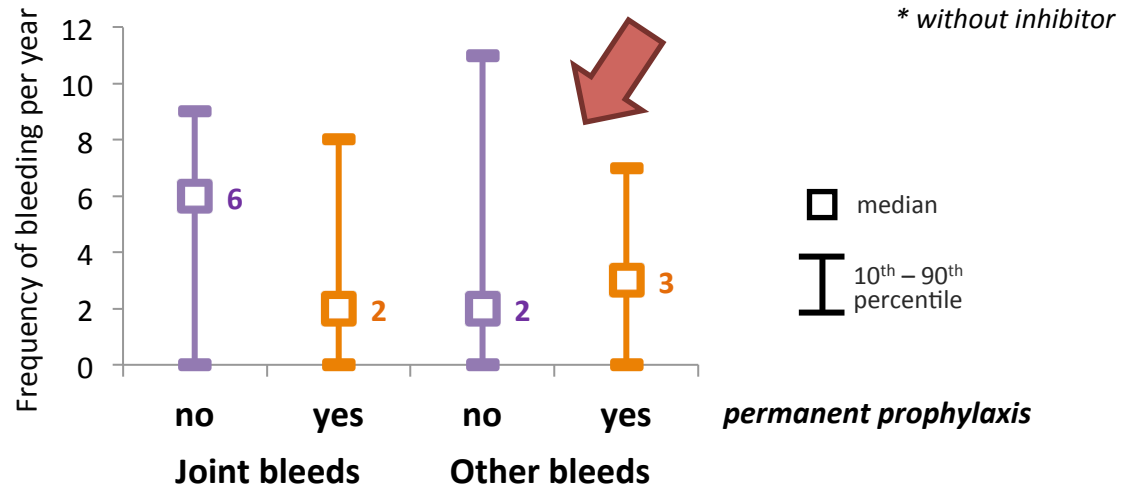
permanent prophylaxis

Frequency of bleeding	Mild*		Moderate*		Severe*		Inhibitor	
N	88		38	7	11	62	3	4
Mean	0.5		2.9	3.3	12.3	7.0	16.0	14.8
Median (min – max)	0 (0 – 7)		1 (0 – 22)	1 (0 – 16)	8 (0 – 59)	6 (0 – 45)	17 (1 – 30)	11.5 (7 – 29)
children on permanent prophylaxis	0 (0%)		7 (15.6%)		62 (84.9%)		4 (57.1%)	
% of drugs (FVIII and FIX) consumed by children on permanent prophylaxis	0 %		6.6 %		75.6 %		10.2 %	

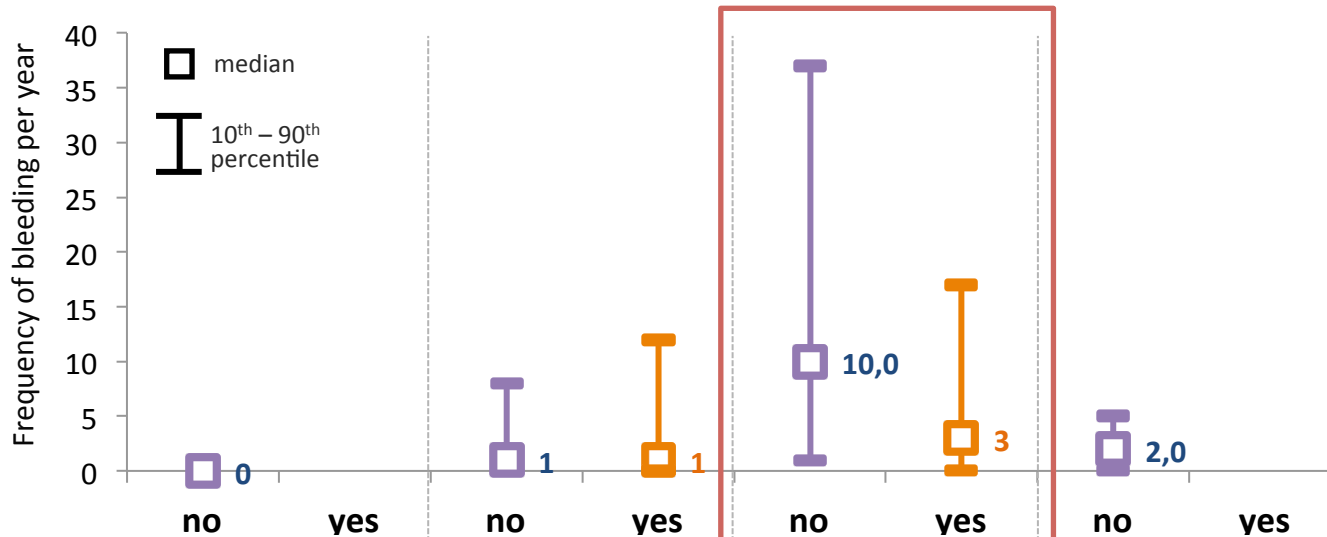
* without inhibitor

Joint and other bleeds according to prophylaxis

Frequency of bleeding	Mild*		Moderate*		Severe*		Inhibitor	
N total	88	0	38	7	11	62	3	4
N valid	86	0	38	7	11	61	3	4
JOINT BLEEDS								
Mean	0.2		1.3	1.9	5.7	3.6	9.0	6.3
Median (range)	0 (0-4)		1 (0-10)	1 (0-10)	6 (0-23)	2 (0-29)	9 (0-18)	6 (4-9)
Total bleeding rate	13		50	13	63	222	27	25
OTHER BLEEDS								
Mean	0.4		1.6	1.4	6.5	3.4	7.0	8.5
Median (range)	0 (0-5)		1 (0-12)	0 (0-6)	2 (0-36)	3 (0-16)	8 (1-12)	5.5 (3-20)
Total bleeding rate	33		61	10	72	209	21	34



Bleeding requiring treatment according to prophylaxis



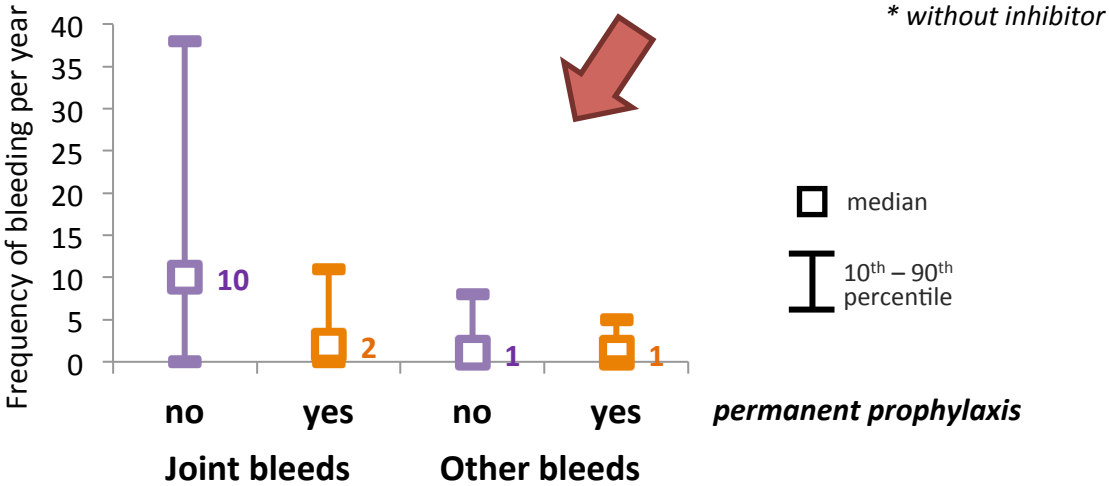
permanent prophylaxis

Frequency of bleeding	Mild*		Moderate*		Severe*		Inhibitor	
N	122	0	34	7	90	57	5	0
Mean	0.4		2.8	3.3	15.5	6.3	1.8	
Median (min – max)	0 (0 – 6)		1 (0 – 30)	1 (0 – 12)	10 (0 – 124)	3 (0 – 35)	2 (0 – 5)	
adults on permanent prophylaxis	0		7 (16.7%)		57 (38.3%)		0	
% of drugs (FVIII and FIX) consumed by adults on permanent prophylaxis	-		3.7 %		56.2 %		-	

