The status of care for persons with <u>haemophilia</u> registered within CNHP registry Annual Report 2024

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Sample size, valid records





This slide describes the process of records' validation within the registry. All patients have signed IC.



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Centres participating in CNHP

	Valid	persons
Paediatric centres	Ν	%
Prague – Dpt. of Pediatric Haematology and Oncology, CUH Motol	110	14.6
Brno – Dpt. of Pediatric Haematology, CUH Brno	69	9.2
Hradec Králové – Dpt. of Pediatric Medicine, UH HK	31	4.1
Ostrava – Dpt. of Pediatric Medicine, UH Ostrava	19	2.5
Ústí n.L. – Pediatric Dpt. – Haematology, Masaryk Hospital	16	2.1
České Budejovice – Pediatric Dpt., Hospital CB	15	2.0
Olomouc – Dpt. of Pediatric Medicine, UH Olomouc	13	1.7
Pilsen – Pediatric Dpt., UH Pilsen	12	1.6

	Valid	persons
Adult centres	N	%
Brno – Dpt. Of Clin Hematol, UH Brno	175	23.3
Ostrava – Blood centre, UH Ostrava	75	10.0
Olomouc – Haemato-Oncology Dpt., UH Olomouc	58	7.7
Pilsen – Dpt. of Biochemistry and Hematology, UH Pilsen	53	7.0
Liberec – Dpt. Of Clin Hematol, Hospital Liberec	48	6.4
Ústí n.L. – Dpt. Of Clin Hematol, Masaryk Hospital	29	3.9
České Budějovice – Dpt. Of Clin Hematol, Hospital CB	25	3.3
Nymburk – Center for Thrombosis and Hemostasis, Nymburk Hospital	4	0.5



Centres contributing to the CNHP registry.

Basic demographics

All N=752



Type of haemophilia





Four children with haemophilia were born in 2024.



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 almost 12% of all registered PWHs.

Persons with haemophilia and inhibitors in 2024

All N=752

Active inhibitors were recorded in 12 persons during 2024

• 1 inhibitor in adult with mild HA newly developed and one child had re-occurence in 2024

PWH with inhibitors:

- 6 children and 6 adults
- 11 haemophilia A and 1 haemophilia B
- 9 in severe, 2 in moderate and 1 in mild haemophilia
- 11 high-titre and 1 low-titre (<5BU) •
- 7 high response and 4 low response inhibitors; this information not available in 1 PWH with inhibitor
- 10 patients were treated with emicizumab
 - 7 patients were treated only with emi, 1 patient with emi and by-pass therapy, and 2 patients with emi and FVIII during the year
- 1 patient with haemophilia B was treated with rFVIIa
- One patient has already been on-going ITT in 2024 (started earlier)

Eradication of inhibitor:

- Six patients with a history of inhibitor (now receiving emicizumab prophylaxis) had repeatedly negative inhibitor levels and were considered inhibitor-free this year
- One patient had transient inhibitor (increased inhibitor level in 2023) and was inhibitor-free in 2024
- One patient with inhibitor was transfered to another center (outside CNHP registry)



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

Number of PWHI further decreased in 2024. Only 1 new inhibitors developed (adult with mild HA receiving FVIII before surgery) and spontaneously disappered without any treatment and reoccured in 1 child with previous history of inhibitors after FVIII treatment for bl eed.

The reason for the decrease of PWHs with inhibitors is caused mainly by disappearing of inhibitors in those on long-t erm prophylais with emi

ABR and treatment regimens in patients with inhibitor

N=12

	Туре	Year of birth	Severity	пт	Emi	By-pass	Titre	Responder	ABR	Joint / other
1	HA	2021	Severe		Yes	OD	high	HR	3	1/2
2	HA	2020	Severe	Yes	Yes		high	NA	3	1/2
3	HA	2016	Severe		Yes		high	LR	2	1/1
4	HA	2015	Severe		Yes		high	HR	0	0/0
5	HA	1977	Severe		Yes		high	HR	0	0/0
6	HA	1975	Severe		Yes		high	HR	0	0/0
7	HA	1971	Severe		Yes		high	LR	0	0/0
8	HA	1956	Severe		Yes		high	LR	0	0/0
9	HA	2011	Moderate		Yes		high	HR	0	0/0
10	HA	1941	Moderate		Yes		high	HR	0	0/0
11	HA	1988	Mild		No		low	LR	1	1/0
12	HB	2007	Severe			Permanent px	high	HR	15	11/4

new in 2024 NA not available



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This slide describes in more details all PWH with "active" inhibitors within CNHP registry. Very little patients with HT inhibitors remained on ITI (only one in fact, being on concomitant emi prophalxis). All HA hi gh titre inhibitor patients were started or switched on/to emicizumab. The number of bleeds, on above mentioned treatment is kept low.

