

The status of care for persons with haemophilia registered within CNHP registry Annual Report 2016

Jan Blatný, Petra Ovesná
on behalf of
Centres contributing to CNHP registry
(Czech National Haemophilia Programme)
July 2017



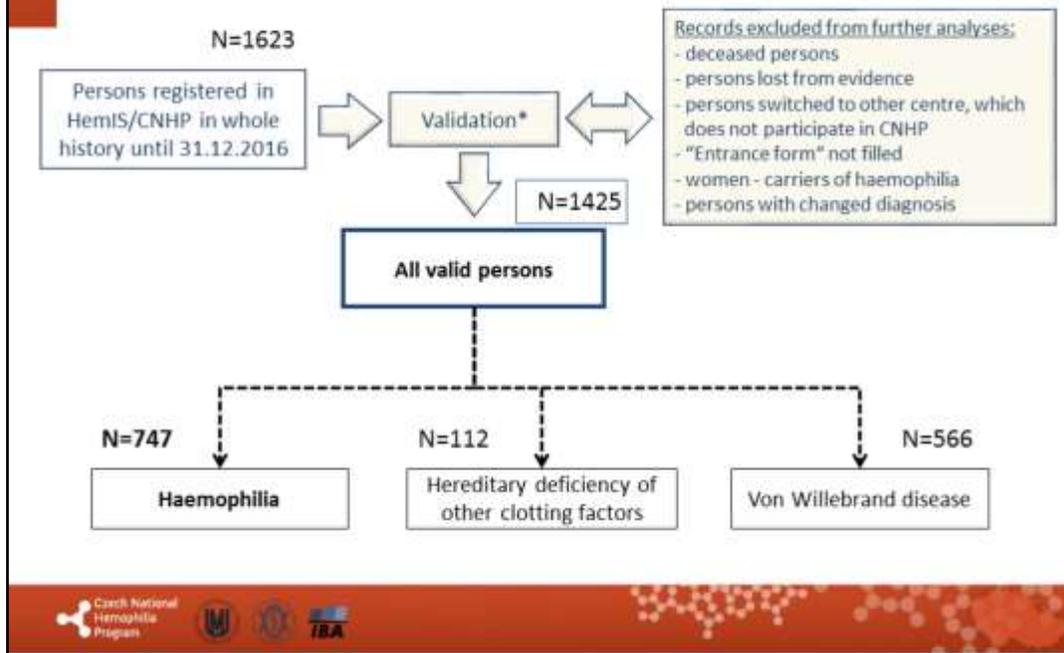
Czech National
Haemophilia
Program



IHA



Sample size, valid records



This slide describes the process of records' validation within the registry.

Part A

Persons with haemophilia (PWH)



Czech National
Hemophilia
Program



ISTA

Centres participating in CNHP

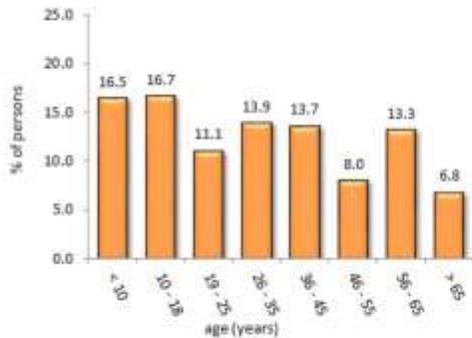
Paediatric centres	Valid persons		Adult centres	Valid persons	
	N	%		N	%
Prague – Dpt. of Pediatric Haematology and Oncology, CUH Motol	85	11.4	Brno – Dpt. Of Clin Hematol, UH Brno	146	19.5
Brno – Dpt. of Pediatric Haematology, CUH Brno	51	6.8	Ostrava – Blood centre, UH Ostrava	77	10.3
Ústí n.L. – Pediatric Dpt. – Haematology, Masaryk Hospital	27	3.6	Hradec Králové – IV. Internal and Hematology Dpt., UH HK	62	8.3
Hradec Králové – Dpt. of Pediatric Medicine, UH HK	25	3.3	Olomouc – Haemato-Oncology Dpt., UH Olomouc	61	8.2
Ostrava – Dpt. of Pediatric Medicine, UH Ostrava	21	2.8	Pilsen – Dpt. of Biochemistry and Hematology, UH Pilsen	49	6.6
České Budejovice – Pediatric Dpt., Hospital CB	14	1.9	Liberec – Dpt. Of Clin Hematol, Hospital Liberec	41	5.5
Pilsen – Pediatric Dpt., UH Pilsen	14	1.9	České Budějovice – Dpt. Of Clin Hematol, Hospital CB	26	3.5
Olomouc – Dpt. of Pediatric Medicine, UH Olomouc	13	1.7	Ústí n.L. – Dpt. Of Clin Hematol, Masaryk Hospital	26	3.5
			Pilsen - Hemacentrum	9	1.2

Centres contributing to the CNHP registry.

Basic demographics

All
N=747

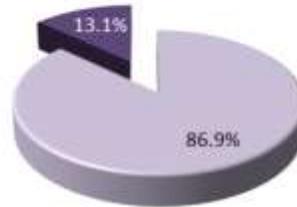
	Actual age* (years)
N	747
Mean	32.5
Median (min - max)	29 (0 - 94)



* age reached in year 2016

Type of haemophilia

- Haemophilia A (N=649)
- Haemophilia B (N=98)



Though the percentage of PWH over 65 years has not been increasing dramatically over last several years, dealing with elderly people with haemophilia will be the challenge for treaters.

All
N=747

Persons with haemophilia and inhibitors in 2016

Active inhibitors were recorded in 19 persons in year 2016 (+ 5 in another centre, not reported here)

- Out of them, 4 inhibitors (all in children with severe HA) newly developed in 2016
 - All in PUPs on rFVIII, 3 x HT/HR, 1 x LT/LR
 - Two of them started ITI in 2016

PWH with inhibitors:

- 10 children and 9 adults
- 18 haemophilia A and 1 haemophilia B
- 16 in severe, 1 in moderate and 2 in mild haemophilia
- 16 high-titre and 3 low-titre (<5BU),
- 13 HR and 3 LR inhibitors; this information not available in 3 PWH with inhibitors
- 6 patients were treated with rFVIIa, 2 patients with aPCC and 4 patients both with rFVIIa and aPCC
 - 5 patients were without any „by-pass“ therapy and 2 patients were without any recorded treatment at all

ITT:

- Four of above mentioned 19 persons (all children) started ITT in 2016
 - ✓ Two developed inhibitors in 2015, two in 2016
- Two children are currently on-going ITT (started earlier)
- ITT was successfully finished in 2 children during 2016, these children are inhibitor free now
 - ✓ Another one child finished ITT successfully during 2016, but inhibitors relapsed at the end of 2016






Summary description of the PWH with inhibitors within registry. There are five other PWH with inhibitors in the centre not participating in CNHP registry.

Please note further increased number of PWH with inhibitors in 2016. Four children with haemophilia A, (all severe PUPs) developed inhibitors in 2016. Most of them were HR inhibitors (**only 1 was LR**). All inhibitors developed on rFVIII, as recombinant factors are treatment of choice in PUPs in Czech Republic

Six children were on ITI in 2016. Two of them started earlier, four started in 2016. ITI was successfully finished in 3 children in 2016, however, in one patient inhibitors relapsed at the end of 2016. No adults were on ITI in 2016.

The number of new inhibitors was thus higher, than the number of successfully achieved ITIs in 2016.

ABR and treatment regimen in patients with inhibitor

N=19

	Type	Year of birth	Severity	ITI	"By-pass" prophylaxis	Titre	Responder	ABR	Joint / other
1	HA	2014	Moderate	Yes	Permanent	High	HR	0	0 / 0
2	HA	2014	Moderate	Yes	Permanent	High	HR	11	2 / 9
3	HA	2015	Moderate	Yes	Permanent	High	HR	0	0 / 0
4	HA	2016	Moderate	Yes	Permanent	High	HR	2	0 / 2
5	HA	2015	Moderate	Yes	Permanent	High	HR	6	0 / 6
6	HA	2004	Moderate	Yes	Permanent	High	HR	7	2 / 5
7	HA	2015	Moderate	Yes	Permanent	High	HR	5	0 / 5
8	HA	2016	Moderate	Yes	Permanent	High	HR	0	0 / 0
9	HA	1971	Moderate	Yes	Permanent	High	HR	0	0 / 0
10	HA	1941	Moderate	Yes	Permanent	High	HR	5	2 / 3
11	HA	1949	Mild	Yes	Permanent	High	NA	10	/
12	HA	1956	Moderate	Yes	Permanent	High	HR	5	2 / 2
13	HA	1971	Moderate	Yes	Permanent	High	HR	0	0 / 0
14	HA	1976	Moderate	Yes	Permanent	High	HR	0	0 / 0
15	HA	1977	Moderate	Yes	Permanent	High	HR	0	0 / 0
16	HA	1988	Moderate	Yes	Permanent	High	NA	0	0 / 0
17	HA	2003	Moderate	Yes	Permanent	High	NA	22	16 / 6
18	HA	1975	Moderate	Yes	Permanent	High	HR	8	7 / 1
19	HB	2007	Moderate	Yes	Permanent	High	HR	25	15 / 10

NA – not available



This slide describes in more details all PWH with “active” inhibitors within CNHP registry. Most, but not all of children with HT inhibitors are on ITI for different reasons. (Reasons not reported here, but often: previous ITI failure, waiting for inhibitors <10BU to start ITI, no consent for ITI provided by parents etc...) No adult PWH was on ITI in 2016.

Patients with inhibitors will be reported separately in details later in 2017.

ABR according to treatment regimen in PWH with inhibitor

N=19

Diagnosis	ITT	"By-pass" prophylaxis	N	ABR (mean)	ABR (median)	Joint / other bleeds (mean)
Haemophilia A	Yes	Permanent	1	7.0	7	2 / 5
		Temporary	4	3.3	1	0 / 1
		OD	1	6.0	6	0 / 6
	No	Permanent	2	15.0	15	11.5 / 3.5
		Temporary	3	1.7	0	0 / 0
		OD	7	2.9	0	0 / 0
Haemophilia B		Temporary	1	25.0	25	15 / 10

Patients with inhibitors, who have frequent joint bleeds, are on permanent prophylaxis with by-passing agents. Despite this, some of them have still high ABR.

Part A.1

Demographic characteristics Haemophilia A



Czech National
Hemophilia
Program



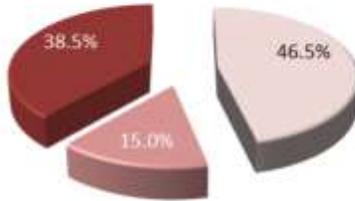
ISTA

Severity of haemophilia A

Haem A
N=649

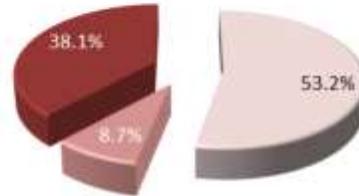
Children (N=213)

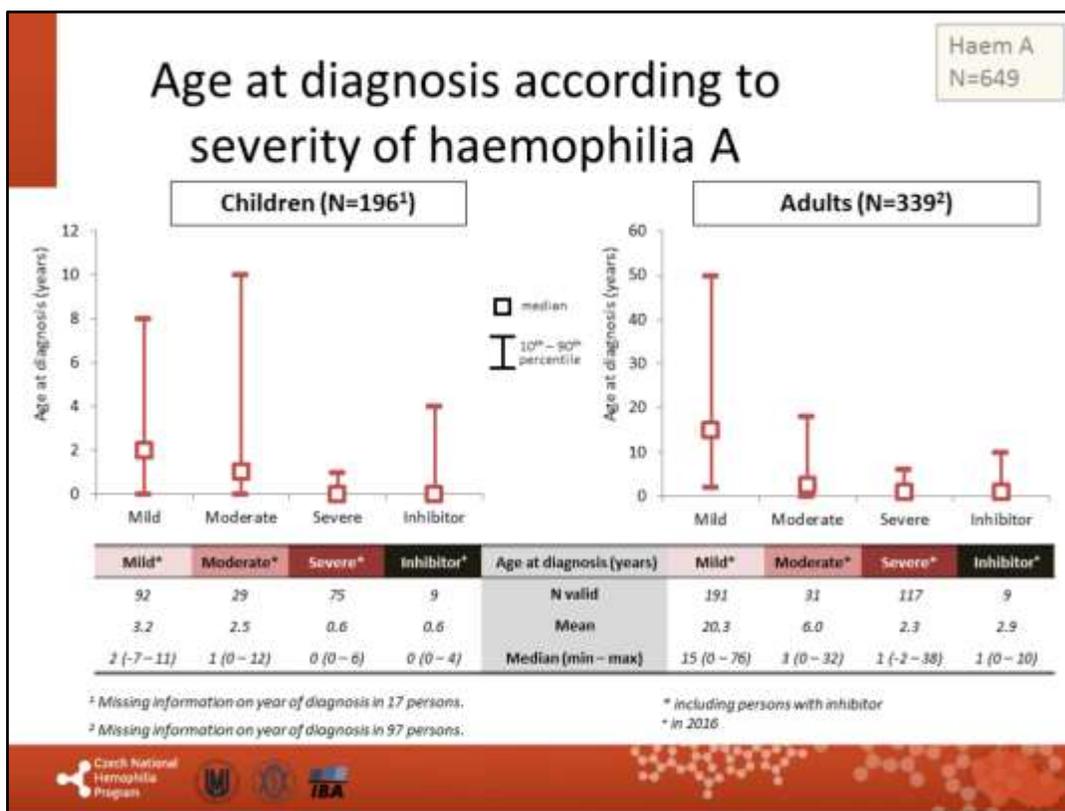
- Mild (N=99)
- Moderate (N=32)
- Severe (N=82)



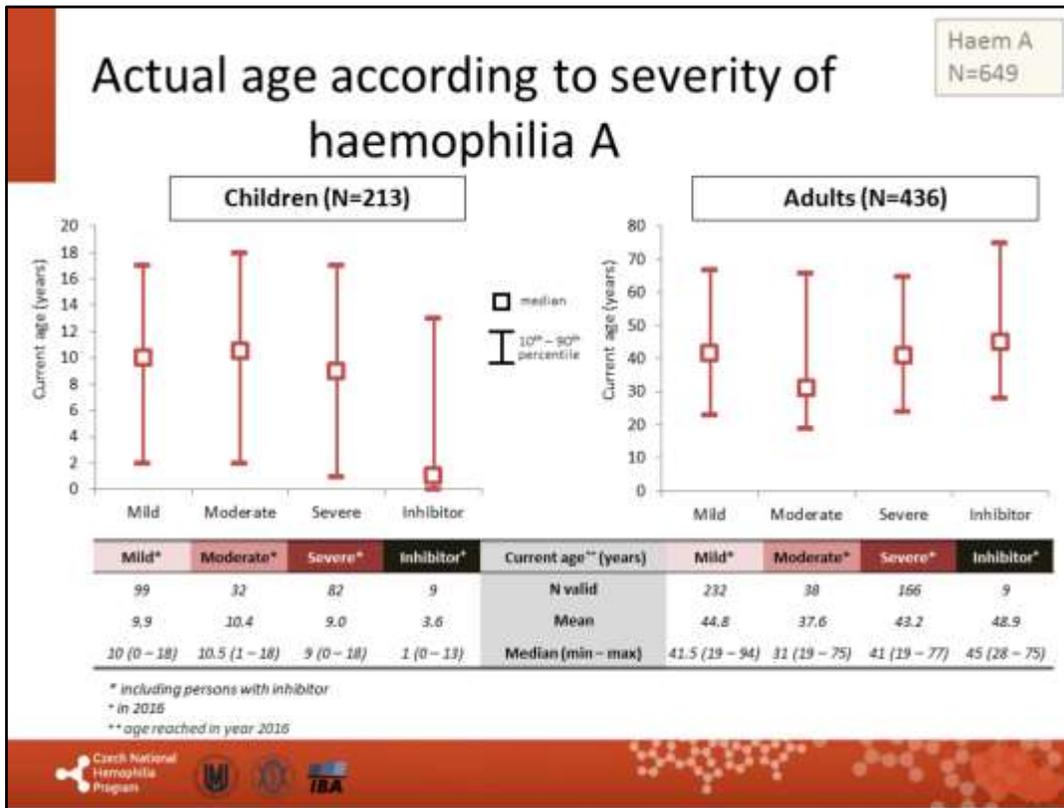
Adults (N=436)

- Mild (N=232)
- Moderate (N=38)
- Severe (N=166)





Median age at diagnosis is different for adults and children with HA. (In the past, the diagnostic options were worse, than they are today.)



