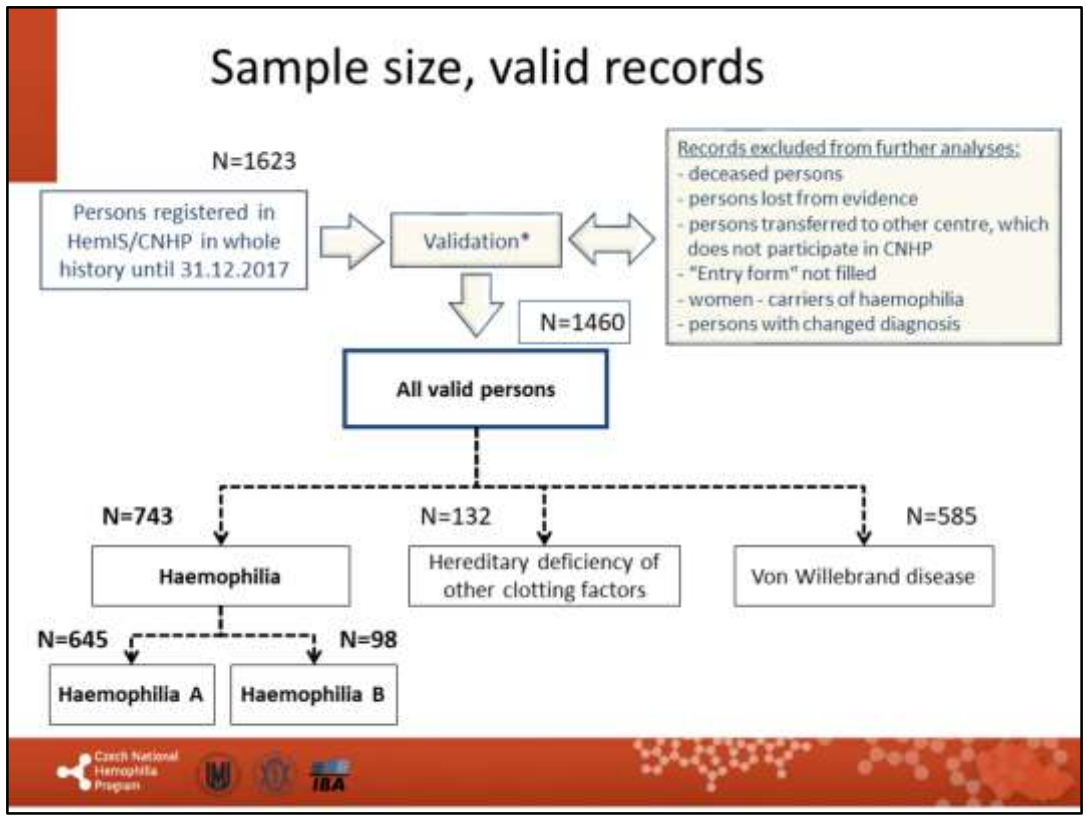
The status of care for persons with haemophilia registered within CNHP registry Annual Report 2017

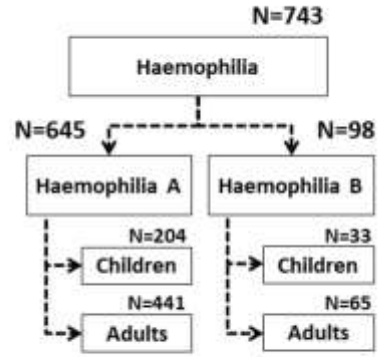
Jan Blatný, Petra Ovesná
on behalf of
Centres contributing to CNHP registry
(Czech National Haemophilia Programme)

Export date: April 2018

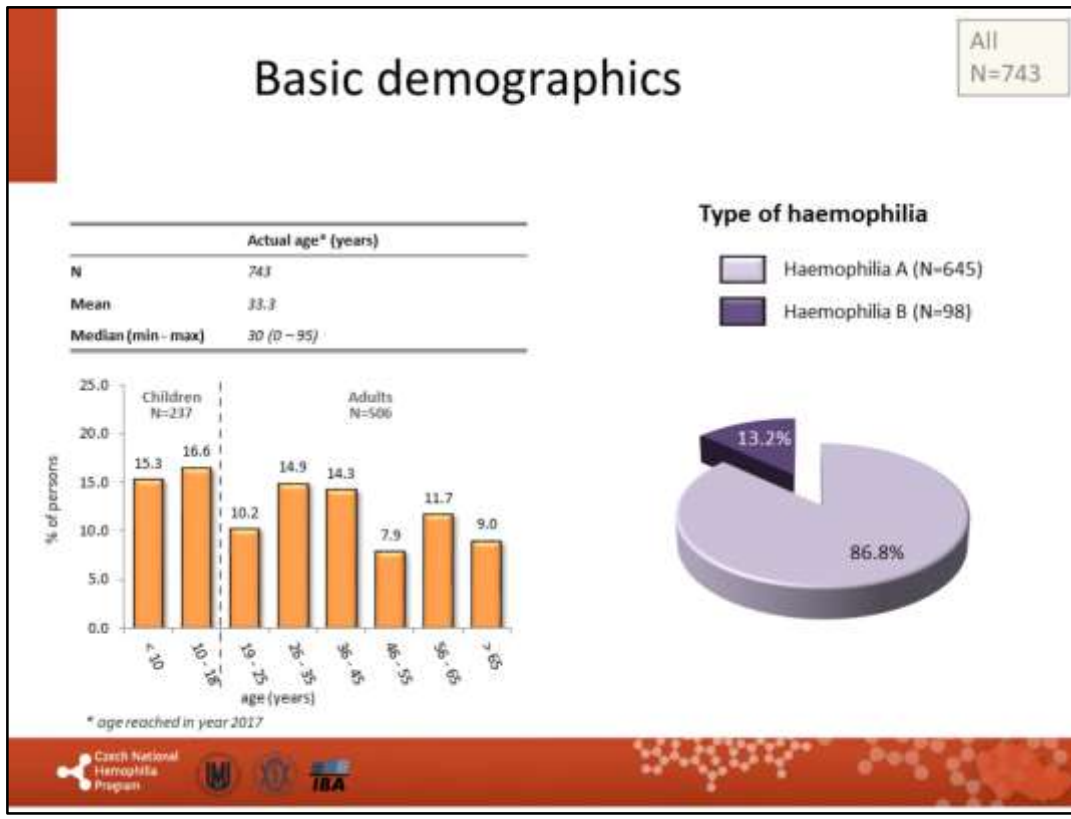


This slide describes the process of records‘ validation within the registry.

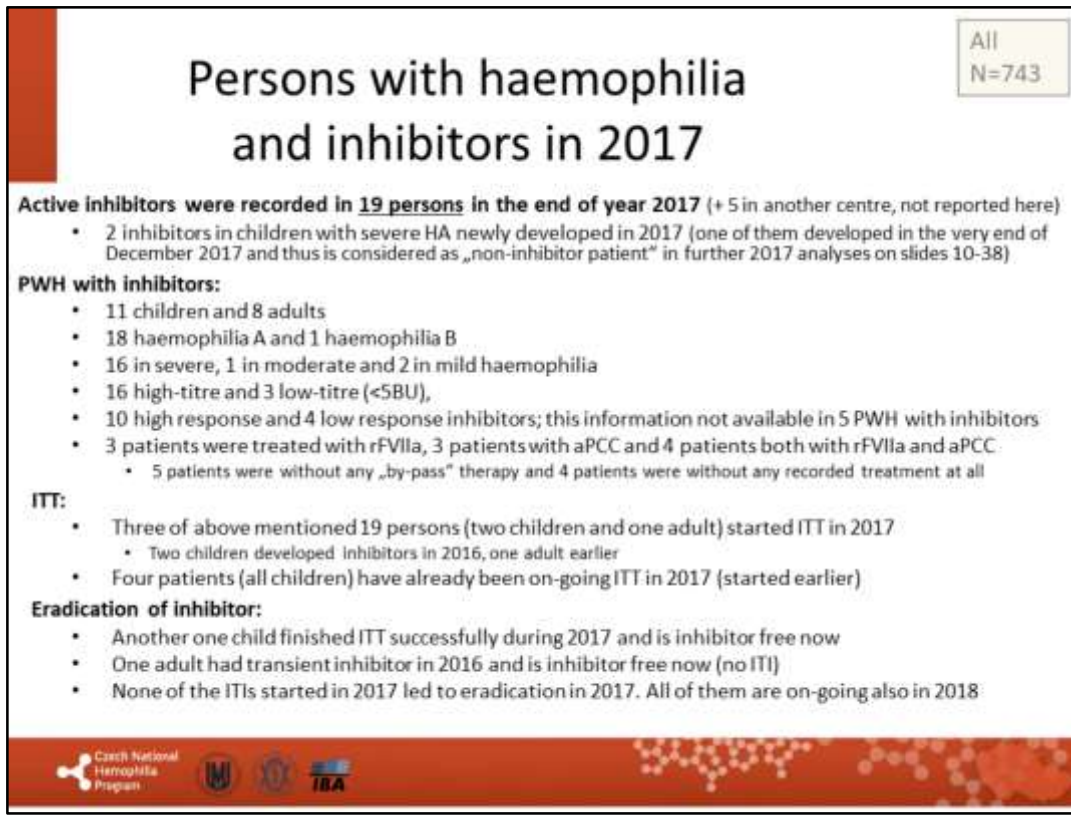
Persons with haemophilia (PWH)



Centres contributing to the CNHP registry.



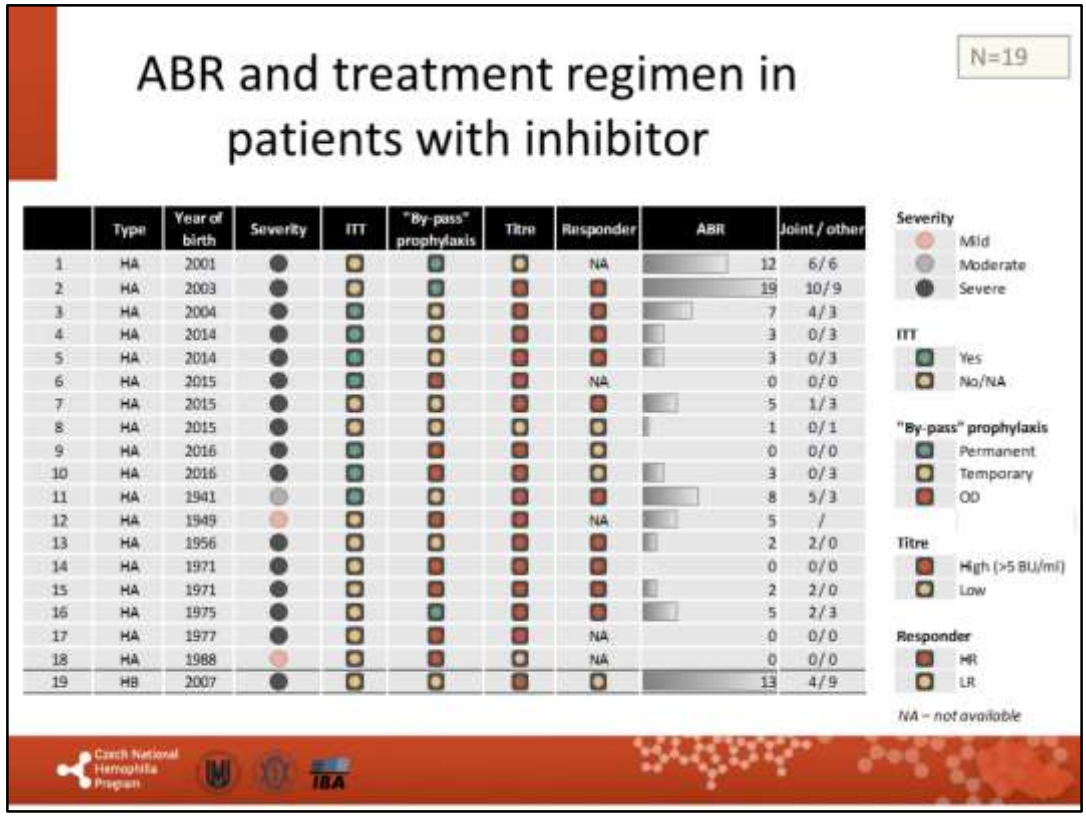
Though the percentage of PWH over 65 years has not been increasing dramatically over last several years, dealing with elderly people with haemophilia will be the challenge for treaters. Currently it counts for almost 10% of all registered PWHs



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

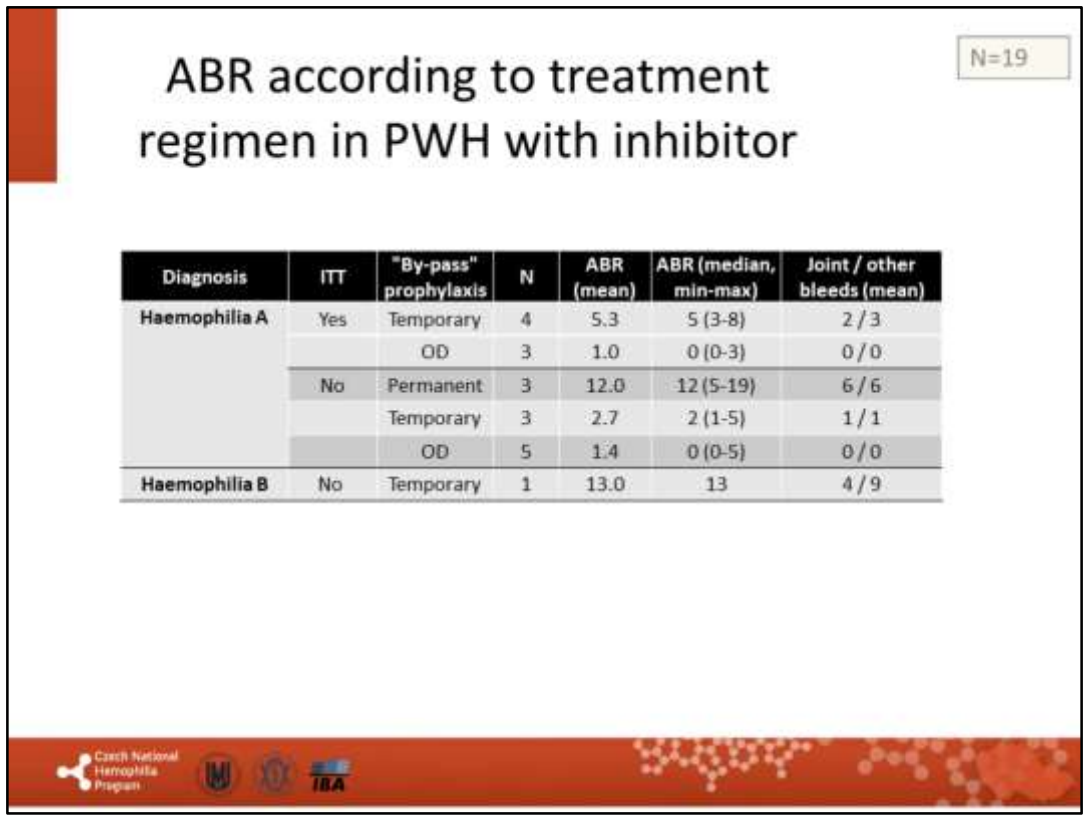
Number of PWHI in 2017 is the same as in 2016. 2 new inhibitors developed and 2 disappeared. One inhibitor developed in PUP on rFVIII and one re-appeared in an adolescent treated with pdFVIII (considered as “non-inhibitor patient” in further 2017 analysis as it appeared in the very end of the year).

Six children and one adult were on ITI in 2017. Four of them started earlier, three started in 2017. ITI was successfully finished in 1 child in 2017.
The number of newly developed inhibitors dropped down compared to 2016.



	Type	Year of birth	Severity	ITT	"By-pass" prophylaxis	Titre	Responder	ABR	Joint / other
1	HA	2001					NA	12	6/6
2	HA	2003						19	10/9
3	HA	2004						7	4/3
4	HA	2014						3	0/3
5	HA	2014						3	0/3
6	HA	2015					NA	0	0/0
7	HA	2015						5	1/3
8	HA	2015						1	0/1
9	HA	2016						0	0/0
10	HA	2016						3	0/3
11	HA	1941						8	5/3
12	HA	1949					NA	5	/
13	HA	1956						2	2/0
14	HA	1971						0	0/0
15	HA	1971						2	2/0
16	HA	1975						5	2/3
17	HA	1977					NA	0	0/0
18	HA	1988					NA	0	0/0
19	HB	2007						13	4/9

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…). One adult PWH was on ITI in 2017.



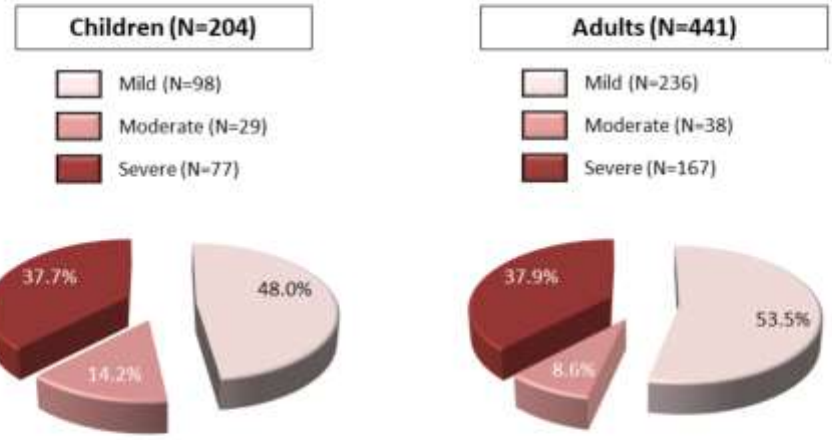
Diagnosis	ITT	"By-pass" prophylaxis	N	ABR (mean)	ABR (median, min-max)	Joint / other bleeds (mean)
Haemophilia A	Yes	Temporary	4	5.3	5 (3-8)	2 / 3
		OD	3	1.0	0 (0-3)	0 / 0
	No	Permanent	3	12.0	12 (5-19)	6 / 6
		Temporary	3	2.7	2 (1-5)	1 / 1
		OD	5	1.4	0 (0-5)	0 / 0
Haemophilia B	No	Temporary	1	13.0	13	4 / 9

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

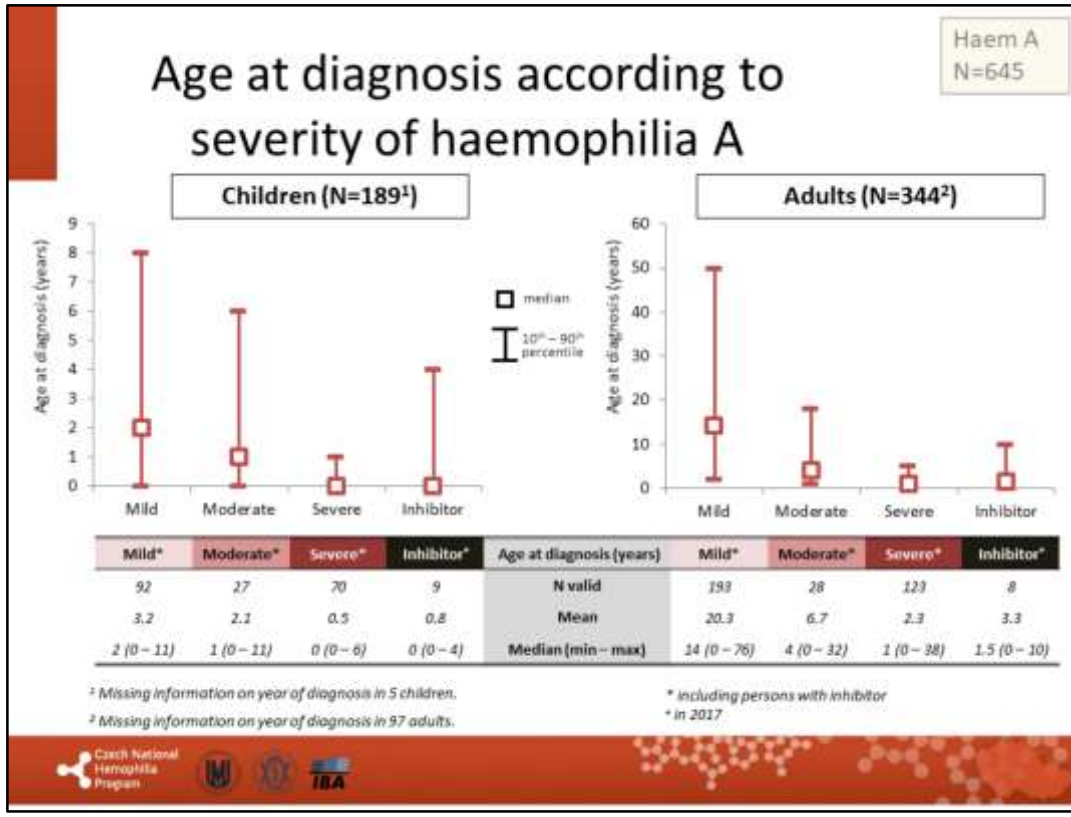
Demographic characteristics
Haemophilia A