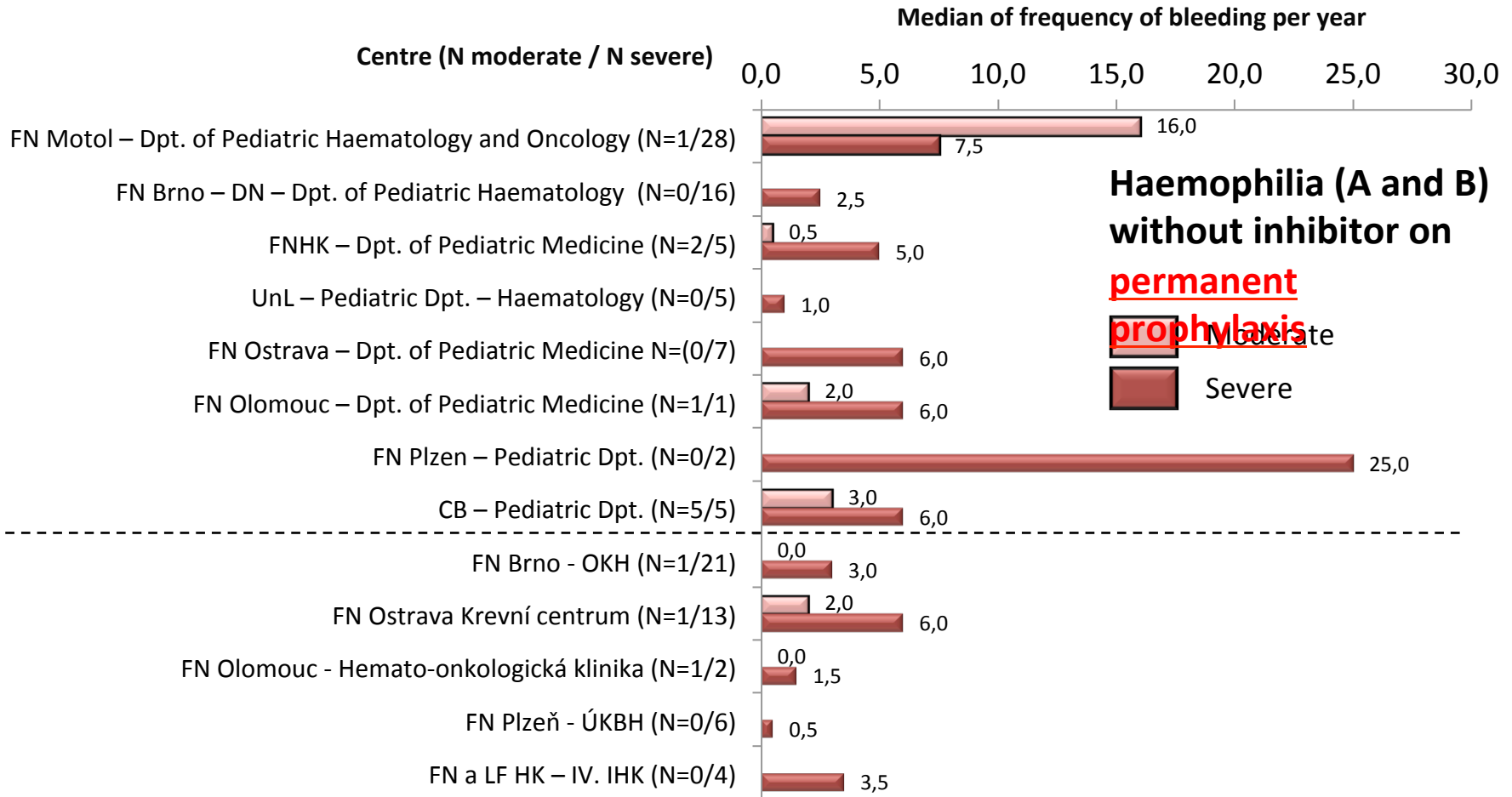
* without inhibitor

Joint and other bleeds according to prophylaxis

Frequency of bleeding	Mild*		Moderate*		Severe*		Inhibitor	
N total	122	0	34	7	90	57	5	0
N valid	107	0	25	6	60	35	3	0
JOINT BLEEDS								
Mean	0.1		1.6	3.7	15.2	3.8	0	
Median (range)	0 (0-5)		0 (0-17)	1 (0-12)	10 (0-124)	2 (0-30)	0	
Total bleeding rate	10		41	22	909	133	0	
OTHER BLEEDS								
Mean	0.2		1.1	0.0	2.6	1.6	0.7	
Median (range)	0 (0-3)		0 (0-13)	0	1 (0-24)	1 (0-8)	0 (0-2)	
Total bleeding rate	19		27	0	154	55	2	



Bleeding requiring treatment according to centres



Bleeding requiring treatment according to centres



Frequency of bleeding in children with haemophilia (A and B) without inhibitor on **permanent prophylaxis**

Child centres	0	10	20	30	N	Mean	Median	Min	Max	Severity
FN Motol – Dpt. of Pediatric Haematology and Oncology	16,0				1	16.0	16.0			Moderate
	7,5				28	8.5	7.5	0	20	Severe
FN Brno – DN – Dpt. of Pediatric Haematology	2,5				16	4.4	2.5	0	17	Severe
	0,5				2	0.5	0.5	0	1	Moderate
FNHK – Dpt. of Pediatric Medicine	5,0				5	4.2	5.0	2	6	Severe
	1,0				5	2.0	1.0	0	6	Severe
FN Ostrava – Dpt. of Pediatric Medicine	6,0				7	7.4	6.0	0	17	Severe
	2,0				1	3.0	3.0			Moderate
FN Olomouc – Dpt. of Pediatric Medicine	6,0									
	25,0				2	25.0	25.0	5	45	Severe
FN Plzen – Pediatric Dpt.	3,0				5	4.8	3.0	0	12	Moderate
	6,0				5	9.4	6.0	1	25	Severe

Bleeding requiring treatment according to centres



Frequency of bleeding in adults with haemophilia (A and B) without inhibitor on **permanent prophylaxis**

Adult centres	0,0	2,0	4,0	6,0	8,0	N	Mean	Median	Min	Max	Severity
FN Brno – OKH	0,0					1	0.0	0.0			Moderate
		3,0				21	6.2	3.0	0	26	Severe
FN Ostrava – Blood centre	2,0					1	2.0	2.0			Moderate
			6,0			13	8.8	6.0	0	35	Severe
FN Olomouc – Haemato-Oncology Dpt.	0,0					1	0.0	0.0			Moderate
		1,5				2	1.5	1.5	0	3	Severe
FN Plzen – UKBH		0,5				6	3.0	0.5	0	15	Severe
FN a LF HK – IV. IHK			3,5			4	5.8	3.5	1	15	Severe

Bleeding requiring treatment according to centres



Frequency of bleeding in children with haemophilia (A and B) without inhibitor **regardless of prophylaxis**