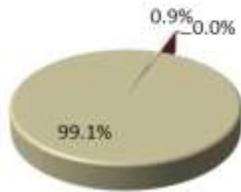
Mean age of Czech adults with HA is around 40 years. Mean age of children with HA is around 10 years.

Hepatitis (ever) experienced

Children
Haem A
N=213

Experienced hepatitis

- Yes (N=0)
- No (N=211)
- Not known (N=2)



No child has hepatitis C.

Data from last annual report of each person.



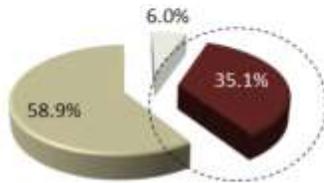
No HepC infection in children since late 90's. None of Czech children with HA is infected with Hepatitis C.

Hepatitis (ever) experienced

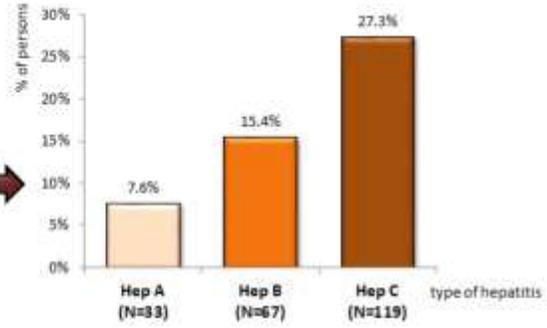
Adults
Haem A
N=436

Experienced hepatitis

- Yes (N=153)
- No (N=257)
- Not known (N=26)



N=153*

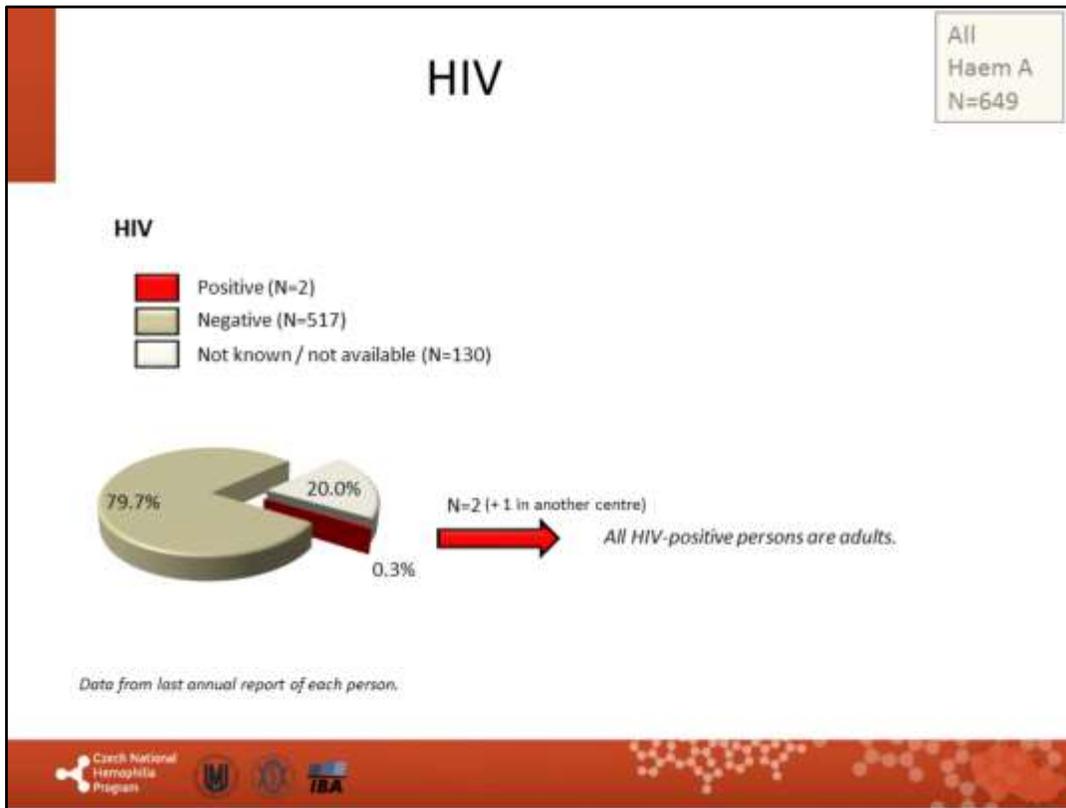


Data from last annual report of each person.

*Total of 219 cases of hepatitis in 153 persons. One person may have more types of hepatitis recorded.



There has been NO NEW HepC infection in 2016.
119 PWHA ever experienced hepatitis, though some of them may have been successfully treated (numbers of successfully treated not shown here).



Very low number of HIV positive PWH due to low/no access to contaminated concentrates in 80s and 90s. Our current treatment is on a very high safety level. No new HIV+ PWH reported since late 90s.

Part A.2

Treatment outcomes and bleeding frequency Haemophilia A



Czech National
Hemophilia
Program



ISTA

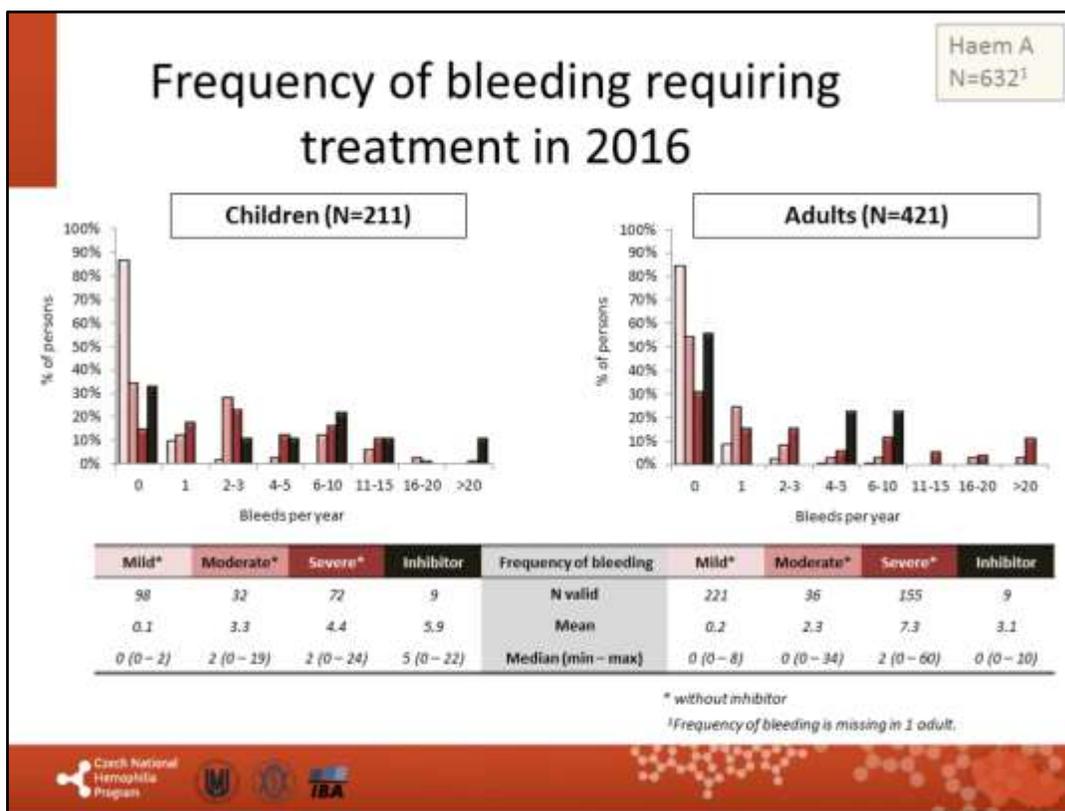
Data from year 2016 – sample size

All
Haem A
N=649

	Valid persons with haemophilia A		→	Persons with annual report in 2016		→	Persons examined in 2016		→	Persons treated in 2016	
	N	%		N	%		N	%		N	%
All	649	100%		633	97.5%		478	73.7%		347	53.5%
of them with inhibitor	18			18			17			14	
Children	213	100%		211	99.1%		182	85.4%		124	58.2%
of them with inhibitor	9			9			9			9	
Adults	436	100%		422	96.8%		296	67.9%		223	51.1%
of them with inhibitor	9			9			8			5	

There are records of nearly 80% of all Czech haemophiliacs in total within the CNHP registry. As for paediatric population, ALL children are recorded. CNHP registry also houses records of over two thirds of adult haemophiliacs in Czech Republic. Further slides display analyses performed only on records, which were updated during 2016. Not all patients came to the centre (especially adults) and not all centres fully reported all data in 2016. Thus not all records have been updated and used for further analyses. Though the data completeness has further improved in 2016, it remains our task to get as close as possible to 100% in future years. This goal shall be reached by introducing of the data monitoring in 2017. (Ideally, percentage of PWH with annual report should be equal to PWH examined and both should be 100%.)

One adult is not included in further detailed analyses of treatment due to only partially filled 2016 annual report.



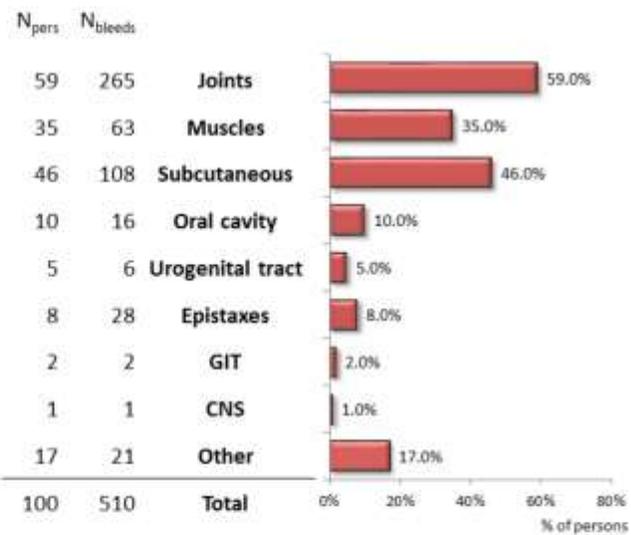
Data shown document good efficacy of care provided to Czech PWH, no matter what age category they are. Mean/Median number of bleedings per year (ABR) is 7,3/2 for adults and 4,4/2 in children with severe HA.

In 2015 the numbers for children were 4,7/3 and for adults 7,4/3.

Location of bleeds in 2016

Children
Haem A
N=211

100 (47.4%) children experienced bleeding requiring treatment at least once in year; 510 bleeds were recorded in total, 30 bleeds required hospitalization. All 100 of these children have recorded location of their bleeds. 111 (52.6%) children recorded no bleed during year 2016.

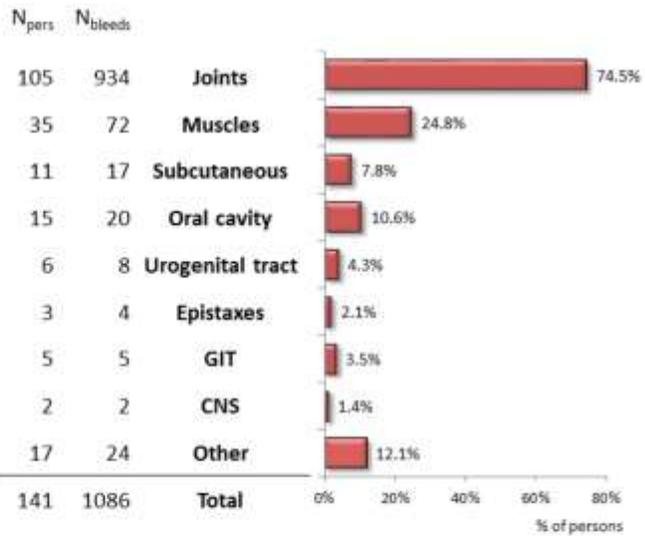


There was one CNS bleed in children with haemophilia in 2016. 52,6% of children had no bleed at all.

Location of bleeds in 2016

Adults
Haem A
N=421¹

153 (36.3%) adults experienced bleeding requiring treatment at least once in year; 1286 bleeds were recorded in total, 38 bleeds required hospitalization. 141 of these 153 adults have recorded location of their bleeds. Localization is not known in 12 adults. 268 (63.7%) adults have recorded no bleed during year 2016.



¹Frequency of bleeding is missing in 1 adult.

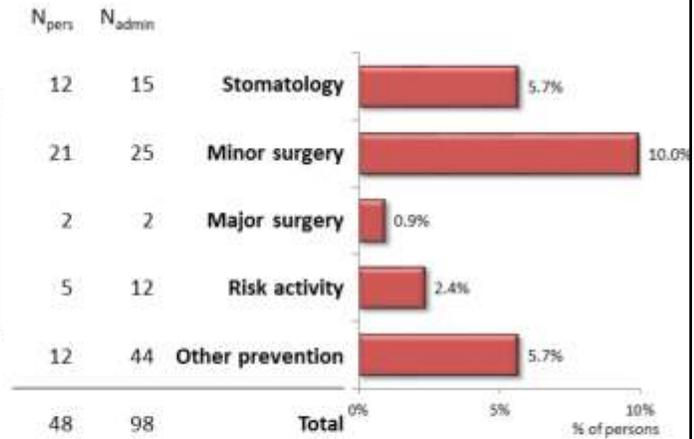


Bleeding events in adults.

Preventive administration in 2016

Children
Haem A
N=211

48 (22.7%) children were given factor to prevent bleeding during/before risk situation.
98 preventive administrations were recorded in total.

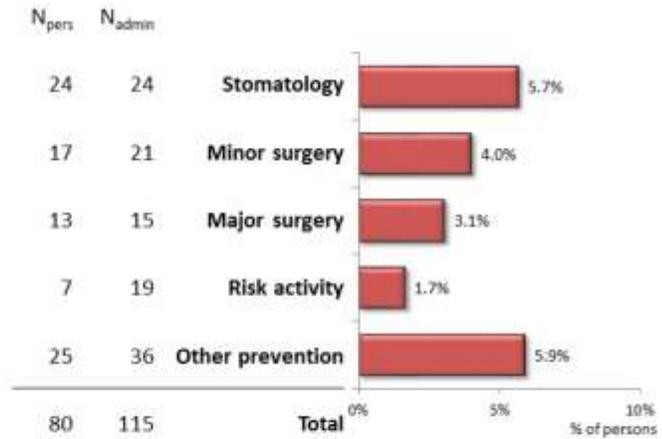


This figure refers to preventive factors administration in children with HA.

Preventive administration in 2016

Adults
Haem A
N=422

80 (19.0%) persons were given factor to prevent bleeding during/before risk situation. 115 preventive administrations were recorded in total.



This figure refers to preventive treatment in adults with HA

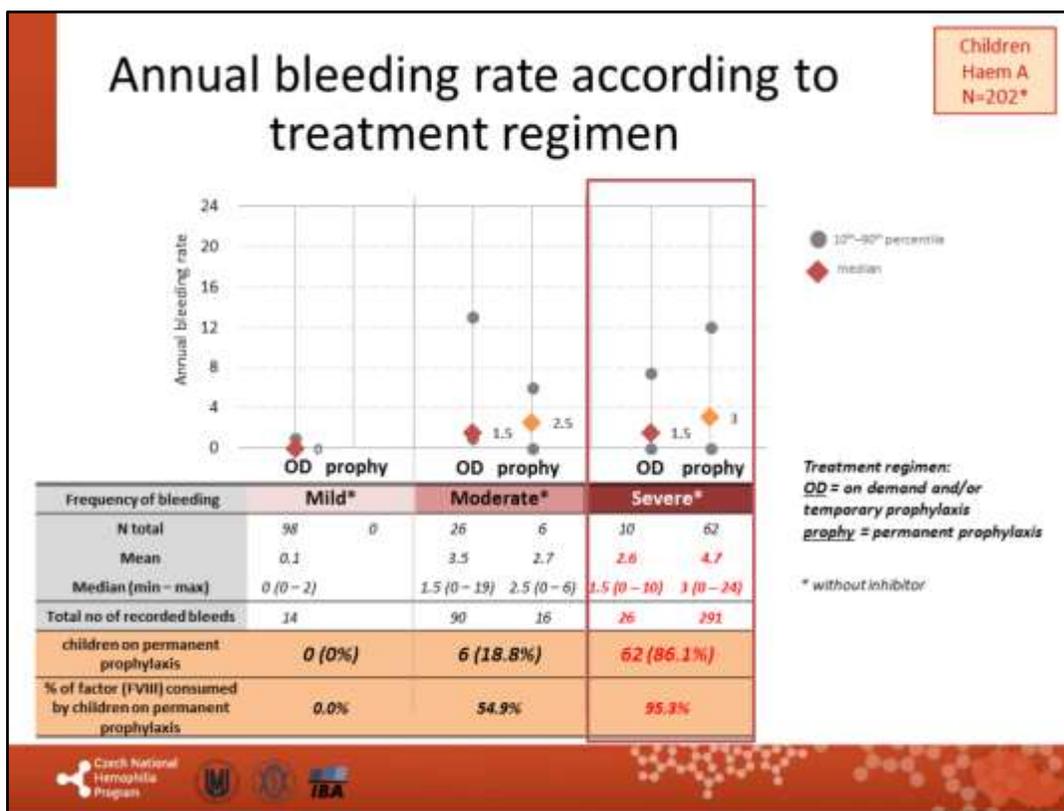
Part A.3

ABR according to treatment regimen Haemophilia A without inhibitor



Czech National
Hemophilia
Program





This slide supports good effect of permanent prophylaxis in children. Rate of prophylaxis decreased from 94,1% in 2015 to 86,1% in 2016 among children with severe haemophilia A. Those children with severe haemophilia, who are not on permanent prophylaxis yet shall be encouraged to do so. (see comment below) Number of bleeds per year (median) in severe haemophilacs A on prophylaxis decreased from 3,5 in 2015 to 3/year in 2016. ABR in children with severe haemophilia A on OD decreased from 3 to 1,5.