Severity of haemophilia A

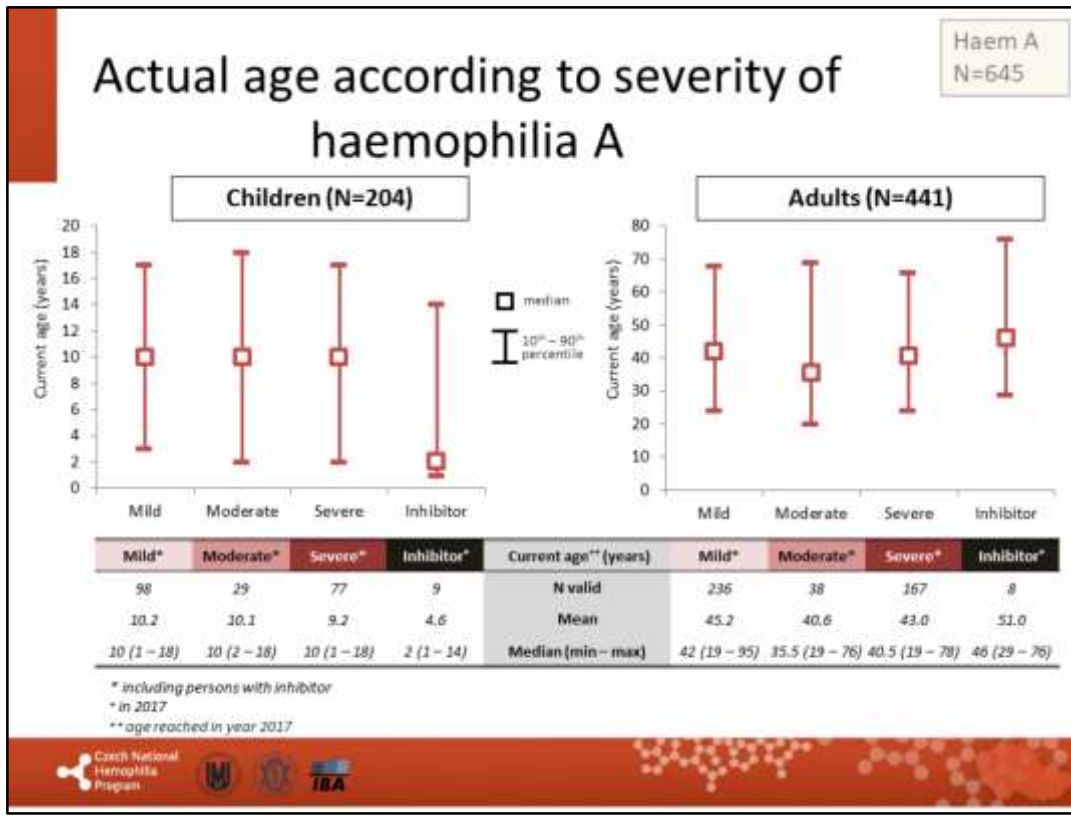
Haem A
N=645



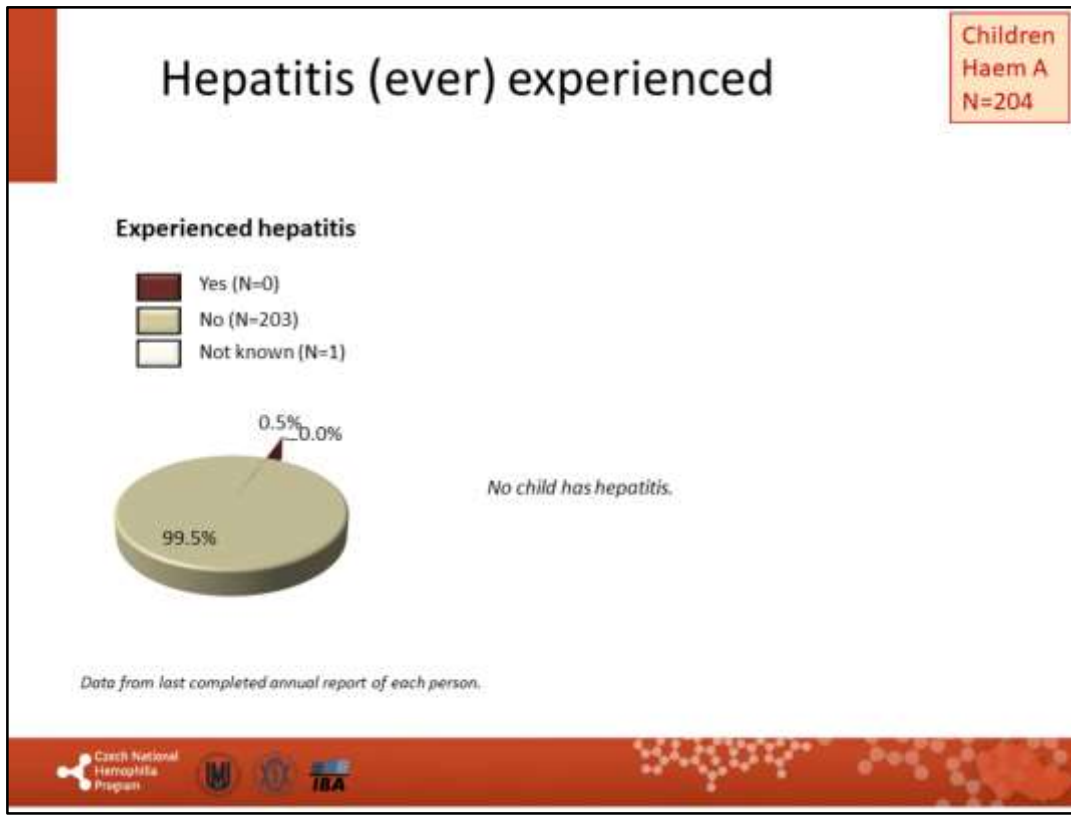
Czech National Hemophilia Program



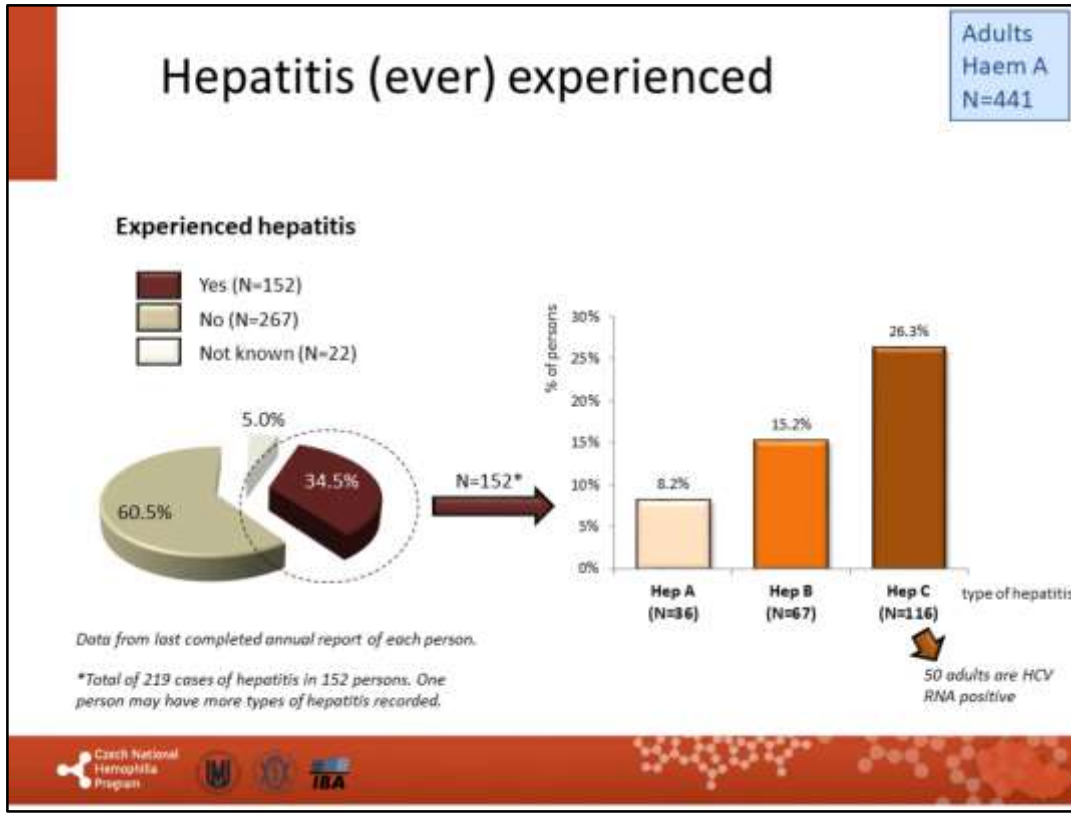
Median age at diagnosis is different for adults and children with HA. (In the past, the diagnostic options were worse, than they are today). All (but one) children wit severe haemophilia are diagnosed before 12 months of age now.



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

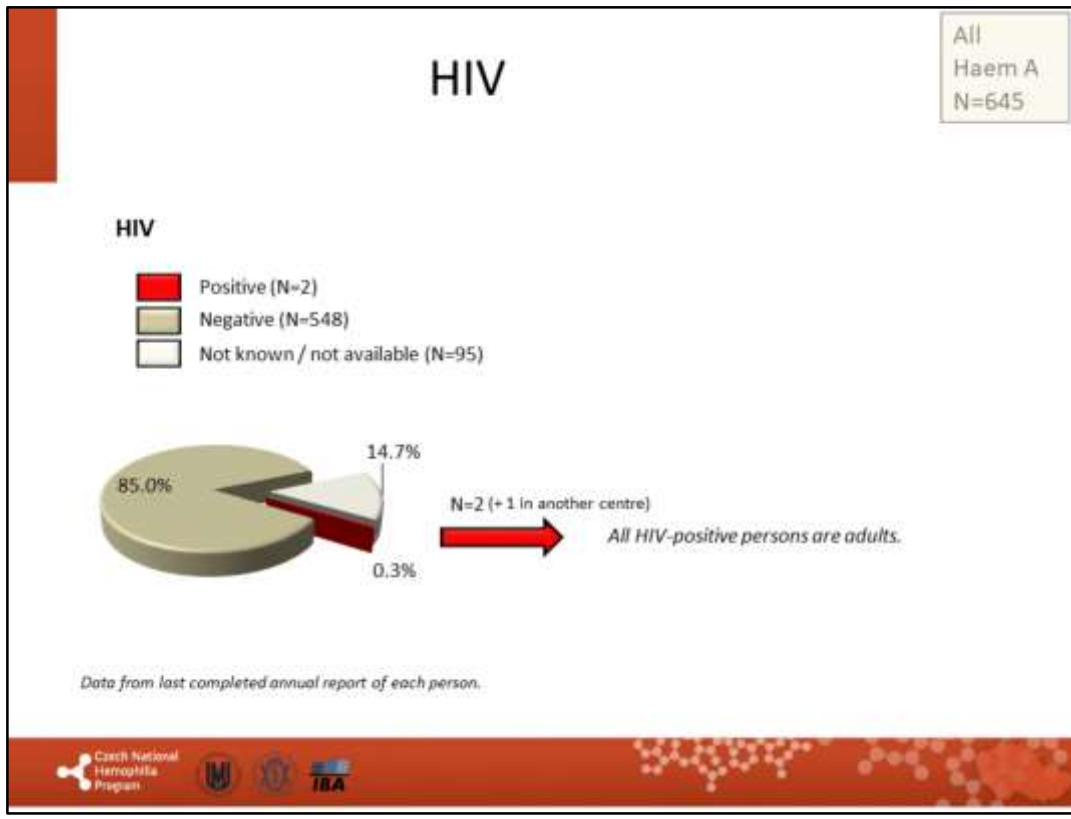


No HepC infection in children since late 90's. None of Czech children with HA is infected with Hepatitis C.



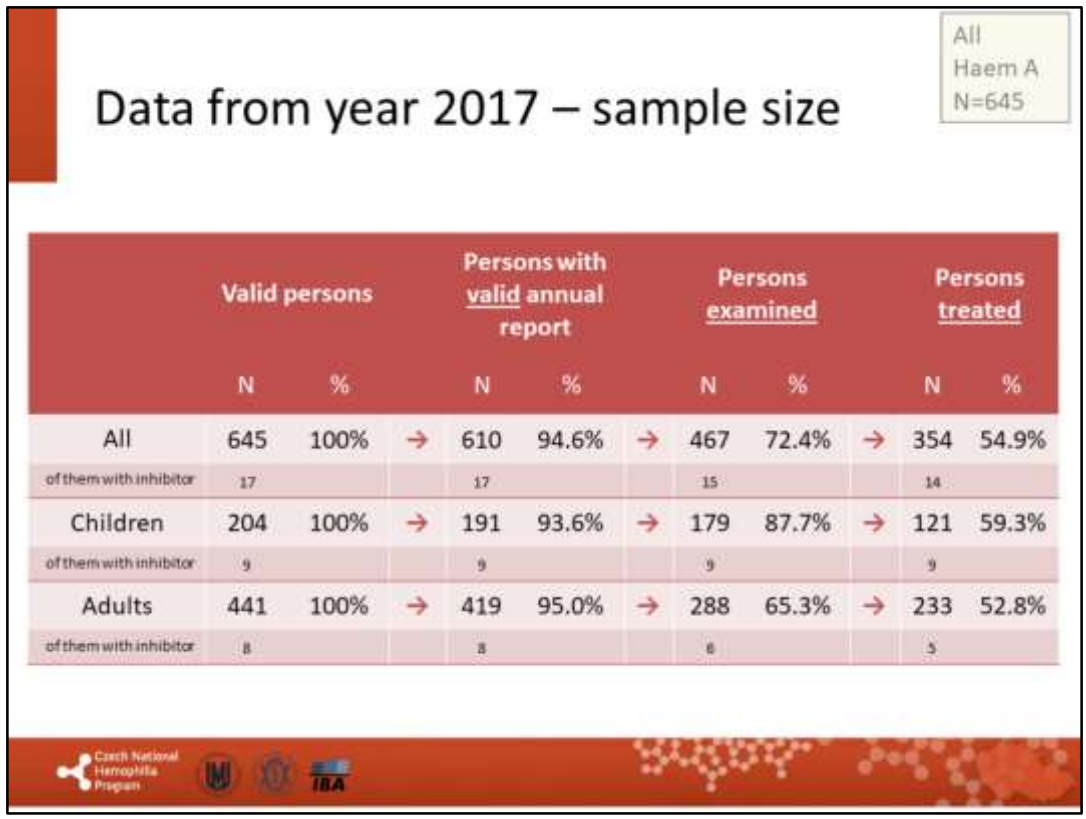
There was NO NEW HepC infection in 2017.
116 PWHA reported as “ever experienced hepatitis” in 2017, though some of them may have already been successfully treated (numbers of successfully treated not shown here). Only 50 adults are currently reported as HCV RNA positive, thus with active disease. New antiviral therapy regimens are widely used in Czech adult PWHs with active HepC infection.

NB 2 HepC positive adults died in 2017 and one was transferred to the centre not participating in CNHP registry.

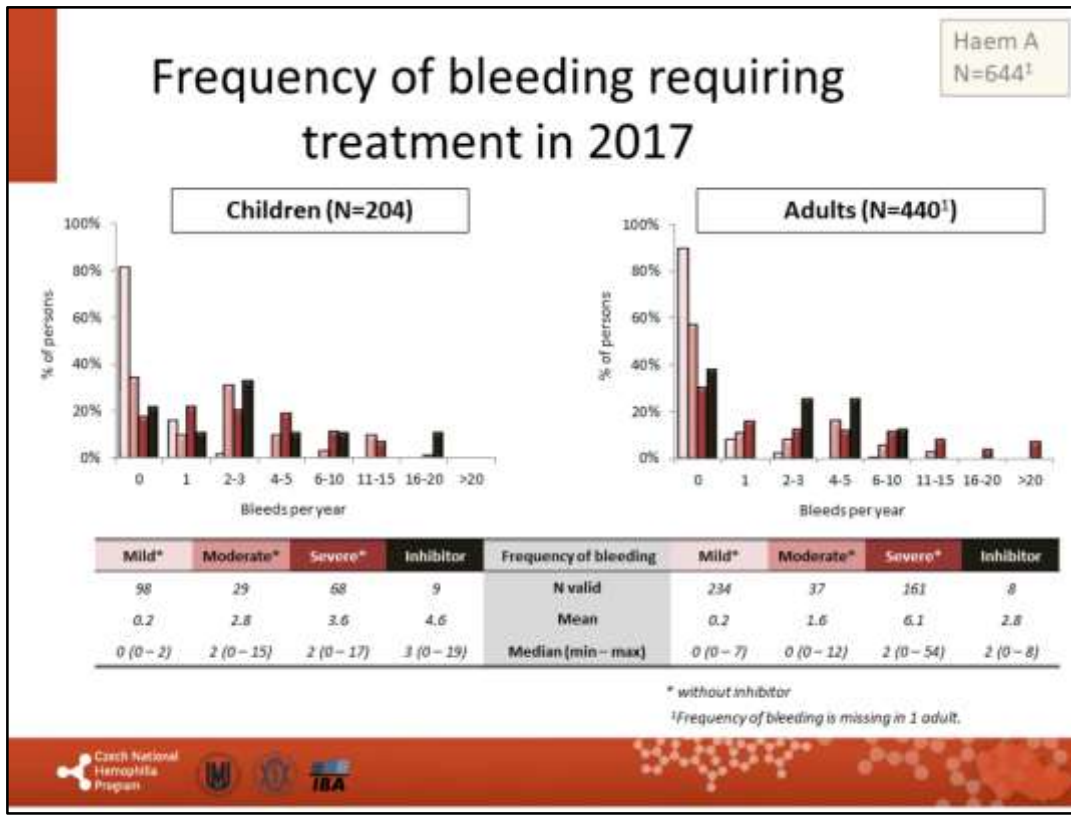


Very low number of HIV positive PWH due to low/no access to contaminated concentrates in 80s and 90s. Our current treatment is on a very high safety level. No new HIV+ PWH reported since late 90s.

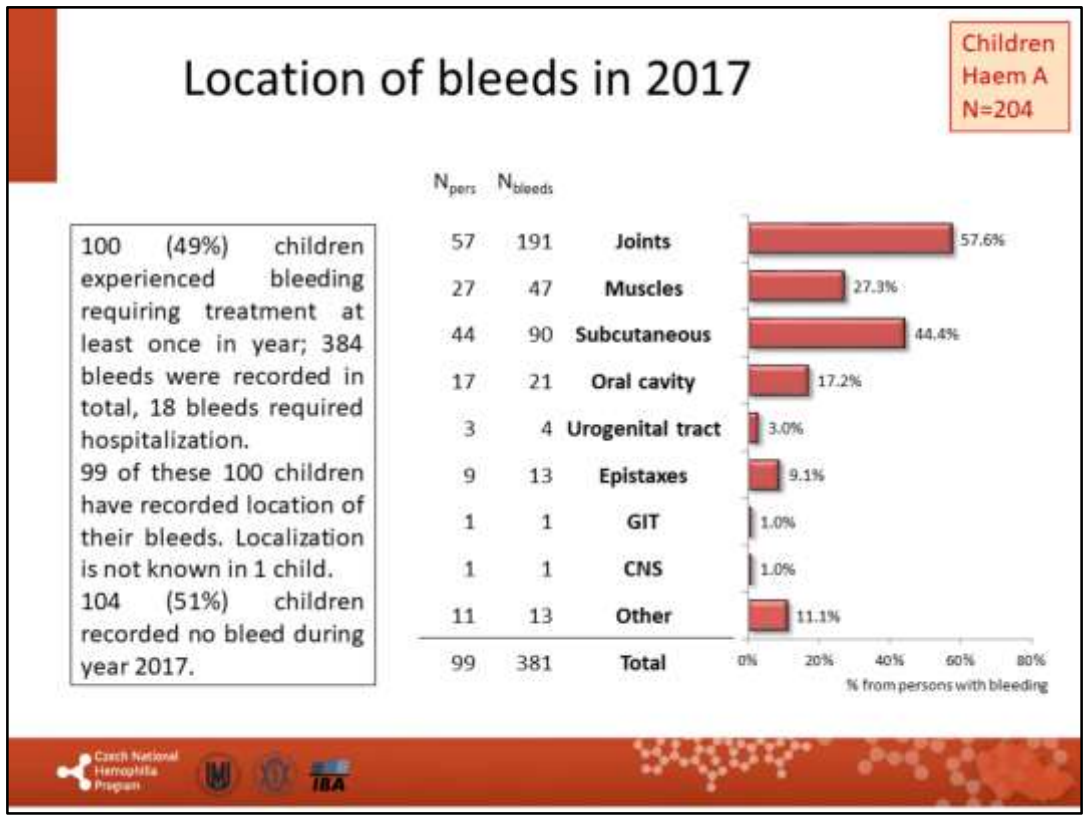
Treatment outcomes and bleeding frequency
Haemophilia A



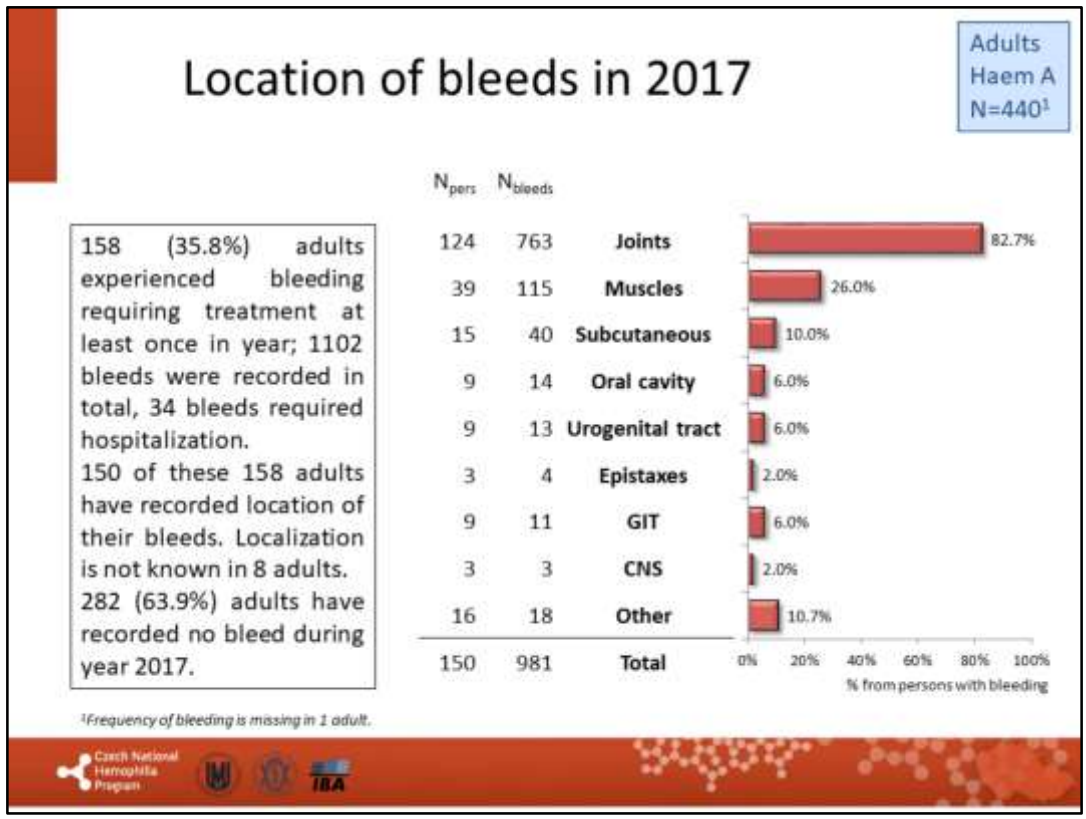
There are records of nearly 70% of all Czech haemophiliacs in total within the CNHP registry. As for paediatric population, ALL children are recorded. CNHP registry also houses records of about two thirds of adult haemophiliacs in Czech Republic. Further slides display analyses performed only on records, which were updated during 2017. Not all patients came to the centre (especially adults) and not all centres fully reported all data in 2017. Thus not all records have been updated and used for further analyses. Data monitoring was introduced in 2017 to further increase the validity of the data within CNHP registry.



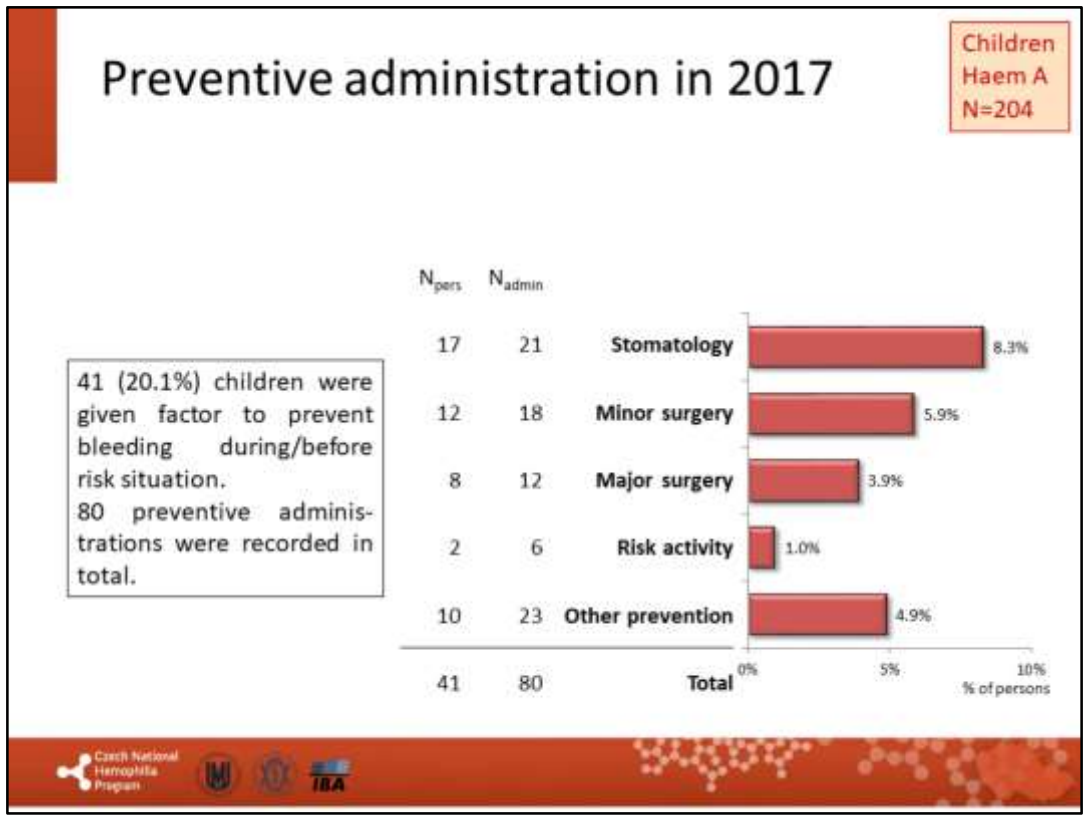
Data shown document good efficacy of care provided to Czech PWH, no matter what age category they are. Mean/Median number of bleedings per year (ABR) is 6.1/2 for adults and 3.6/2 for children with severe haemophilia A.
In 2016 the numbers for adults were 7.3/2 and for children 4.4/2.



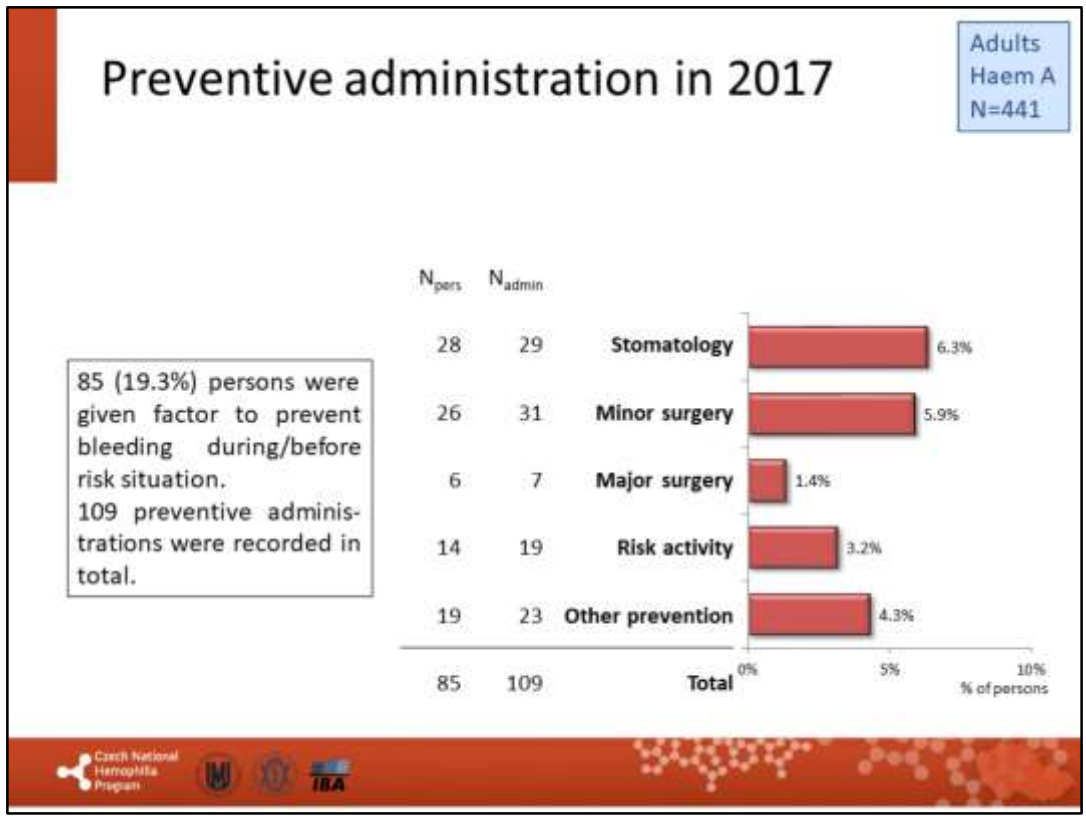
There was one CNS bleed in children with haemophilia in 2017. 51% of children had no bleed at all.