Child centres	0	5	10	N	Mean	Median	Min	Max	% on permanent prophylaxis
FN Motol – Dpt. of Pediatric Haematology and Oncology	2,0			14	4.6	2.0	0	22	7.1
		8,0		37	8.6	8.0	0	20	75.7
FN Brno – DN – Dpt. of Pediatric Haematology	1,0			7	1.4	1.0	0	4	0.0
		2,0		17	4.2	2.0	0	17	94.1
FNHK – Dpt. of Pediatric Medicine	1,0			9	1.2	1.0	0	3	22.2
		5,0		5	4.2	5.0	2	6	100.0
UnL – Pediatric Dpt. – Haematology	0,0			2	0.0	0.0	0	0	0.0
		1,0		7	2.6	1.0	0	8	71.4
FN Ostrava – Dpt. of Pediatric Medicine	3,5			8	4.8	3.5	0	10	0.0
		4,5		10	11.2	4.5	0	59	70.0
FN Olomouc – Dpt. of Pediatric Medicine	1,0			3	1.0	1.0	0	2	33.3
		6		1	6.0	6.0			100.0
FN Plzen – Pediatric Dpt.		5,0		3	16.7	5.0	0	45	66.7
CB – Pediatric Dpt.	3,0			7	4.3	3.0	0	12	71.4
		6,0		5	9.4	6.0	1	25	100.0

Bleeding requiring treatment according to centres

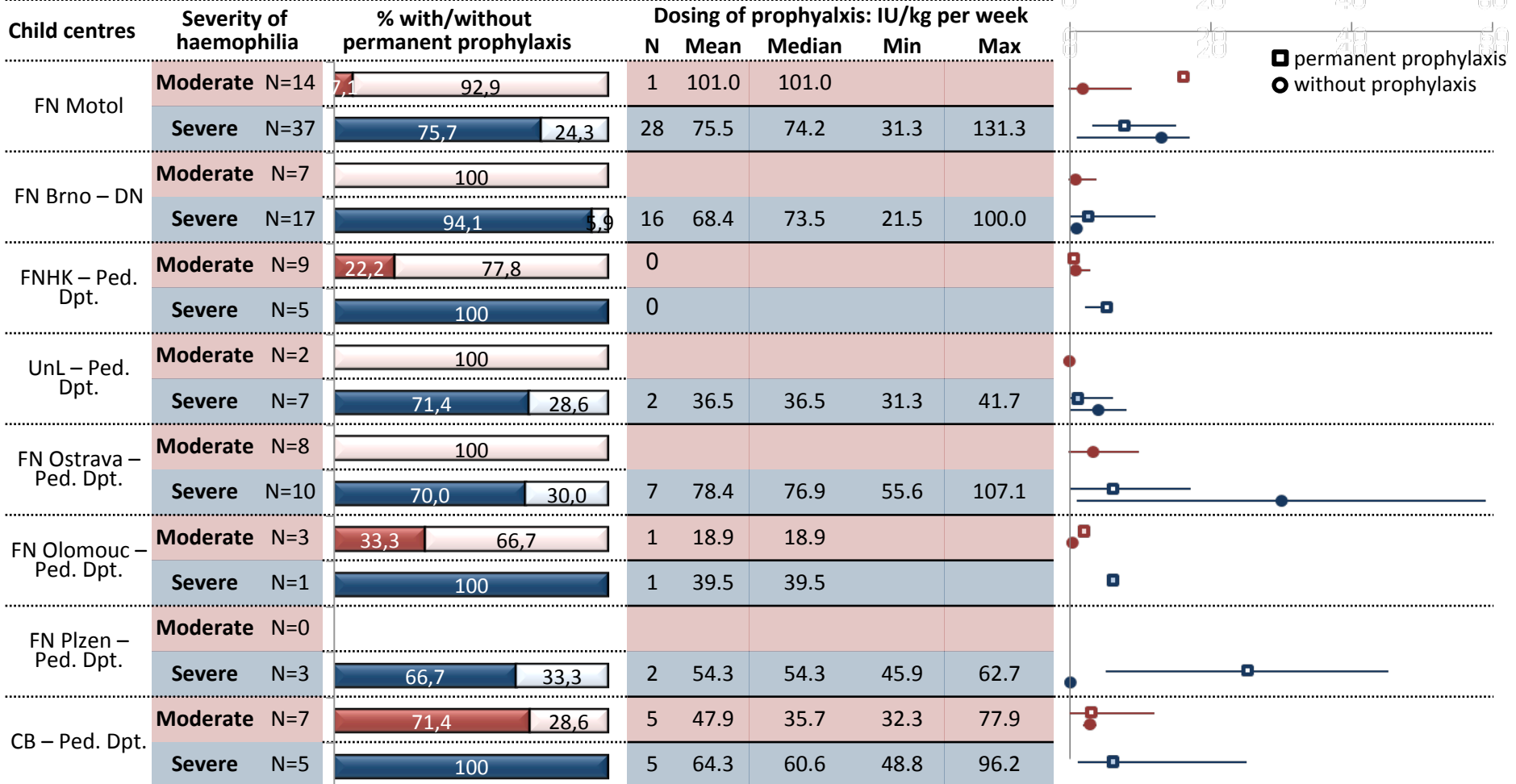


Frequency of bleeding in adults with haemophilia (A and B) without inhibitor **regardless of prophylaxis**

Adult centres	0,0	5,0	10,0	15,0	20,0	N	Mean	Median	Min	Max	% on permanent prophylaxis
FN Brno – OKH	0,0					21	1.8	0.0	0	12	4.8
		4,0				39	7.8	4.0	0	30	53.8
FN Ostrava – Blood centre		4,0				7	8.4	4.0	0	30	14.3
			7,0			31	10.5	7.0	0	35	41.9
FN Olomouc – Haemato-Oncology Dpt.	0,5					8	0.8	0.5	0	2	12.5
			14,0			23	17.9	14.0	0	53	8.7
FN Plzen – UKBH	1					5	1.0	1.0	0	3	0.0
		5,0				19	9.4	5.0	0	35	31.6
FN a LF HK – IV. IHK	0,0					1	0.0	0.0			0.0
			18,0			10	34.6	18.0	1	124	40.0

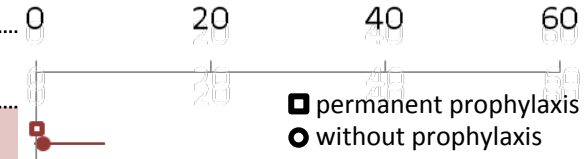
Prophylaxis according to centres

Frequency of bleeding
(median, 10th and 90th percentile)



Prophylaxis according to centres

Frequency of bleeding
(median, 10th and 90th percentile)



Adult centres	Severity of haemophilia	N	% with/without prophylaxis	Dosing of prophylaxis: IU/kg per week			
				N	Mean	Median	Min
FN Brno – OKH	Moderate	N=21	95,2	0			
	Severe	N=39	53,8 / 46,2	21	51.3	48.4	26.9 / 105.3
FN Ostrava – Blood centre	Moderate	N=7	14,3 / 86	0			
	Severe	N=31	41,9 / 58,1	0			
FN Olomouc – HOK	Moderate	N=8	12,5 / 87,5	1	11.8	11.8	
	Severe	N=23	8,7 / 91,3	2	28.9	28.5	14.9 / 42.9
FN Plzen – UKBH	Moderate	N=5	100				
	Severe	N=19	31,6 / 68,4	0			
FN a LF HK – IV. IHK	Moderate	N=1	100				
	Severe	N=10	40,0 / 60,0	3	23.7	21.7	0.9 / 48.4