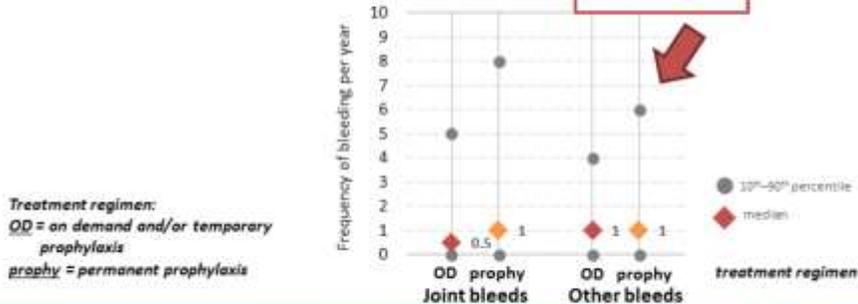
We should, however, still bear in mind, that over 2 bleeds/year may lead to significant joint damage, and we shall further work on this issue! We are likely able to prevent almost all spontaneous bleeds, but we should focus on trauma bleeds in still more and more active children. This is true specially for children with severe haemophilia.

Joint and other bleeds according to treatment regimen

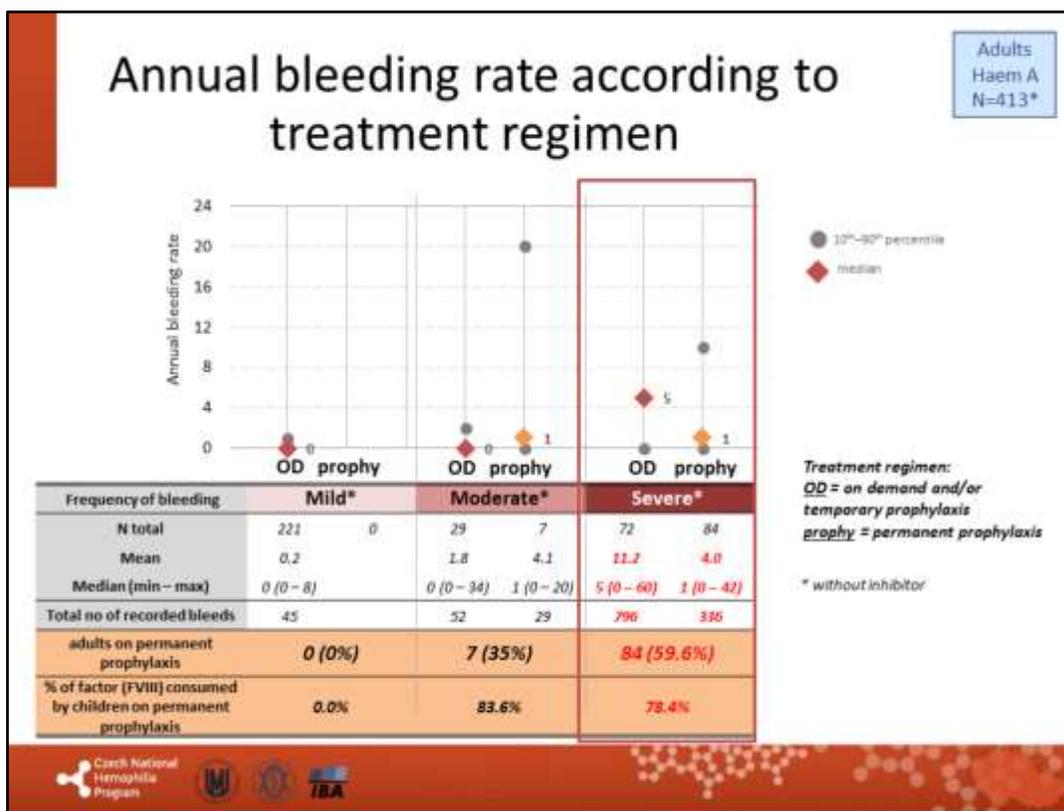
Children
Haem A
N=201*

Frequency of bleeding	Mild*		Moderate*		Severe*	
	OD	prophy	OD	prophy	OD	prophy
Treatment regimen	OD	prophy	OD	prophy	OD	prophy
N valid	97	0	26	6	10	62
JOINT BLEEDS						
Mean	0.0		1.8	1.7	1.3	2.8
Median (range)	0 (0-1)		0 (0-18)	2 (0-3)	0.5 (0-2)	1 (0-18)
Total no of recorded bleeds	3		46	10	13	169
OTHER BLEEDS						
Mean	0.1		1.7	1.0	1.1	2.0
Median (range)	0 (0-2)		1 (0-9)	0 (0-4)	1 (0-4)	1 (0-9)
Total no of recorded bleeds	10		44	6	10	122

* without inhibitor; missing location of bleeds in 1 child



Children with HA on permanent prophylaxis had median of joint bleeds per year below 2 for the first time in the history of CNHP registry. This is, indeed, a great success, however, there are still children, who have over 10 joint bleeds per year! Please note also very high - and thus unacceptable - number of joint bleeds in some children with moderate HA, when treated „on-demand“ (interval range 0-18)! These children definitely deserve prophylaxis.



Prophylaxis works very well in Czech adult PWHs! It is able to decrease bleedings from 5 to 1 (median numbers). In 2015 median ABR in adult PWHs with severe haemophilia A was 10 on OD and 2 on prophylaxis.

Rate of prophylaxis increased from 54,8% in 2015 to 59,6% among adults with severe haemophilia A.

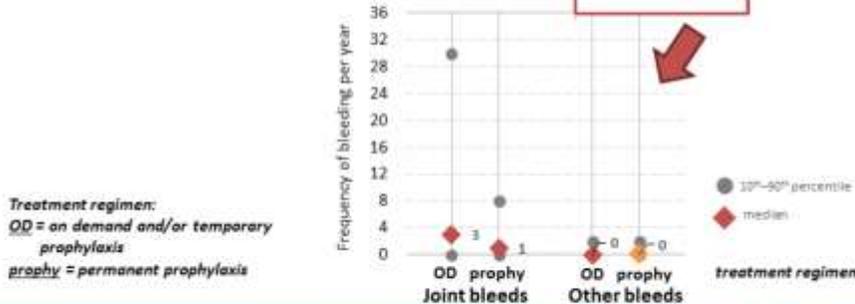
Use of prophylaxis will certainly increase the factor consumption in adults, but the benefit shown as far less bleedings is undoubted.

Joint and other bleeds according to treatment regimen

Adults
Haem A
N=398*

Frequency of bleeding	Mild*		Moderate*		Severe*	
	OD	prophy	OD	prophy	OD	prophy
Treatment regimen	OD	prophy	OD	prophy	OD	prophy
N valid	221	0	29	7	64	77
JOINT BLEEDS						
Mean	0.1		1.6	2.1	9.4	2.9
Median (range)	0 (0-4)		0 (0-34)	0 (0-8)	1 (0-60)	1 (0-23)
Total no of recorded bleeds	17		47	15	580	222
OTHER BLEEDS						
Mean	0.1		0.2	2.0	0.8	0.6
Median (range)	0 (0-5)		0 (0-1)	0 (0-12)	0 (0-7)	0 (0-20)
Total no of recorded bleeds	28		6	14	49	48

* without inhibitor; missing location of bleeds in 15 adults



Median of joint bleeds per year is below 2 also in adults with severe HA on prophylaxis. It is however seen, that some adult PWHA still have significant number of joint bleeds despite the prophylaxis. Wide interval range for those with severe and moderate HA treated “on demand” suggests, that more adults with HA should be commenced on prophylaxis.

As described later in this report, doses for adults (in IU/kg/year) are still significantly lower, than in children with the same disease.

ABR according to treatment regimen and age

Adults
Haem A
N=413*

* without inhibitor

Frequency of bleeding	Mild*		Moderate*		Severe*	
	OD	Prophy.	OD	Prophy.	OD	Prophy.
Treatment regimen	OD	Prophy.	OD	Prophy.	OD	Prophy.
N total	180	0	18	4	69	61
Mean	0.2		2.5	6.8	11.7	4.1
Median (min – max)	0 (0 – 8)		0 (0 – 34)	3.5 (0 – 20)	5.5 (0 – 60)	1 (0 – 40)
Total no of recorded bleeds	34		45	27	795	253
adults on permanent prophylaxis	0 (0%)		4 (18.2%)		61 (46.9%)	
% of factor (FVIII) consumed by children on permanent prophylaxis	0.0%		77.6%		73.2%	

Adults (haem A) born before 1990
N=332

Frequency of bleeding	Mild*		Moderate*		Severe*	
	OD	Prophy.	OD	Prophy.	OD	Prophy.
Treatment regimen	OD	Prophy.	OD	Prophy.	OD	Prophy.
N total	41	0	11	3	3	23
Mean	0.3		0.6	0.7	0.1	3.6
Median (min – max)	0 (0 – 3)		1 (0 – 2)	1 (0 – 1)	0 (0 – 1)	1 (0 – 42)
Total no of recorded bleeds	11		7	2	1	83
adults on permanent prophylaxis	0 (0%)		3 (21.4%)		23 (88.5%)	
% of factor (FVIII) consumed by children on permanent prophylaxis	0.0%		90.3%		96.6%	

Adults (haem A) born in 1990 or later
N=81



This important table shows in general significant difference in bleeding rates between adult PWH born before 1990 (when concentrates and thus also prophylaxis became available in CZ) and PWH born later. This difference, however, disappears, when comparing adults with severe haemophilia A on prophylaxis. In both groups the medians and interval ranges are similar. In other words, prophylaxis works very well also in those, with already damaged joints. We advocate for more tertiary prophylaxis in adult PWH.

Joint and other bleeds according to treatment regimen and age

Adults
Haem A
N=398*

* without inhibitor; missing location of bleeds in 15 adults

Frequency of bleeding	Mild*		Moderate*		Severe*		
	OD	prophy	OD	prophy	OD	prophy	
Treatment regimen	OD	prophy	OD	prophy	OD	prophy	
N valid	180	0	18	4	61	55	
JOINT BLEEDS							
Mean	0.1		2.4	3.8	9.8	3.1	Adults (haem A) born before 1990 N=318
Median (range)	0 (0-4)		0 (0-34)	3.5 (0-8)	1 (0-60)	1 (0-33)	
Total no of recorded bleeds	13		44	15	579	169	
OTHER BLEEDS							
Mean	0.1		0.1	3.0	0.8	0.4	Adults (haem A) born in 1990 or later N=80
Median (range)	0 (0-5)		0 (0-1)	0 (0-12)	0 (0-7)	0 (0-3)	
Total no of recorded bleeds	21		2	12	49	19	

Frequency of bleeding	Mild*		Moderate*		Severe*		
	OD	prophy	OD	prophy	OD	prophy	
Treatment regimen	OD	prophy	OD	prophy	OD	prophy	
N valid	41	0	11	3	3	22	
JOINT BLEEDS							
Mean	0.1		0.3	0.0	0.1	2.4	Adults (haem A) born in 1990 or later N=80
Median (range)	0 (0-1)		0 (0-2)	0 (0-0)	0 (0-1)	1 (0-22)	
Total no of recorded bleeds	4		3	0	1	53	
OTHER BLEEDS							
Mean	0.2		0.4	0.7	0.0	1.3	Adults (haem A) born in 1990 or later N=80
Median (range)	0 (0-2)		0 (0-1)	1 (0-1)	0 (0-0)	0 (0-20)	
Total no of recorded bleeds	7		4	2	0	29	



The same is true for joint bleeds in adults. Situation significantly improved compared to 2015, some frequent bleeders however still remain, especially between adults with severe HA born before 1990 and still treated “on demand”. They are, indeed, the candidates for tertiary prophylaxis.

Part A.4

ABR according to centres Haemophilia A (PWHA)