ABR according to treatment regimen in PWH with inhibitor

N=12

Diagnosis	ITT	Emi/by-pass prophylaxis	N	ABR (mean)	ABR (median, min-max)	Joint / other bleeds (median)
Haemophilia A	Yes	Emi px	1	3.00	3 (3-3)	1/2
		OD	0	-	-	-
	No	Emi px	9	0.56	0 (0-3)	0/0
		OD	1	1.00	1 (1-1)	1/0
Haemophilia B	No	BPA permanent	1	15.00	15 (15-15)	11/4



(Almost all) Patients with inhibitors, are on permanent prophylaxis with emicizumab. This treatment led to minimal ABR in all HA inhibitor patients.

Demographic characteristics Haemophilia A







Haem A N=647







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Median age at diagnosis is different for adults and children with HA. (In the past, the diagnostic options were worse, than they are today). Most children with severe haemophilia are diagnosied before 12 months of age now, what is constantly lowering the median/mean age of diagnosis in children year by year.





* including persons with inhibitor

in 2024 age reached in year 2024



Mean age of Czech adults with HA is over 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 2023.





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 No new HIV+ PWH reported since late 90s.

Treatment outcomes and bleeding frequency Haemophilia A



Data from year 2024 – sample size

All	
Haem A	
N=647	

	Valid persons		Persons with <u>valid</u> annual report			Pe <u>exa</u>	Persons <u>treated</u>				
	Ν	%		Ν	%		Ν	%		Ν	%
All	647	100%	\rightarrow	627	96.9%	\rightarrow	479	74.0%	\rightarrow	336	51.9%
of them with inhibitor	11			11			11			11	
Children	241	100%	\rightarrow	241	100.0%	\rightarrow	211	87.6%	\rightarrow	126	52.3%
of them with inhibitor	5			5			5			5	
Adults	406	100%	\rightarrow	386	95.1%	\rightarrow	268	66.0%	\rightarrow	210	51.7%
of them with inhibitor	6			6			6			6	



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There are records of nearly 75% of all Czech haemophiliacs in total within the CNHP registry in 2024. As for paediatric population, ALL children are recorded. CNHP registry also houses records of about 65% of adult haemophiliacs in Czech Republic. Further slides display analyses performed only on records, which were updated during 2024. Not all patients came to the centre (especially adults) and not all centres fully reported all data (including detailed info about bleeding episodes) in 2024. Thus, not all records have been updated and used for further analyses. Data monitoring has been introduced since 2017 to further increase the validity of the data within CNHP registry. Last data monitoring by the teams of auditors was done in all centres in 2023.





Data shown support good efficacy of care provided to Czech PWH, no matter what age category they are. Mean/Median number of bleedings per year (ABR) is 0.8/0 for ch ildren and 10,9/0 for adults with severe haemophilia A without inhibitors. WAS 0,9/0 for children and 1,2/0 for adults in 2023.

The median of ABR is kept 0 for children and adults in CZ since 2021. This year, median ABR was 0 also for adult PWHs with inhibitors.

Location of bleeds in 2024

55

(22.8%)

hospitalization.

their bleeds.

recorded no

during year 2024.





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There was no CNS bleed in children with haemophilia in 2024. Percentage of children with no bleed significantly increased from 70,4 to 77,2 from 2023 to 2024.

Location of bleeds in 2024



during year 2024. ¹Frequency of bleeding is missing in 3 adult.

no

is

66

of

(16.4%)

hospitalization.

Localization

recorded

their

known in 2 adults.



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Number of "non-bleeders" in adults further increased compared to 2023 (from 80,9% to 83,6%). What is even more important is further si gnificant decrease in total number of bleeds in adult PWHs compared to 2023 (from 213 to 174).