Consumption of drugs

Drug	Total annual consumption	Number of treated persons	Average annual consumption per treated person	Number of examined persons	Average annual consumption per examined person
<i>Immunate</i>	8 447 750 IU	124	68 127.0 IU		17 822.3 IU
<i>Fanhdi</i>	5 870 250 IU	78	75 259.6 IU		12 384.5 IU
<i>Octanate</i>	2 080 750 IU	20	104 037.5 IU		4 389.8 IU
<i>Haemoctin</i>	381 500 IU	3	127 166.7 IU		804.9 IU
FVIII				474	
<i>Advate</i>	4 026 993 IU	61	66 016.3 IU		8 495.8 IU
<i>Kogenate</i>	5 300 750 IU	36	147 243.1 IU		11 183.0 IU
<i>Recombinate</i>	1 858 000 IU	21	88 476.2 IU		3 919.8 IU
<i>Bax 855</i>	96 284 IU	5	19 256.8 IU		203.1 IU
<i>Other recombinant</i>	241 500 IU	4	60 375.0 IU		509.5 IU
FVIII celkem	28 303 777 IU	322	87 899.9 IU		59 712.6 IU
<i>Immunine</i>	1 633 040 IU	43	37 977.7 IU		21 208.3 IU
<i>Octanine</i>	1300880 IU	19	68 467.4 IU		16 894.5 IU
<i>Other recombinant</i>	639 957 IU	4	159 989.3 IU	77	8 311.1 IU
FIX celkem	3 573 877 IU	58	61 618.6 IU		46 414.0 IU
aPCC					
<i>Feiba</i>	35 000 IU	3	11 666.7 IU		
rFVIIa					
<i>NovoSeven</i>	1140 mg	5	228.0 mg		
Plasma-derived factors - TOTAL*	19 714 170 IU	277	71 170.3 IU		35 585.1 IU
Recombinant factors - TOTAL*	12 163 484 IU	123	98 890.1 IU	554	21 955.7 IU
TOTAL CONSUMPTION *	31 877 654 IU	383	83 231.5 IU		57 540.9 IU

•plasma-derived factors = Immunate, Fanhdi, Octanate, Immunine, Octanine, Other plasma-derived

•recombinant factors = Advate, Kogenate, Recombinate, BAX 326, Other recombinant

*TOTAL CONSUMPTION = all mentioned drugs excluding Feiba and NovoSeven

Consumption of drugs

Drug	Total annual consumption	Number of treated persons	Average annual consumption per treated child	Number of examined children	Average annual consumption per examined child
<i>Immunate</i>	1 633 500 IU	25	65 340.0 IU		8 926.2 IU
<i>Fanhdi</i>	1 158 250 IU	12	96 520.8 IU		6 329.2 IU
<i>Octanate</i>	1 692 750 IU	13	130 211.5 IU		9 250.0 IU
<i>Haemoctin</i>	165 000 IU	1	165 000.0 IU		901.6 IU
FVIII				183	
<i>Advate</i>	2 838 993 IU	50	56 779.9 IU		15 513.6 IU
<i>Kogenate</i>	2 200 750 IU	24	91 697.9 IU		12 026.0 IU
<i>BAX 855</i>	65 284 IU	3	21 761.3 IU		356.7 IU
<i>Studie gena 13</i>	241 500 IU	4	60 375.0 IU		1 319.7 IU
FVIII celkem	9 996 027 IU	116	86 172.6 IU		54 623.1 IU
<i>Immunine</i>	575 140 IU	16	35 946.3 IU		17 428.5 IU
<i>Octanine</i>	267 580 IU	8	33 447.5 IU	33	8 108.5 IU
<i>Other recombinant</i>	212 214 IU	3	70 738.0 IU		6 430.7 IU
FIX celkem	1 054 934 IU	21	50 235.0 IU		31 967.7 IU
aPCC					
<i>Feiba</i>	23 000 IU	2	11 500.0 IU		
rFVIIa					
<i>NovoSeven</i>	695 mg	4	173.8 mg		
Plasma-derived factors - TOTAL*	5 492 220 IU	72	76 280.8 IU		25 426.9 IU
Recombinant factors - TOTAL*	5 558 741 IU	77	72 191.4 IU	216	25 734.9 IU
TOTAL CONSUMPTION *	11 050 961 IU	139	79 503.3 IU		51 161.9 IU

•plasma-derived factors = Immunate, Fanhdi, Octanate, Immunine, Octanine, Other plasma-derived

•recombinant factors = Advate, Kogenate, Recombinate, BAX 326, Other recombinant

*TOTAL CONSUMPTION = all mentioned drugs excluding Feiba and NovoSeven

Consumption of drugs

Drug	Total annual consumption	Number of <u>treated</u> persons	Average annual consumption per <u>treated</u> person	Number of <u>examined</u> adults	Average annual consumption per <u>examined</u> adult
<i>Immunate</i>	6 814 250 IU	99	68 830.8 IU		23 416.7 IU
<i>Fanhdi</i>	4 712 000 IU	66	71 393.9 IU		16 192.4 IU
<i>Octanate</i>	388 000 IU	7	55 428.6 IU		1 333.3 IU
<i>Haemoctin</i>	216 500 IU	2	108 250.0 IU		744.0 IU
FVIII				291	
<i>Advate</i>	1 188 000 IU	11	108 000.0 IU		4 082.5 IU
<i>Kogenate</i>	3 100 000 IU	12	258 333.3 IU		10 652.9 IU
<i>Recombinate</i>	1 858 000 IU	21	88 476.2 IU		6 384.9 IU
<i>BAX 855</i>	31 000 IU	2	15 500.0 IU		106.5 IU
FVIII celkem	18 307 750 IU	206	88 872.6 IU		62 913.2 IU
<i>Immunine</i>	1 057 900 IU	27	39 181.5 IU		24 043.2 IU
<i>Octanine</i>	1 033 000 IU	11	93 936.4 IU		23 484.1 IU
<i>Other recombinant</i>	427 743 IU	1	427 743.0 IU	44	9 721.4 IU
FIX celkem	2 518 943 IU	37	68 079.5 IU		57 248.7 IU
aPCC					
<i>Feiba</i>	12 000 IU	1	12 000.0 IU		
rFVIIa					
<i>NovoSeven</i>	445 mg	1	445.0 mg		
Plasma-derived factors - TOTAL*	14 221 950 IU	205	69 375.4 IU		42 453.6 IU
Recombinant factors - TOTAL*	6 604 743 IU	46	143 581.4 IU	335	19 715.7 IU
TOTAL CONSUMPTION *	20 826 693 IU	244	85 355.3 IU		62 169.2 IU

•plasma-derived factors = Immunate, Fanhdi, Octanate, Immunine, Octanine, Other plasma-derived

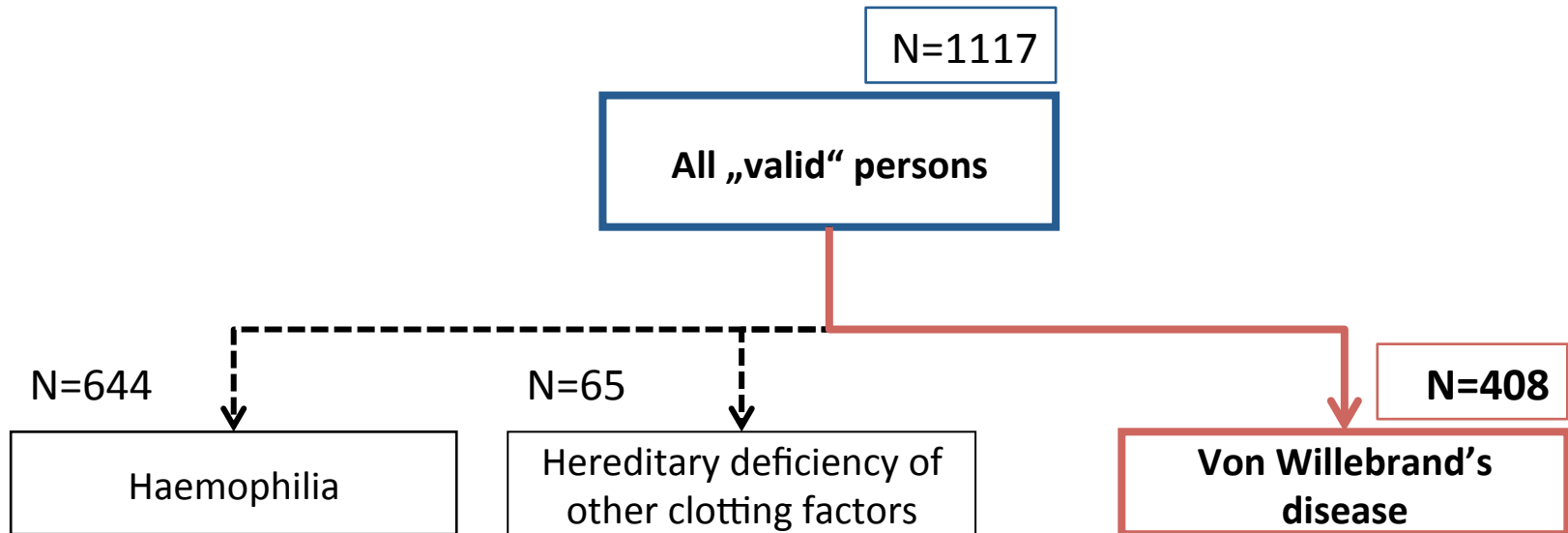
•recombinant factors = Advate, Kogenate, Recombinate, BAX 326, Other recombinant