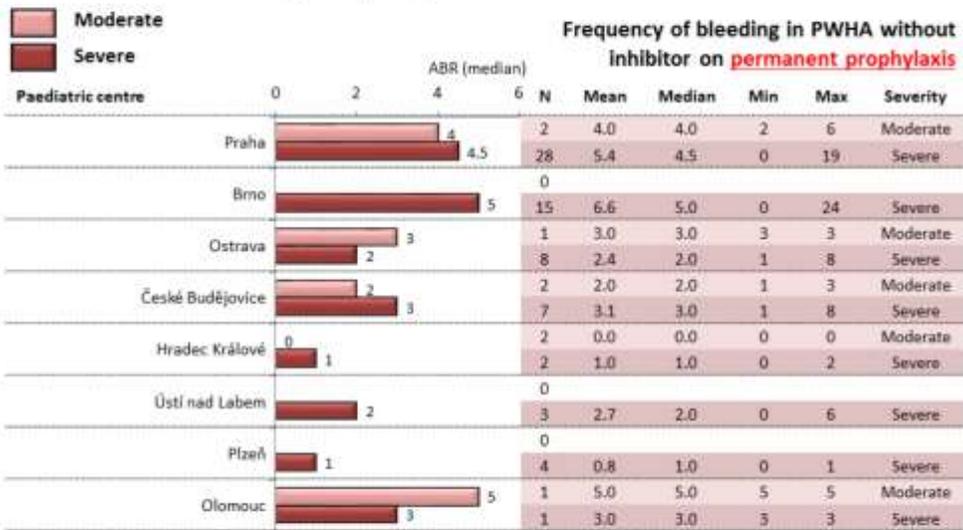
Czech National
Hemophilia
Program



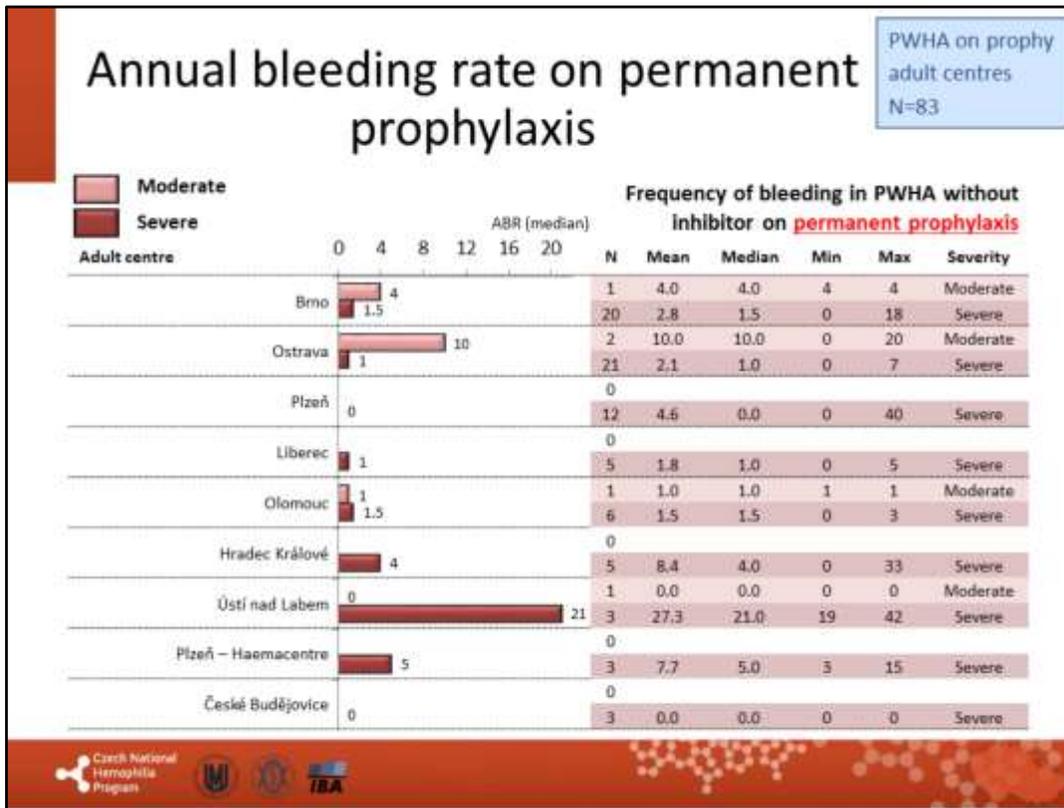
ISTA

Annual bleeding rate on permanent prophylaxis

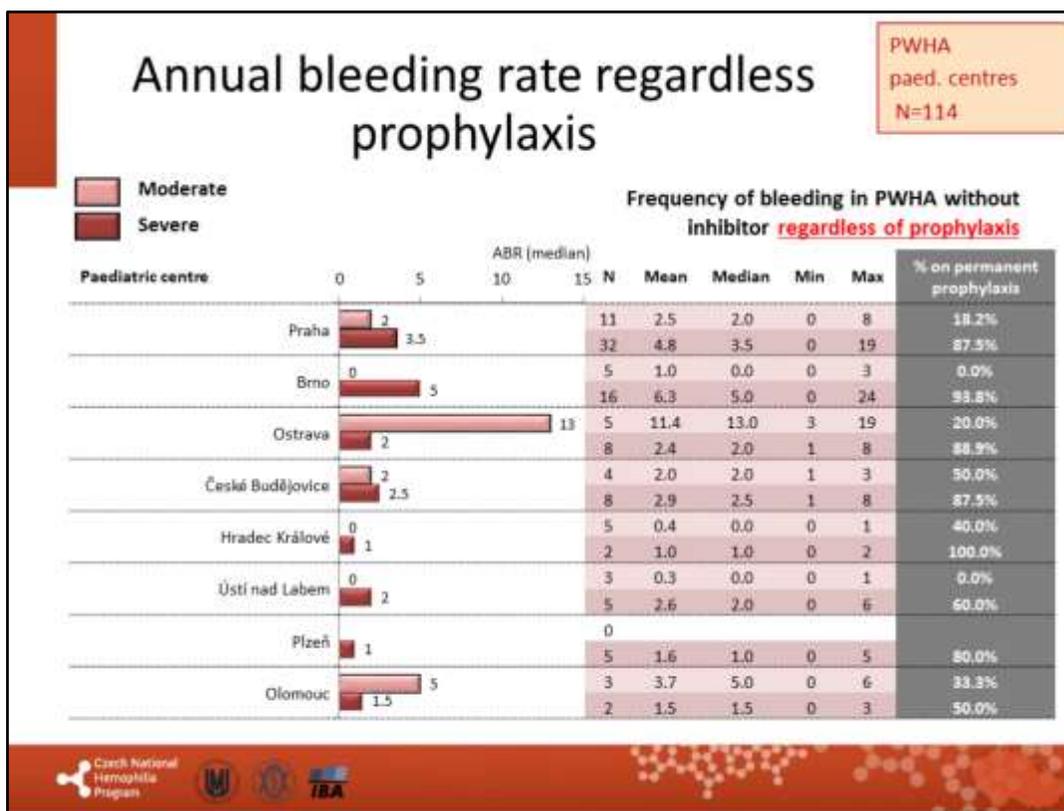
PWHA on prophylaxis
paed. centres
N=76



In vast majority of paediatric centres, severe haemophiliacs on prophylaxis bleed not more than 4 times per year (median). We should continue in our focus on individualized/tailored prophylaxis and shall offer it to all, who may benefit from this approach. This should also minimize the differences in ABR between centres. It is still an important challenge for all paediatric centres.



In centres using prophylaxis in adults, the ABR differs significantly. There are also adults with severe haemophilia, who have no bleed per year on permanent prophylaxis. This should encourage us to promote further prophylaxis in more adult PWH.



Ideally, children on prophylaxis should have same (lower) bleeding pattern as/than those, who do not need prophylaxis. This is in fact the goal of prophylaxis! Those, who bleed, should be given prophylaxis to decrease the bleeding rate. Those, who have not more than one joint bleed per year without prophylaxis probably do not need it. Paediatric centres should work further on this issue to reflect the fact, that children in these days want to live very active life. The discrepancy between centres should be minimized or should even disappear to guarantee the same level of care nation-wide.

Annual bleeding rate regardless prophylaxis

PWHA
adult centres
N=181

Moderate
Severe

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

Adult centre	ABR (median)					N	Mean	Median	Min	Max	% on permanent prophylaxis
	0	10	20	30	40						
Brno	0					15	0.7	0.0	0	4	6.7%
	2					32	5.0	2.0	0	30	60.6%
Ostrava	1.5					6	5.0	1.5	0	20	33.3%
	1					29	2.8	1.0	0	13	72.4%
Plzeň	0					2	0.0	0.0	0	0	0.0%
	0.5					20	10.5	0.5	0	48	57.1%
Liberec	0					1	0.0	0.0	0	0	0.0%
	3					11	6.3	3.0	0	28	45.5%
Olomouc	1					1	1.0	1.0	1	1	100.0%
	5.5					20	8.3	5.5	0	35	30.0%
Hradec Králové	0.5					2	0.5	0.5	0	1	0.0%
	3					13	9.6	3.0	0	37	33.3%
Ústí nad Labem	0					3	0.0	0.0	0	0	33.3%
	37.5					8	36.3	37.5	10	60	33.3%
Plzeň – Haemacentre	0					1	34.0	34.0	34	34	0.0%
	4					4	5.8	4.0	0	15	75.0%
České Budějovice	0					1	0.0	0.0	0	0	0.0%
	0					12	0.3	0.0	0	3	25.0%

Czech National Hemophilia Program



Similar information for adults. High ABR in some centres might be due to an individual with very severe phenotype and/or perhaps poor compliance. On the other hand, dealing with those patients should be a challenge for respective centres.

Prophylactic regimens and treatment outcomes

PWHA
paed. centres
N=114

Paediatric centre	Severity	Total N	% of patients	N	PERMANENT PROPHYLAXIS						ON-DEMAND / TEMPORARY PROPHY		
					Dosing of prophylaxis (IU/kg per week)				ABR		N	ABR	
					Mean	Median	Min	Max	Mean	Median		Mean	Median
Praha	Moderate	11	18.2%	2	64.1	64.1	60.4	67.7	4.0	4.0	9	2.1	1.0
	Severe	32	87.5%	28	82.2	86.3	34.0	119.7	5.4	4.5	4	0.8	0.5
Brno	Moderate	5	0.0%	0							5	1.0	0.0
	Severe	16	93.8%	15	78.4	75.0	36.1	145.8	6.6	5.0	1	2.0	2.0
Ostrava	Moderate	5	20.0%	1	71.4	71.4	71.4	71.4	3.0	3.0	4	13.5	13.5
	Severe	8	88.0%	8	79.0	77.2	52.4	115.4	2.4	2.0	0	0.0	0.0
Č. Budějovice	Moderate	4	50.0%	2	46.2	46.2	23.1	69.2	2.0	2.0	2	2.0	2.0
	Severe	8	87.5%	7	65.2	71.4	29.4	83.9	3.1	3.0	1	1.0	1.0
Hradec Králové	Moderate	5	40.0%	2	45.8	45.8	12.2	79.5	0.0	0.0	3	0.7	1.0
	Severe	2	100.0%	2	79.4	79.4	58.8	100.0	1.0	1.0	0	0.0	0.0
Ústí nad Labem	Moderate	3	0.0%	0							3	0.3	0.0
	Severe	5	60.0%	3	55.5	54.1	53.6	58.8	2.7	2.0	2	2.5	2.5
Píseň	Moderate	0	0.0%	0							0	0.0	0.0
	Severe	5	80.0%	4	63.6	73.7	23.0	84.0	0.8	1.0	1	5.0	5.0
Olomouc	Moderate	3	33.3%	1	47.6	47.6	47.6	47.6	5.0	5.0	2	3.0	3.0
	Severe	2	50.0%	1	50.0	50.0	50.0	50.0	3.0	3.0	1	0.0	0.0



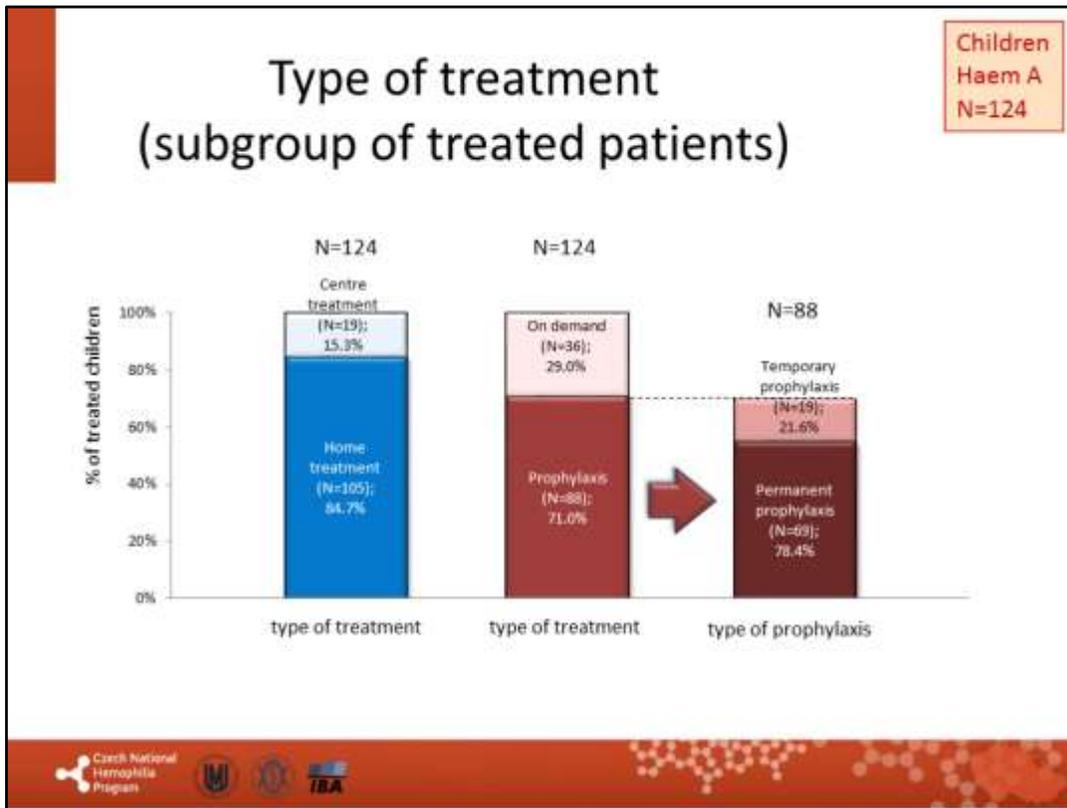
More detailed description of prophylactic dosing/regimens used by different paediatric centres within CNHP and its correlation with annual bleeding rates in respective centres.

Prophylactic regimens and treatment outcomes

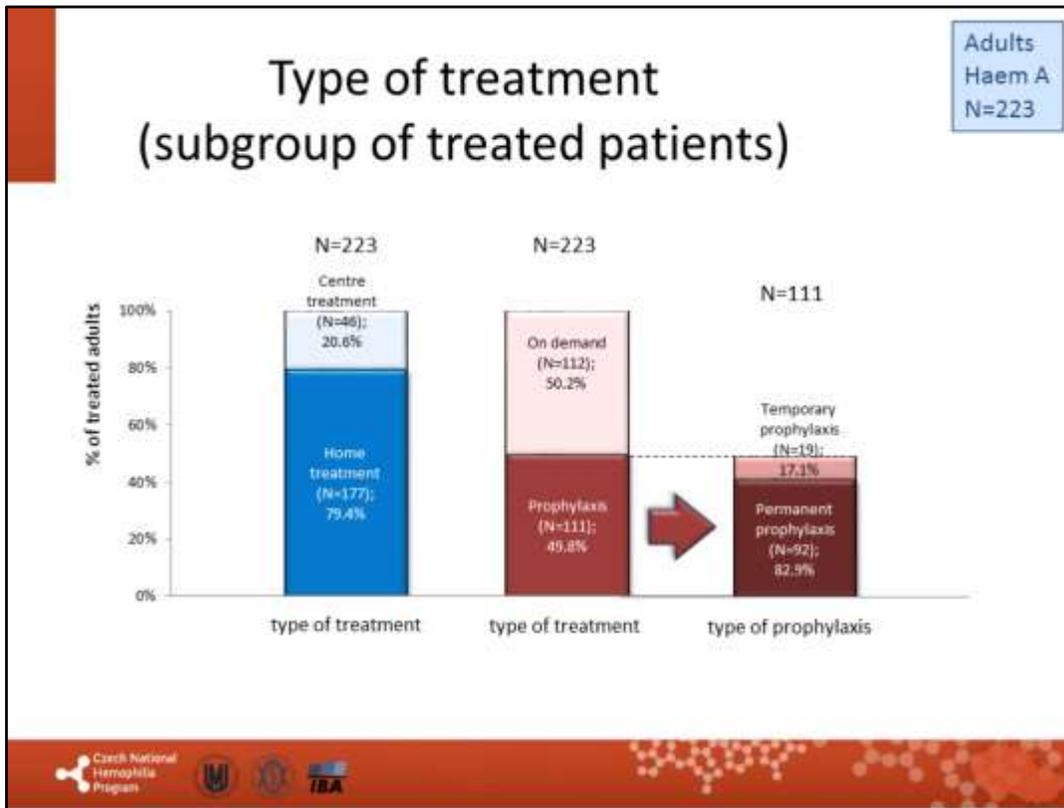
PWHA
adult centres
N=182

Adult centre	Severity	Total N	% of patients	N	PERMANENT PROPHYLAXIS							ON-DEMAND / TEMPORARY PROPHY			
					Dosing of prophylaxis (IU/kg per week)				ABR		Age	N	ABR		Age
					Mean	Median	Min	Max	Mean	Median	Median		Mean	Median	Median
Brno	Moderate	15	6.7%	1	42.9	42.9	42.9	42.9	4.0	4.0	27	14	0.4	0.0	39
	Severe	32	60.6%	20	50.2	37.6	10.9	233.3	2.8	1.5	34	12	8.6	7.0	55
Ostrava	Moderate	6	33.3%	2	39.0	39.0	23.5	54.5	10.0	10.0	66	4	2.5	1.5	51
	Severe	29	72.4%	21	50.5	52.3	15.6	92.3	2.0	1.0	37	8	4.6	4.0	62
Píseň	Moderate	2	0.0%	0								2	0.0	0.0	35
	Severe	20	57.1%	12	33.9	34.9	14.7	60.0	4.6	0.0	48	8	19.3	13.5	46
Liberec	Moderate	1	0.0%	0								1	0.0	0.0	35
	Severe	11	45.5%	5	55.9	51.7	37.3	94.3	1.8	1.0	32	6	10.0	9.0	62
Olomouc	Moderate	1	100.0%	1	41.1	41.1	41.1	41.1	1.0	1.0	26	0	0.0	0.0	0
	Severe	20	30.0%	6	44.4	43.2	13.7	100.0	1.5	1.5	27	14	11.2	10.5	56
Hradec Králové	Moderate	2	0.0%	0								2	0.5	0.5	21
	Severe	13	33.3%	5	65.5	65.9	52.6	83.3	8.4	4.0	33	8	10.4	3.0	30
Ústí n. Labem	Moderate	3	33.3%	1	60.0	60.0	60.0	60.0	0.0	0.0	24	2	0.0	0.0	21
	Severe	9	33.3%	3	41.3	31.7	6.9	85.2	27.3	21.0	31	5	41.6	52.0	37
Píseň - Haemacentre	Moderate	1	0.0%	0					0.0	0.0	0	1	34.0	34.0	47
	Severe	4	75.0%	3	33.4	21.4	18.3	60.5	7.7	5.0	43	1	0.0	0.0	34
Č. Budějovice	Moderate	1	0.0%	0								1	0.0	0.0	70
	Severe	12	25.0%	3	59.9	70.6	34.1	75.0	0.0	0.0	40	9	0.4	0.0	51

More detailed description of prophylactic dosing/regimens used by different adult centres within CNHP and its correlation with annual bleeding rates in respective centres.



Over 80% of children treated in 2016 took the advantage of home treatment. 71% of treated children were commenced on any type of prophylaxis (was 64% in 2015) and 78% out of those on prophylaxis were on permanent prophylaxis in 2016 (was 92% in 2015).



80% of adults treated in 2016 took the advantage of home treatment (no change compared to 2015). 50% of treated adults were commenced on any type of prophylaxis (was 45% in 2015) and 83% out of those on prophylaxis were on permanent prophylaxis in 2016 (was 79% in 2015).