This figure refers to preventive factor's administration in children with HA, applied less often, than in 2023.





This figure refers to preventive treatment in adults with HA. No significant change compared to 2023

ABR according to treatment regimen Haemophilia A without inhibitor



Annual bleeding rate according to treatment regimen



Frequency of bleeding	Mi	ld*	Mode	erate*	Seve	ere*	* without inhibite
Treatment regimen	OD	prophy	OD	prophy	OD	prophy	
N valid	121	1	13	9	2	90	
Mean	0.1	0.0	0.3	0.4	0.5	0.8	
Median (min – max)	0 (0 – 3)	0 (0 – 0)	0 (0 – 4)	0 (0 – 2)	0.5 (0 – 1)	0 (0 – 6)	
Total no of recorded bleeds	15	0	4	4	1	72	
Children on permanent prophylaxis	1 (0.8%)		9 (40.9%)		90 (9)	7.8%)	Treatment regim <u>OD</u> = on demand
% of factor (FVIII) consumed by children on permanent prophylaxis	0.4%		96.2%		95.	7%	temporary proph <u>prophy</u> = perman prophylaxis (facto
Location of bleeding	Mi	ld*	Mode	erate⁺	Seve	ere*	
Treatment regimen	OD	nronhu	00	nronhy	00	prophy	
		propriy	00	propriy	00	propriy	
N valid	121	1 1	13	9	2	90	
N valid JOINT BLEEDS	121	1 1	13	9	2	90	
N valid JOINT BLEEDS Mean	121 0.0	1 0	0.1	9 0.2	2	90 0.3	
N valid JOINT BLEEDS Mean Median (range)	0.0 0 (0 - 2)	1 0 0 (0 - 0)	0.1 0 (0 - 1)	9 0.2 0 (0 - 1)	2 0.0 0 (0 - 0)	90 0.3 0 (0 - 4)	
N valid JOINT BLEEDS Mean Median (range) Total no of recorded bleeds	0.0 0 (0 - 2) 2	1 0 0 (0 - 0) 0	0.1 0 (0 - 1) 1	9 0.2 0 (0 - 1) 2	2 0.0 0 (0 - 0) 0	90 0.3 0 (0 - 4) 25	
N valid JOINT BLEEDS Mean Median (range) Total no of recorded bleeds OTHER BLEEDS	121 0.0 0 (0 - 2) 2	0 0 (0 - 0) 0	0.1 0 (0 - 1) 1	9 0.2 0 (0 - 1) 2	2 0.0 0 (0 - 0) 0	90 0.3 0 (0 - 4) 25	
N valid JOINT BLEEDS Mean Median (range) Total no of recorded bleeds OTHER BLEEDS Mean	121 0.0 0 (0 - 2) 2 0.1	0 0 (0 - 0) 0	13 0.1 0 (0 - 1) 1 0.2	9 0.2 0 (0 - 1) 2 0.2	2 0.0 0 (0 - 0) 0	90 0.3 0 (0 - 4) 25 0.5	
N valid JOINT BLEEDS Mean Median (range) Total no of recorded bleeds OTHER BLEEDS Mean Median (range)	$ \begin{array}{c} 0.0 \\ 0 (0 - 2) \\ 2 \\ 0.1 \\ 0 (0 - 3) \end{array} $	1 0 (0 - 0) 0 (0 - 0) 0 (0 - 0)	$ \begin{array}{c} 0.1 \\ 0.(0-1) \\ 1 \\ 0.2 \\ 0.(0-3) \end{array} $	$\begin{array}{c} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 $	0.0 0 (0 - 0) 0 0.5 0.5 (0 - 1)	90 0.3 0 (0 - 4) 25 0.5 0 (0 - 6)	

eatment regimen: <u>)</u> = on demand and/or <u>o – on demand unayon</u> mporary prophylaxis <u>ophy</u> = permanent ophylaxis (factor or emi)

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This slide confirms good effect of permanent prophylaxis in children. Rate of prophylaxis (factor or emi) is almost 100% among children with severe haemophilia A. Number of bleeds per year (median) in severe haemophiliacs A on prophylaxis is kept on 0.