Bleeding events in adults.

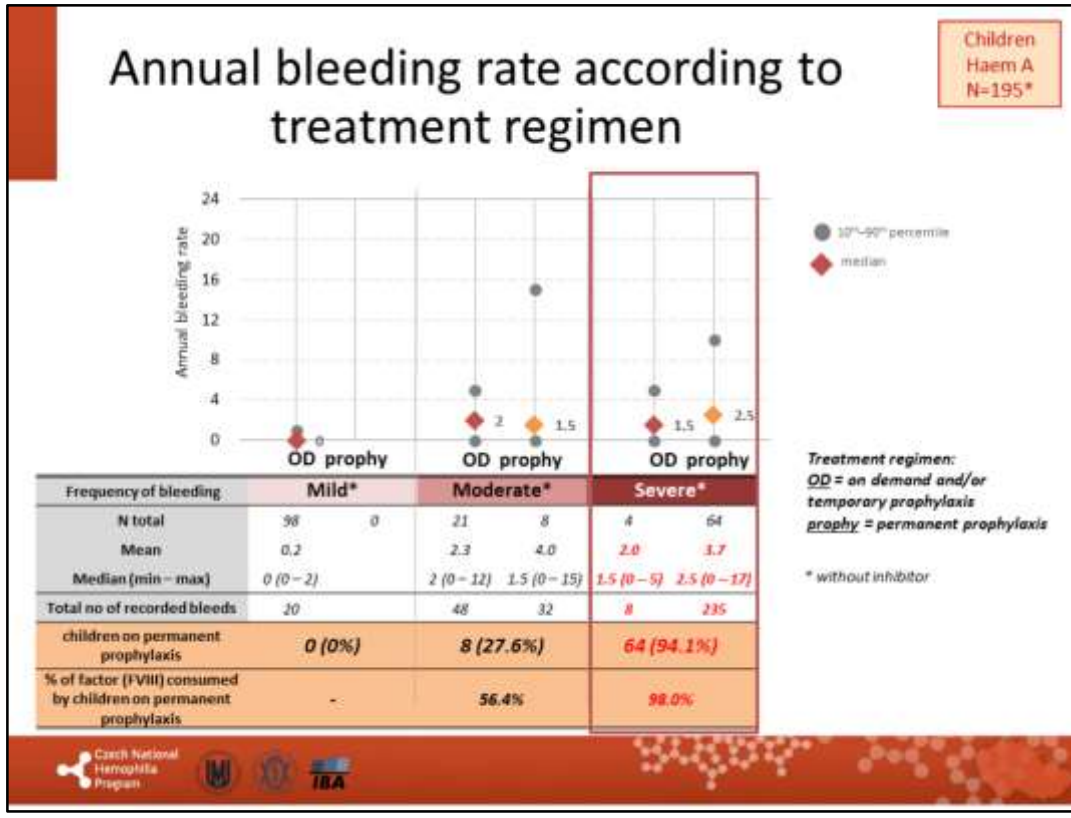


This figure refers to preventive factors administration in children with HA.



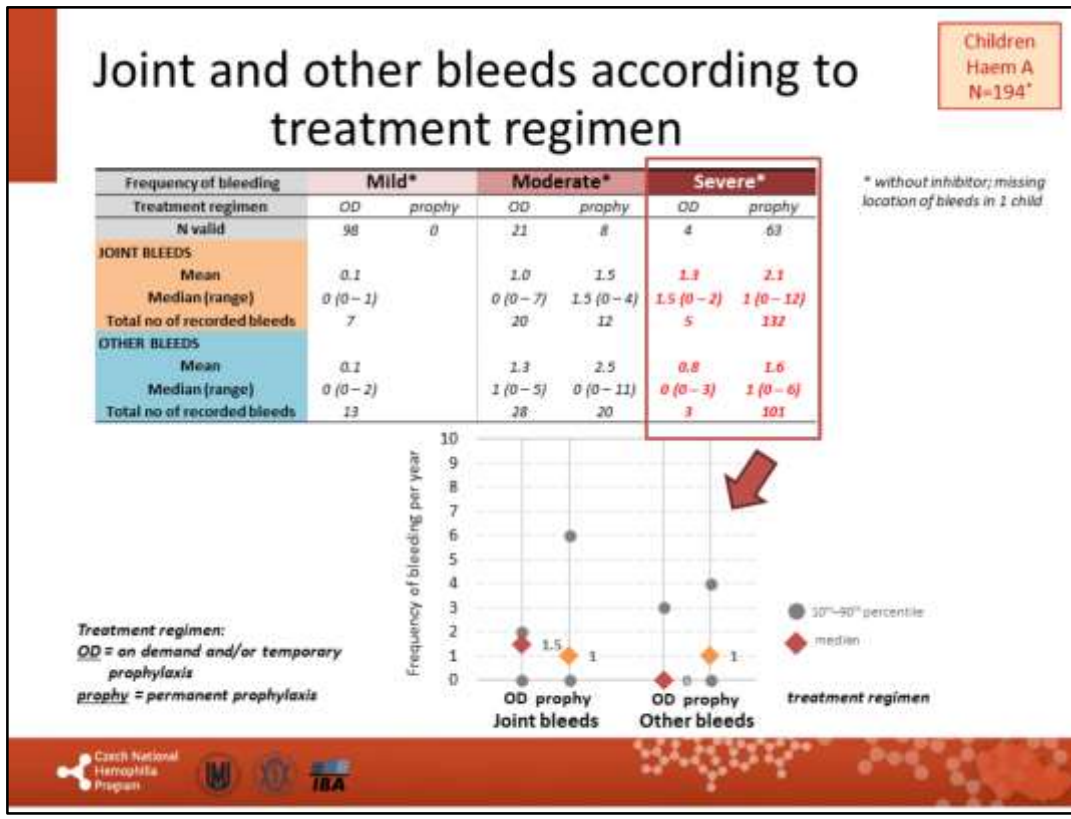
This figure refers to preventive treatment in adults with HA.

ABR according to treatment regimen
Haemophilia A without inhibitor

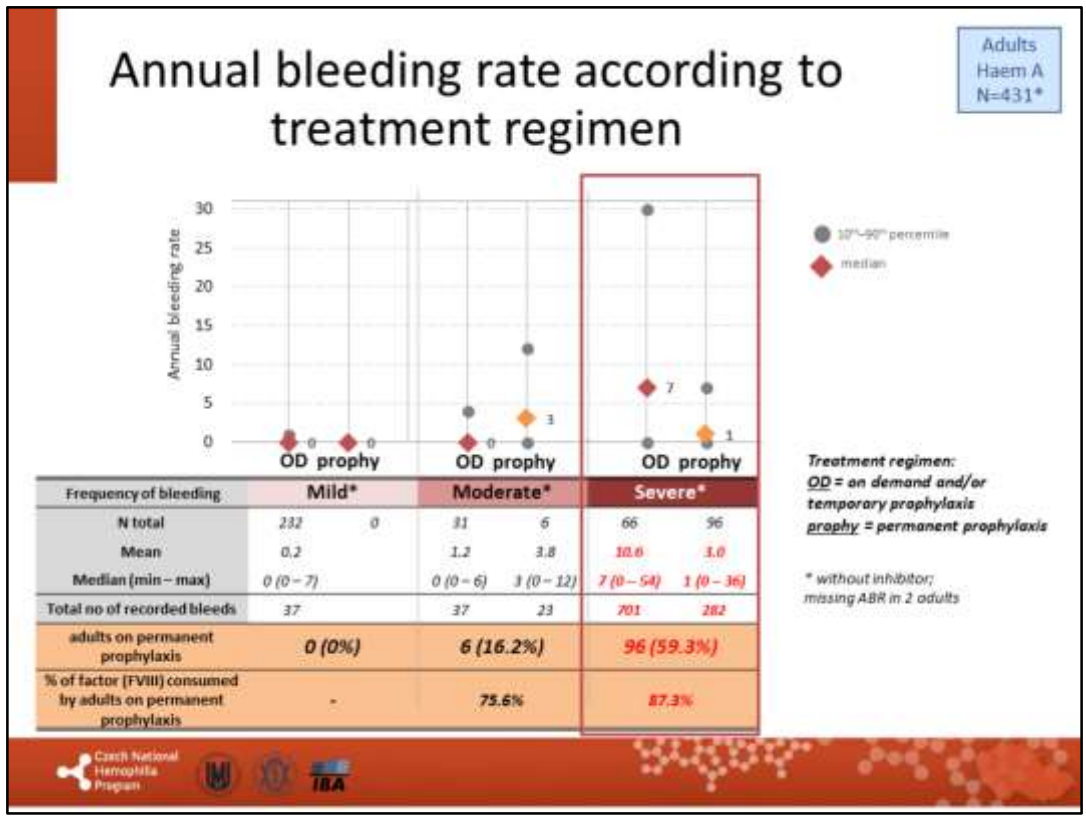


This slide confirms good effect of permanent prophylaxis in children. Rate of prophylaxis increase again over 94% in 2017 (was temporary below 90% in 2016) among children with severe haemophilia A. Those children with severe haemophilia, who are not on permanent prophylaxis yet shall be encouraged to do so. (see comment below)
Number of bleeds per year (median) in severe haemophiliacs A on prophylaxis decreased from 3 in 2016 to 2.5/year in 2017. Maximal ABR in children with severe HA decreased significantly during 2017
ABR in children with severe haemophilia A on OD remained 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.

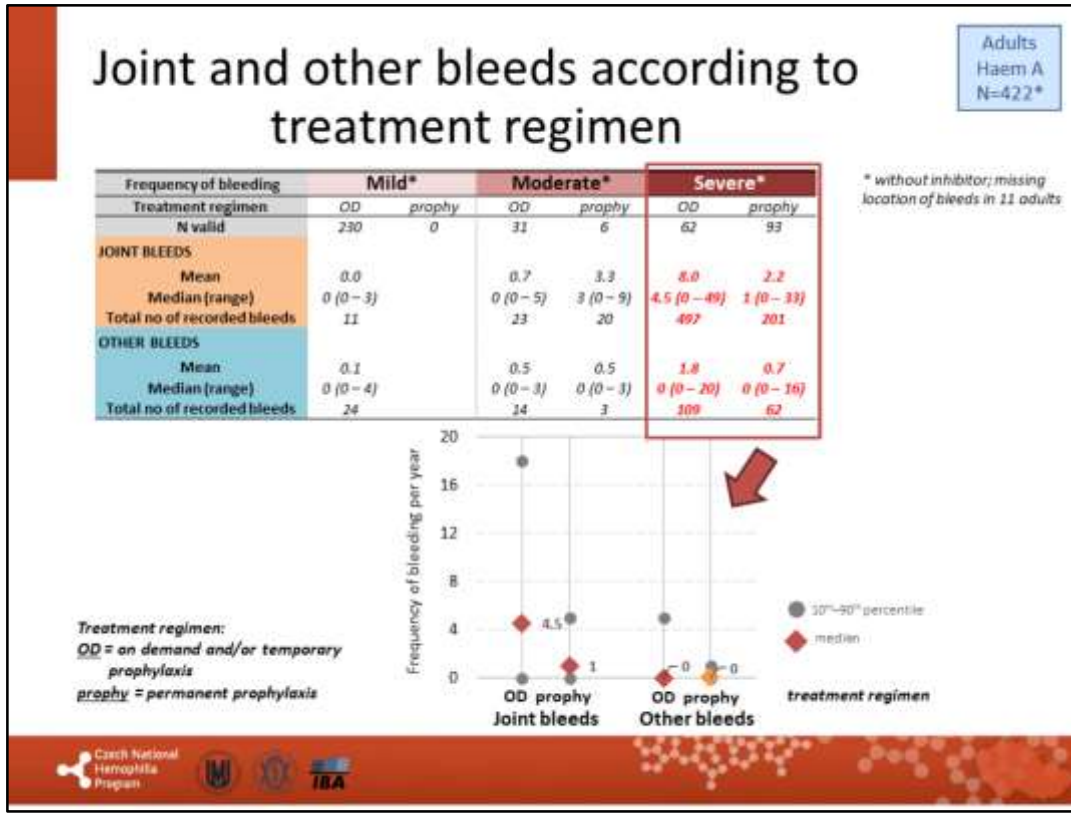


Children with HA on permanent prophylaxis keep median of joint bleeds per year below 2. This is, indeed, a great success, however, there are still children, who have over 10 joint bleeds per year!
Joint bleeds in children with moderate HA decreased as well, but still some of them deserve prophylaxis!



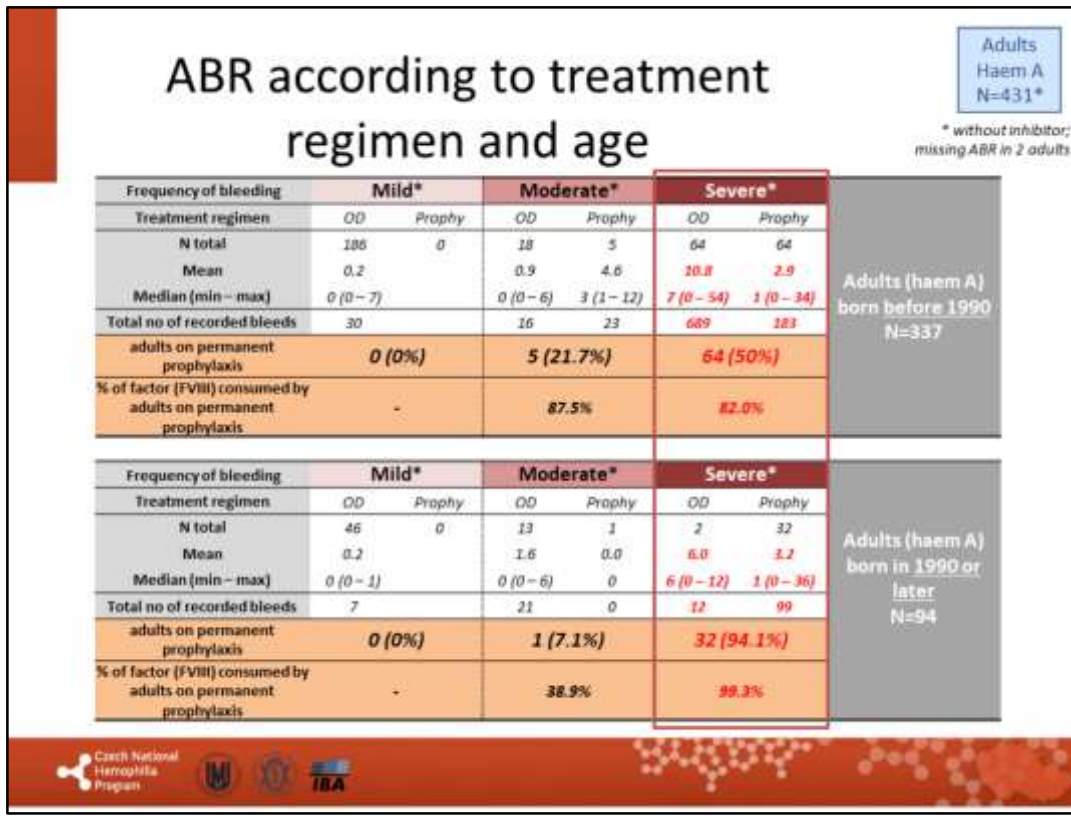
Prophylaxis works very well in Czech adult PWHs! It is able to decrease bleedings from 7 to 1 (median). In 2016 median ABRs in adult PWHs with severe haemophilia were similar to 2017 figures for both OD and prophylaxis treatment.

Rate of prophylaxis remained around 60% among adults with severe haemophilia A.



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. No major change from 2016.

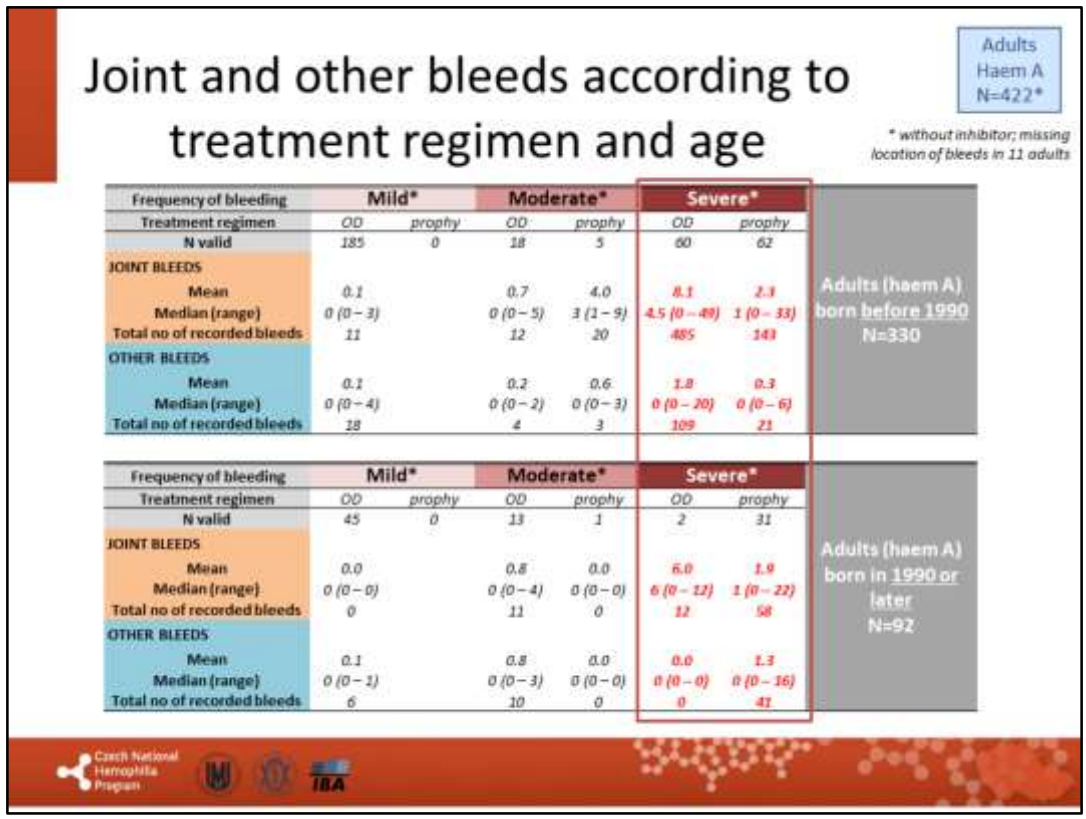
As described later in this report, doses for adults (in IU/kg/year) are still significantly lower, than in children with the same disease.



Frequency of bleeding	Mild*		Moderate*		Severe*	
Treatment regimen	OD	Prophy	OD	Prophy	OD	Prophy
N total	186	0	18	5	64	64
Mean	0.2		0.9	4.6	10.8	2.9
Median (min – max)	0 (0 – 7)		0 (0 – 6)	3 (1 – 12)	7 (0 – 54)	1 (0 – 34)
Total no of recorded bleeds	30		16	23	689	183
adults on permanent prophylaxis	0 (0%)		5 (21.7%)		64 (50%)	
% of factor (FVIII) consumed by adults on permanent prophylaxis	-		87.5%		82.0%	

Frequency of bleeding	Mild*		Moderate*		Severe*	
Treatment regimen	OD	Prophy	OD	Prophy	OD	Prophy
N total	46	0	13	1	2	32
Mean	0.2		1.6	0.0	6.0	1.2
Median (min – max)	0 (0 – 1)		0 (0 – 6)	0	6 (0 – 12)	1 (0 – 36)
Total no of recorded bleeds	7		21	0	12	99
adults on permanent prophylaxis	0 (0%)		1 (7.1%)		32 (94.1%)	
% of factor (FVIII) consumed by adults on permanent prophylaxis	-		38.9%		99.3%	

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 further advocate for more tertiary prophylaxis in adult PWH.

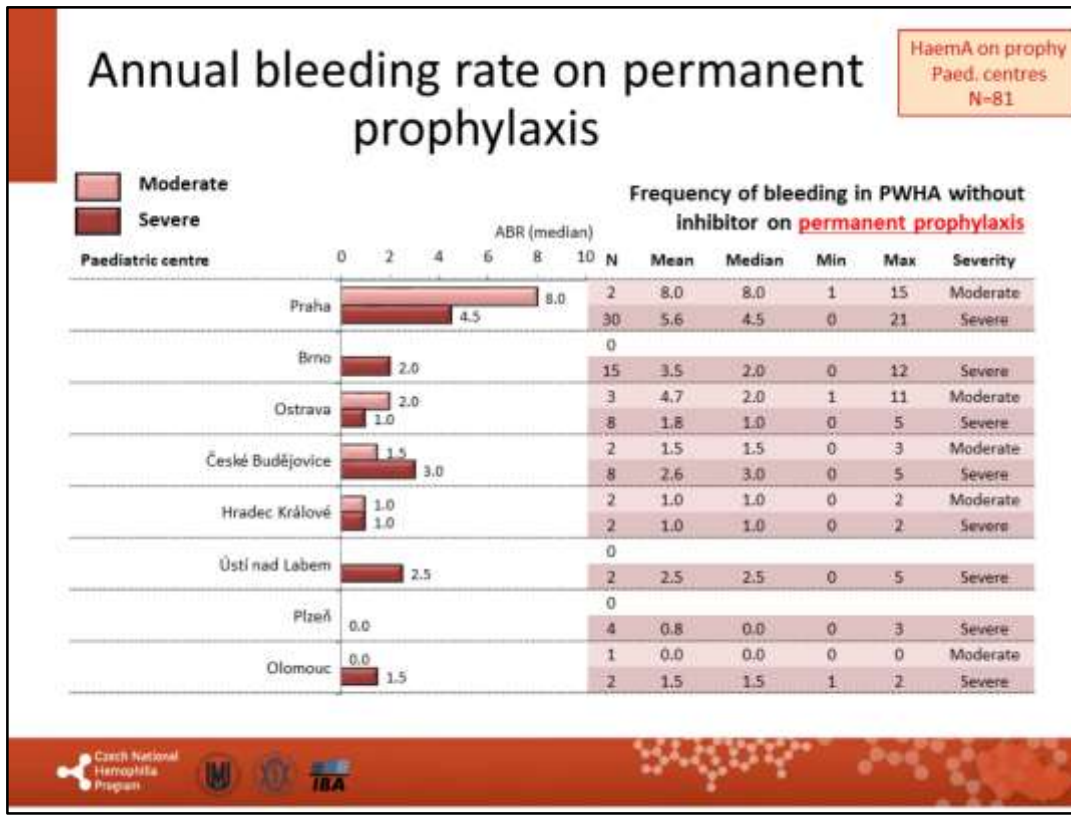


Frequency of bleeding	Mild*		Moderate*		Severe*	
Treatment regimen	OD	prophy	OD	prophy	OD	prophy
N valid	185	0	18	5	60	62
JOINT BLEEDS						
Mean	0.1		0.7	4.0	8.1	2.3
Median (range)	0 (0 – 3)		0 (0 – 5)	3 (1 – 9)	4.5 (0 – 49)	1 (0 – 33)
Total no of recorded bleeds	11		12	20	485	143
OTHER BLEEDS						
Mean	0.1		0.2	0.6	1.8	0.3
Median (range)	0 (0 – 4)		0 (0 – 2)	0 (0 – 3)	0 (0 – 20)	0 (0 – 6)
Total no of recorded bleeds	18		4	3	109	21

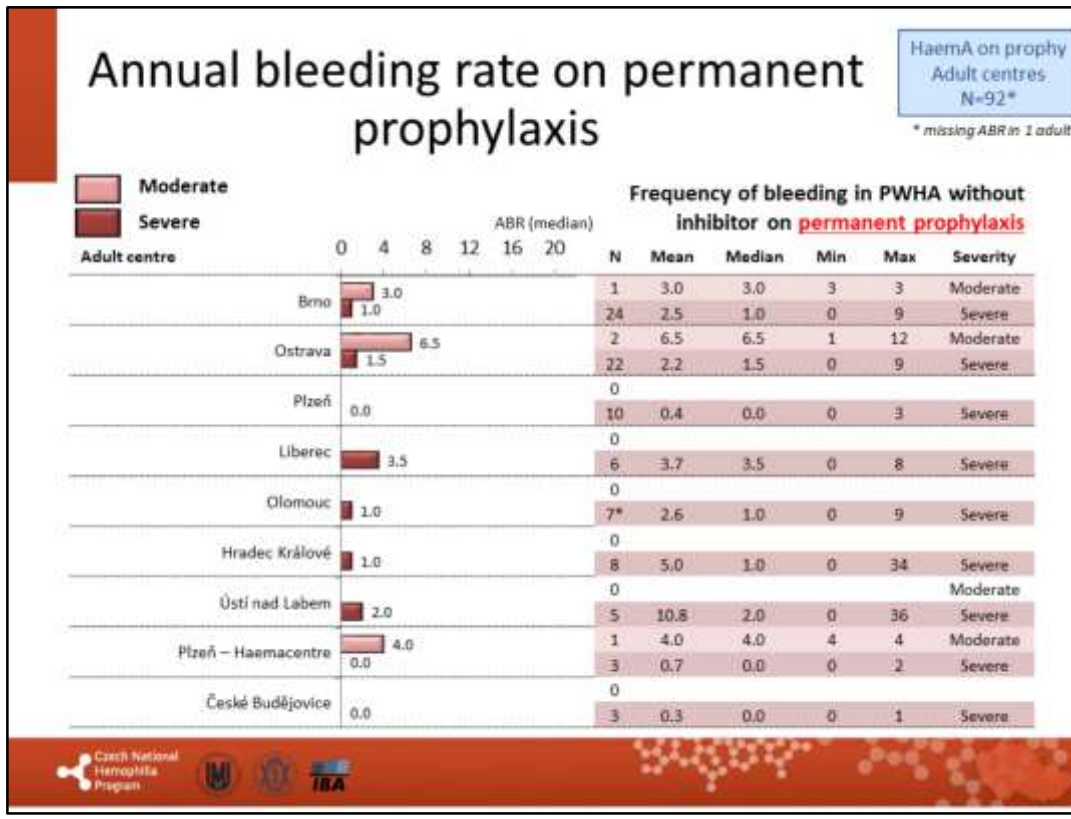
Frequency of bleeding	Mild*		Moderate*		Severe*	
Treatment regimen	OD	prophy	OD	prophy	OD	prophy
N valid	45	0	13	1	2	31
JOINT BLEEDS						
Mean	0.0		0.8	0.0	6.0	1.9
Median (range)	0 (0 – 0)		0 (0 – 4)	0 (0 – 0)	6 (0 – 12)	1 (0 – 22)
Total no of recorded bleeds	0		11	0	12	58
OTHER BLEEDS						
Mean	0.1		0.8	0.0	0.0	1.3
Median (range)	0 (0 – 1)		0 (0 – 3)	0 (0 – 0)	0 (0 – 0)	0 (0 – 16)
Total no of recorded bleeds	6		10	0	0	41

The same is true for joint bleeds in adults. Some frequent bleeders however still remain, especially among adults with severe HA born before 1990 and still treated “on demand”. They are, indeed, the candidates for tertiary prophylaxis.