Part B.1

Demographic characteristics Haemophilia B



Czech National
Hemophilia
Program



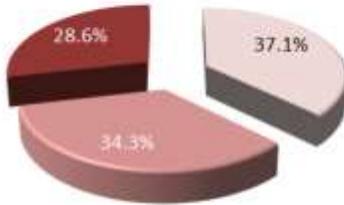
ISTA

Severity of haemophilia B

Haem B
N=98

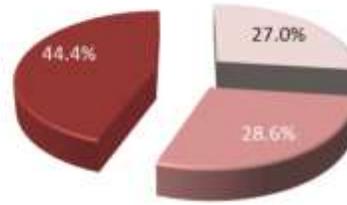
Children (N=35)

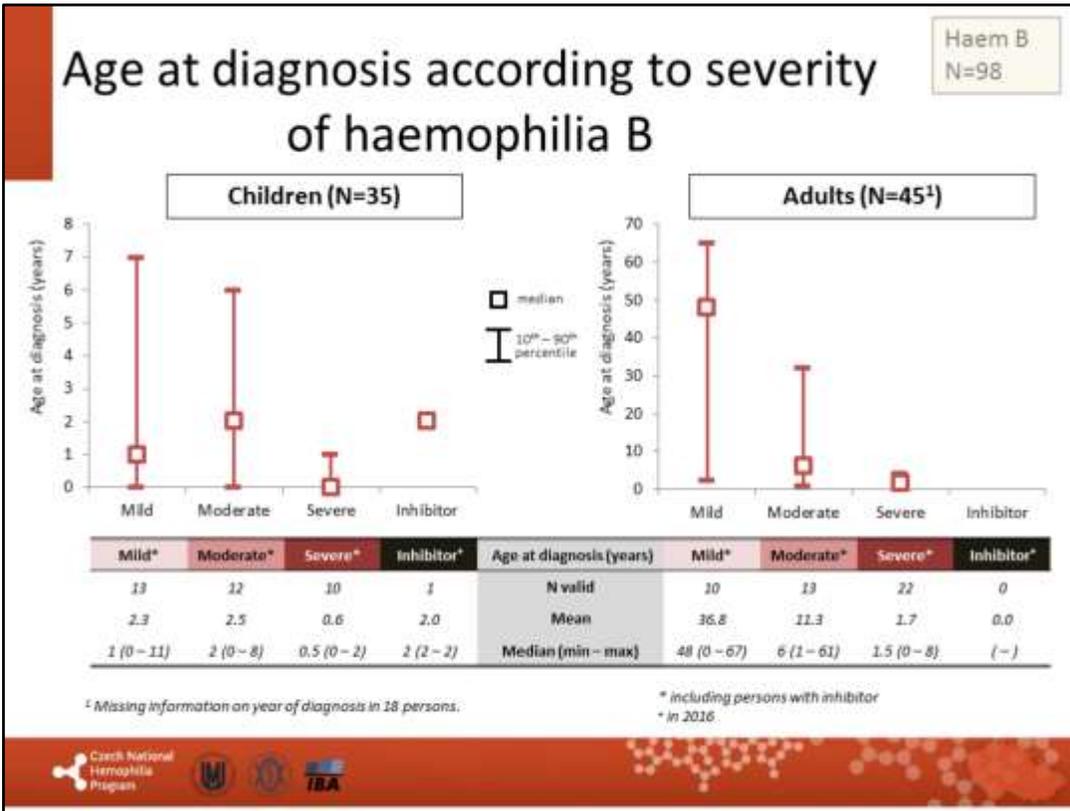
- Mild (N=13)
- Moderate (N=12)
- Severe (N=10)



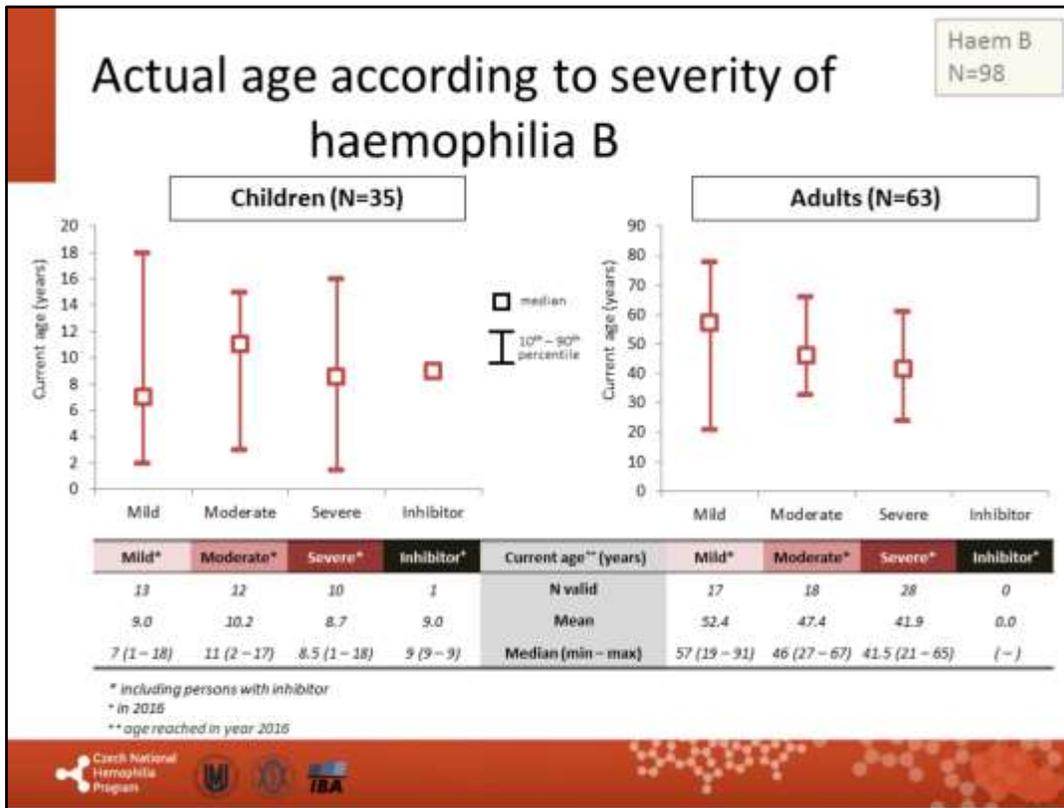
Adults (N=63)

- Mild (N=17)
- Moderate (N=18)
- Severe (N=28)





There is no major difference in demographics between HA and HB.



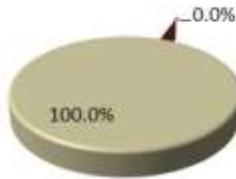
There is no major difference in demographics between HA and HB, perhaps adults with HB are slightly older than those, with HA.

Hepatitis (ever) experienced

Children
Haem B
N=35

Experienced hepatitis

- Yes (N=0)
- No (N=35)



No child has hepatitis C.

Data from last annual report of each person.



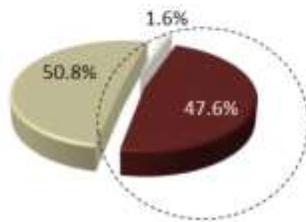
NO HepC infection in children since late 90's. None of Czech children with HB is infected with Hepatitis C.

Hepatitis (ever) experienced

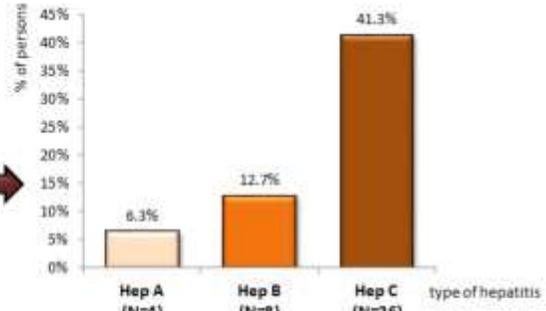
Adults
Haem B
N=63

Experienced hepatitis

- Yes (N=30)
- No (N=32)
- Not known (N=1)



N=30*

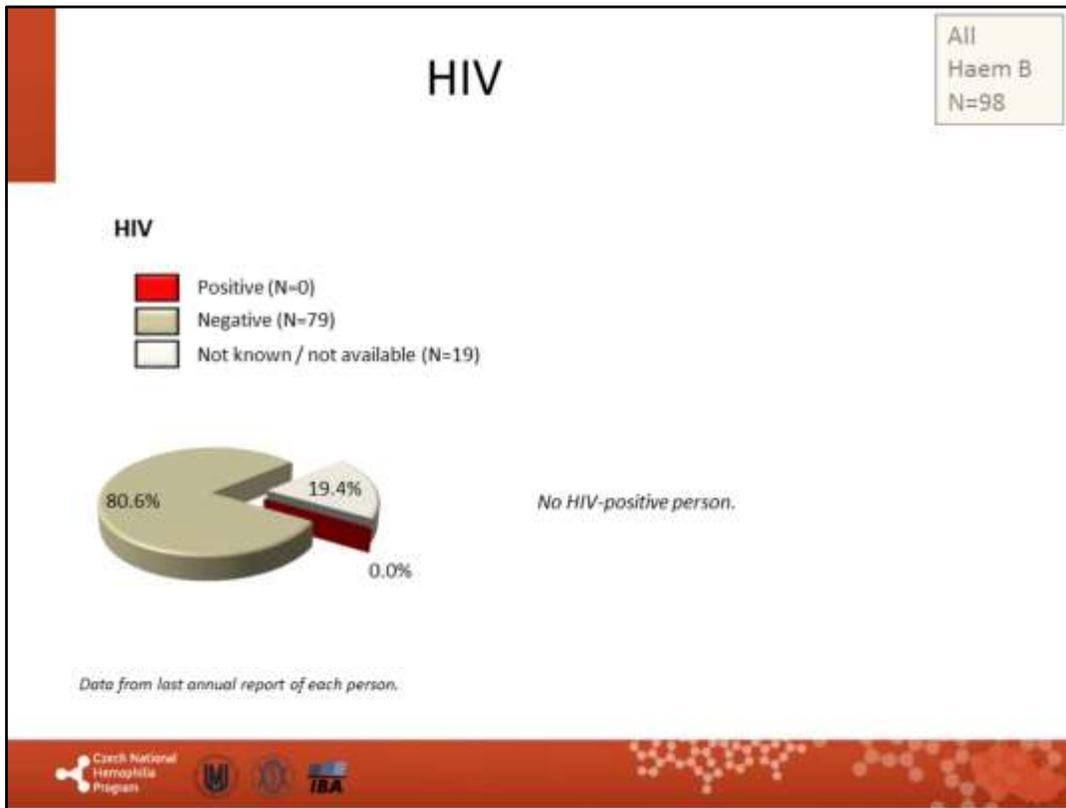


Data from last annual report of each person.

*Total of 38 cases of hepatitis in 30 persons. One person may have more types of hepatitis recorded.



There has been NO NEW HepC infection in 2016.
26 PWHB ever experienced hepatitis, though some of them may have been successfully treated (numbers of successfully treated not shown here).



Very low number of HIV positive PWH due to low/no access to contaminated concentrates in 80s and 90s. Our current treatment is on a very high safety level. No new HIV reported in any PWH since late 90s.

Part B.2

Treatment outcomes and bleeding frequency Haemophilia B



Czech National
Hemophilia
Program



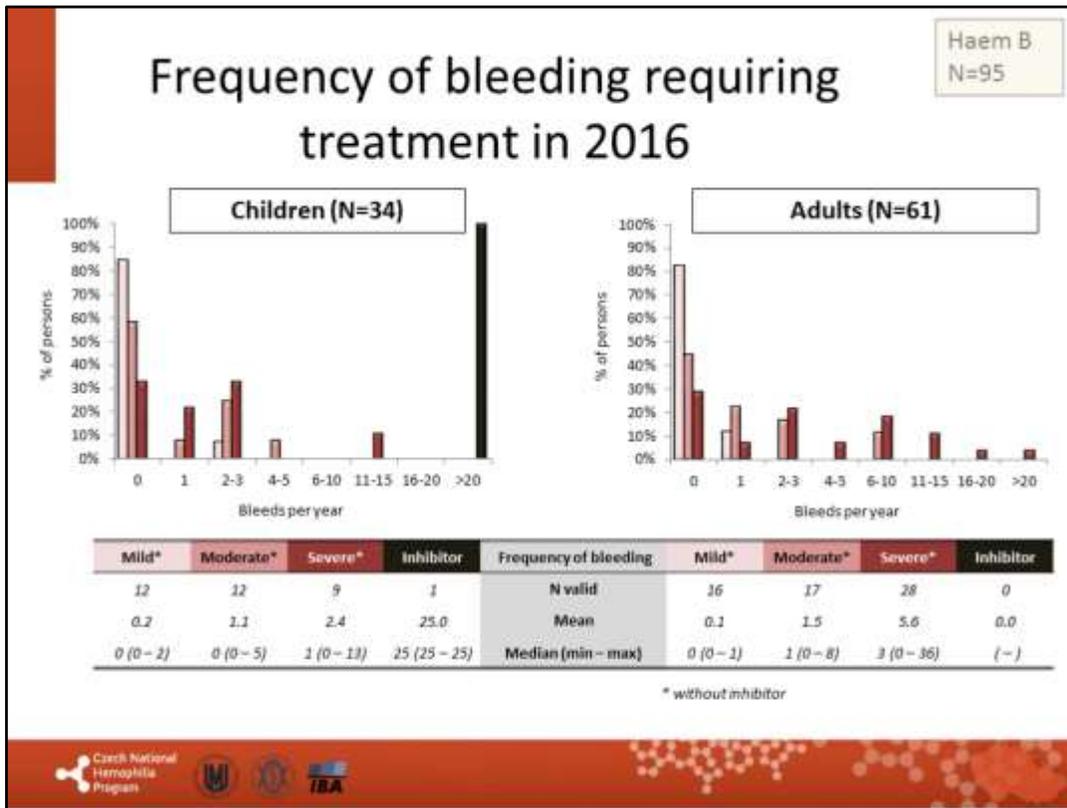
ISTA

Data from year 2016 – sample size

All
Haem B
N=98

	Valid persons		→	Persons with annual report in 2016		→	Persons examined in 2016		→	Persons treated in 2016	
	N	%		N	%		N	%		N	%
All	98	100%	→	95	96.9%	→	84	85.7%	→	63	64.3%
of them with inhibitor	1			1			1			1	
Children	35	100%	→	34	97.1%	→	33	94.3%	→	19	54.3%
of them with inhibitor	1			1			1			1	
Adults	63	100%	→	61	96.8%	→	51	81.0%	→	44	69.8%
of them with inhibitor	-			-			-			-	

See previous comment for the same slide related to HA.

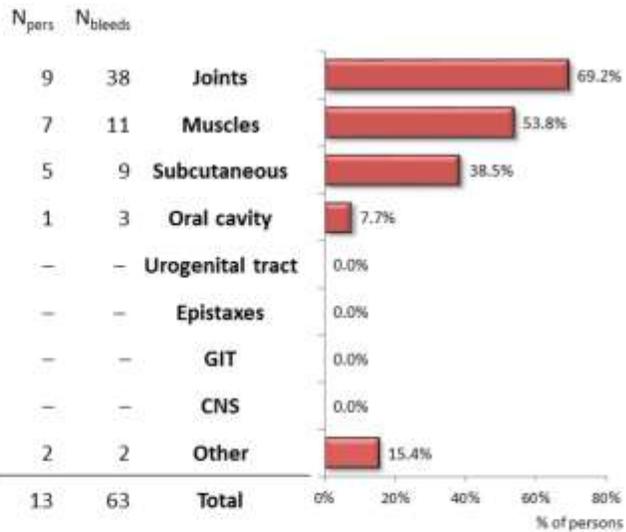


Data shown document good efficacy of care provided to Czech PWH, no matter what age category they are. Mean/Median number of bleedings per year (ABR) is 5,6/3 for adults and 2,4/1 in children with severe HB.

Location of bleeds in 2016

Children
Haem B
N=34

13 (38.2%) children experienced bleeding requiring treatment at least once in year; 63 bleeds were recorded in total, 2 bleeds required hospitalization. All 13 of these children have recorded location of their bleeds.
21 (61.8%) children recorded no bleed during year 2016.