It is true also for joint bleeds, see the lower figure on the slide. The total number of joint bleeds decrease almost 5 times compared to 2023!!!

Annual bleeding rate according to treatment regimen



Frequency of bleeding	IVII	ld*	Node	erate*	Severe*		
Treatment regimen	OD	prophy	OD	prophy	OD	prophy	
N valid	219	0	27	8	26	117	
Mean	0.1	0.0	0.6	1.0	2.9	0.5	
Median (min – max)	0 (0 – 3)	(-)	0 (0 – 10)	0.5 (0 – 5)	0 (0 – 35)	0 (0 - 7)	
Total no of recorded bleeds	16	16 0		8	76	57	
Adults on permanent prophylaxis	0 (0)%)	8 (22	2.9%)	119 (8	1.5%)	
% of factor (FVIII) consumed by adults on permanent prophylaxis	0.0% 85.3%			91.	91.2%		
Location of bleeding	Mild*		Moderate*		Severe*		
	OD prophy						
Treatment regimen	OD	prophy	OD	prophy	OD	prophy	
Treatment regimen N valid	0D 219	prophy 0	0D 27	prophy 8	0D 24	prophy 117	
Treatment regimen N valid JOINT BLEEDS	OD 219	prophy 0	0D 27	prophy 8	0D 24	prophy 117	
Treatment regimen N valid JOINT BLEEDS Mean	0D 219 0.0	prophy 0 0	0D 27 0.1	prophy 8 0.8	0D 24 1.7	prophy 117 0.3	
Treatment regimen N valid JOINT BLEEDS Mean Median (range)	OD 219 0.0 0 (0 - 1)	prophy 0 0 (-)	OD 27 0.1 0 (0 - 3)	prophy 8 0.8 0 (0 - 4)	0D 24 1.7 0 (0 - 25)	prophy 117 0.3 0 (0 - 4)	
Treatment regimen N valid JOINT BLEEDS Mean Median (range) Total no of recorded bleeds	0D 219 0.0 0 (0 - 1) 6	<i>prophy</i> 0 0 (-) 0	OD 27 0.1 0 (0 - 3) 4	prophy 8 0.8 0 (0 - 4) 6	0D 24 1.7 0 (0 - 25) 41	prophy 117 0.3 0 (0 - 4) 33	
Treatment regimen N valid JOINT BLEEDS Mean Median (range) Total no of recorded bleeds OTHER BLEEDS	OD 219 0.0 0 (0 - 1) 6	0 0 (-) 0	OD 27 0.1 0 (0 - 3) 4	prophy 8 0.8 0 (0 - 4) 6	0D 24 1.7 0 (0 - 25) 41	prophy 117 0.3 0 (0 - 4) 33	
Treatment regimen N valid Modian (range) Total no of recorded bleeds OTHER BLEEDS Mean Median (range) Total no of modian (range) Mean	OD 219 0.0 0 (0 - 1) 6	<i>prophy</i> 0 (-) 0	OD 27 0.1 0 (0 - 3) 4 0.4	prophy 8 0.8 0 (0 - 4) 6 0.3	0D 24 1.7 0 (0 - 25) 41 0.7	prophy 117 0.3 0 (0 – 4) 33 0.2	
Treatment regimen N valid JOINT BLEEDS Mean Median (range) Total no of recorded bleeds OTHER BLEEDS Mean Median (range)	OD 219 0.0 0 (0 - 1) 6 0.0 0 (0 - 3)	prophy 0 (-) 0 (-)	0D 27 0.1 0 (0 - 3) 4 0.4 0 (0 - 9)	prophy 8 0.8 0 (0 - 4) 6 0.3 0 (0 - 1)	0D 24 1.7 0 (0 - 25) 41 0.7 0 (0 - 10)	prophy 117 0.3 0 (0 - 4) 33 0.2 0 (0 - 4)	

* without inhibitor; missing frequency of bleeding in 3 adults; missing location of bleeds in 2 adults

Treatment regimen: <u>OD</u> = on demand and/or temporary prophylaxis <u>prophy</u> = permanent prophylaxis (factor or emi)



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Prophylaxis works very well in Czech adult PWHsI It keeps the median of ABR in all severe haemophiliacs with prophylaxis below 1. Was 0 in 2023, though ?! Rate of prophylaxis (factor or emi) is kept around 92% among adults with severe haemophilia A.