*TOTAL CONSUMPTION = all mentioned drugs excluding Feiba and NovoSeven

Part B

Persons with Von Willebrand's disease

Sample size



Cca 1000 symptomatic vWDs should be in CZ
408 of them are in CNHP registry so far

Number of patients in participating centres

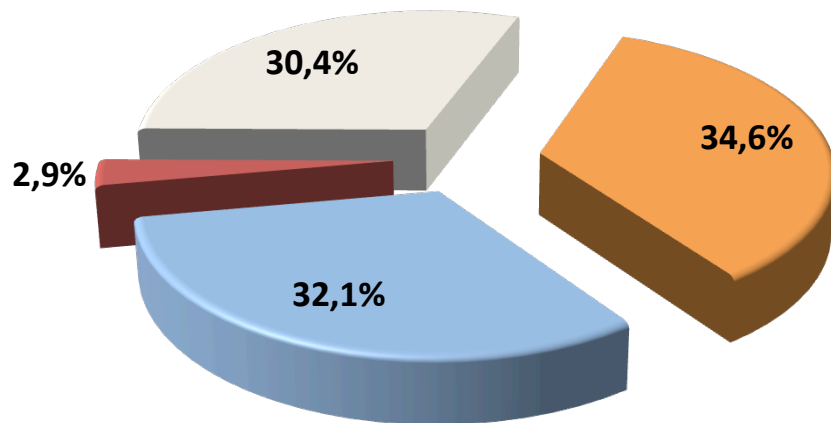
N=408





Paediatric centres	Valid patients	
	N	%
FN Plzen – Pediatric Dpt.	24	5.9
FN Motol – Dpt. of Pediatric Haematology and Oncology	18	4.4
FN Brno – DN – Dpt. of Pediatric Haematology	15	3.7
UnL – Pediatric Dpt. – Haematology	6	1.5
FNHK – Dpt. of Pediatric Medicine	2	0.5
FN Olomouc – Dpt. of Pediatric Medicine	1	0.2

Adult centres	Valid patients	
	N	%
FN Brno – OKH	181	44.4
FN Ostrava – Blood centre	62	15.2
FN Plzen – UKBH	65	15.9
KN Liberec – OKH	22	5.4
FN Olomouc – Haemato-Oncology Dpt.	11	2.7
CB – OKH	1	0.2

Type of Von Willebrand's disease

N=408

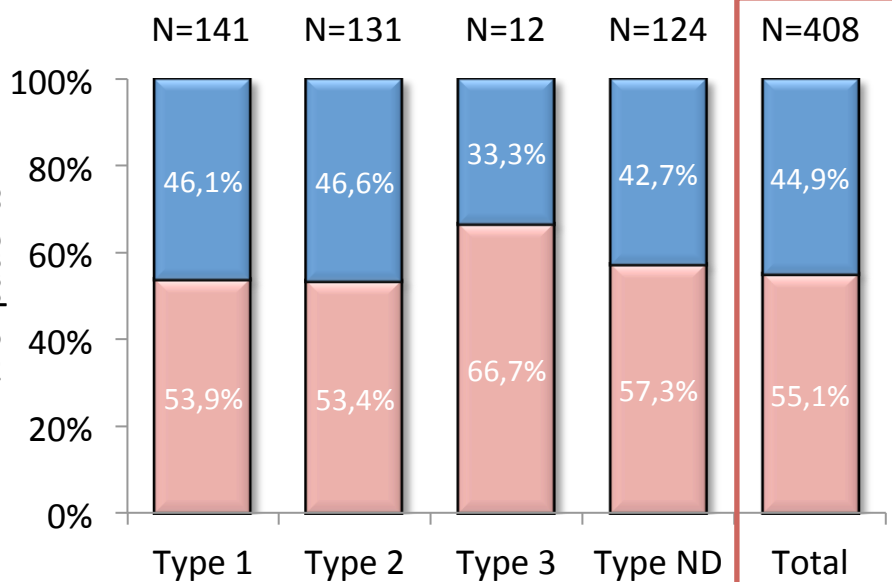
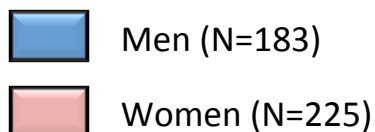


		Patients	
Type of disease		N	%
	Type 1	141	34.6
	Type 2	131	32.1
	<i>Type 2A</i>	63	15.4
	<i>Type 2B</i>	8	2.0
	<i>Type 2M</i>	20	4.9
	<i>Type 2N</i>	7	1.7
	<i>Type 2 (not specified)</i>	33	8.1
	Type 3	12	2.9
	Type not determined / unfilled	124	30.4
Total		408	100.0

Sex and age of patients

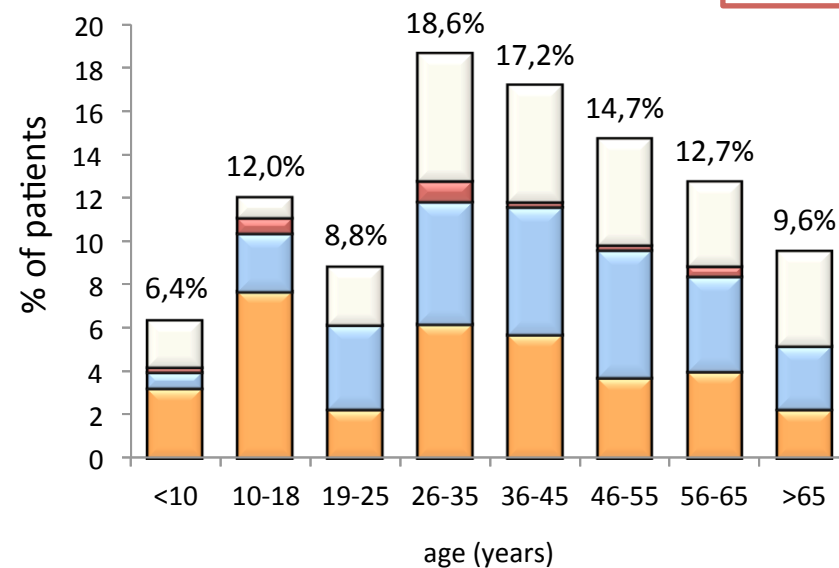
N=408

Sex



Current age*

	Type 1	Type 2	Type 3	Type ND	Total
N	141	131	12	124	408
Mean	33.4	40.5	31.9	42.0	38.3
Median	32	39	31.5	41	37
min - max	2 - 85	6 - 76	6 - 62	2 - 87	2 - 87