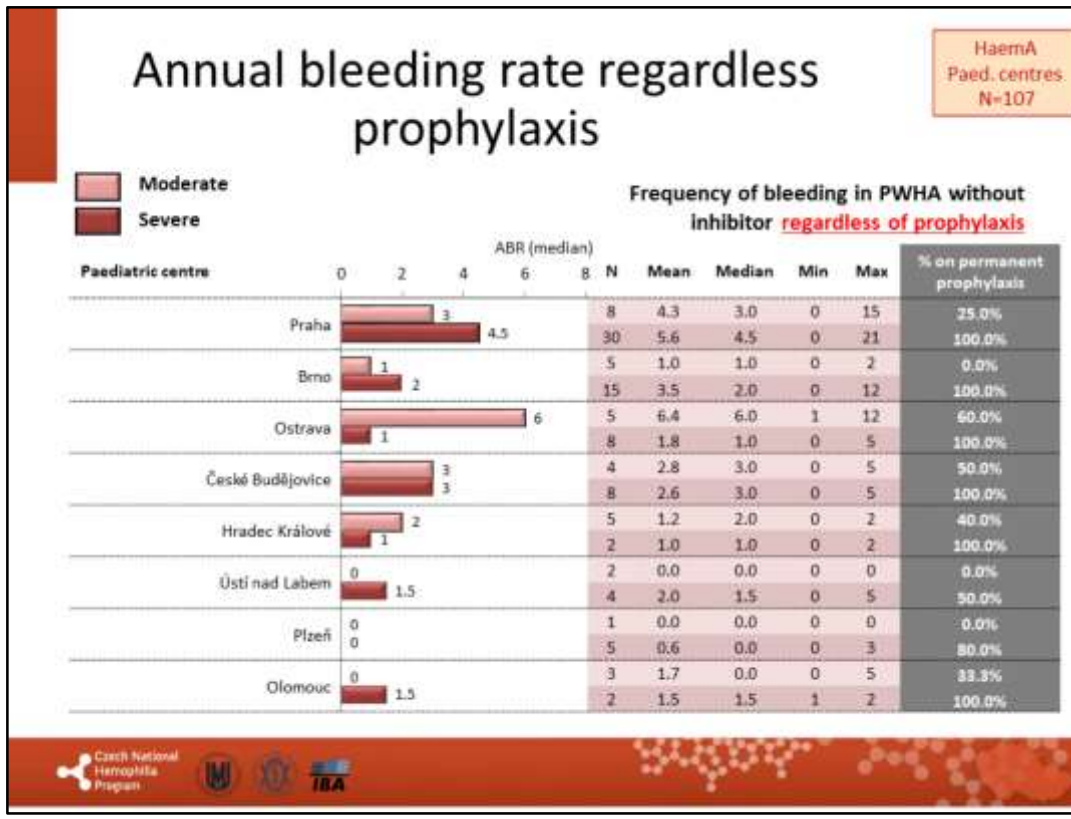
ABR according to centres
Haemophilia A (PWHA)



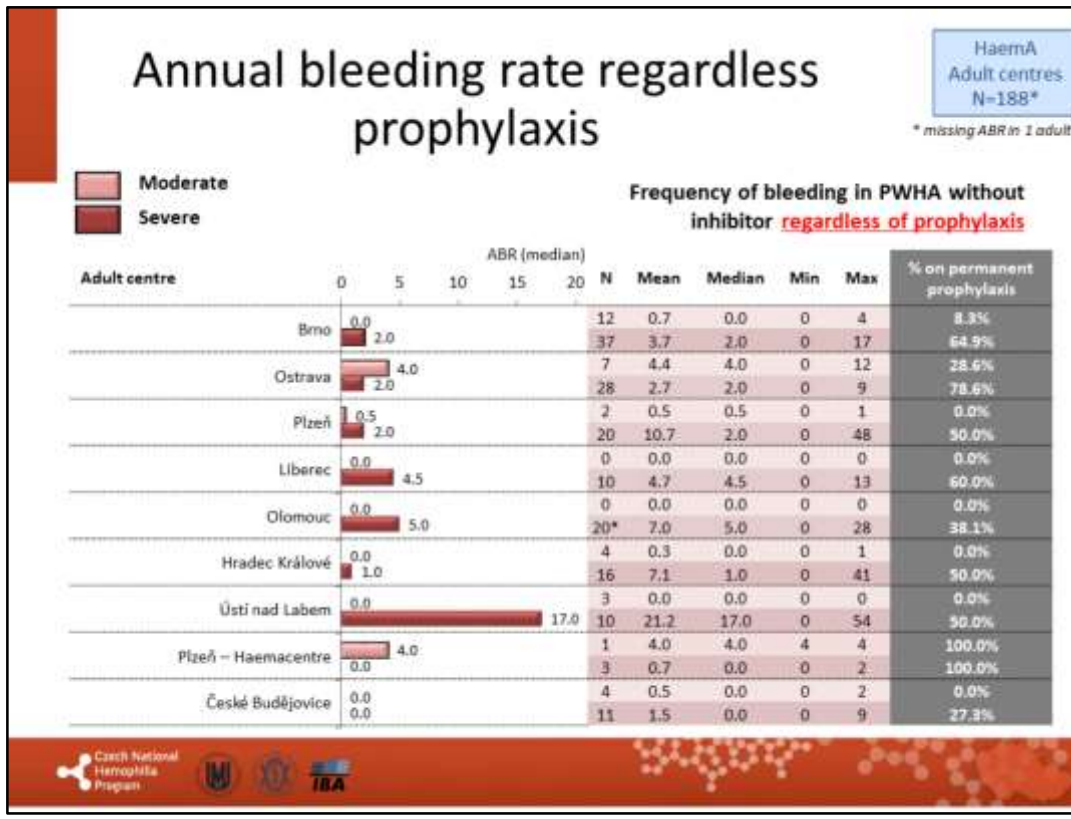
In vast majority of paediatric centres, severe haemophiliacs on prophylaxis bleed not more than 4 times per year (median). We should continue to focus on individualized/tailored prophylaxis and shall offer it to all, who may benefit from this approach. This should also minimize the differences in ABR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



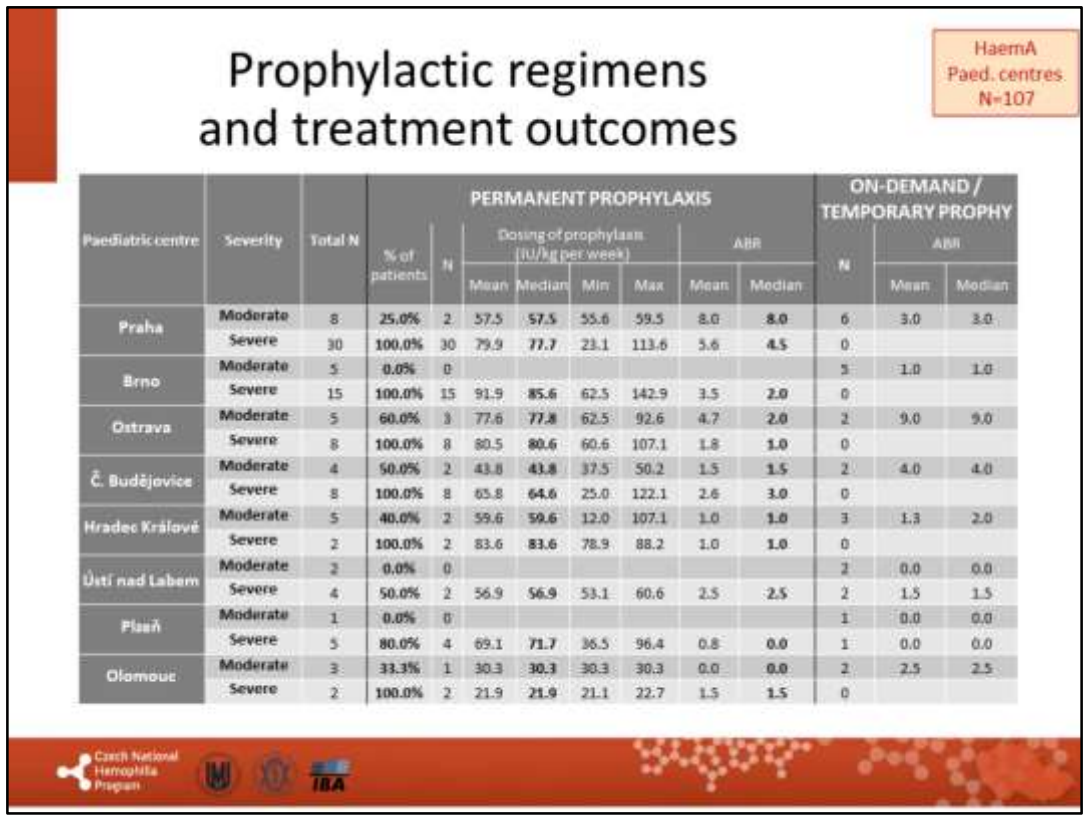
In 2017 the difference between centres in ABR of adults with severe HA on prophylaxis diminished significantly compared to 2016.



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.

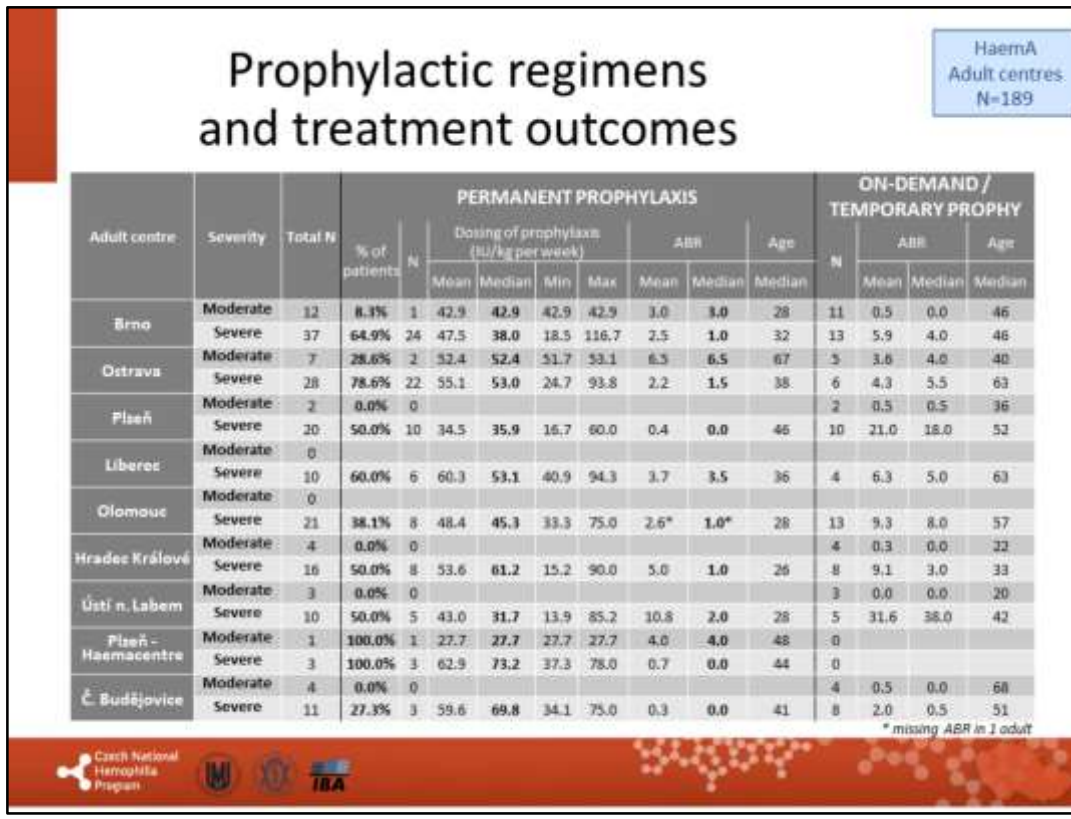


Similar information for adults. High ABR in some centres might be due to an individual with very severe phenotype and/or perhaps poor compliance. On the other hand, dealing with those patients should be a challenge for respective centres.



Paediatric centre	Severity	Total N	PERMANENT PROPHYLAXIS								ON-DEMAND / TEMPORARY PROPHY		
			% of patients	N	Dosing of prophylaxis (IU/kg per week)				ABR		N	ABR	
					Mean	Median	Min	Max	Mean	Median		Mean	Median
Praha	Moderate	8	25.0%	2	57.5	57.5	55.6	59.5	8.0	8.0	6	3.0	3.0
	Severe	30	100.0%	30	79.9	77.7	23.1	113.6	5.6	4.5	0		
Brno	Moderate	5	0.0%	0							5	1.0	1.0
	Severe	15	100.0%	15	91.9	85.6	62.5	142.9	3.5	2.0	0		
Ostrava	Moderate	5	60.0%	3	77.6	77.8	62.5	92.6	4.7	2.0	2	9.0	9.0
	Severe	8	100.0%	8	80.5	80.6	60.6	107.1	1.8	1.0	0		
Č. Budějovice	Moderate	4	50.0%	2	43.8	43.8	37.5	50.2	1.5	1.5	2	4.0	4.0
	Severe	8	100.0%	8	65.8	64.6	25.0	122.1	2.6	3.0	0		
Hradec Králové	Moderate	5	40.0%	2	59.6	59.6	12.0	107.1	1.0	1.0	3	1.3	2.0
	Severe	2	100.0%	2	83.6	83.6	78.9	88.2	1.0	1.0	0		
Ústí nad Labem	Moderate	2	0.0%	0							2	0.0	0.0
	Severe	4	50.0%	2	56.9	56.9	53.1	60.6	2.5	2.5	2	1.5	1.5
Plzeň	Moderate	1	0.0%	0							1	0.0	0.0
	Severe	5	80.0%	4	69.1	71.7	36.5	96.4	0.8	0.0	1	0.0	0.0
Olomouc	Moderate	3	33.3%	1	30.3	30.3	30.3	30.3	0.0	0.0	2	2.5	2.5
	Severe	2	100.0%	2	21.9	21.9	21.1	22.7	1.5	1.5	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

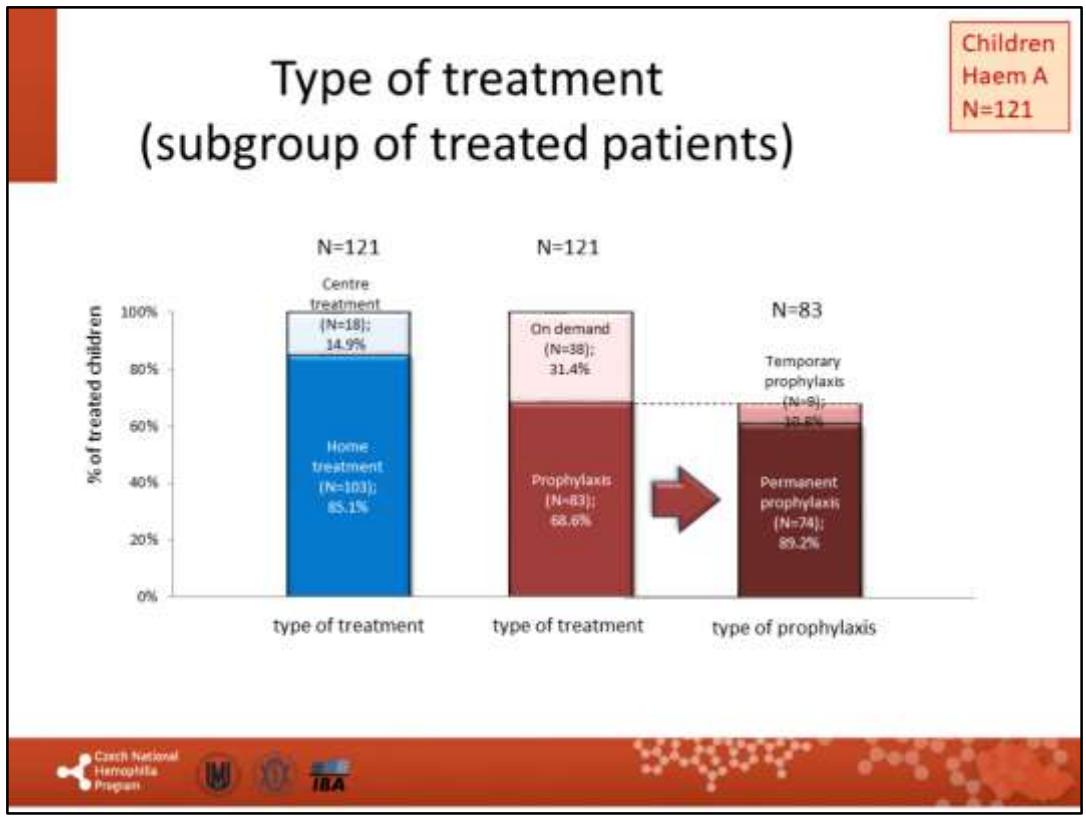
HaemA Adult centres N=189

Adult centre	Severity	Total N	PERMANENT PROPHYLAXIS									ON-DEMAND / TEMPORARY PROPHY			
			% of patients	N	Dosing of prophylaxis (IU/kg per week)				ABR		Age	N	ABR		Age
					Mean	Median	Min	Max	Mean	Median	Median		Mean	Median	Median
Brno	Moderate	12	8.3%	1	42.9	42.9	42.9	42.9	3.0	3.0	28	11	0.5	0.0	46
	Severe	37	64.9%	24	47.5	38.0	18.5	116.7	2.5	1.0	32	13	5.9	4.0	46
Ostrava	Moderate	7	28.6%	2	52.4	52.4	51.7	53.1	6.5	6.5	67	5	3.6	4.0	40
	Severe	28	78.6%	22	55.1	53.0	24.7	93.8	2.2	1.5	38	6	4.3	5.5	63
Plzeň	Moderate	2	0.0%	0								2	0.5	0.5	36
	Severe	20	50.0%	10	34.5	35.9	16.7	60.0	0.4	0.0	46	10	21.0	18.0	52
Liberec	Moderate	0													
	Severe	10	60.0%	6	60.3	53.1	40.9	94.3	3.7	3.5	36	4	6.3	5.0	63
Olomouc	Moderate	0													
	Severe	21	38.1%	8	48.4	45.3	33.3	75.0	2.6*	1.0*	28	13	9.3	8.0	57
Hradec Králové	Moderate	4	0.0%	0								4	0.3	0.0	22
	Severe	16	50.0%	8	53.6	61.2	15.2	90.0	5.0	1.0	26	8	9.1	3.0	33
Ústí n. Labem	Moderate	3	0.0%	0								3	0.0	0.0	20
	Severe	10	50.0%	5	43.0	31.7	13.9	85.2	10.8	2.0	28	5	31.6	38.0	42
Plzeň - Haemacentre	Moderate	1	100.0%	1	27.7	27.7	27.7	27.7	4.0	4.0	48	0			
	Severe	3	100.0%	3	62.9	73.2	37.3	78.0	0.7	0.0	44	0			
Č. Budějovice	Moderate	4	0.0%	0								4	0.5	0.0	68
	Severe	11	27.3%	3	59.6	69.8	34.1	75.0	0.3	0.0	41	8	2.0	0.5	51

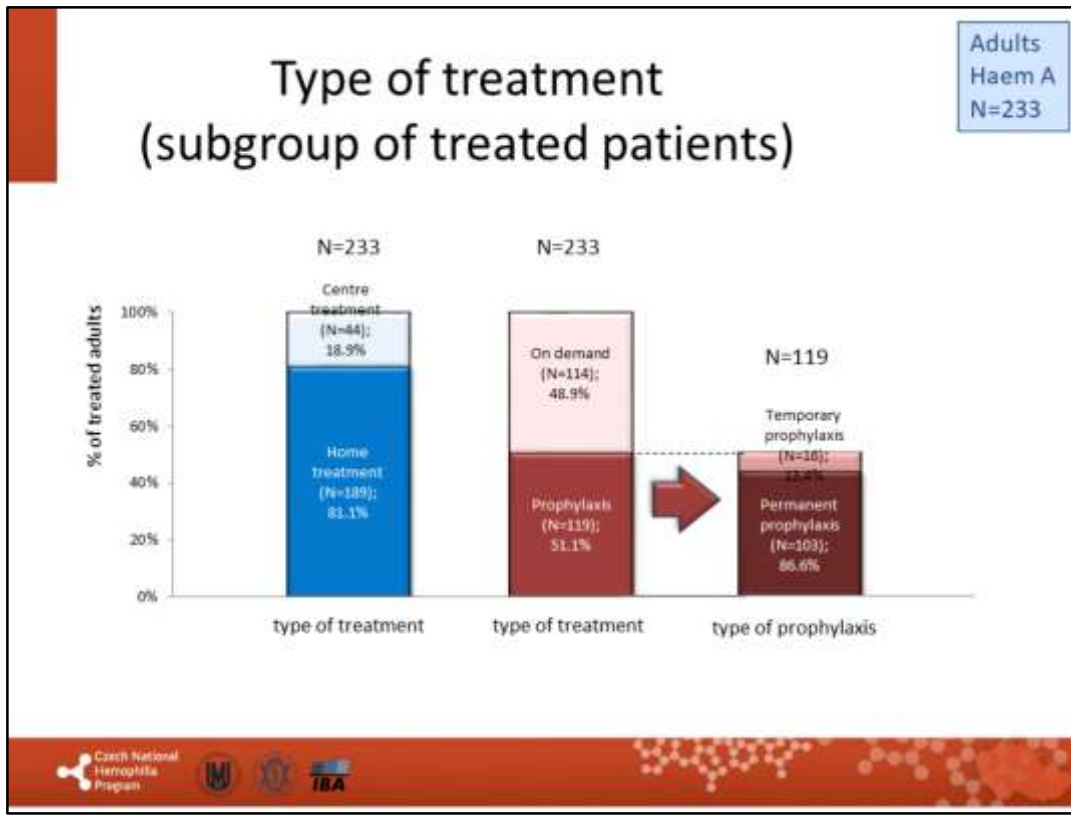
* missing ABR in 1 adult

Czech National Hemophilia Program

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 85% of children treated in 2017 took the advantage of home treatment. 68% of treated children were commenced on any type of prophylaxis (was 71% in 2016) and 89% out of those on prophylaxis were on permanent prophy in 2017 (was 78% in 2016).