Median of joint bleeds per year is 0 in adults with severe HA (both on prophy and OD)! It is however seen, that some adult PWHA still have significant number of joint bleeds despite the prophylaxis.

ABR according to treatment regimen and age

							* without inhib frequency of bleeding missing location o
Frequency of bleeding	Mi	ld*	Mode	erate*	Seve	ere*	
Treatment regimen	OD	Prophy	OD	Prophy	OD	Prophy	
N valid	153	0	16	6	20	74	
Mean	0.1	0.0	0.1	1.2	3.7	0.5	Adults (baom A)
Median (min – max)	0 (0 – 3)	(-)	0 (0 – 1)	0.5 (0 – 5)	0 (0 – 35)	0 (0 – 5)	horn before 1990
Total no of recorded bleeds	12	0	1	7	74	35	N=269
Adults on permanent prophylaxis	0 ()%)	6 (2)	7.3%)	76 (7	8.4%)	11-205
% of factor (FVIII) consumed by adults on permanent prophylaxis	0.	0%	83	.7%	89.	8%	
Frequency of bleeding	Mi	ld*	Mode	erate*	Seve	ere*	
Treatment regimen	OD	Prophy	OD	Prophy	OD	Prophy	
N valid	66	0	11	2	6	43	Adults (baom A)
Mean	0.1	0.0	1.4	0.5	0.3	0.5	horn in 1990 or
Median (min – max)	0 (0 – 2)	(-)	0 (0 – 10)	0.5 (0 – 1)	0 (0 – 1)	0 (0 – 7)	later
Total no of recorded bleeds	4	0	15	1	2	22	N=128
Adults on permanent prophylaxis	0 (0)%)	2 (15	5.4%)	43 (8	7.8%)	11-120
% of factor (FVIII) consumed by adults on permanent prophylaxis	0.0	0%	87.	.9%	93.	9%	

Adults Haem A N=397*



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This important table shows in general difference in bleeding rates between adult PWH born before 1990 (when concentrates and thus also prophylaxis became available in CZ) and PWH and born later. This is now however true only for means and intervals. Median of ABR in severe HA on prophylaxis is below 1 for both groups.

Prophylaxis thus works very well also in most of those, with already damaged joints. This is clearly seen on median ABR for the "older" group. We thus further advocate for more tertiary prophylaxis in adult PWH.



							* without inhi frequency of bleedi missing location	ibitor; ing in 3 n of ble
Frequency of bleeding	Mi	ld*	Mod	erate*	Sev	ere*		
Treatment regimen	OD	prophy	OD	prophy	OD	prophy		
N valid	153	0	16	6	18	74		
JOINT BLEEDS								
Mean	0.0	0	0.0	0.8	2.2	0.3	Adults (haem A)	
Median (range)	0 (0 - 1)	(-)	0 (0 – 0)	0 (0 – 4)	0 (0 – 25)	0 (0 – 4)	born <u>before 1990</u>	
Total no of recorded bleeds	3	0	0	5	40	25	N=267	
OTHER BLEEDS								
Mean	0.1	0	0.1	0.3	0.9	0.1		
Median (range)	0 (0 – 3)	(–)	0 (0 - 1)	0 (0 – 1)	0 (0 - 10)	0 (0 – 3)		
Total no of recorded bleeds	9	0	1	2	16	10		
Frequency of bleeding	Mi	ld*	Mod	erate*	Seve	ere*		
Treatment regimen	OD	prophy	OD	prophy	OD	prophy		
N valid	66	0	11	2	6	43		
OINT BLEEDS							Adults (haem A)	
Mean	0.0	0	0.4	0.5	0.2	0.2	born in 1990 or	
Median (range)	0 (0 - 1)	(-)	0 (0 – 3)	0.5 (0 – 1)	0 (0 – 1)	0 (0 – 3)		
Total no of recorded bleeds	3	0	4	1	1	8	iater	
OTHER BLEEDS							N=128	
Mean	0.0	0	1.0	0.0	0.2	0.3		
Median (range)	0 (0 – 1)	(-)	0 (0 – 9)	0 (0 – 0)	0 (0 – 1)	0 (0 – 4)		
Total no of recorded bleeds	1	0	11	0	1	14		

Haem A N=395*



The same is true for joint bleeds in adults. Some frequent bleeders however still remain, especially among adults with severe HA born before 1990. They are, indeed, either new candidates for tertiary prophylaxis, or they may need more intensive prophylaxis.