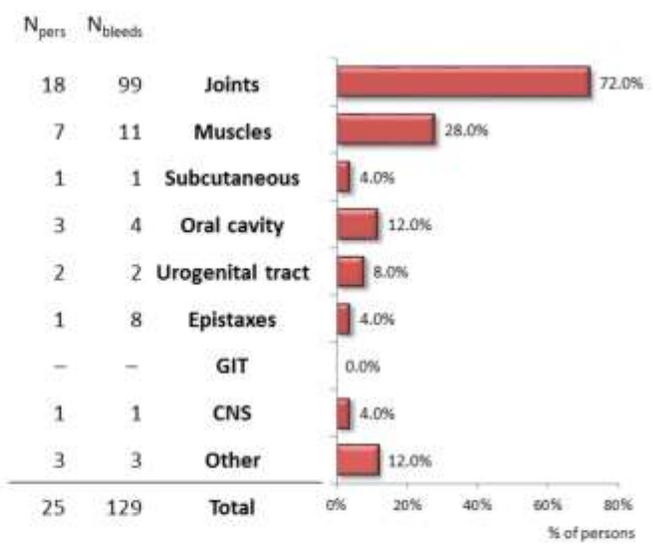


There was no CNS bleed in children with haemophilia B in 2016. 61,6% of children had no bleed at all.

Location of bleeds in 2016

Adults
Haem B
N=61

31 (50.8%) adults experienced bleeding requiring treatment at least once in year; 185 bleeds were recorded in total, 2 bleeds required hospitalization. 25 of these 31 adults have recorded location of their bleeds. Localization is not known in 6 adults. 30 (49.2%) adults have recorded no bleed during year 2016.

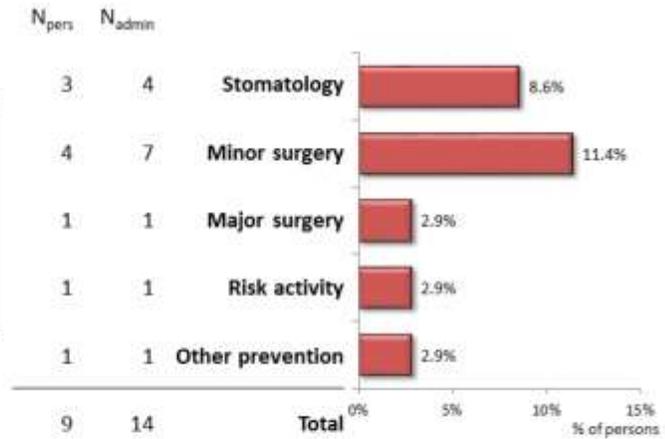


Bleeding events in adults.

Preventive administration in 2016

Children
Haem B
N=34

9 (26.5%) children were given factor to prevent bleeding during/before risk situation. 14 preventive administrations were recorded in total.

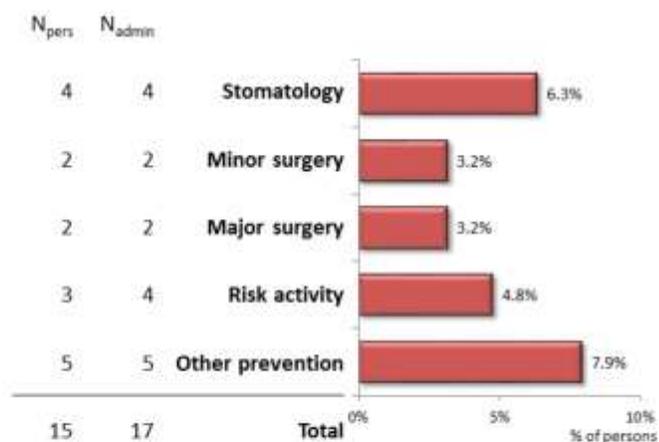


This figure refers to preventive factors administration in children with HB.

Preventive administration in 2016

Adults
Haem B
N=61

15 (24.6%) persons were given factor to prevent bleeding during/before risk situation.
17 preventive administrations were recorded in total.



This figure refers to preventive factors administration in adults with HB.

Part B.3

ABR according to treatment regimen Haemophilia B without inhibitor

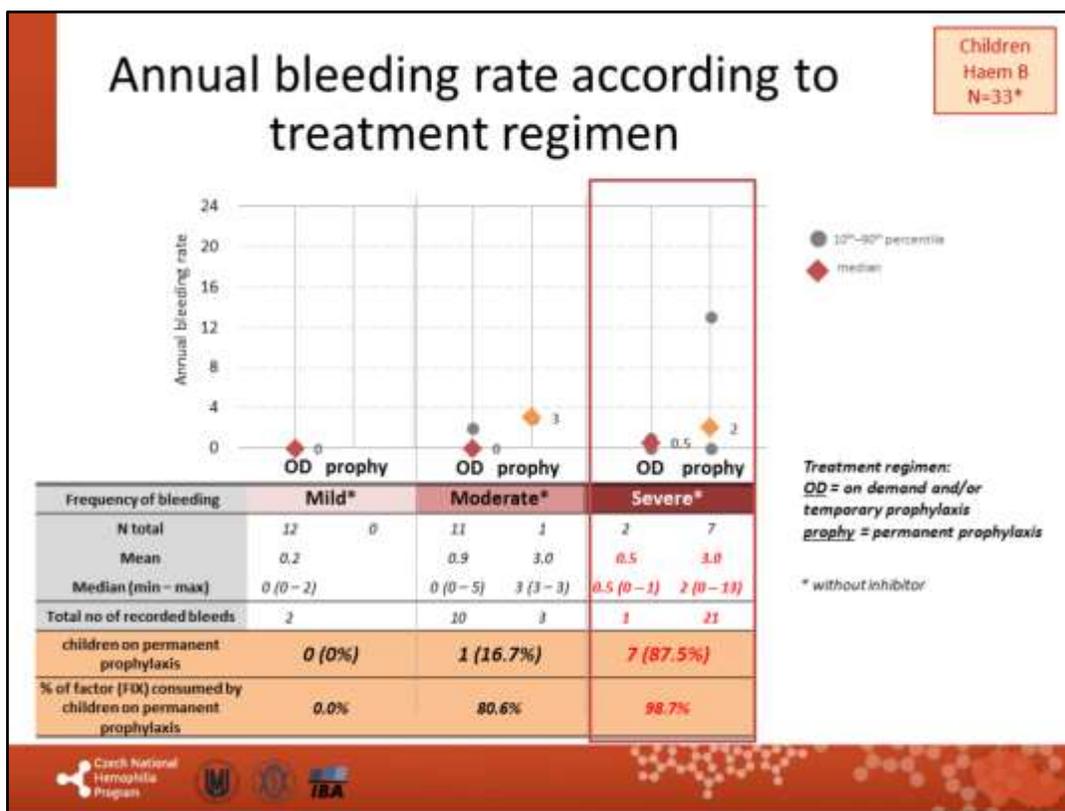


Czech National
Hemophilia
Program



ISTA





The data on bleeding rate in children with HB. The interval range in children with severe HB should be smaller, though. In general, less bleeds in children with HB.

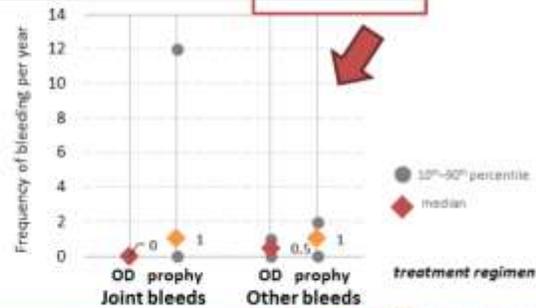
Joint and other bleeds according to treatment regimen

Children
Haem B
N=33*

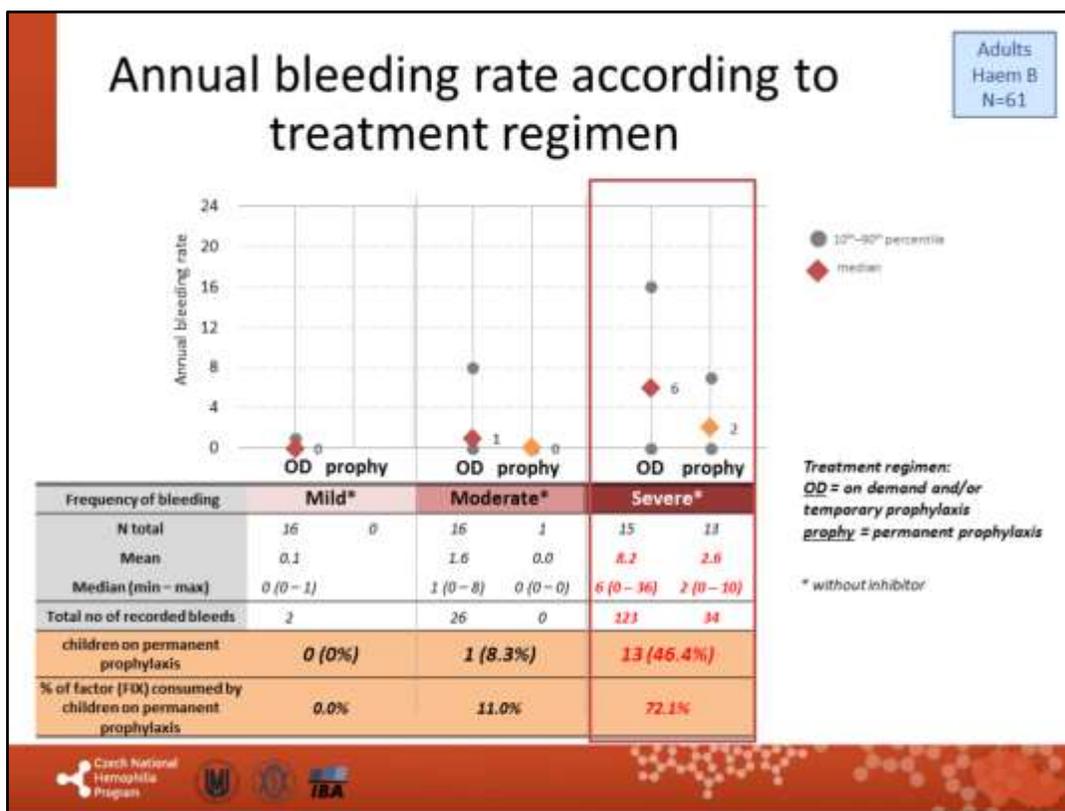
Frequency of bleeding	Mild*		Moderate*		Severe*	
	OD	prophy	OD	prophy	OD	prophy
Treatment regimen	OD	prophy	OD	prophy	OD	prophy
N valid	12	0	11	1	2	7
JOINT BLEEDS						
Mean	0.0		0.4	3.0	0.0	2.3
Median (range)	0 (0-0)		0 (0-2)	3 (3-3)	0 (0-0)	1 (0-12)
Total no of recorded bleeds	0		4	3	0	16
OTHER BLEEDS						
Mean	0.2		0.5	0.0	0.5	0.9
Median (range)	0 (0-2)		0 (0-3)	0 (0-0)	0.5 (0-1)	1 (0-2)
Total no of recorded bleeds	2		6	0	1	6

* without inhibitor

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



The same is true for joint bleeds.



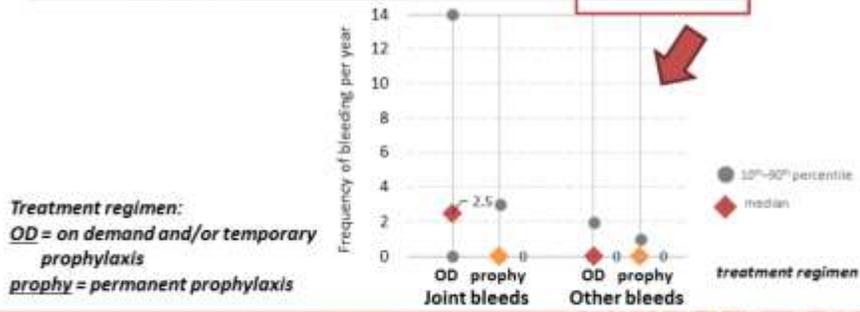
As well as in HA, adults with severe haemophilia B, who bleed frequently should be commenced on prophylaxis.

Joint and other bleeds according to treatment regimen

Adults
Haem B
N=55*

Frequency of bleeding	Mild*		Moderate*		Severe*	
	OD	prophy	OD	prophy	OD	prophy
Treatment regimen	OD	prophy	OD	prophy	OD	prophy
N valid	15	0	14	1	14	11
JOINT BLEEDS						
Mean	0.0		0.1	0.0	5.5	1.5
Median (range)	0 (0-0)		0 (0-1)	0 (0-0)	2.5 (0-15)	0 (0-7)
Total no of recorded bleeds	0		2	0	77	17
OTHER BLEEDS						
Mean	0.1		1.0	0.0	0.7	0.5
Median (range)	0 (0-1)		0 (0-8)	0 (0-0)	0 (0-5)	0 (0-2)
Total no of recorded bleeds	1		14	0	10	5

* without inhibitor; missing location of bleeds in 6 adults



The same is true also for joint bleeds in PWHB.

Part B.4

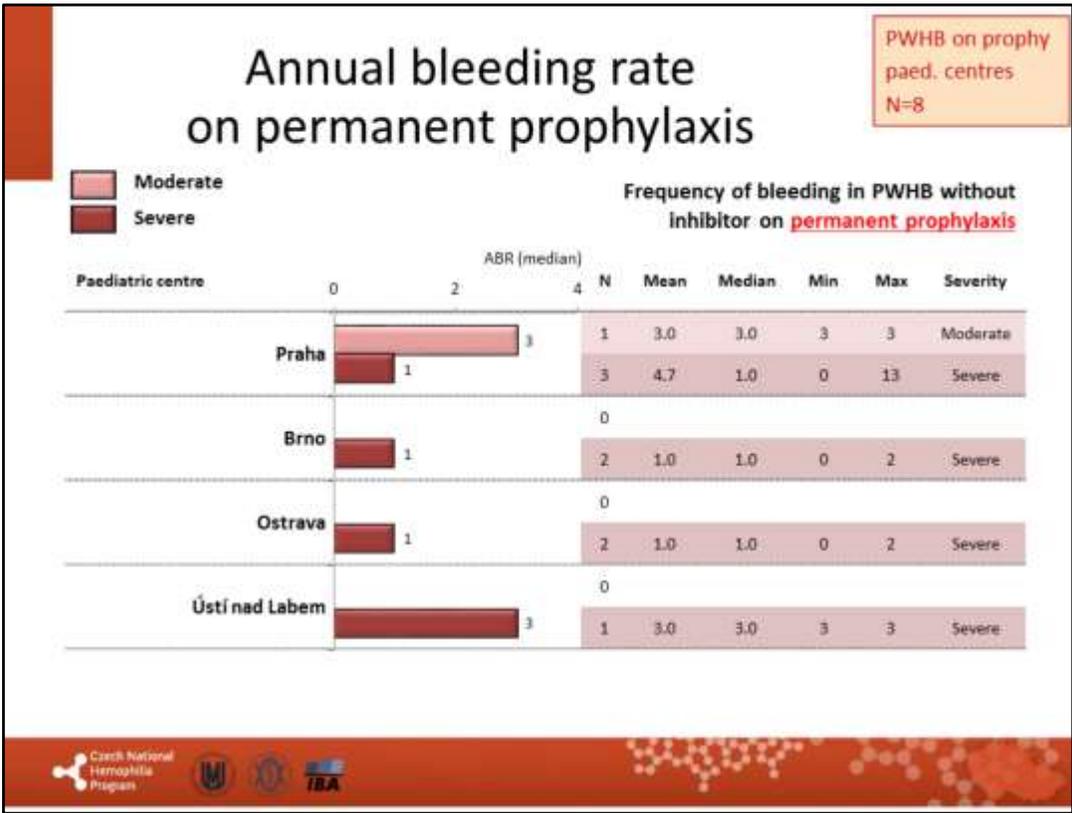
ABR according to centres Haemophilia B (PWHB)