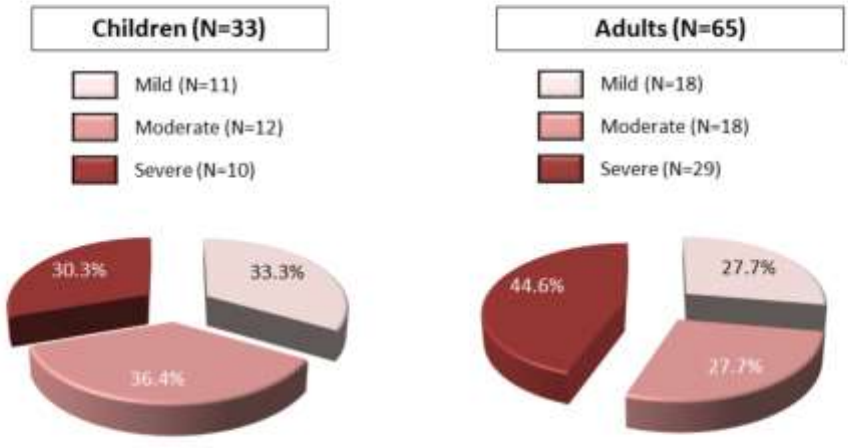


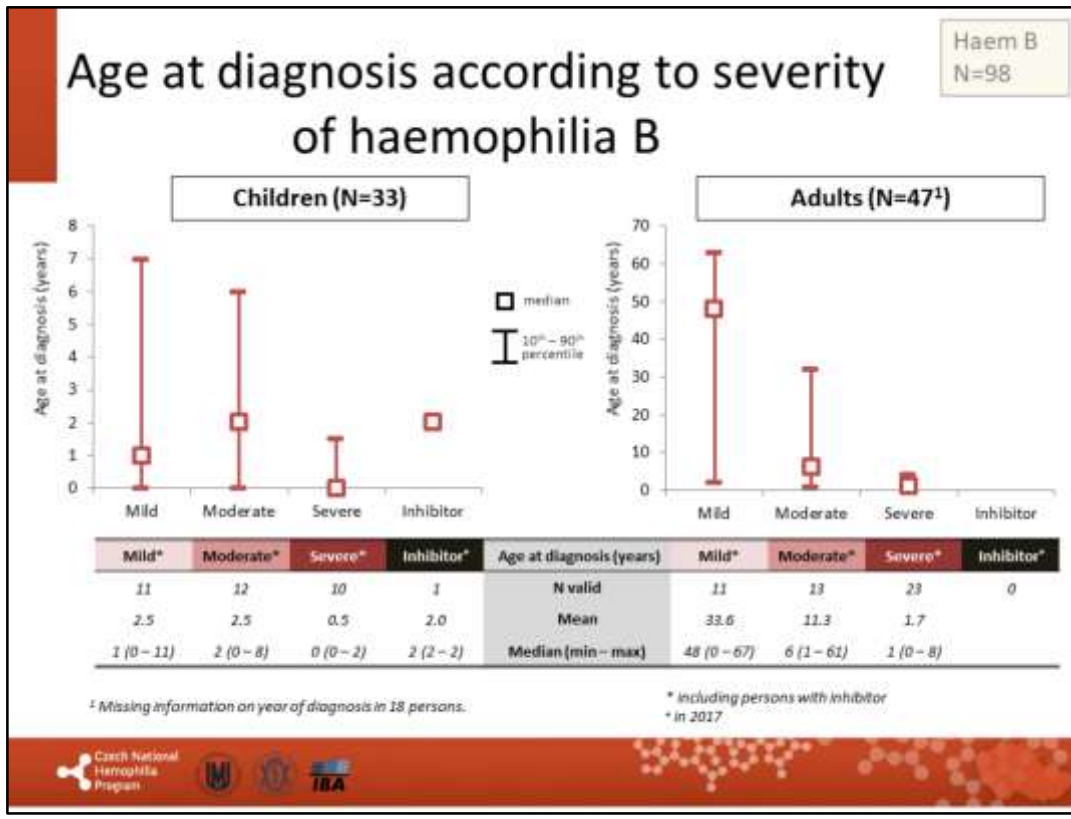
81% of adults treated in 2017 took the advantage of home treatment (no change compared to 2016). Over 50% of treated adults were commenced on any type of prophylaxis (was similar in 2016) and 86.6% out of those on prophylaxis were on permanent prophy in 2017 (was 83% in 2016).

Demographic characteristics
Haemophilia B

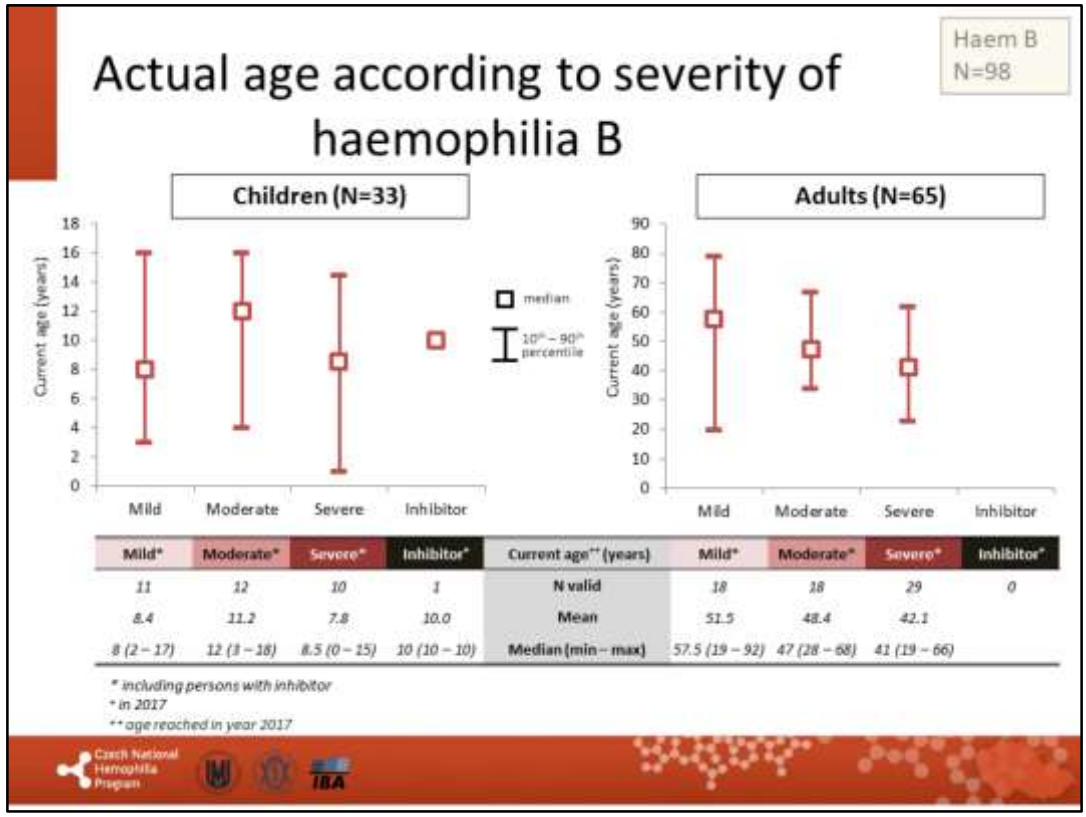
Severity of haemophilia B

Haem B
N=98

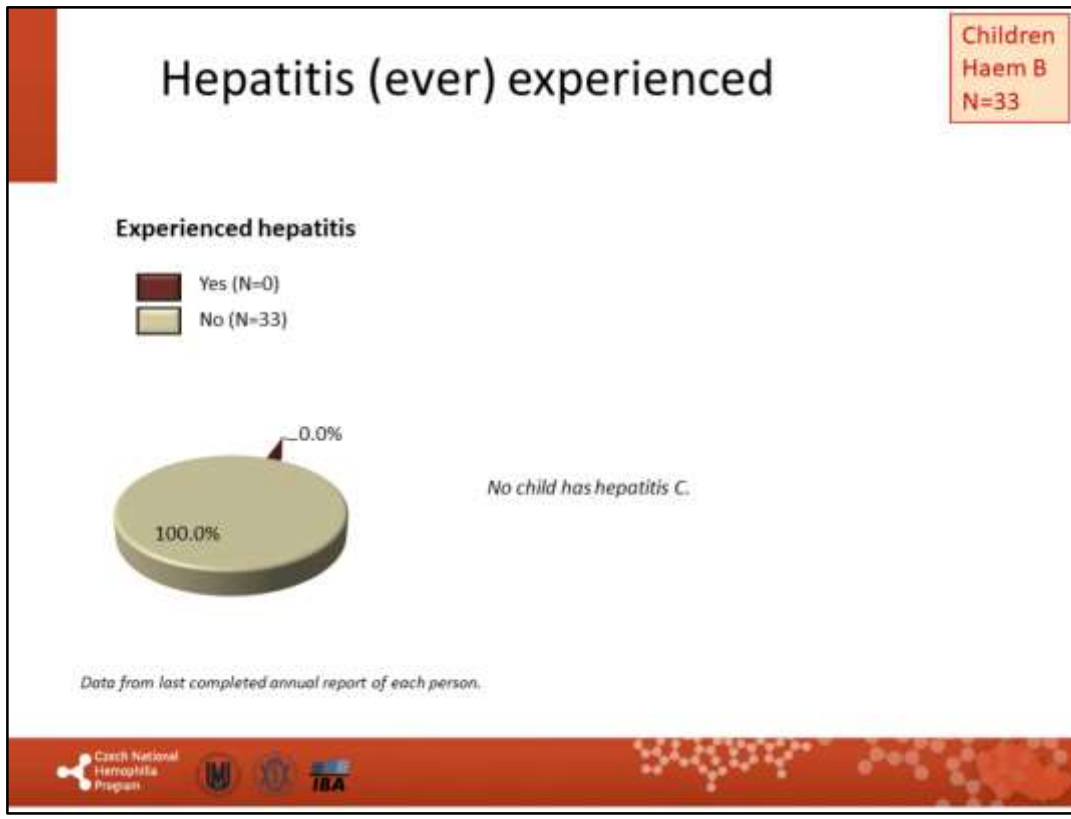




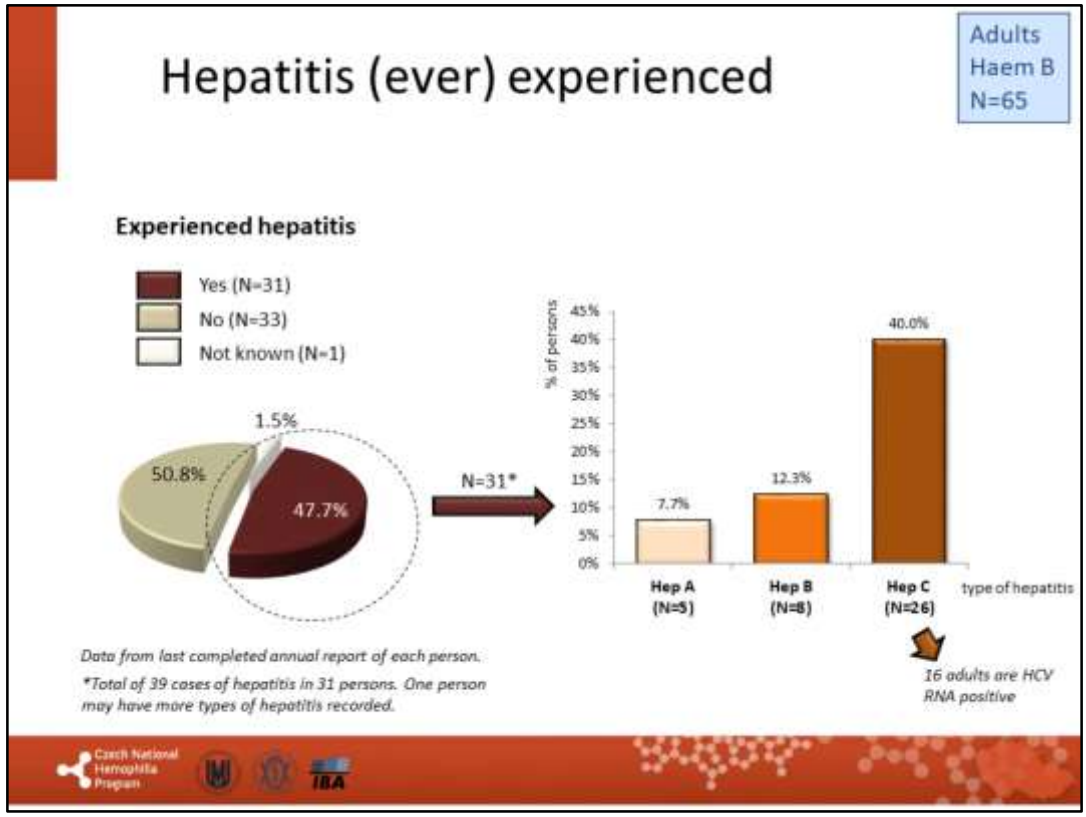
There is no major difference in demographics between HA and HB.



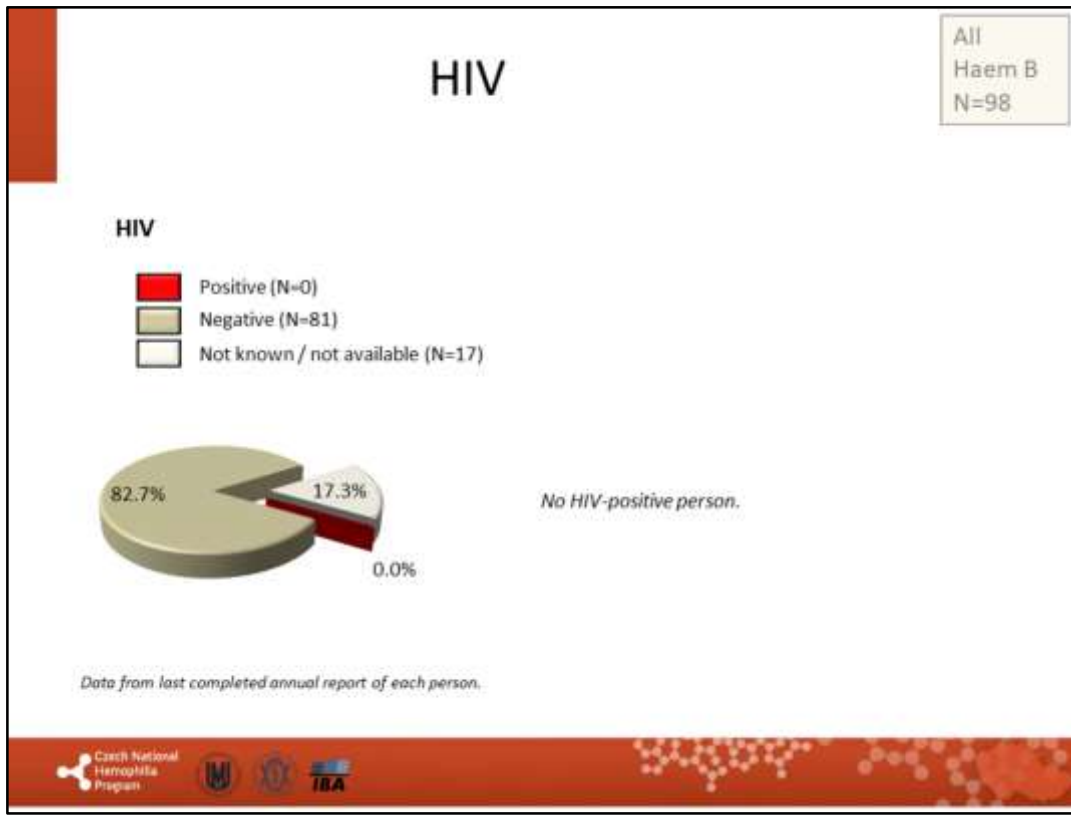
There is no major difference in demographics between HA and HB, perhaps adults with HB are slightly older than those, with HA.



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

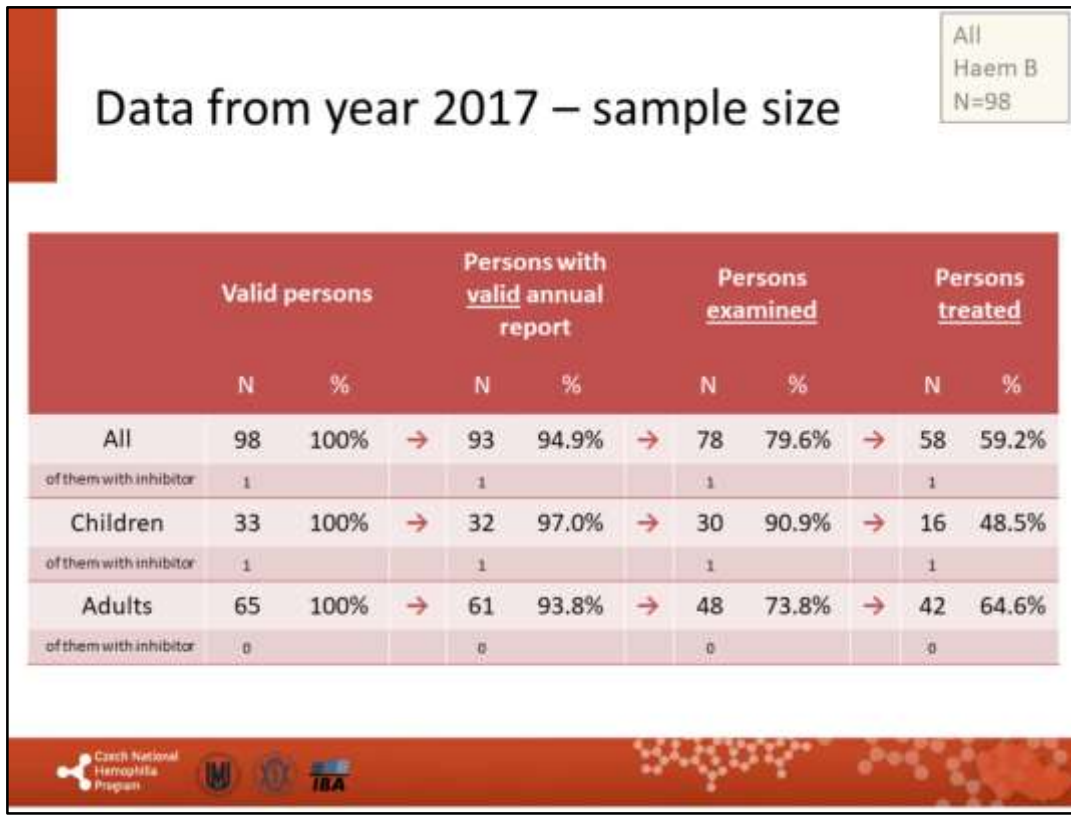


There was NO NEW HepC infection in 2017.
26 PWHB ever experienced hepatitis, though some of them may have been successfully treated (numbers of successfully treated not shown here). 16 adults reported as HCV RNA positive, thus with active disease. New antiviral treatment available for all, who need it.

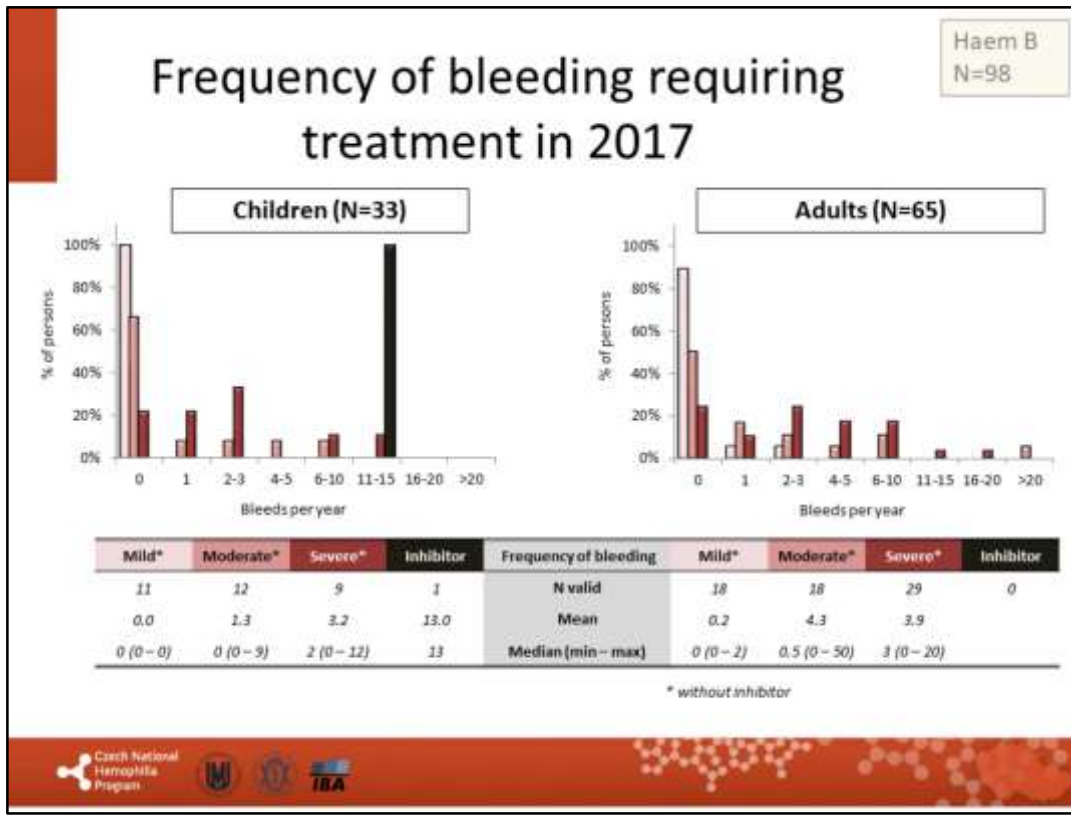


Very low number of HIV positive PWH due to low/no access to contaminated concentrates in 80s and 90s. Our current treatment is on a very high safety level. No new HIV reported in any PWH since late 90s.

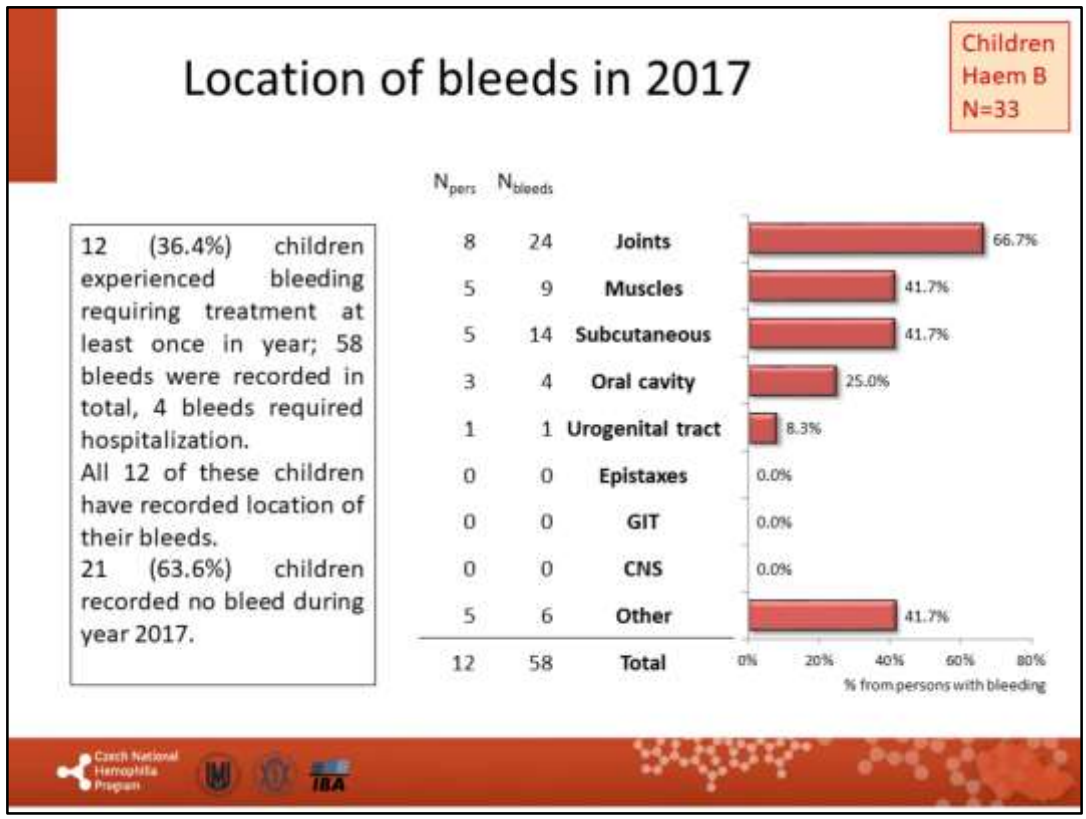
Treatment outcomes and bleeding frequency
Haemophilia B



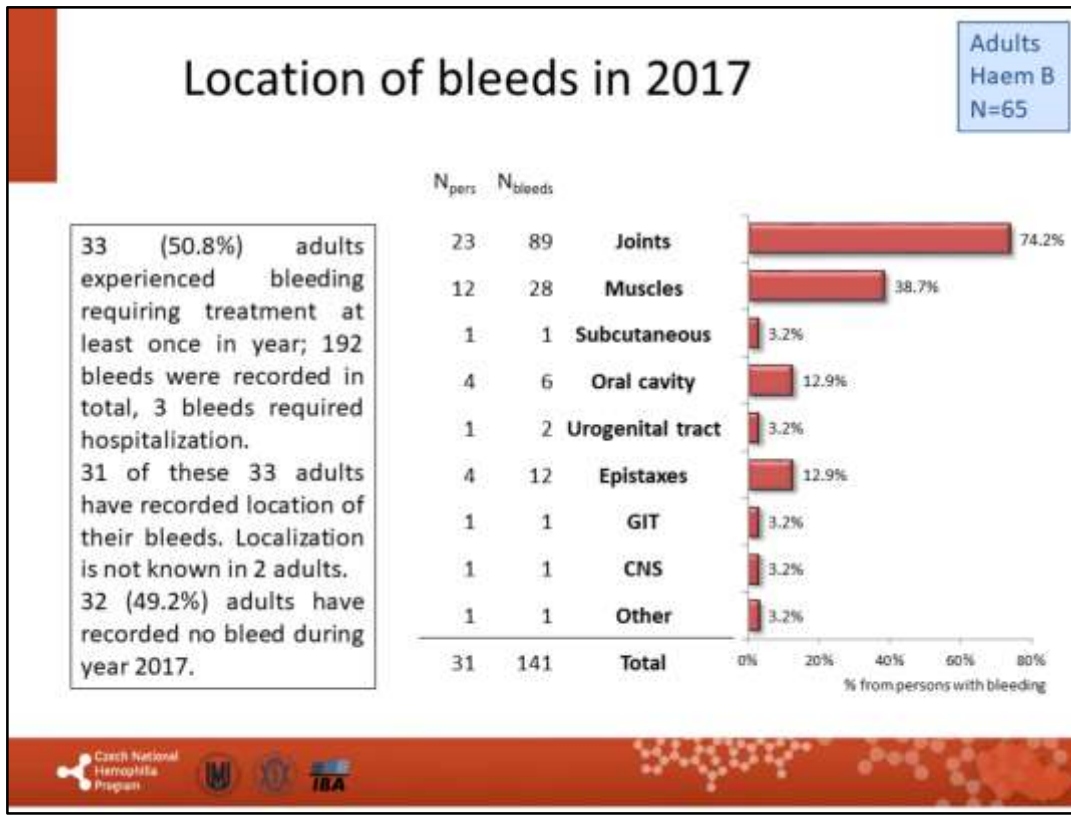
See previous comment for the same slide related to HA.