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Only around 31% of bleeds in children with haemophilia are joint bleeds. Soft tissue bleeds are in 34% subcutaneous bleeds. The most of all bleeds in children are traumatic bleeds.

Detailed treatment of bleeds

	Children Haem A N=104*
	11-104
*	number of bleed

	Joints	Muscles	Subcuta- neous	Oral cavity	Urogenital tract	Epistaxes	GIT	CNS	Other	Total
No. of bleeds	33	19	34	6	0	2	1	0	9	104
FVIII consumption per bleed (IU), valid N	27	19	28	5		1	1		8	89
geometric mean	2497.3	2545.2	1359.9	574.3		1500.0	10500.0		1990.2	1887.9
median	2500.0	2500.0	1500.0	500.0		1500.0	10500.0		2250.0	1500.0
min – max	500-20000	500-19000	500-8000	250-4000		1500-1500	10500-10500		500-6250	250-20000
sum	97 200	68 750	47 750	5 500		1 500	10 500		20 250	251 450
No. of doses per bleed										
geometric mean	1.5	1.4	1.2	1.0		1.0	7.0		1.6	1.3
median	1	1	1	1		1	7		1	1
min – max	0–8	1–10	0–4	1–1		0–1	7–7		0–9	0–10
Duration of therapy per bleed, days										
geometric mean	2.0	1.7	2.5	2.7		4.6	5.0		1.7	2.1
median	1	1	1	3		5	5		2	1
min – max	1–21	1–7	1-1500	1–12		3–7	5–5		1–7	1–1500
N (%) with hospitalization	2 (6.1%)	1 (5.3%)	0 (0%)	1 (16.7%)		0 (0%)	1 (100%)		1 (11.1%)	6 (5.8%)
N (%) with rebleeding	5 (15.2%)	0 (0%)	1 (2.9%)	0 (0%)		0 (0%)	0 (0%)		1 (11.1%)	7 (6.7%)



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In median, the dose used to treat joint bleed in children was 2500 IU FVIII administered in 1 infusion within one day. Muscle bleeds were often treated similarly. Some bleeds were however cesed only on prophylaxis with no extra dose needed. Compared to 2023, bleeds in 2024 needed less factor and less time to heal.





The situation is different in adults, though. Over 58% of bleeds in adults with haemophilia are joint bleeds, though their total number significantly decreased compared to 2023. Soft tissue bleeds are in 32% muscle bleeds. The most of all bleeds in adults are spontaneous ones (i.e. 68% of joint bleeds). This is probably mainly due to already damaged joints especially in people born before 1990.

Detailed treatment of bleeds

	Adults							
	Haem A							
	N=156*							
* number of bleed								

	Joints	Muscles	Subcuta- neous	Oral cavity	Urogenital tract	Epistaxes	GIT	CNS	Other	Total
No. of bleeds	91	32	9	5	7	0	4	0	8	156
FVIII consumption per bleed (IU), valid N	87	31	9	5	6		4		7	149
geometric mean	2862.9	2876.9	4313.2	1918.6	2167.5		8795.6		8572.4	3110.0
median	3000.0	1000.0	4000.0	2000.0	4000.0		16750.0		9000.0	3000.0
min – max	500-91000	1000-86000	1000-26000	1000-6500	10-24000		2000-47500		1000-63000	10-91000
sum	502 500	304 000	62 500	12 500	44 000		83 000		150 000	1 158 510
No. of doses per bleed										
geometric mean	1.7	1.9	1.7	1.3	2.8		4.8		4.3	1.9
median	1	1	1	1	3		9		5	1
min – max	0–37	0–34	1–13	1–2	0–7		1–32		1–21	0–37
Duration of therapy per bleed, days										
geometric mean	1.7	2.0	1.9	1.3	2.7		25.6		4.0	2.0
median	1	1	1	1	4		15		5	1
min – max	1–30	1–45	1–13	1–2	1–6		1–2000		1–21	1–2000
N (%) with hospitalization	5 (5.5%)	4 (12.5%)	1 (11.1%)	0 (0%)	1 (14.3%)		2 (50%)		2 (25%)	15 (9.6%)
N (%) with rebleeding	4 (4.4%)	1 (3.1%)	0 (0%)	0 (0%)	1 (14.3%)		0 (0%)		0 (0%)	6 (3.8%)