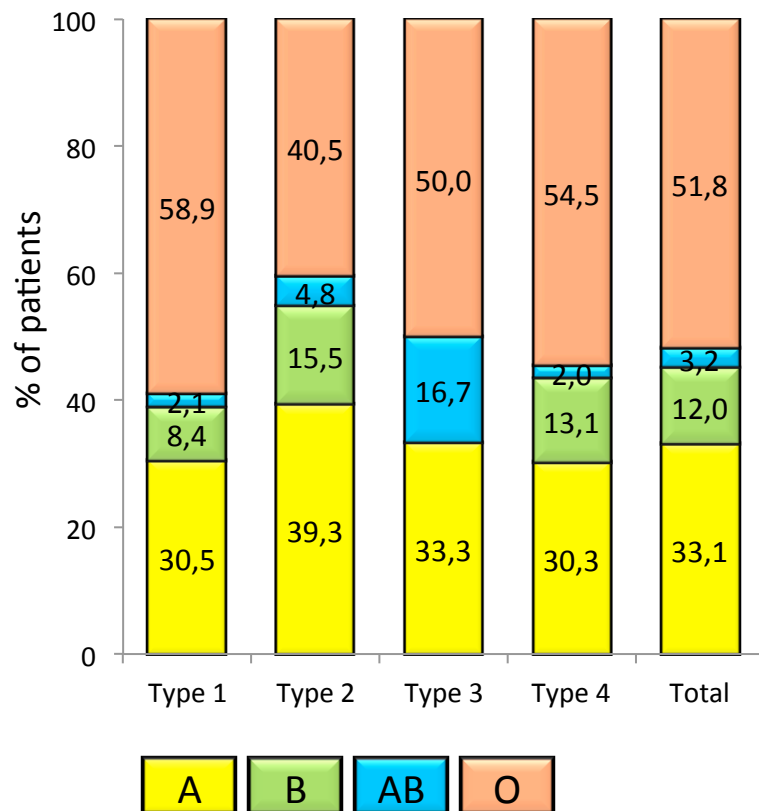


Type ND = not determined or unfilled

* age reached in year 2013

Blood group

N=408

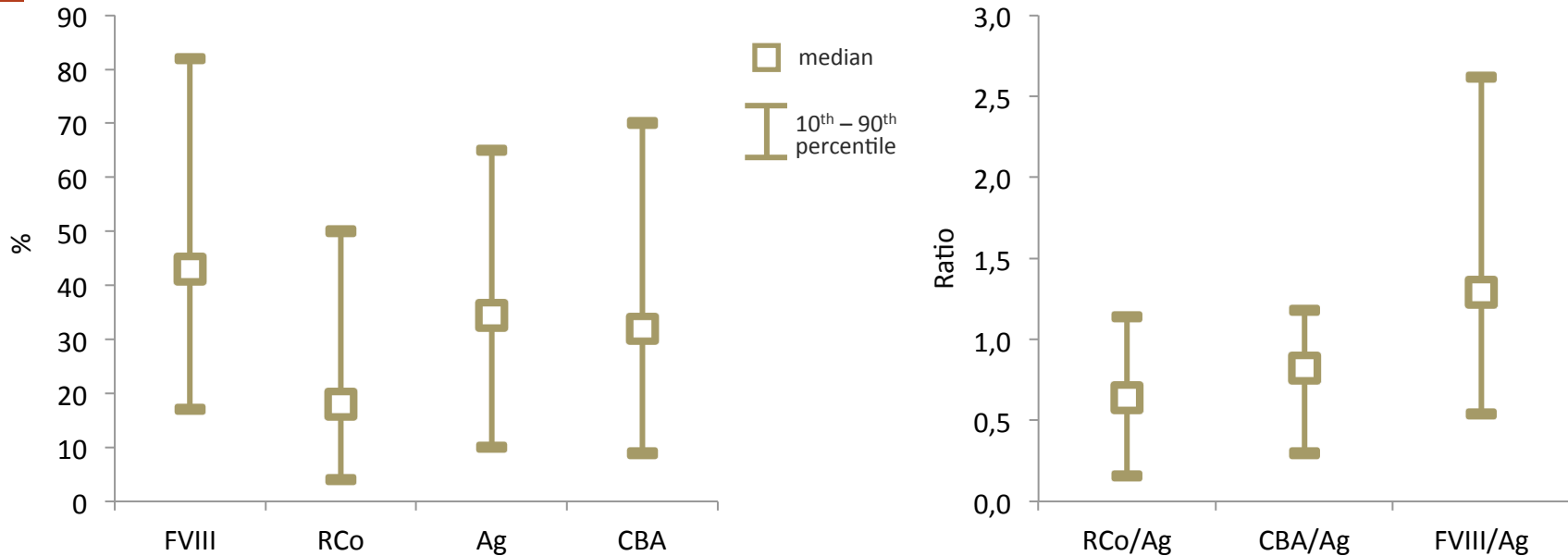


%¹ - % of total N
 %² - % of valid N

Blood group	A	B	AB	O	ND	Total N	Valid N
Type 1	N	29	8	2	56	46	141
	%¹	20.6	5.7	1.4	39.7	32.6	100
	%²	30.5	8.4	2.1	58.9		100
Type 2	N	33	13	4	34	47	131
	%¹	25.2	9.9	3.1	26.0	35.9	100
	%²	39.3	15.5	4.8	40.5		100
Type 3	N	2	0	1	3	6	12
	%¹	16.7	0.0	8.3	25.0	50.0	100
	%²	33.3	0.0	16.7	50.0		100
Type ND	N	30	13	2	54	25	124
	%¹	24.2	10.5	1.6	43.5	20.2	100
	%²	30.3	13.1	2.0	54.5		100
Total	N	94	34	9	147	124	408
	%¹	23.0	8.3	2.2	36.0	30.4	100
	%²	33.1	12.0	3.2	51.8		100