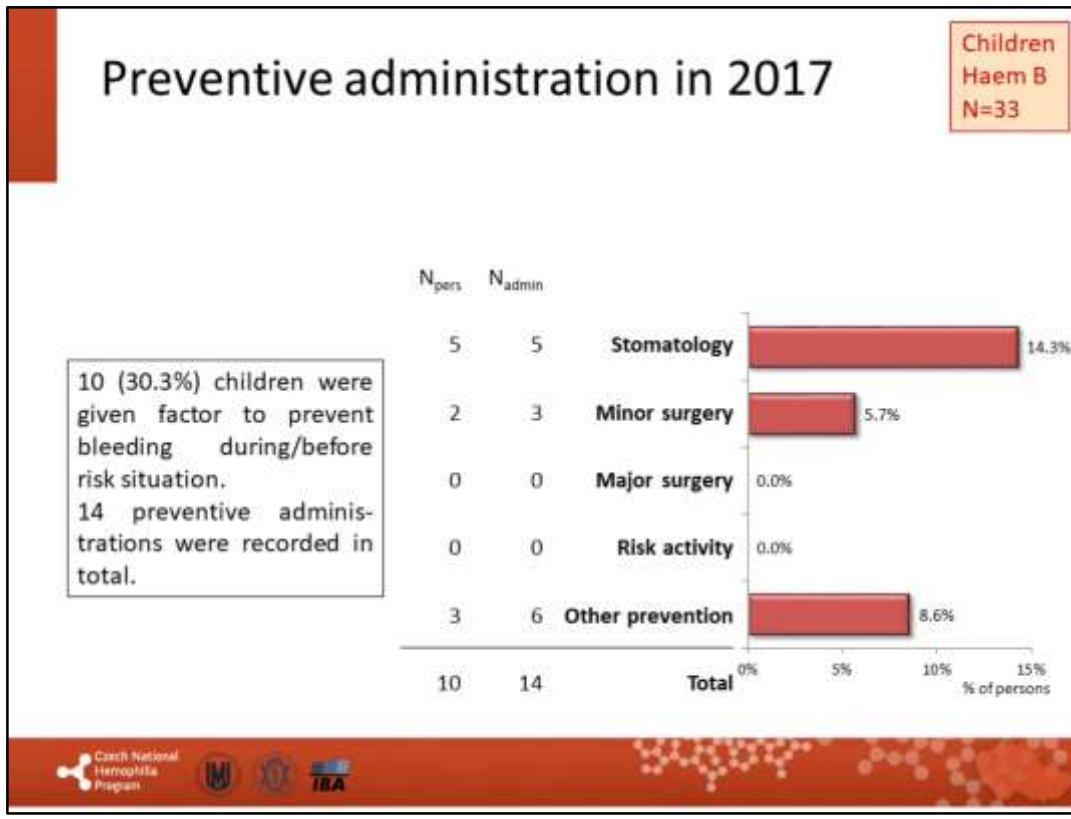
Data shown document good efficacy of care provided to Czech PWH, no matter what age category they are. Mean/Median number of bleedings per year (ABR) is 3.9/3 for adults and 3.2/2 in children with severe HB.



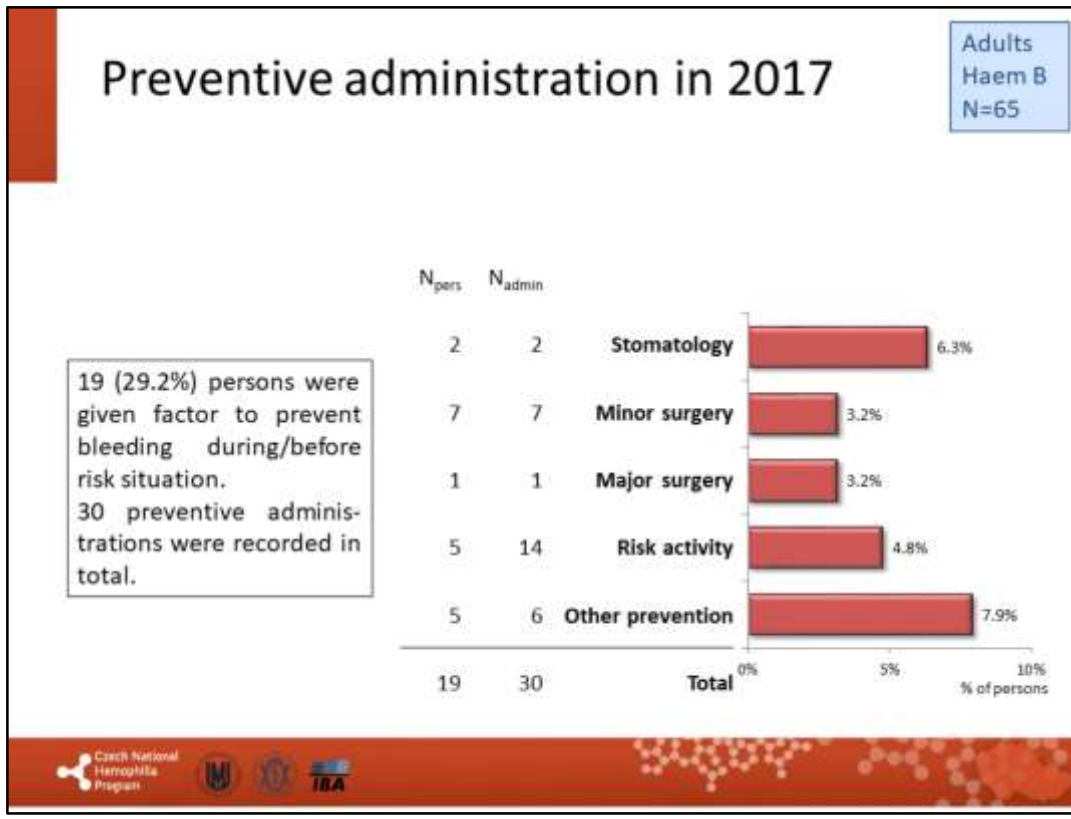
There was no CNS bleed in children with haemophilia B in 2017. 63.6% of children had no bleed at all.



Bleeding events in adults.

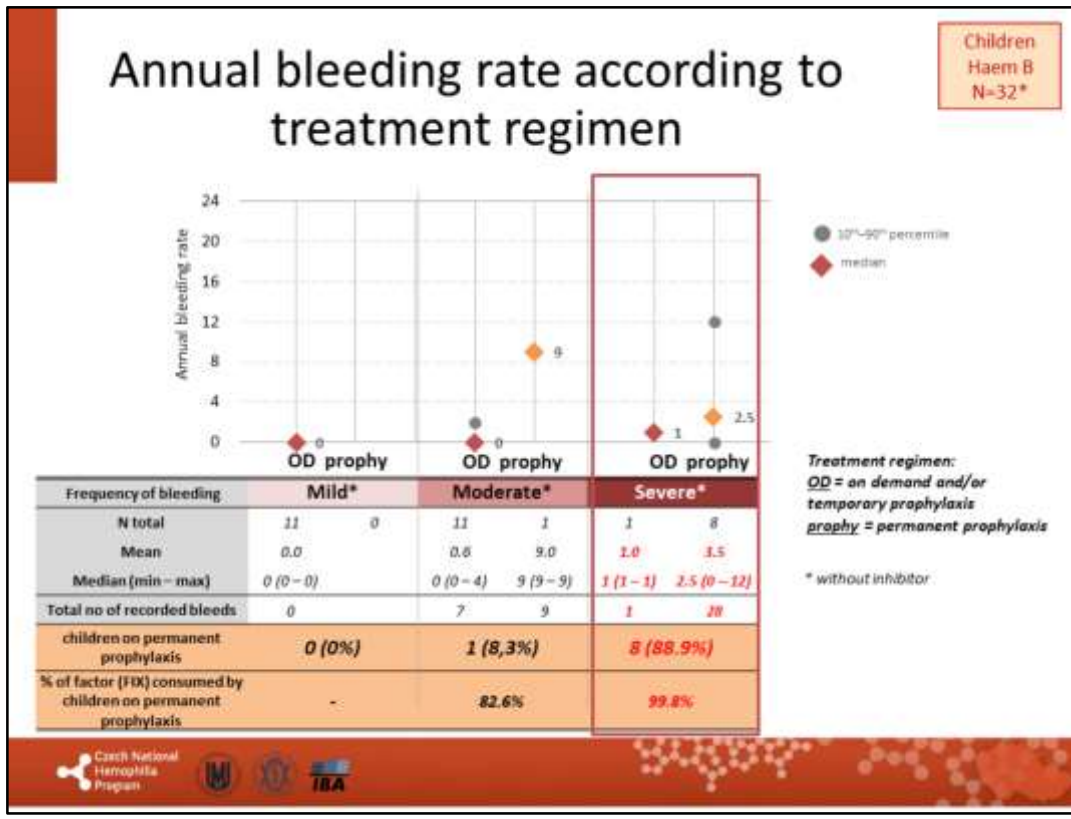


This figure refers to preventive factors administration in children with HB.



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

ABR according to treatment regimen
Haemophilia B without inhibitor



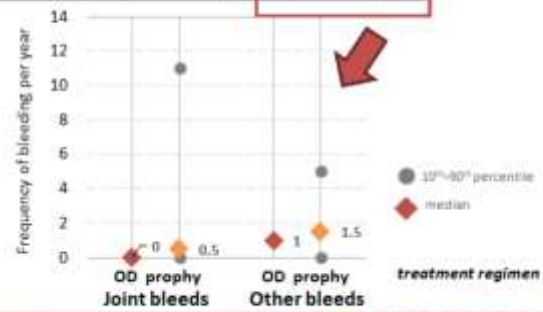
The data on bleeding rate in children with HB.. In general, less bleeds in children with HB. No major change compared to 2016

Joint and other bleeds according to treatment regimen

Children
Haem B
N=32*

Frequency of bleeding	Mild*		Moderate*		Severe*	
Treatment regimen	OD	prophy	OD	prophy	OD	prophy
N valid	11	0	11	1	1	8
JOINT BLEEDS						
Mean	0.0		0.3	2.0	0.0	1.9
Median (range)	0 (0 – 0)		0 (0 – 2)	2 (2 – 2)	0 (0 – 0)	0.5 (0 – 11)
Total no of recorded bleeds	0		3	2	0	15
OTHER BLEEDS						
Mean	0.0		0.4	7.0	1.0	1.6
Median (range)	0 (0 – 0)		0 (0 – 3)	7 (7 – 7)	1 (1 – 1)	1.5 (0 – 5)
Total no of recorded bleeds	0		4	7	1	13

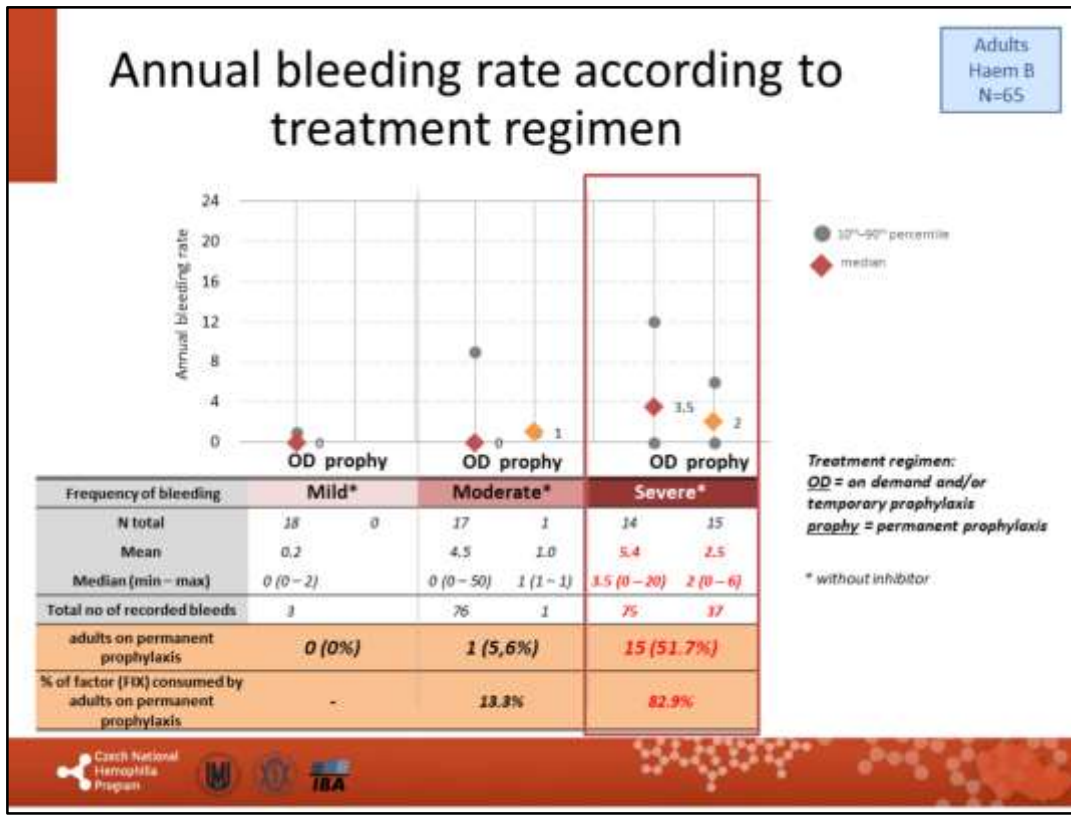
* without inhibitor



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

Czech National Hemophilia Program

The same is true for joint bleeds.



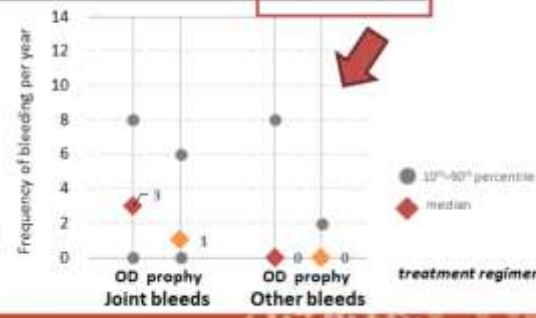
As well as in HA, adults with severe haemophilia B, who bleed frequently should be commenced on prophylaxis.

Joint and other bleeds according to treatment regimen

Adults
Haem B
N=63*

Frequency of bleeding	Mild*		Moderate*		Severe*	
Treatment regimen	OD	prophy	OD	prophy	OD	prophy
N valid	18	0	16	1	14	14
JOINT BLEEDS						
Mean	0.1		0.6	1.0	3.6	1.9
Median (range)	0 (0 – 1)		0 (0 – 4)	1 (1 – 1)	3 (0 – 12)	1 (0 – 6)
Total no of recorded bleeds	1		10	1	51	26
OTHER BLEEDS						
Mean	0.1		1.0	0.0	1.7	0.7
Median (range)	0 (0 – 2)		0 (0 – 9)	0 (0 – 0)	0 (0 – 10)	0 (0 – 4)
Total no of recorded bleeds	2		16	0	24	10

* without inhibitor; missing location of bleeds in 2 adults

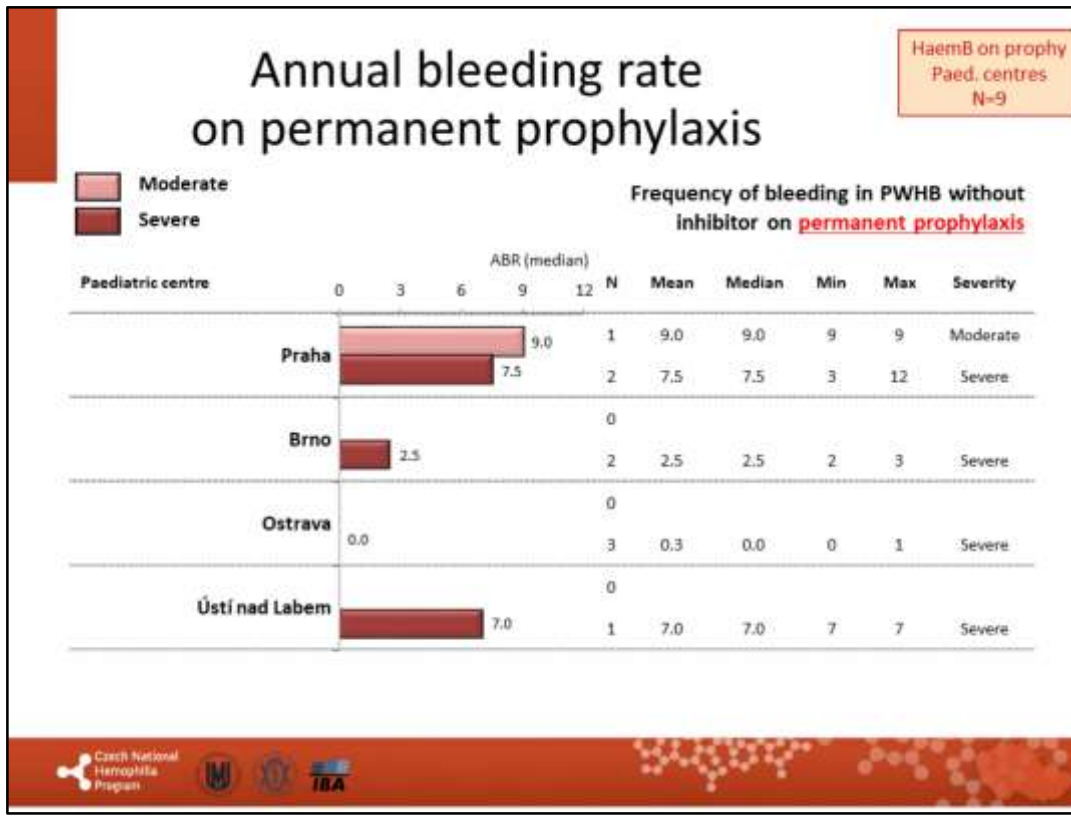


Treatment regimen:
OD = on demand and/or temporary prophylaxis
prophy = permanent prophylaxis

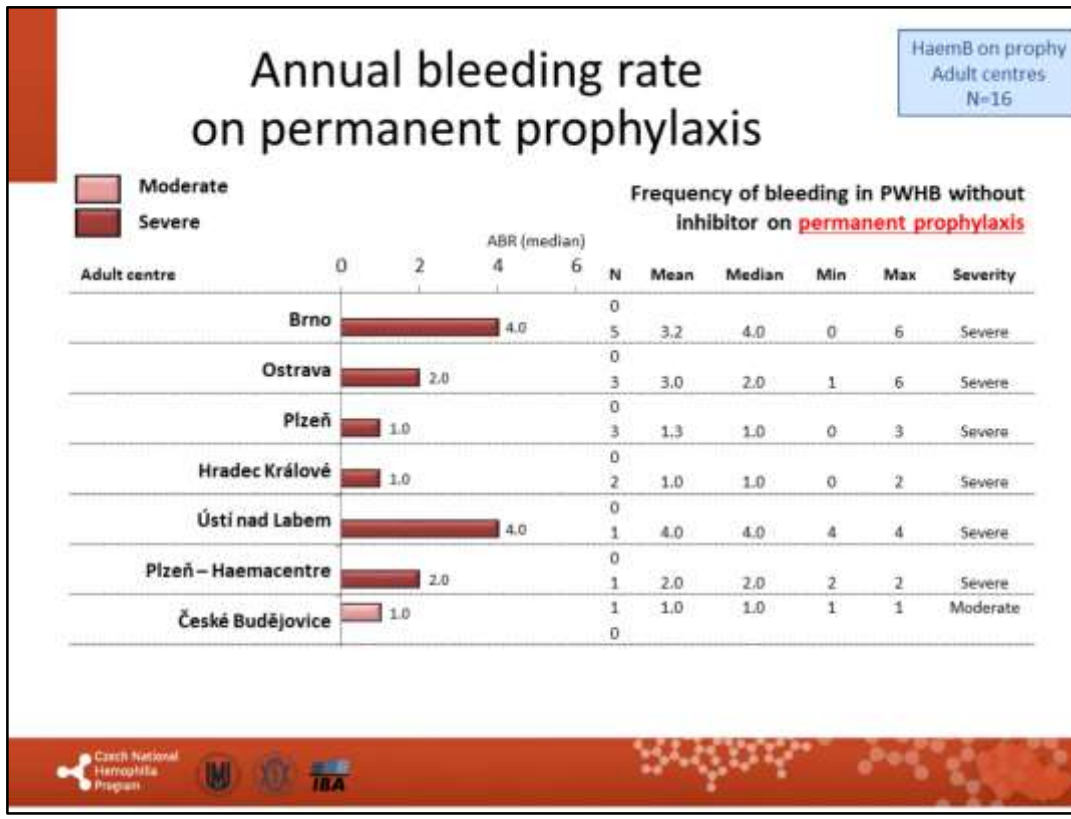
Czech National Hemophilia Program

The same is true also for joint bleeds in PWHB.

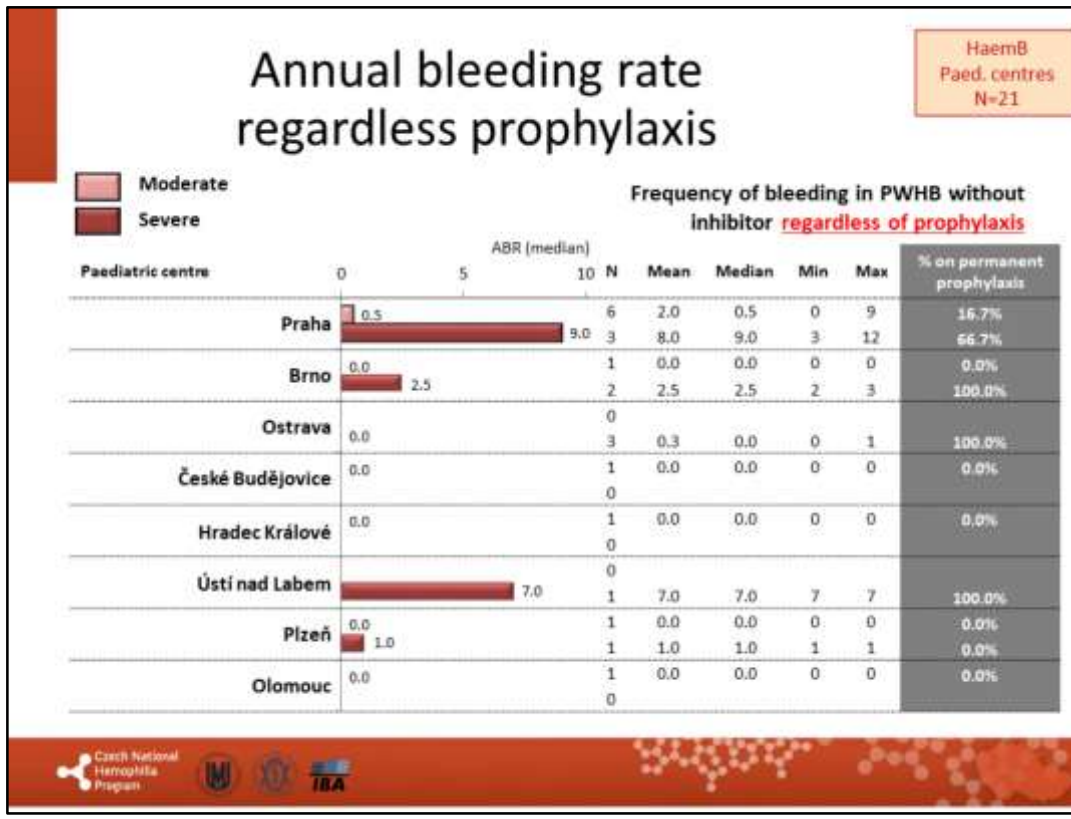
ABR according to centres
Haemophilia B (PWHB)



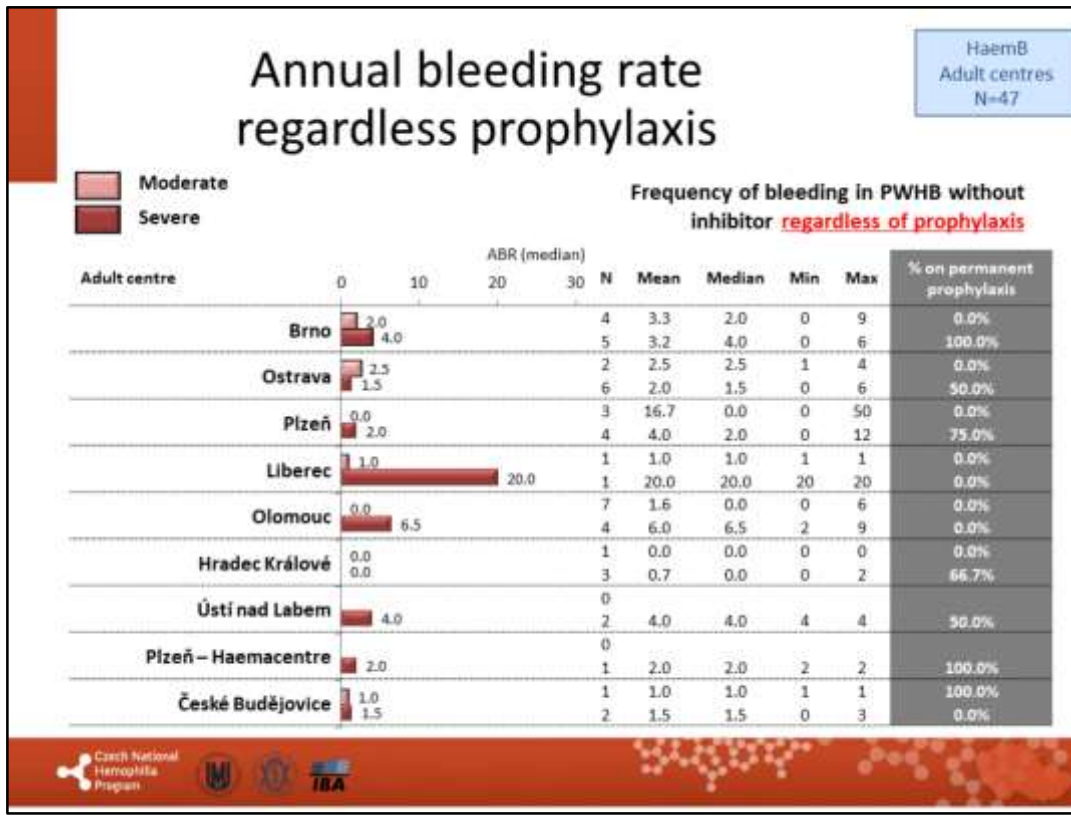
Not all centres treat children with HB. The median ABR increased significantly in certain centres compared to 2016. Though this is, indeed, due to small total numbers, the adequate action has to be taken by respective centres.