Czech National
Hemophilia
Program



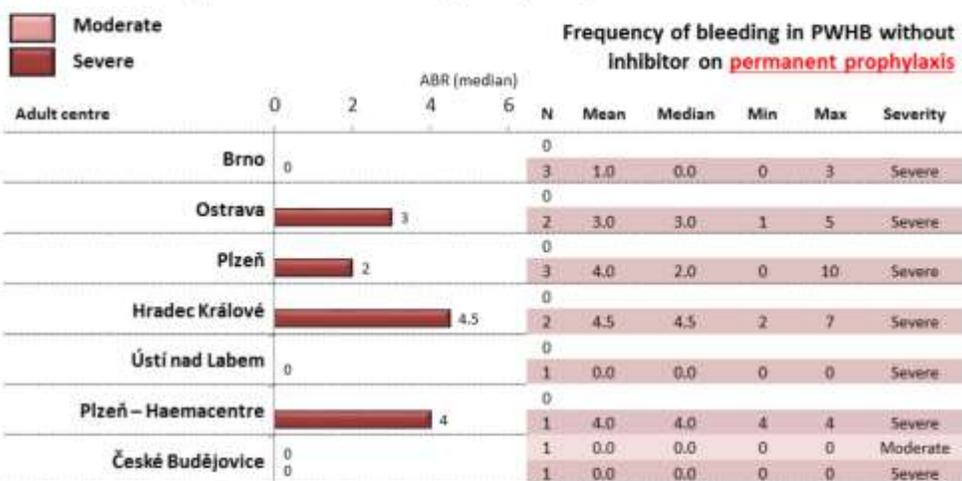
ISTA



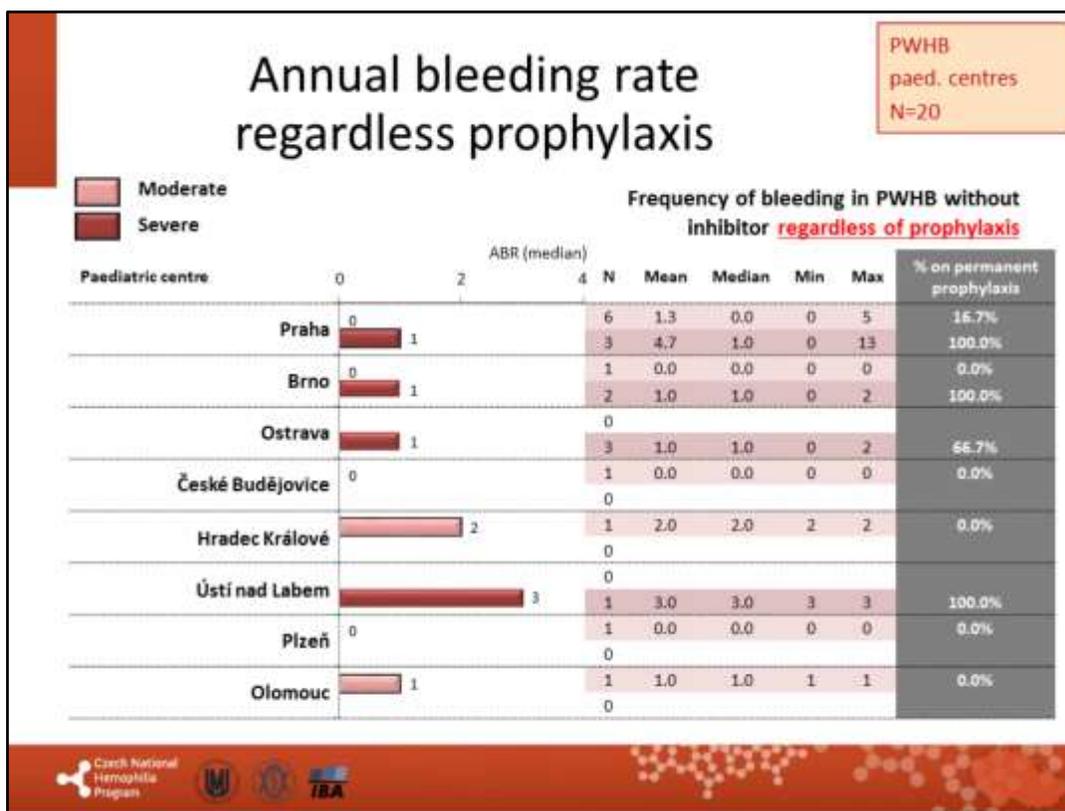
Not all centres treat children with HB. The median ABR is relatively low, but at least one child with severe HB has ABR over 10 despite of prophylaxis.

Annual bleeding rate on permanent prophylaxis

PWHB on prophylaxis
adult centres
N=14



Similar situation for adults with HB. HB, though, means significantly less burden for patients, compared to adults with HA.



This slide describes the treatment of children with HB regardless of prophylaxis in those centres, which treat PWHB.

Annual bleeding rate regardless prophylaxis

PWHB
adult centres
N=46

Moderate
Severe

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

Adult centre	ABR (median)		N	Mean	Median	Min	Max	% on permanent prophylaxis
	Moderate	Severe						
Brno	1	3	4	2.5	1.0	0	8	0.0%
	1	1	5	4.2	3.0	0	15	60.0%
Ostrava	2	1	2	2.0	2.0	2	2	0.0%
	1	1	6	3.0	1.0	0	11	33.3%
Pízeň	2	6	3	3.3	2.0	0	8	0.0%
	1	1	4	12.0	6.0	0	36	75.0%
Liberec	0	16	1	0.0	0.0	0	0	0.0%
	1	1	1	16.0	16.0	16	16	0.0%
Olomouc	0.5	7.5	6	0.7	0.5	0	2	0.0%
	1	1	4	9.0	7.5	6	15	0.0%
Hradec Králové	0	2	1	0.0	0.0	0	0	0.0%
	1	1	3	3.0	2.0	0	7	66.7%
Ústí nad Labem	1.5	0	2	1.5	1.5	0	3	50.0%
	1	1	0	0	0	0	0	0.0%
Pízeň – Haemacentre	4	0	1	4.0	4.0	4	4	100.0%
	1	1	1	0.0	0.0	0	0	100.0%
České Budějovice	0	1	2	1.0	1.0	0	2	50.0%
	1	1	1	0.0	0.0	0	0	0.0%

Czech National Hemophilia Program



This slide describes the treatment of adults with HB regardless of prophylaxis in those centres, which treat PWHB.

Prophylactic regimens and treatment outcomes

PWHB
paed. centres
N=20

Paediatric centre	Severity	Total N	% of patients	N	PERMANENT PROPHYLAXIS						ON-DEMAND / TEMPORARY PROPHY		
					Dosing of prophylaxis (IU/kg per week)				ABR		N	ABR	
					Mean	Median	Min	Max	Mean	Median		Mean	Median
Praha	Moderate	6	16.7%	1	58.8	58.8	58.8	58.8	3.0	3.0	5	1.0	0.0
	Severe	3	100.0%	3	66.5	55.0	53.6	91.0	4.7	1.0	0		
Brno	Moderate	1	0.0%	0							1	0.0	0.0
	Severe	2	100.0%	2	33.0	33.0	33.0	33.0	2.0	2.0	0		
Ostrava	Moderate	0											
	Severe	3	66.7%	2	60.6	60.6	59.6	61.5	1.0	1.0	1	1.0	1.0
Č. Budějovice	Moderate	1	0.0%	0							1	0.0	0.0
	Severe	0											
Hradec Králové	Moderate	1	0.0%	0							1	2.0	2.0
	Severe	0											
Ústí nad Labem	Moderate	0											
	Severe	1	100.0%	1	55.8	55.8	55.8	55.8	3.0	3.0	0		
Píseň	Moderate	1	0.0%	0							1	0.0	0.0
	Severe	0											
Olomouc	Moderate	1	0.0%	0							1	1.0	1.0
	Severe	0											

More detailed description of prophylactic dosing/regimens used by different paediatric centres within CNHP and its correlation with annual bleeding rates in respective centres.

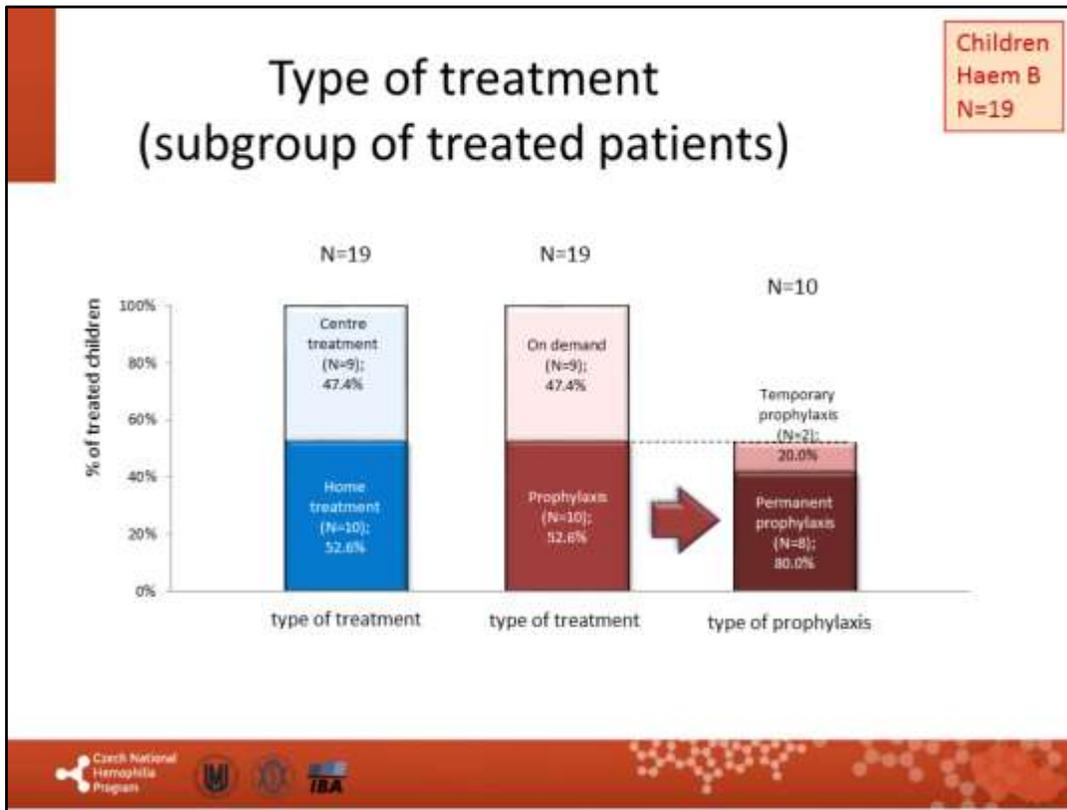
Prophylactic regimens and treatment outcomes

PWHB
adult centres
N=46

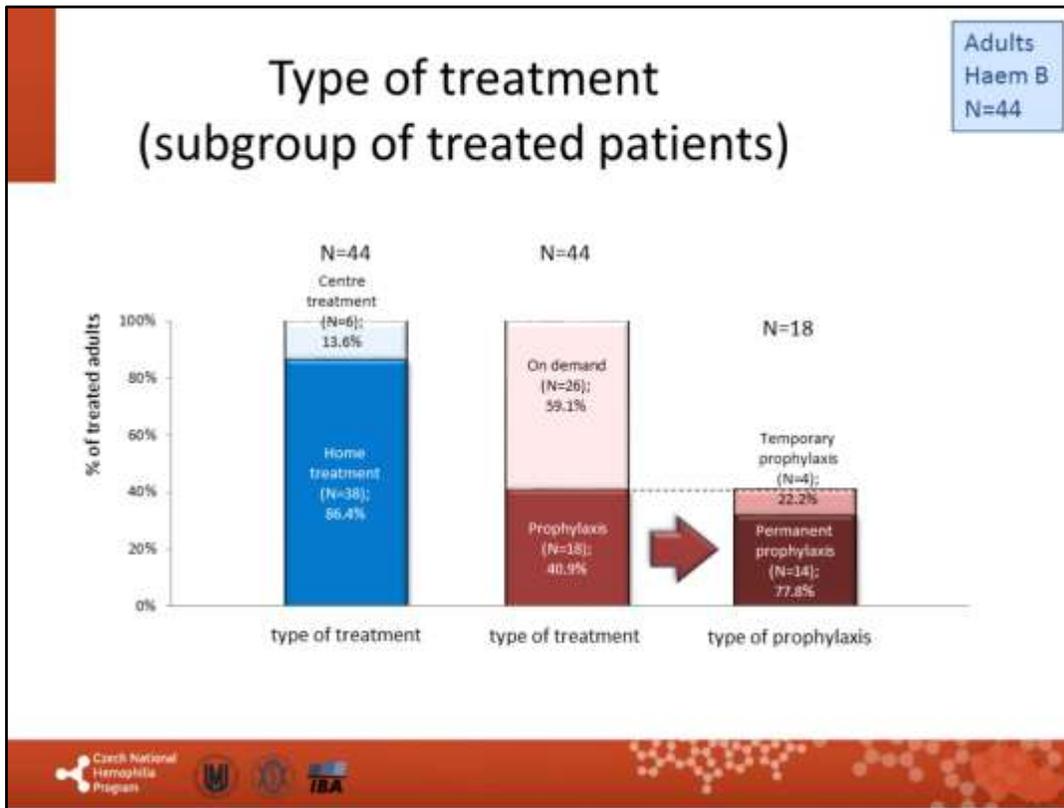
Adult centre	Severity	Total N	% of patients		PERMANENT PROPHYLAXIS							ON-DEMAND / TEMPORARY PROPHY				
					N	Dosing of prophylaxis (IU/kg per week)				ABR		Age	N	ABR		Age
						Mean	Median	Min	Max	Mean	Median	Median		Mean	Median	Median
Brno	Moderate	4	0.0%	0								4	2.5	1.0	47	
	Severe	5	60.0%	3	50.5	48.0	46.2	57.2	1.0	0.0	24	2	9.0	9.0	61	
Ostrava	Moderate	2	0.0%	0								2	2.0	2.0	25	
	Severe	6	33.3%	2	45.8	45.8	37.9	53.7	3.0	3.0	43	4	3.0	0.5	53	
Píseň	Moderate	3	0.0%	0					0.0	0.0	0	3	3.3	2.0	54	
	Severe	4	75.0%	3	8.1	6.1	5.3	13.0	4.0	2.0	40	1	36.0	36.0	34	
Liberec	Moderate	1	0.0%	0								1	0.0	0.0	43	
	Severe	1	0.0%	0								1	16.0	16.0	24	
Olomouc	Moderate	6	0.0%	0								6	0.7	0.5	43	
	Severe	4	0.0%	0								4	9.0	7.5	49	
Hradec Králové	Moderate	1	0.0%	0								1	0.0	0.0	62	
	Severe	3	66.7%	2	108.2	108.2	108.2	108.2	4.5	4.5	38	1	0.0	0.0	60	
Ústí n. Labem	Moderate	0														
	Severe	2	50.0%	1	49.3	49.3	49.3	49.3	0.0	0.0	21	1	3.0	3.0	45	
Píseň - Haemacentre	Moderate	0														
	Severe	1	100.0%	1	37.5	37.5	37.5	37.5	4.0	4.0	35	0				
Č. Budějovice	Moderate	1	100.0%	1	6.7	6.7	6.7	6.7	0.0	0.0	50	0				
	Severe	2	50.0%	1	42.1	42.1	42.1	42.1	0.0	0.0	53	1	2.0	2.0	43	



More detailed description of prophylactic dosing/regimens used by different adult centres within CNHP and its correlation with annual bleeding rates in respective centres.



Only 52,5% of children treated in 2016 took the advantage of home treatment. 52% of treated children were commenced on any type of prophylaxis and 80% out of those on prophylaxis were on permanent prophyl in 2016.



86% of adults treated in 2016 took the advantage of home treatment. 40% of treated adults were commenced on any type of prophylaxis and 78% out of those on prophylaxis were on permanent prophylaxis in 2016.