Factor levels

N=408

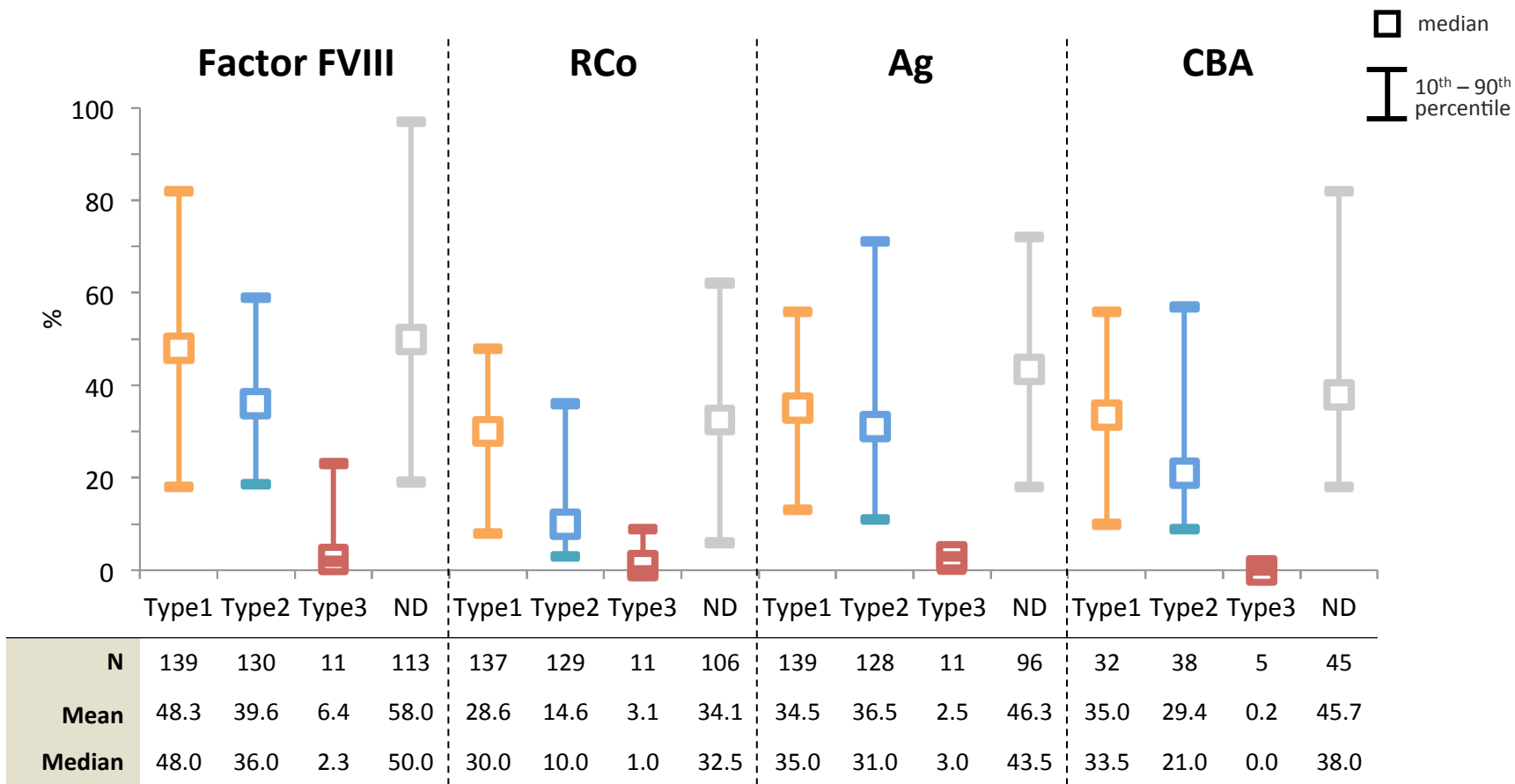


Factor FVIII*	RCo	Ag	CBA		RCo/Ag	CBA/Ag	FVIII/Ag
393	383	374	120	N	366	118	369
47.0	24.7	37.3	35.8	Mean	0.77	0.87	1.84
43 (0–219)	18 (0–135)	34.5 (0–177)	32 (0–127)	Median (min – max)	0.64 (0–15.8)	0.82 (0–11.1)	1.29 (0–42.4)

* Factor FVIII was assessed by coagulati on method in 372 patients, by chromogenic method in 16 patients and method is missing in 5 patient

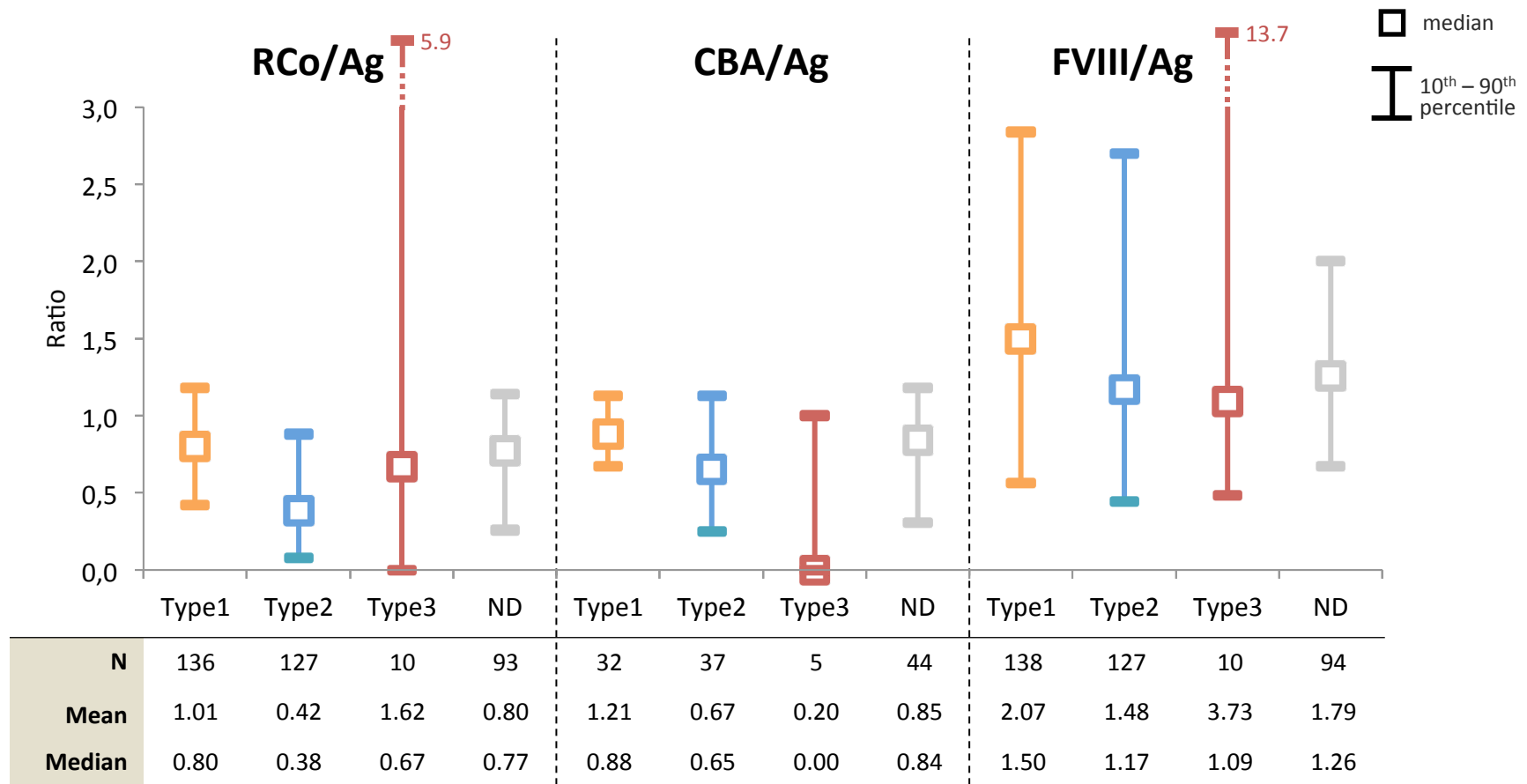
Factor levels according to type of VWD disease I.

N=408



Factor levels according to type of VWD disease II.