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In median, the dose used to treat joint bleed in adults increased to 3000 IU FVIII administered in one infusion within one day. Muscle bleeds were often treated with total dose of 1000 IU FVIII administered in 1 infusions. Doses are similar or lower than in children, though the weight of adults is approximately 3x higher, compared to children. Some adults still received ONLY 500 IU to treat the joint/muscle bleed!!!

ABR according to centres Haemophilia A (PWHA)



Annual bleeding rate on permanent prophylaxis

HaemA on
prophy
Paed. centres
N=106

Moderate			F	Frequency of bleeding in PWHA without							
Severe		ABR (median)		inhibitor on permanent prophylaxis							
Paediatric centre	(0 2	4 _N	Mean	Median	Min	Max	Severity			
	_ Draha	0	5	0.6	0.0	0	2	Moderate			
		<u></u>	39	1.0	0.0	0	5	Severe			
	Brno	0	1	0.0	0.0	0	0	Moderate			
		ŏ	27	0.4	0.0	0	3	Severe			
c	- Istrava	0	0								
		ŏ	7	0.4	0.0	0	2	Severe			
České Budi			0								
Ceske Duur		0	12	0.2	0.0	0	1	Severe			
Hradec k	rálové	0	1	0.0	0.0	0	0	Moderate			
		<u> </u>	2	1.0	1.0	0	2	Severe			
lístí nad	– Lahem	1	1	1.0	1.0	1	1	Moderate			
osti nuu		0 -	3	1.0	0.0	0	3	Severe			
	– Plzeň		0								
Ρι.		1	4	2.0	1.0	0	6	Severe			
04	mour	0	1	0.0	0.0	0	0	Moderate			
Olomouc		1	3	0.7	1.0	0	1	Severe			



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In none of paediatric centres, severe haemophiliacs on prophylaxis bleed more than 1 times per year (median). We, however, should continue to focus on individualized/tailored prophylaxis in all with severe phenotype and shall offer it to all, who may benefit from this approach. This should further minimize the differences in ABR between centres, also in patients with moderate haemophilia.

Annual bleeding rate on permanent prophylaxis

HaemA on
prophy
Adult centres
N=118

Moderate					Fr	requenc	y of blee	ding in	PWHA	without
Severe	ſ	h	ABR (median)	4		inhit	bitor on p	erman	ent pro	phylaxis
Adult centre		,	2	-	Ν	Mean	Median	Min	Max	Severity
	Drmo	0.5	5		2	0.5	0.5	0	1	Moderate
	ыпо	0			34	0.5	0.0	0	4	Severe
	Octrovo		1.0		3	2.0	1.0	0	5	Moderate
	Ustrava	0	-		26	0.7	0.0	0	5	Severe
	Direž				0					
	Pizen	0			16	0.1	0.0	0	1	Severe
	1.16	0.0			2	0.0	0.0	0	0	Moderate
	LIDEIEC	0			7	0.6	0.0	0	3	Severe
	Olemeure		1.0		1	1.0	1.0	1	1	Moderate
	Joniouc	0			12	0.5	0.0	0	5	Severe
Úctí pa	d Laborn	_			0					
USUITI		0			9	0.4	0.0	0	2	Severe
České D	džiouioo	_			0					
Ceske Bl	idejovice	0			3	0.7	0.0	0	2	Severe
	a seconda a secondar	•			0					
	Numburk 0		3	2.3	0.0	0	7	Severe		



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In 2024 the difference in ABR of adults with severe HA on prophylaxis is low between centres. All adult PWHs with severe dis disease on permanent prophylaxis had median of ABR below 1 in all centres for the first time. (Was 0 though in 2023?!)