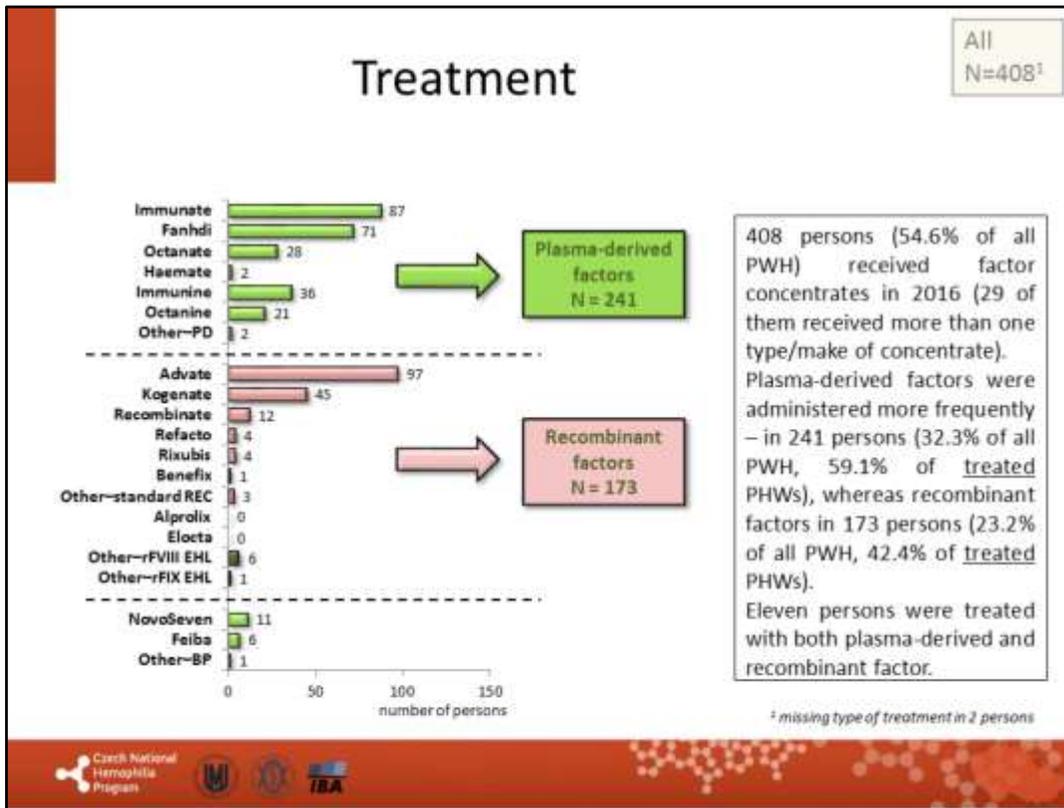
Part C.1

Treatment data and factor consumption Haemophilia A and B

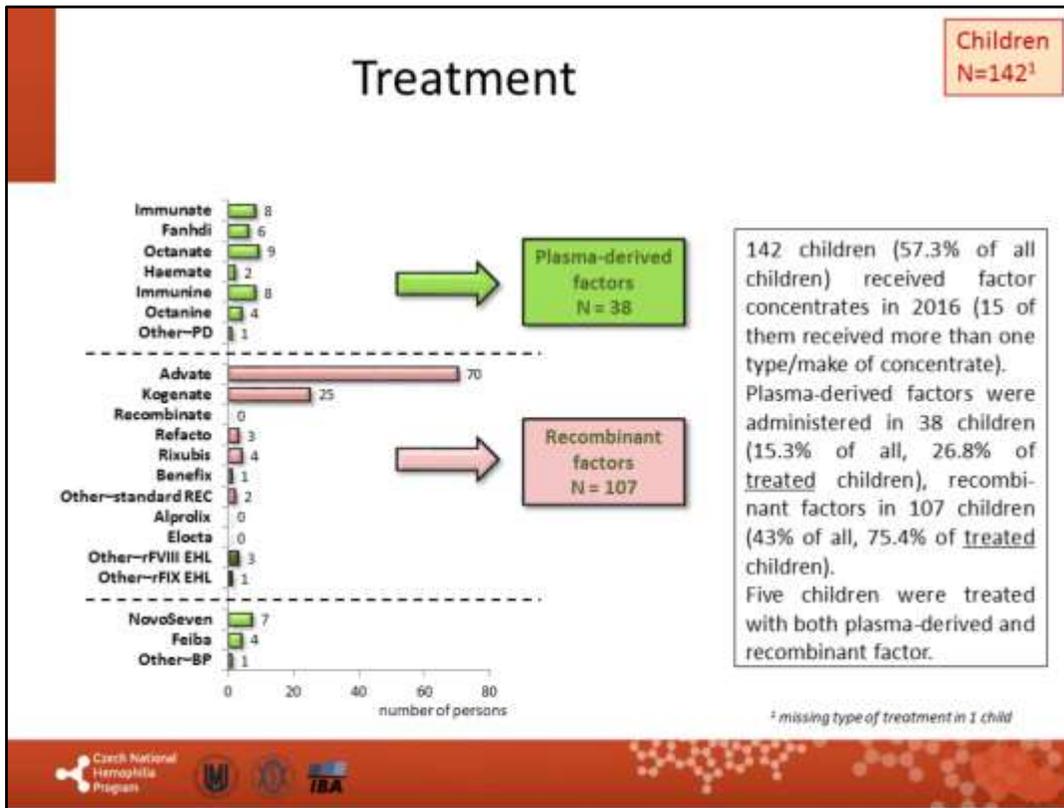


Czech National
Hemophilia
Program

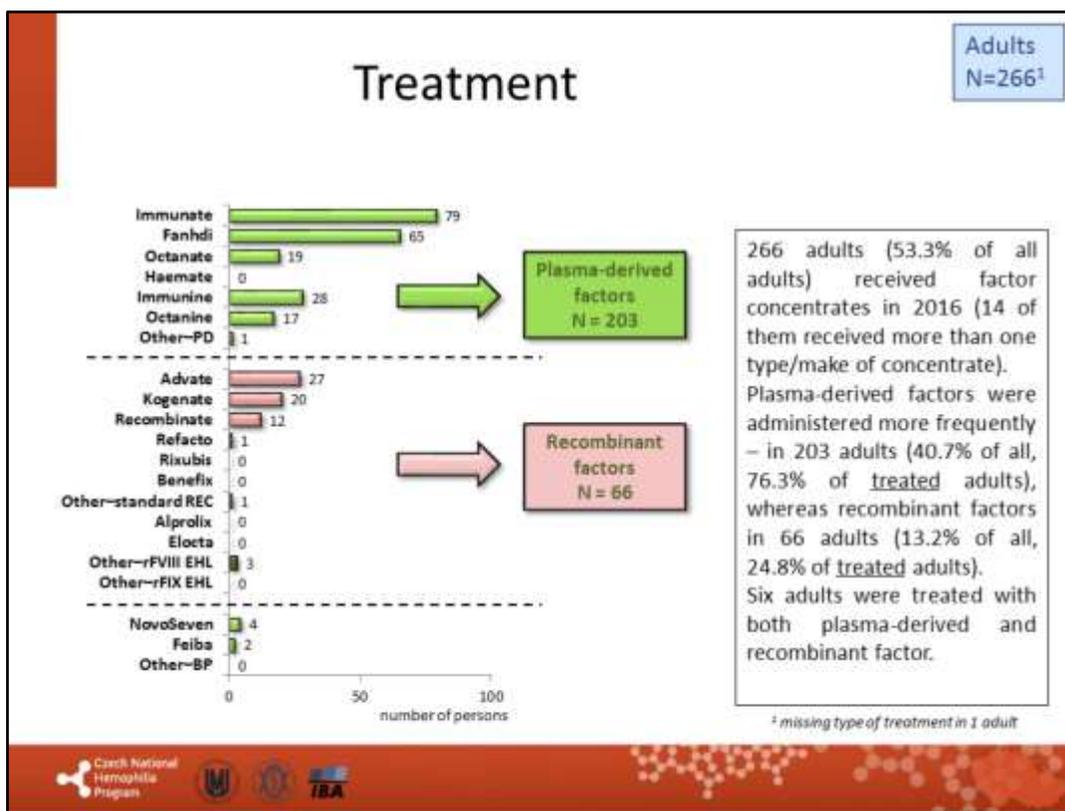




42% of PWH registered in CNHP registry and treated with any factor concentrate were treated with recombinants in 2016. The number of PWH treated with recombinants is gradually increasing over last several years. This is not only due to the recommendation of CNHP to treat PUPs with recombinants (since 2006), but also reflects switches of older children and adults to rFVIII in some cases.



Over 75% of children, who were given factor concentrate in 2016, were treated with recombinants.



Number of adult PWH treated with recombinants is slowly increasing (currently 25% of those treated with factor concentrate in 2016 and registered within CNHP registry).

Comparison of treatment in years 2015 and 2016

All

	2016			2015		
	N	% of all PWH	% treated PWH	N	% of all PWH	% treated PWH
All persons with treatment	414	55.4	100.0	423	57.5	100.0
<i>Plasma-derived factor</i>	241	32.3	58.2	261	35.5	61.7
<i>Recombinant factor</i>	173	23.2	41.8	162	22.0	38.3
Without treatment	333	44.6	-	313	42.5	-
Total	747	100.0	-	736	100.0	-

This table compares data between 2015 and 2016. E.g. you can see, that percentage of patients treated with recombinant concentrates and registered within CNHP registry changed from 38,3% in 2015 to 41,8% in 2016.

Comparison of treatment in years 2015 and 2016

Children

	2016			2015		
	N	% of all PWH	% treated PWH	N	% of all PWH	% treated PWH
All children with treatment	145	58.5	100.0	138	56.3	100.0
<i>Plasma-derived factor</i>	38	15.3	26.2	42	17.1	30.4
<i>Recombinant factor</i>	107	43.1	73.8	96	39.2	69.6
Without treatment	103	41.5	-	107	43.7	-
Total	248	100.0	-	245	100.0	-

This table compares data between 2015 and 2016. E.g. you can see, that percentage of patients treated with recombinant concentrates and registered within CNHP registry changed from 69,6% in 2015 to 73,8% in 2016.

Comparison of treatment in years 2015 and 2016

Adults

	2016			2015		
	N	% of all PWH	% treated PWH	N	% of all PWH	% treated PWH
All children with treatment	269	108.5	185.5	285	116.3	206.5
<i>Plasma-derived factor</i>	203	81.9	140.0	219	89.4	158.7
<i>Recombinant factor</i>	66	26.6	45.5	66	26.9	47.8
Without treatment	230	92.7	-	206	84.1	-
Total	499	201.2	-	491	200.4	-

This table compares data between 2015 and 2016. E.g. you can see, that percentage of patients treated with recombinant concentrates and registered within CNHP registry changed from 47,8% in 2015 to 45,5% in 2016.

Consumption of drugs

All

Drug (IU)	Total annual consumption	Number of treated persons	Consumption per treated person	Number of valid persons	Average annual consumption per valid person
FVIII (IU)					
<i>Immunate</i>	6 317 635	87	72 616.5		
<i>Fanhdli</i>	7 376 500	71	103 894.4		
<i>Octanate</i>	2 825 500	28	100 910.7		
<i>Haemate P</i>	2 475 500	2	1 237 750.0		
<i>Other plasma-derived</i>	312 500	1	312 500.0		
FVIII PD total	19 307 635	185	104 365.6		
<i>Advate</i>	12 574 800	97	129 637.1		
<i>Kogenate</i>	6 114 500	45	135 877.8		
<i>Recombinate</i>	2 149 000	12	179 083.3		
<i>Refacto</i>	374 000	4	93 500.0		
<i>Other recombinant</i>	859 000	3	286 333.3		
FVIII REC total*	22 071 300	158	139 691.8		
FVIII total*	41 378 935	338	123 151.6	649	63 758.0
FIX (IU)					
<i>Immune</i>	1 723 200	36	47 866.7		
<i>Octanine</i>	2 101 000	21	100 047.6		
<i>Other plasma-derived</i>	26 500	1	26 500.0		
FIX PD total	3 850 700	56	68 762.5		
<i>Rixubis</i>	128 000	4	32 000.0		
<i>Benefix</i>	158 000	1	158 000.0		
<i>Other recombinant</i>	271 506	3	90 502.0		
FIX REC total*	557 506	8	69 688.3		
FIX total*	4 408 206	60	73 470.1	98	44 981.7
EHL (IU)					
<i>FVIII</i>	1 508 101.0	6	251 350.2		
<i>FIX</i>	166 381.0	1	166 381.0		
„by-pass“					
<i>Feiba (U)</i>	1 752 475	6	292 079.2		
<i>NovoSeven (mg)</i>	4 121.0	11	374.6		
<i>Other rFVIIa (mg)</i>	134.4	1	134.4		

* excluding patients treated with EHL





Absolute numbers of respective concentrates in this figure refer ONLY to the records within CNHP registry, which have been updated in 2016. The most important information on this slide is „Average annual consumption per treated person“. This reflects nationwide consumption of factor concentrate per treated PWH.

„Average annual consumption per valid person“ gives us an information on the consumption per patient, regardless of his treatment status and severity of the disease. It also enables us to estimate the national-wide consumption of FVIII. As we do know, that there were 937 haemophilia A patients in 2016 (WFH survey 2016) the total consumption was approximately 59 741 246 IU of FVIII/year in the Czech Republic. (SUKL reported 64 235 500 units of FVIII purchased in CZ during 2016). In other words, it means, that the total consumption was about 5,6 IU/capita of FVIII in 2016 (SUKL reported 6 IU/capita). This is a significant increase (over 1IU/capita, cca 20%) compared to 2015, probably due to 4 ITI (some of them high dosed) commenced in children in 2016 as well as increased number and perhaps dose of prophylaxis in adults.

Number of haemophiliacs B in the Czech Republic was 139 in 2016, the total consumption was approx. 6 252 498 IU of FIX/year, i.e. 0.59 IU/capita, thus no major change compared to 2015 (SUKL reported 6 944 750 IU of FIX purchased in 2016). New recombinant FIX were introduced in 2016.

EHL (Extended Half-Life) products are currently used only through clinical trials, though two of them were registered in CZ in 2016

Significant increase in aPCC consumption is caused mainly by aPCC prophylaxis in two children with inhibitors (in one as a part of Bonn ITI regimen), but more aPCC was used also in adults in 2016.

Consumption of drugs

Children

Drug (IU)	Total annual consumption	Number of treated persons	Consumption per treated person	Number of valid persons	Average annual consumption per valid person
FVIII (IU)					
<i>Immunate</i>	650 750	8	81 343.8		
<i>Fanhdil</i>	1 260 500	6	210 083.3		
<i>Octanate</i>	1 699 000	9	188 777.8		
<i>Haemate P</i>	2 475 500	2	1 237 750.0		
<i>Other plasma-derived</i>	312 500	1	312 500.0		
FVIII PD total	6 398 250	26	246 086.5		
<i>Advate</i>	6 822 800	70	97 468.6		
<i>Kogenate</i>	2 488 000	25	99 520.0		
<i>Recombinate</i>	0				
<i>Refacto</i>	154 000	3	51 333.3		
<i>Other recombinant</i>	0				
FVIII REC total*	9 464 800	96	98 591.7		
FVIII total*	15 863 050	120	132 192.1	213	74 474.4
FIX (IU)					
<i>Immunine</i>	463 200	8	57 900.0		
<i>Octanine</i>	90 000	4	22 500.0		
<i>Other plasma-derived</i>	0				
FIX PD total	553 200	12	46 100.0		
<i>Rixubis</i>	128 000	4	32 000.0		
<i>Benefix</i>	158 000	1	158 000.0		
<i>Other recombinant</i>	221 500	2	110 753.0		
FIX REC total*	507 500	7	72 500.9		
FIX total*	1 060 700	16	66 294.1	35	30 305.9
EHL (IU)					
<i>FVIII</i>	516 256.0	3	172 085.3		
<i>FIX</i>	166 381.0	1	166 381.0		
„by-pass“					
<i>Feiba (U)</i>	1 508 975	4	377 243.8		
<i>NovoSeven (mg)</i>	1 529.0	7	218.4		
<i>Other rFVIIa (mg)</i>	134.4	1	134.4		

* excluding patients treated with EHL

Absolute numbers of respective concentrates in this figure refer ONLY to the records within CNHP registry, which have been updated in 2016. The most important information on this slide is „Average annual consumption per treated person“. This reflects nation-wide consumption of factor concentrate per treated child with haemophilia.

Please note, that amount of FVIII is higher in children (median age 10 years), than in adults (median age around 40 years)! Thus, children with average weight around 25 kg had comparable or even higher consumption of FVIII to an adult weighting around 75 kg in average. Situation is similar for FIX

Consumption of drugs

Adults

Drug (IU)	Total annual consumption	Number of treated persons	Consumption per treated person	Number of valid persons	Average annual consumption per valid person
FVIII (IU)					
<i>Immunate</i>	5 666 885	79	71 732.7		
<i>FanhdI</i>	6 116 000	65	94 092.3		
<i>Octanate</i>	1 128 500	19	59 289.5		
<i>Haemate P</i>	0				
<i>Other plasma-derived</i>	0				
FVIII PD total	12 909 385	159	81 191.1		
<i>Advate</i>	5 752 000	27	213 037.0		
<i>Kogenate</i>	3 626 500	20	181 325.0		
<i>Recombinate</i>	2 149 000	12	179 083.3		
<i>Refacto</i>	220 000	1	220 000.0		
<i>Other recombinant</i>	859 000	3	286 333.3		
FVIII REC total*	12 606 500	62	203 330.6		
FVIII total*	25 515 885	216	118 129.1	436	58 522.7
FIX (IU)					
<i>Immunine</i>	1 200 000	28	45 000.0		
<i>Octanine</i>	2 011 000	17	118 294.1		
<i>Other plasma-derived</i>	26 500	1	26 500.0		
FIX PD total	3 237 500	44	74 943.2		
<i>Rixubis</i>	0				
<i>Benefix</i>	0				
<i>Other recombinant</i>	50 000	1	50 000.0		
FIX REC total*	50 000	1	50 000.0		
FIX total*	3 347 500	44	76 079.5	63	53 134.9
EHL (IU)					
<i>FVIII</i>	991 845.0	3	330 615.0		
<i>FIX</i>	0.0				
„by-pass“					
<i>Feiba (U)</i>	243 500	2	121 750.0		
<i>NovoSeven (mg)</i>	2 592.0	4	648.0		
<i>Other rFVIIa (mg)</i>	0				

* excluding patients treated with EHL



The same data for adults with haemophilia in 2016.