N=408



Bleeding score¹ according to sex

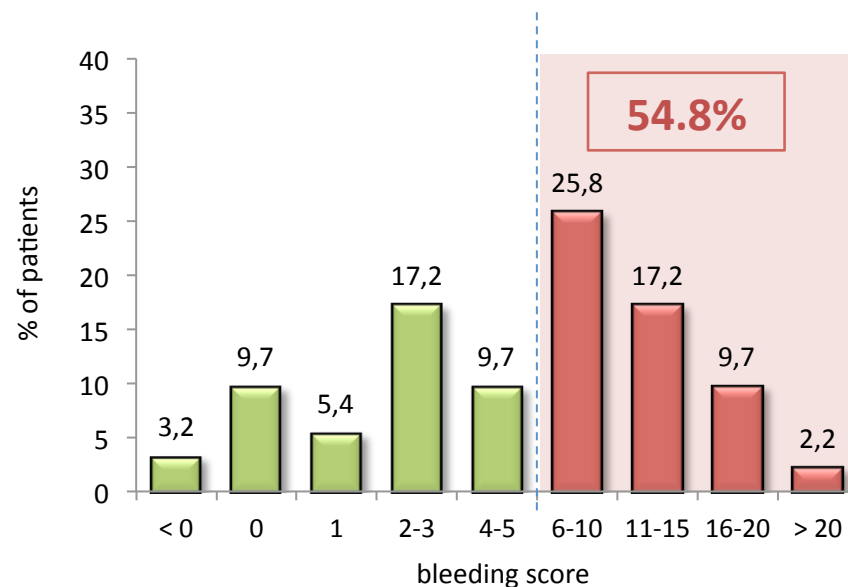
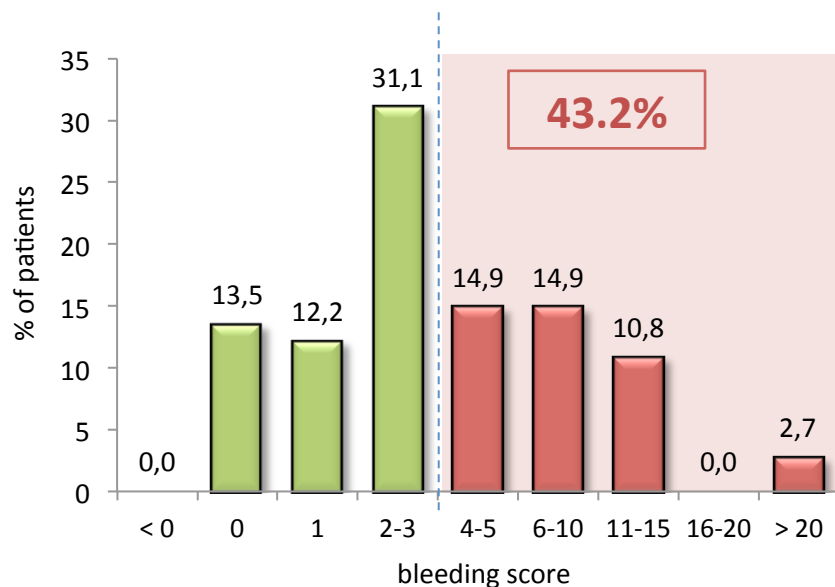
N=167²

Men

N	74
Mean	4.5
Median (min - max)	3 (0 – 25)

Women

N	93
Mean	7.1
Median (min - max)	6 (-3 – 23)



¹ Adult and Pediatric Vincenza VWD Bleeding Questionnaire and Scoring System

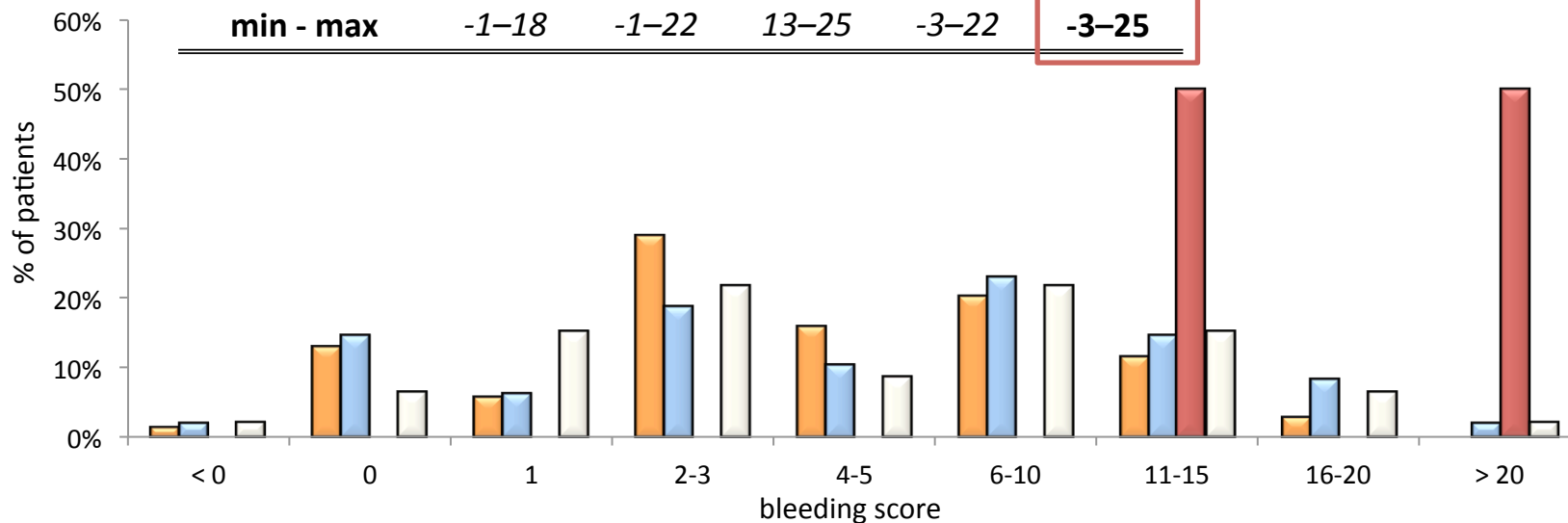
² Missing information on bleeding score in 241 patients.

Bleeding score¹ according to type of disease

N=167²

Bleeding score

	Type 1	Type 2	Type 3	Type ND	Total
N total	141	131	12	124	408
N valid	69	48	4	46	167
Mean	4.8	6.4	18.8	6.1	5.9
Median	4.0	5.0	18.5	4.0	4.0
min - max	-1-18	-1-22	13-25	-3-22	-3-25



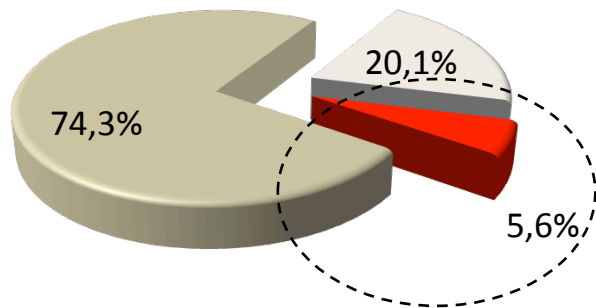
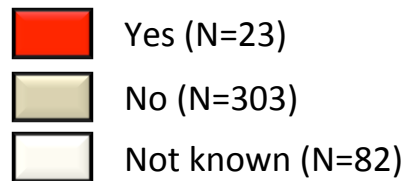
¹ Adult and Pediatric Vincenza VWD Bleeding Questionnaire and Scoring System

² Missing information on bleeding score in 241 patients.

Other diseases

N=408

Experienced hepatitis



*11x hepatitis A
7x hepatitis B
2x hepatitis A+B
3x hepatitis C*

None of the patients is HIV positive.

Consumption of drugs in year 2013

N=408

	Number of treated patients total (type1/type2/type3/typeND)	Total annual consumption	Average annual consumption per treated patient
Fanhdi	15 (11/3/1/0)	42 250 IU	2 816.7 IU
Haemate P	58 (9/23/7/19)	905 900 IU	15 619.0 IU
<i>of them on prophylaxis</i>	<i>4 (0/0/4/0)</i>	<i>215 500 IU</i>	<i>53 875.0 IU</i>
Immunate	2 (1/0/0/1)	13 000 IU	6 500.0 IU
Wilate	6 (1/5/0/0)	141 300 IU	23 550.0 IU
<i>of them on prophylaxis</i>	<i>1 (0/1/0/0)</i>	<i>37 800 IU</i>	<i>37 800.0 IU</i>
Willfact	2 (0/0/2/0)	237 000 IU	118 500.0 IU
<i>of them on prophylaxis</i>	<i>2 (0/0/2/0)</i>	<i>237 000 IU</i>	<i>118 500.0 IU</i>
Total	83 (22/31/10/20)	1 339 450 IU	16 138.0 IU
<i>of them on prophylaxis</i>	<i>7 (0/1/6/0)</i>	<i>490 300 IU</i>	<i>70 043.0 IU</i>
Total - type 1	22	53 500 IU	<u>2 431.8 IU</u>
Total - type 2	31	546 950 IU	<u>17 643.5 IU</u>
Total - type 3	10	568 100 IU	<u>56 810.0 IU</u>
Total - type ND	20	170 900 IU	<u>8 545.0 IU</u>