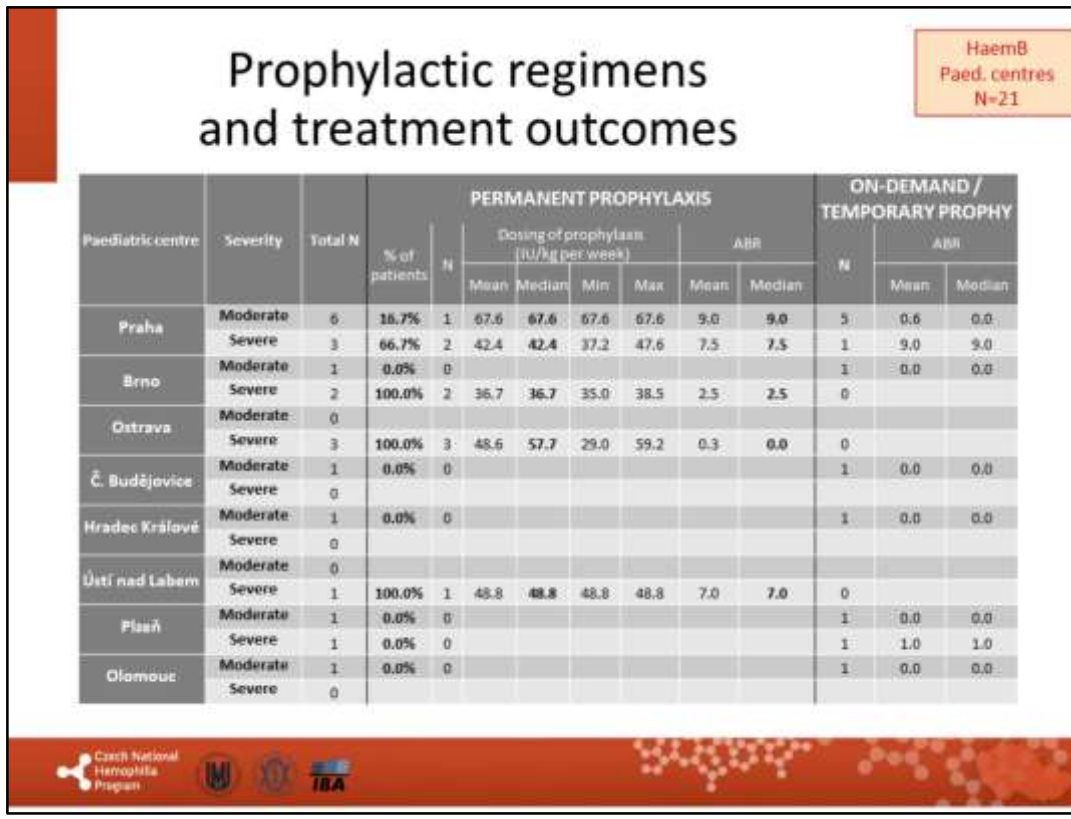
Similar situation for adults with HB. HB means significantly less burden for patients, compared to adults with HA.



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

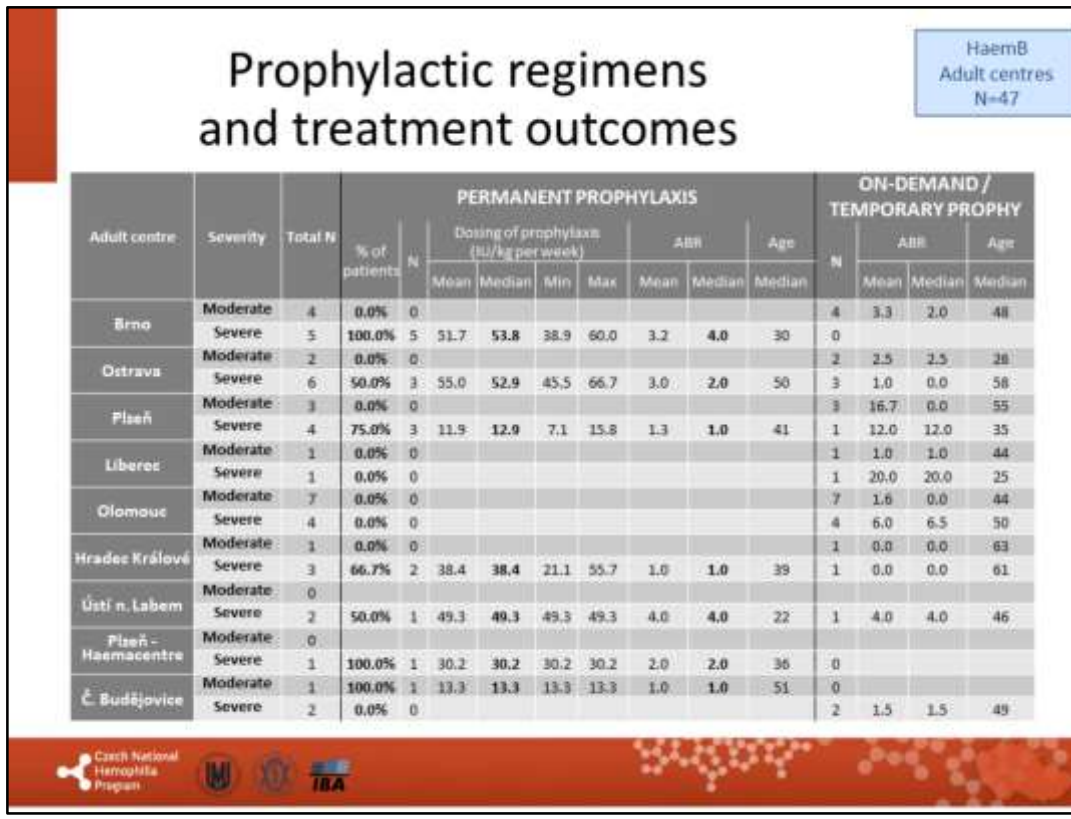


This slide describes the treatment of adults with HB regardless of prophylaxis in those centres, which treat PWHB.



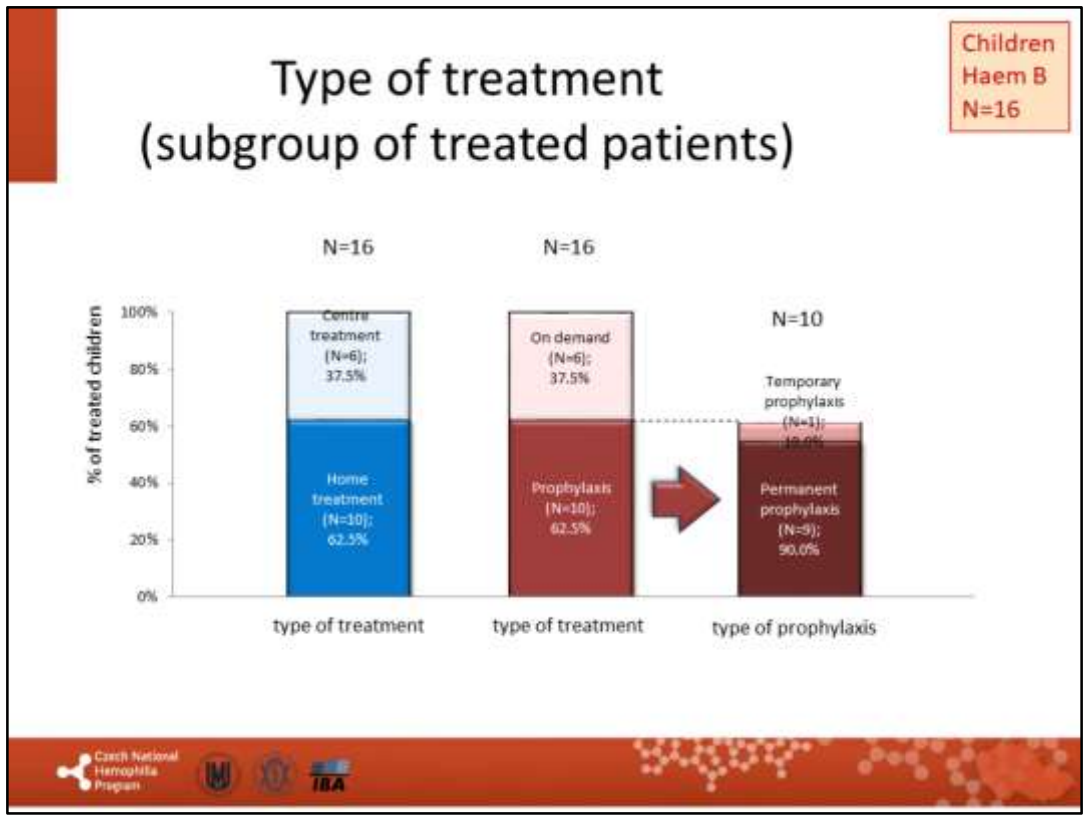
Paediatric centre	Severity	Total N	% of patients	N	PERMANENT PROPHYLAXIS						ON-DEMAND / TEMPORARY PROPHY		
					Dosing of prophylaxis (IU/kg per week)				ABR		N	ABR	
					Mean	Median	Min	Max	Mean	Median		Mean	Median
Praha	Moderate	6	16.7%	1	67.6	67.6	67.6	67.6	9.0	9.0	5	0.6	0.0
	Severe	3	66.7%	2	42.4	42.4	37.2	47.6	7.5	7.5	1	9.0	9.0
Brno	Moderate	1	0.0%	0							1	0.0	0.0
	Severe	2	100.0%	2	36.7	36.7	35.0	38.5	2.5	2.5	0		
Ostrava	Moderate	0											
	Severe	3	100.0%	3	48.6	57.7	29.0	59.2	0.3	0.0	0		
Č. Budějovice	Moderate	1	0.0%	0							1	0.0	0.0
	Severe	0											
Hradec Králové	Moderate	1	0.0%	0							1	0.0	0.0
	Severe	0											
Ústí nad Labem	Moderate	0											
	Severe	1	100.0%	1	48.8	48.8	48.8	48.8	7.0	7.0	0		
Plzeň	Moderate	1	0.0%	0							1	0.0	0.0
	Severe	1	0.0%	0							1	1.0	1.0
Olomouc	Moderate	1	0.0%	0							1	0.0	0.0
	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.

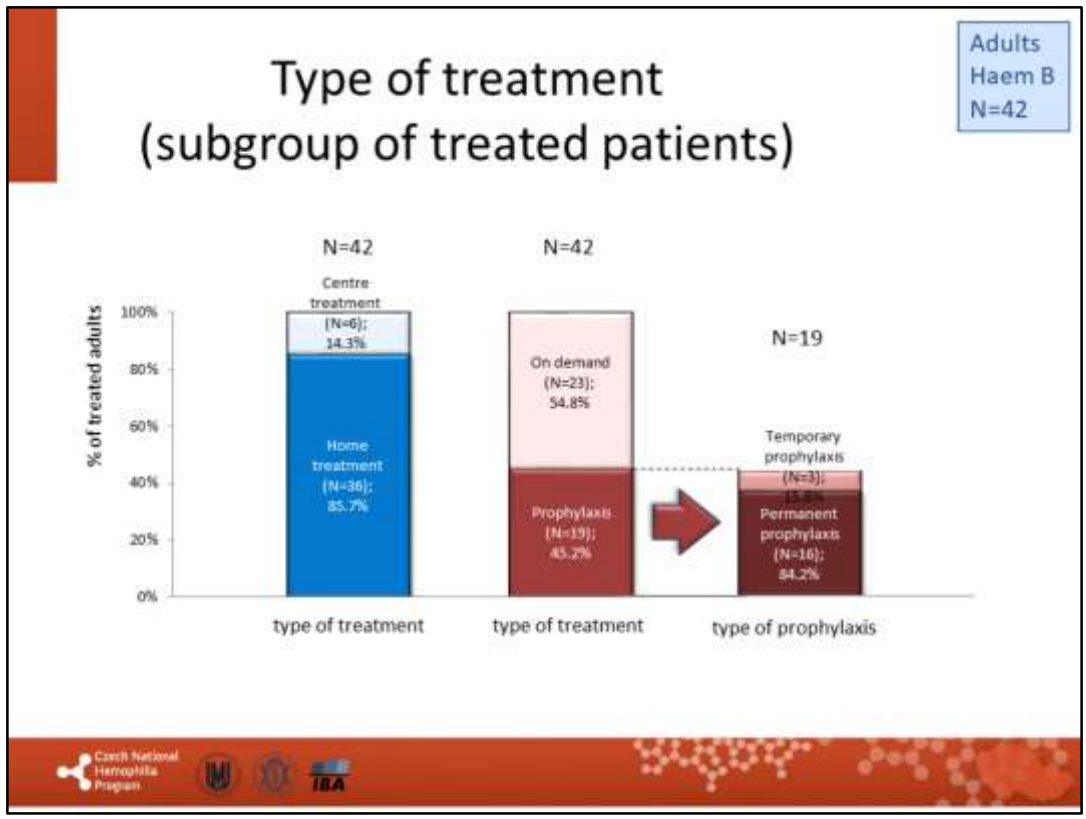


Adult centre	Severity	Total N	PERMANENT PROPHYLAXIS									ON-DEMAND / TEMPORARY PROPHY			
			% of patients	N	Dosing of prophylaxis (IU/kg per week)				ABR		Age	N	ABR		Age
					Mean	Median	Min	Max	Mean	Median	Median		Mean	Median	Median
Brno	Moderate	4	0.0%	0								4	3.3	2.0	48
	Severe	5	100.0%	5	51.7	53.8	38.9	60.0	3.2	4.0	30	0			
Ostrava	Moderate	2	0.0%	0								2	2.5	2.5	38
	Severe	6	50.0%	3	55.0	52.9	45.5	66.7	3.0	2.0	50	3	1.0	0.0	58
Plzeň	Moderate	3	0.0%	0								3	16.7	0.0	55
	Severe	4	75.0%	3	11.9	12.9	7.1	15.8	1.3	1.0	41	1	12.0	12.0	35
Liberec	Moderate	1	0.0%	0								1	1.0	1.0	44
	Severe	1	0.0%	0								1	20.0	20.0	25
Olomouc	Moderate	7	0.0%	0								7	1.6	0.0	44
	Severe	4	0.0%	0								4	6.0	6.5	50
Hradec Králové	Moderate	1	0.0%	0								1	0.0	0.0	63
	Severe	3	66.7%	2	38.4	38.4	21.1	55.7	1.0	1.0	39	1	0.0	0.0	61
Ústí n. Labem	Moderate	0													
	Severe	2	50.0%	1	49.3	49.3	49.3	49.3	4.0	4.0	22	1	4.0	4.0	46
Plzeň - Haemacentre	Moderate	0													
	Severe	1	100.0%	1	30.2	30.2	30.2	30.2	2.0	2.0	36	0			
Č. Budějovice	Moderate	1	100.0%	1	13.3	13.3	13.3	13.3	1.0	1.0	51	0			
	Severe	2	0.0%	0								2	1.5	1.5	49

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

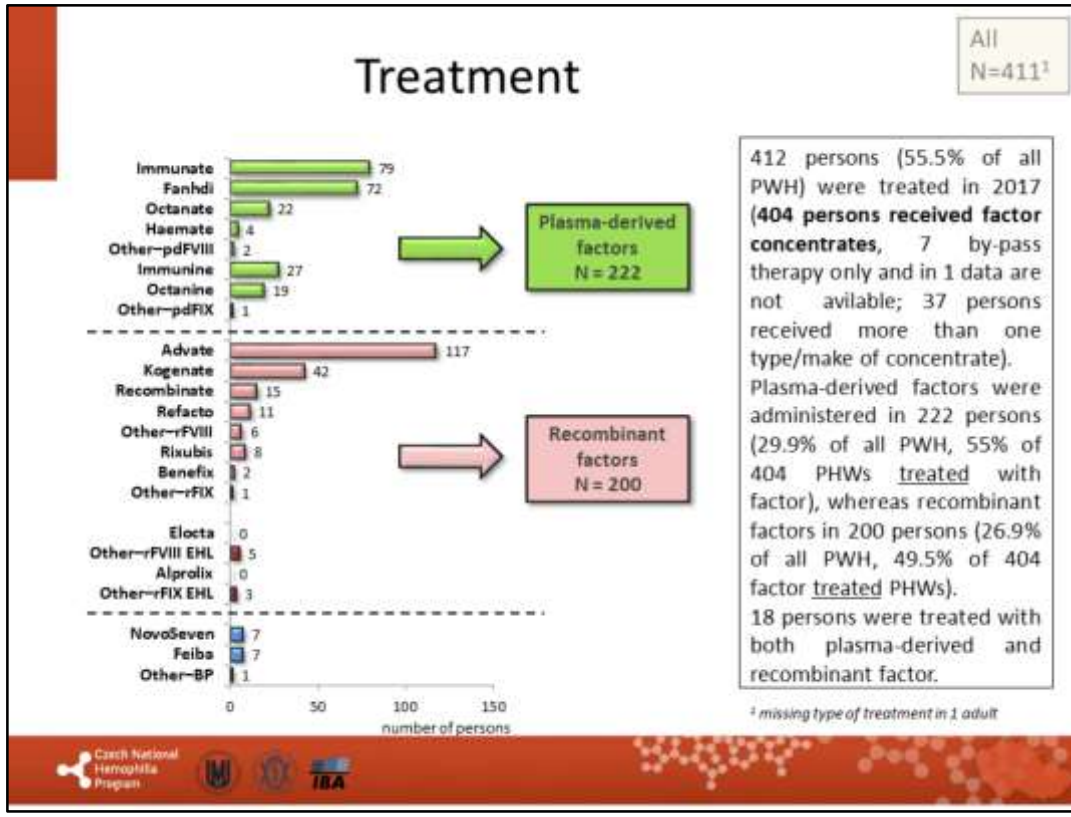


62.5% of children treated in 2017 took the advantage of home treatment (was 52% in 2016).
All children with home treatment were on (any type of) prophylaxis and 90% out of those on prophylaxis were on permanent prophy in 2017 (was 80% in 2016).

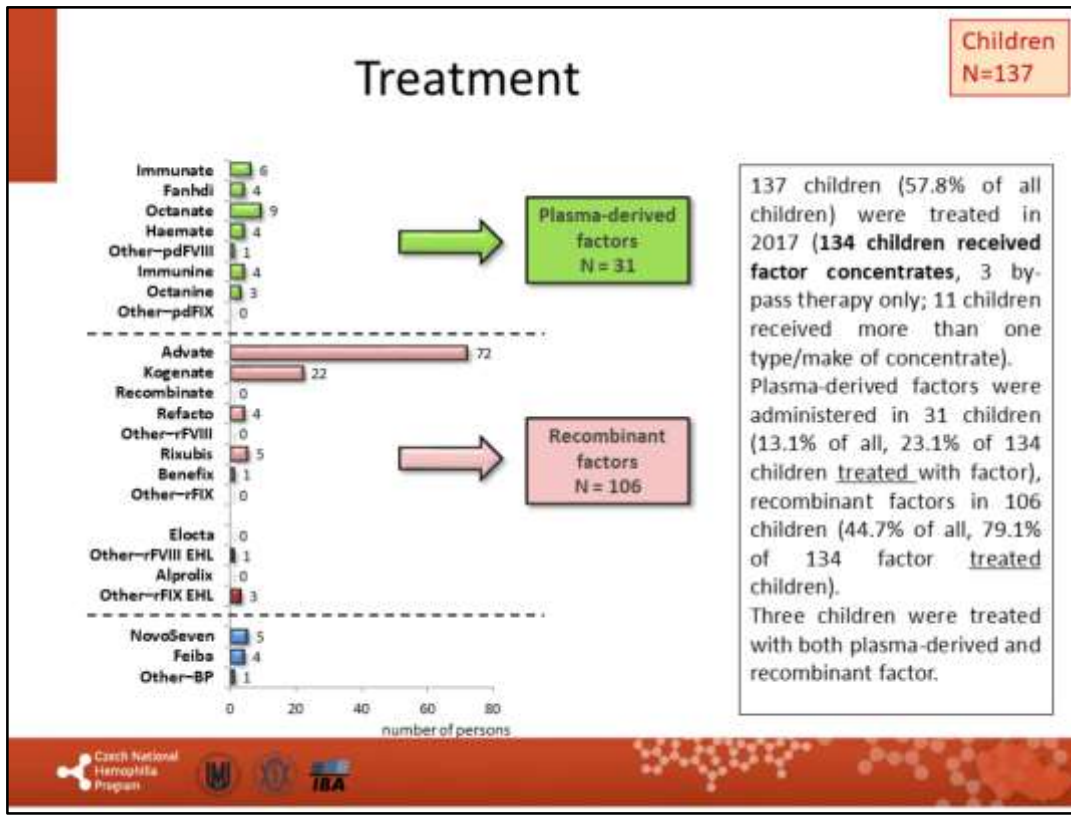


86% of adults treated in 2017 took the advantage of home treatment. 45% of treated adults were commenced on any type of prophylaxis and 84% out of those on prophylaxis were on permanent prophy in 2017 (was 77% in 2016).

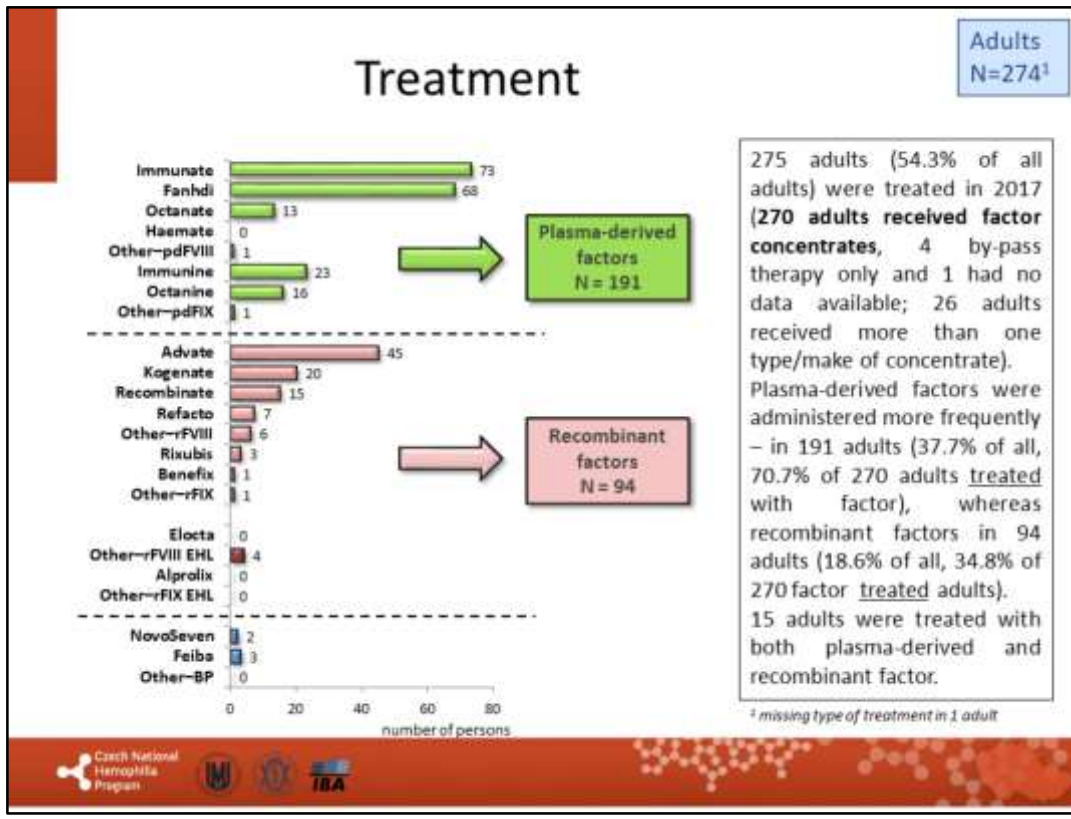
Treatment data and factor consumption Haemophilia A and B



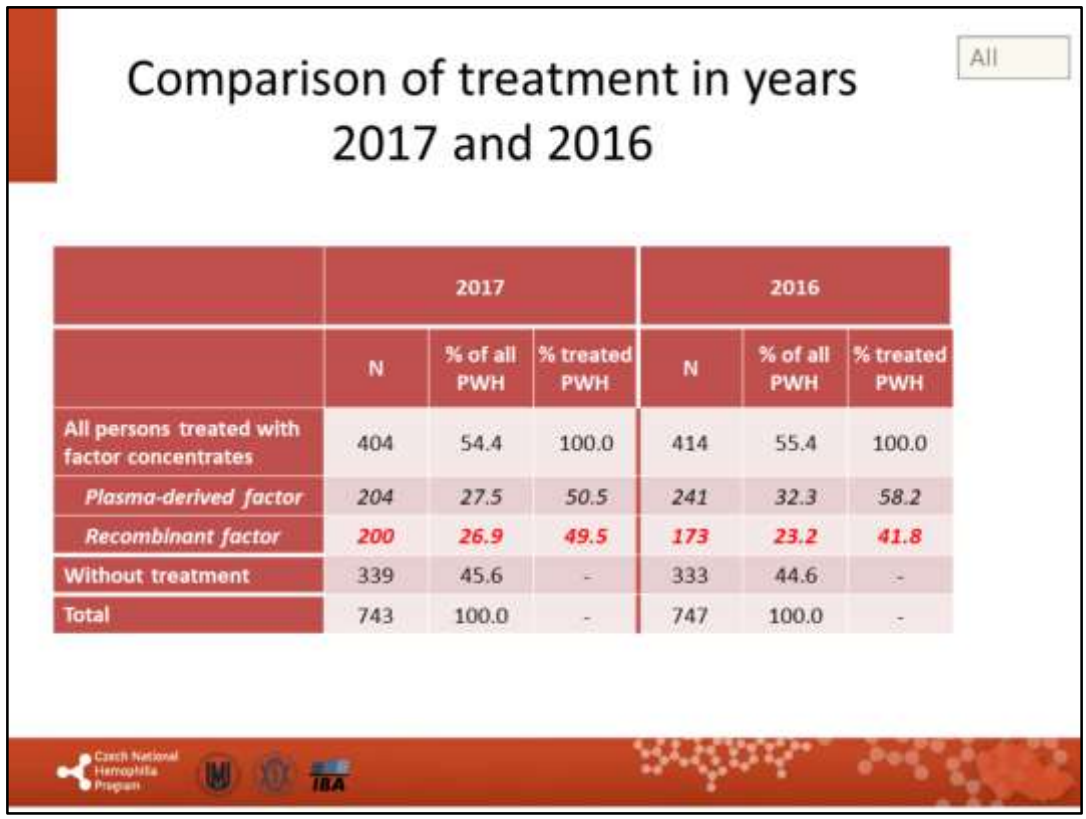
49.5% of PWH registered in CNHP registry and treated with any factor concentrate were treated with recombinants in 2017. The number of PWH treated with recombinants is further increasing over last several years (was 42% in 2016). This is not only due to the recommendation of CNHP to treat PUPs with recombinants (since 2006), but also reflects switches of older children and adults to rFVIII in some cases.



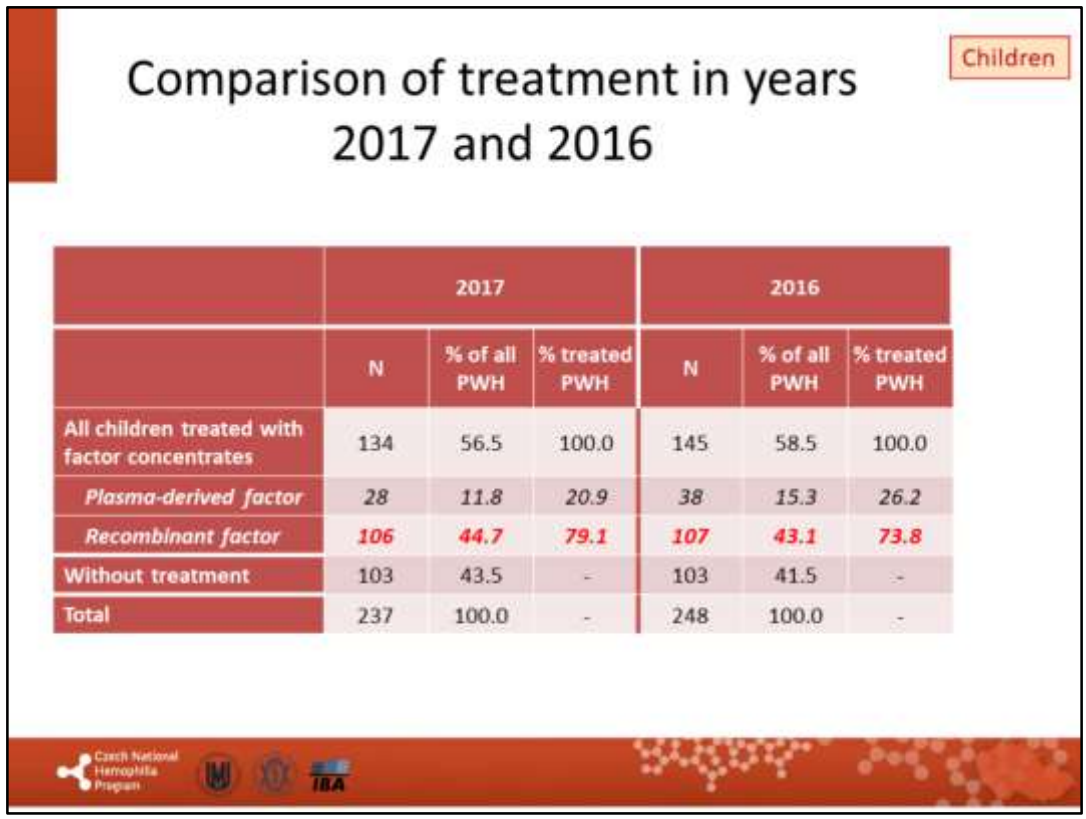
Over 79% of children, who were given factor concentrate in 2017, were treated with recombinants.



Number of adult PWH treated with recombinants is slowly increasing (currently 35% of those treated with factor concentrate in 2017 and registered within CNHP registry (was 25% in 2016).

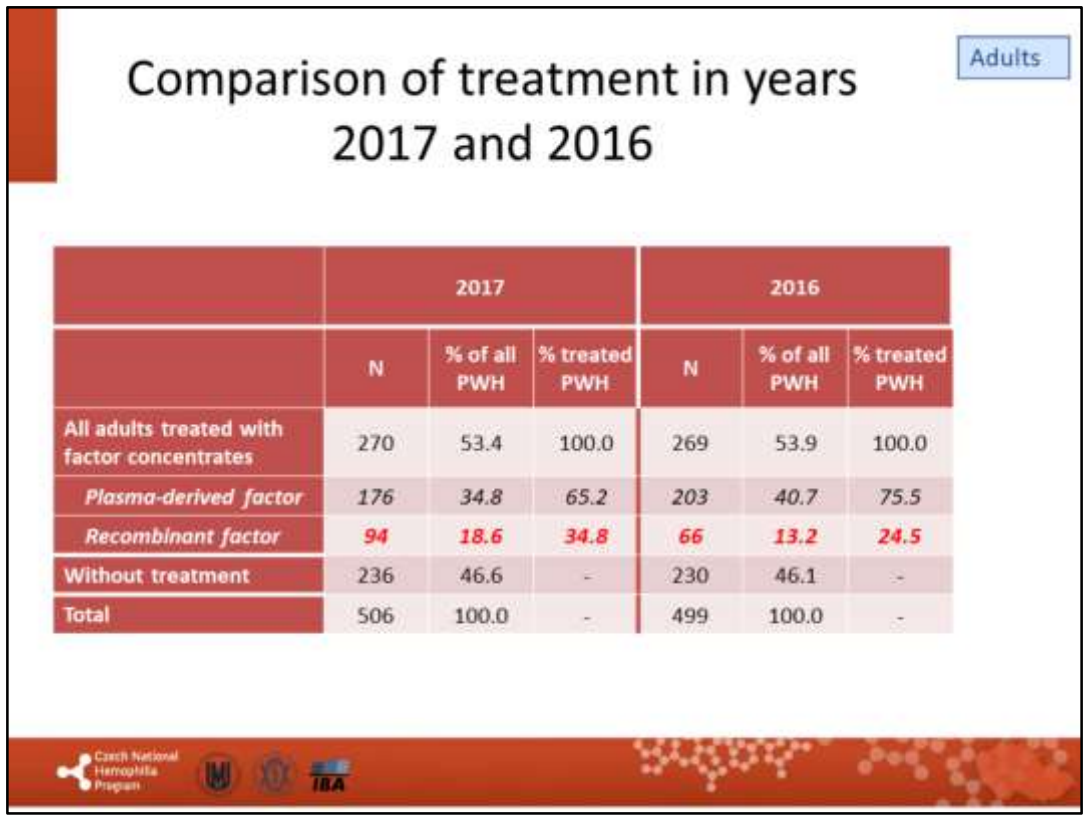


This table compares data between 2016 and 2017. E.g. you can see, that percentage of patients treated with recombinant concentrates and registered within CNHP registry changed from 41.8% in 2016 to 49.5% in 2017.

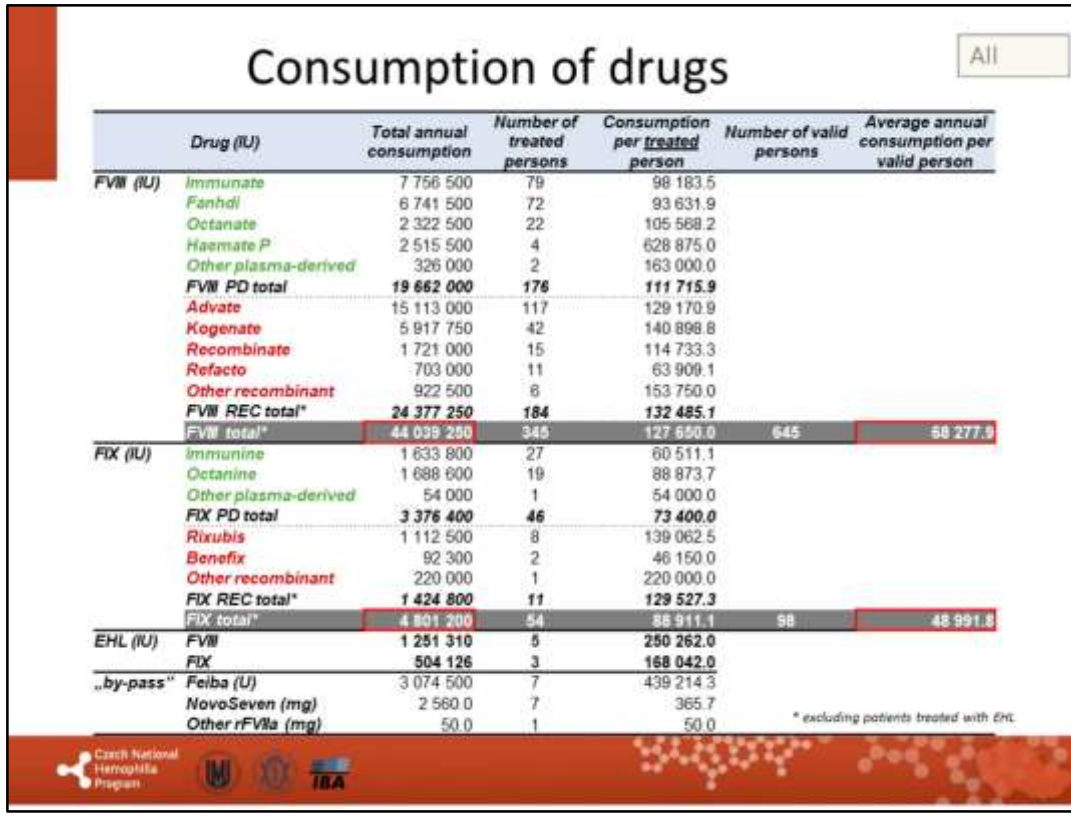


	2017			2016		
	N	% of all PWH	% treated PWH	N	% of all PWH	% treated PWH
All children treated with factor concentrates	134	56.5	100.0	145	58.5	100.0
Plasma-derived factor	*28*	*11.8*	*20.9*	*38*	*15.3*	*26.2*
Recombinant factor	***106***	***44.7***	***79.1***	***107***	***43.1***	***73.8***
Without treatment	103	43.5	-	103	41.5	-
Total	237	100.0	-	248	100.0	-

This table compares data between 2016 and 2017. E.g. you can see, that percentage of patients treated with recombinant concentrates and registered within CNHP registry changed from 73.8% in 2016 to 79.1% in 2017.



This table compares data between 2016 and 2017. E.g. you can see, that percentage of patients treated with recombinant concentrates and registered within CNHP registry changed from 24.5% in 2016 to 34.8% in 2017.



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)	Immunate	7 756 500	79	98 183.5		
	Fanhdi	6 741 500	72	93 631.9		
	Octanate	2 322 500	22	105 568.2		
	Haemate P	2 515 500	4	628 875.0		
	Other plasma-derived	326 000	2	163 000.0		
	FVIII PD total	**19 662 000**	**176**	**111 715.9**		
	Advate	15 113 000	117	129 170.9		
	Kogenate	5 917 750	42	140 898.8		
	Recombinate	1 721 000	15	114 733.3		
	Refacto	703 000	11	63 909.1		
	Other recombinant	922 500	6	153 750.0		
	FVIII REC total*	**24 377 250**	**184**	**132 485.1**		
	FVIII total*	**44 039 250**	**345**	**127 650.0**	**645**	**68 277.9**
FIX (IU)	Immunine	1 633 800	27	60 511.1		
	Octanine	1 688 600	19	88 873.7		
	Other plasma-derived	54 000	1	54 000.0		
	FIX PD total	**3 376 400**	**46**	**73 400.0**		
	Rixubis	1 112 500	8	139 062.5		
	Benefix	92 300	2	46 150.0		
	Other recombinant	220 000	1	220 000.0		
	FIX REC total*	**1 424 800**	**11**	**129 527.3**		
	FIX total*	**4 801 200**	**54**	**88 911.1**	**98**	**48 991.8**
EHL (IU)	**FVIII**	**1 251 310**	**5**	**250 262.0**		
	FIX	**504 126**	**3**	**168 042.0**		
„by-pass"	Feiba (U)	3 074 500	7	439 214.3		
	NovoSeven (mg)	2 560.0	7	365.7		
	Other rFVIIa (mg)	50.0	1	50.0		

* excluding patients treated with EHL

Czech National Hemophilia Program

IBA

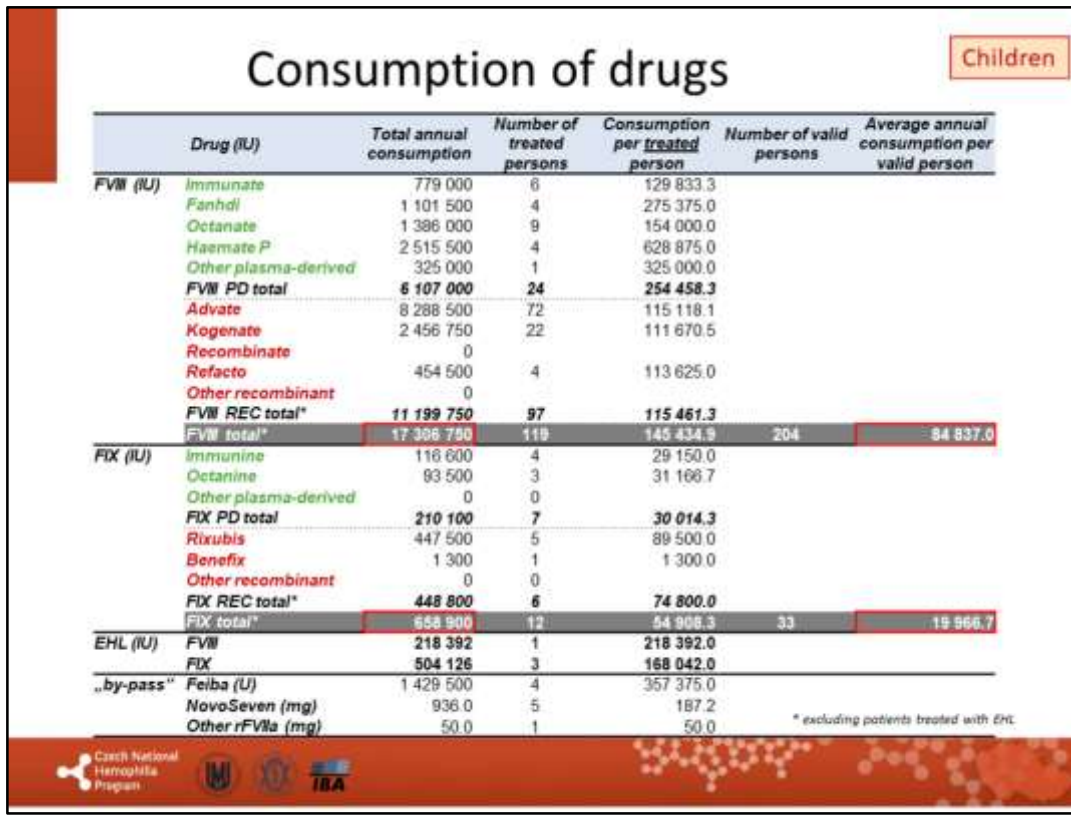
Absolute numbers of respective concentrates in this figure refer ONLY to the records within CNHP registry, which have been updated in 2017. The most important information on this slide is „Average annual consumption per treated person". This reflects nation-wide consumption of factor concentrate per 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 936 haemophilia A patients in 2017 (WFH survey 2017) the total consumption was approximately 63 908 114 IU of FVIII/year in the Czech Republic. (SUKL reported 67 267 000 units of FVIII purchased in CZ during 2017). In other words, it means, that the total consumption was about 6 IU/capita of FVIII in 2017 (SUKL reported 6,34 IU/capita). This is further increased (almost 0,5IU/capita, cca 10%) compared to 2016, probably due to further increase in the numbers of ITIs and more adults on prophylaxis.

Number of haemophiliacs B in the Czech Republic was 141 in 2017, the total consumption was approx. 6 907 731IU of FIX/year, i.e. 0.65 IU/capita (SUKL reported 7 800 000 IU of FIX purchased in 2017, i.e. 0,73 IU/capita).
One can see further increase of rFIX consumption during 2017 (rFIX introduced to Czech market in 2016).

EHL (Extended Half-Life) products were in 2017 used only through clinical trials. Though two of them were registered in CZ in 2016, they still do not have an official price and thus can not be purchased through health insurance system.

Significant further increase in aPCC consumption is caused mainly by aPCC prophylaxis in several children with inhibitors (in one as a part of Bonn ITI regimen), but more aPCC was used also in adults in 2017.



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)	Immunate	779 000	6	129 833.3		
	Fanhdi	1 101 500	4	275 375.0		
	Octanate	1 386 000	9	154 000.0		
	Haemate P	2 515 500	4	628 875.0		
	Other plasma-derived	325 000	1	325 000.0		
	FVIII PD total	**6 107 000**	**24**	**254 458.3**		
	Advate	8 288 500	72	115 118.1		
	Kogenate	2 456 750	22	111 670.5		
	Recombinate	0				
	Refacto	454 500	4	113 625.0		
	Other recombinant	0				
	FVIII REC total*	**11 199 750**	**97**	**115 461.3**		
	FVIII total*	**17 306 750**	**119**	**145 434.9**	**204**	**84 837.0**
FIX (IU)	Immunine	116 600	4	29 150.0		
	Octanine	93 500	3	31 166.7		
	Other plasma-derived	0	0			
	FIX PD total	**210 100**	**7**	**30 014.3**		
	Rixubis	447 500	5	89 500.0		
	Benefix	1 300	1	1 300.0		
	Other recombinant	0	0			
	FIX REC total*	**448 800**	**6**	**74 800.0**		
	FIX total*	**658 900**	**12**	**54 908.3**	**33**	**19 966.7**
EHL (IU)	**FVIII**	**218 392**	**1**	**218 392.0**		
	FIX	**504 126**	**3**	**168 042.0**		
„by-pass"	Feiba (U)	1 429 500	4	357 375.0		
	NovoSeven (mg)	936.0	5	187.2		
	Other rFVIIa (mg)	50.0	1	50.0		

* excluding patients treated with EHL

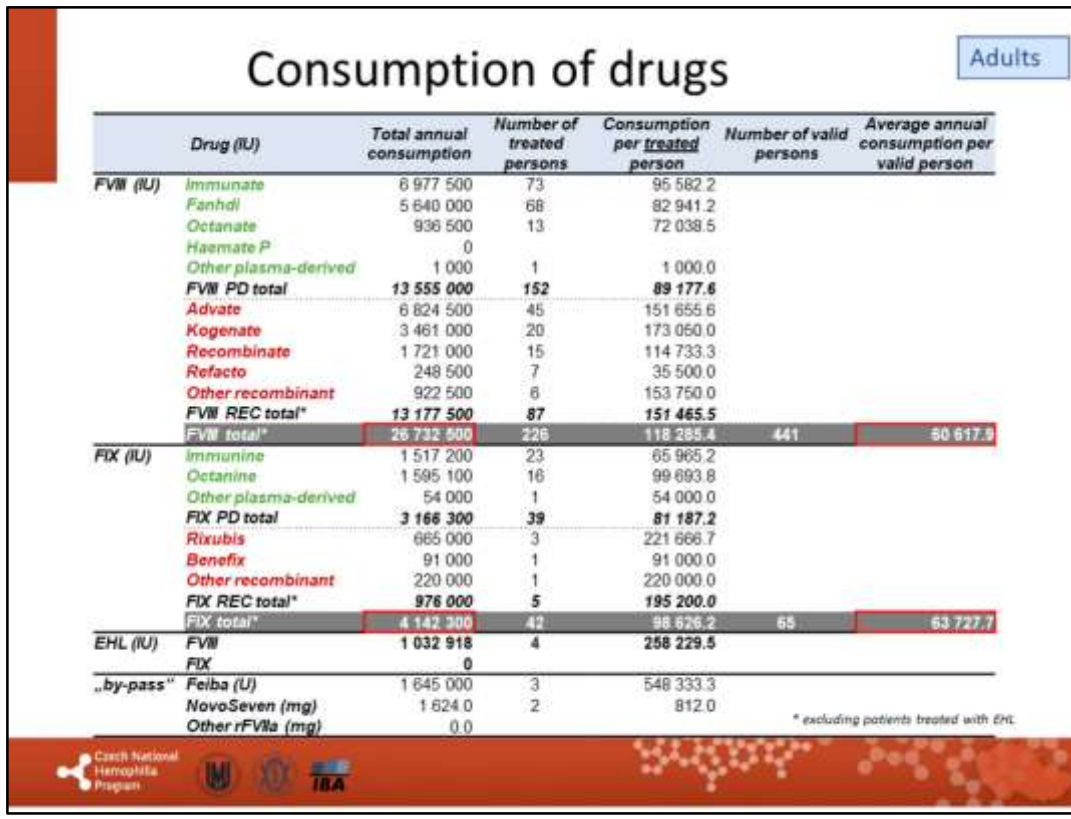
Czech National Hemophilia Program

IBA

Absolute numbers of respective concentrates in this figure refer ONLY to the records within CNHP registry, which have been updated in 2017. 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 used in children (median age 10 years) is higher, 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.

If calculated in „paediatric IU/capita“ (total number of units used in children divided by the total number of children in the country), the figure would be 8,4 IU/capita. Figures for paediatric IU/capita of FIX would not be precise enough, as significant number of children with HB are in clinical trials including EHL FIX products.



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)	Immunate	6 977 500	73	95 582.2		
	Fanhdi	5 640 000	68	82 941.2		
	Octanate	936 500	13	72 038.5		
	Haemate P	0				
	Other plasma-derived	1 000	1	1 000.0		
	FVIII PD total	**13 555 000**	**152**	**89 177.6**		
	Advate	6 824 500	45	151 655.6		
	Kogenate	3 461 000	20	173 050.0		
	Recombinate	1 721 000	15	114 733.3		
	Refacto	248 500	7	35 500.0		
	Other recombinant	922 500	6	153 750.0		
	FVIII REC total*	**13 177 500**	**87**	**151 465.5**		
	FVIII total*	**26 732 500**	**226**	**118 285.4**	**441**	**60 617.5**
FIX (IU)	Immunine	1 517 200	23	65 965.2		
	Octanine	1 595 100	16	99 693.8		
	Other plasma-derived	54 000	1	54 000.0		
	FIX PD total	**3 166 300**	**39**	**81 187.2**		
	Rixubis	665 000	3	221 666.7		
	Benefix	91 000	1	91 000.0		
	Other recombinant	220 000	1	220 000.0		
	FIX REC total*	**976 000**	**5**	**195 200.0**		
	FIX total*	**4 142 300**	**42**	**98 626.2**	**65**	**63 727.7**
EHL (IU)	**FVIII**	**1 032 918**	**4**	**258 229.5**		
	FIX	**0**				
„by-pass"	Feiba (U)	1 645 000	3	548 333.3		
	NovoSeven (mg)	1 624.0	2	812.0		
	Other rFVIIa (mg)	0.0				

* excluding patients treated with EHL

Czech National Hemophilia Program

The same data for adults with haemophilia in 2017.

Estimation of „adult IU/capita (total number of IU used by adults divided by the total number of adults in the country) is 5,2 IU/capita for FVIII and 0,8 IU/capita for FIX. This estimation covers whole adult population, including patients from the centre not participating in CNHP registry