Annual bleeding rate regardless prophylaxis

HaemA	
Paed.	
centres	
N=120	

Moderate Severe				Frequency of bleeding in PWHA without inhibitor <u>regardless of prophylaxis</u>							
Paediatric centre	(D 2 ^{ABR (median)}	6 м	Mean	Median	Min	Max	% on permanent prophylaxis			
	Draha	0	9	0.4	0.0	0	2	55.6%			
	Fialla	0.5	40	1.0	0.5	0	5	97.5%			
	Brno	0	5	0.0	0.0	0	0	20.0%			
		Ō	27	0.4	0.0	0	3	100.0%			
	- Ostrava	0	0	0.0	0.0	0	0	0.0%			
Ostrava		Ŏ		0.4	0.0	0	2	100.0%			
České Budžievies		0	2	0.0	0.0	0	0	0.0%			
Ceske Buu	ejovice	Ŏ		0.2	0.0	0	1	100.0%			
Livedee		0		0.0	0.0	0	0	100.0%			
Hrauec	Kraiove	— 1	2	1.0	1.0	0	2	100.0%			
المعر أعفارًا	Labam	— 1	1	1.0	1.0	1	1	100.0%			
Usu nau	Labern	0	3	1.0	0.0	0	3	100.0%			
	Disež	4	1	4.0	4.0	4	4	0.0%			
	Pizen	1		2.0	1.0	0	6	100.0%			
		0	3	0.0	0.0	0	0	33.3%			
Olomoue		— 1		0.7	1.0	0	1	100.0%			



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Ideally, children on prophylaxis should have same (lower) bleeding rate as (than) those, who do not need prophylaxis. This is in fact the goal of prophylaxis! Those, who bleed, should be on prophylaxis to decrease the bleeding rate. Those, who have not more than one joint bleed per year without prophylaxis probably do not eed 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 further minimized or should ideally disappear to guarantee the same level of care nation-wide.

Annual bleeding rate regardless prophylaxis

HaemA
Adult
centres
N=172*
* missing ABR in 3
adults

Moderate Severe	Frequency of bleeding in PWHA without inhibitor <mark>regardless of prophylaxis</mark>								
Adult centre	0 2 ^{ABR (median)} 6	N	Mean	Median	Min	Max	% on permanent prophylaxis		
Brno	0.0 0.0	15 42	0.2	0.0	0	1	13.3% 81.0%		
Ostrava	0.0 0.0	7	0.9	0.0	0	5	42.9% 89.7%		
Plzeň	0.0 0.0	3 20	0.0 1.0	0.0 0.0	0	0 12	0.0% 80.0%		
Liberec	0.0 0.0	3 10	0.0 2.0	0.0 0.0	0 0	0 15	66.7% 70.0%		
Olomouc	2.0	2 14	2.0 2.9	2.0 0.0	1 0	3 35	50.0% 82.4%		
Ústí nad Labem	0.0 0.0	3 10	0.0 0.4	0.0 0.0	0 0	0 2	0.0% 90.0%		
České Budějovice	0.0 5.0	2 9	5.0 0.7	5.0 0.0	0 0	10 2	0.0% 33.3%		
Nymburk	0.0	0	2.3	0.0	0	7	100.0%		



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Similar information for adults.
Prophylactic regimens and treatment outcomes

HaemA	
Paed.	
centres	
N=120	

		ty Total N		PERMANENT PROPHYLAXIS										ON-DEMAND / TEMPORARY PROPHY		
Paediatric centre	Severity		% of N		Dosing of p Si	orophylaxis HL	Dosing of	prophylaxis HL	Dosing propi	of EMI nylaxis		BR		A	BR	
			patients		(IU/kg p	er week) Median	(IU/Kg p	er week) Median	(mg/kg)	per week)	Mean	Median		Mean	Median	
	Moderate	9	55.6%	5	82.8	82.8	64.1	68.0	IVICALI	Wedian	0.6	0.0	4	0.3	0.0	
Praha	Severe	40	97.5%	39	70.0	88.5	72.8	70.7	1.7	1.5	1.0	0.0	1	1.0	1.0	
	Moderate	5	20.0%	1					1.3	1.3	0.0	0.0	4	0.0	0.0	
Brno	Severe	27	100.0%	27			83.6	87.5	1.3	1.2	0.4	0.0	0			
	Moderate	0	0.0%	0									0			
Ustrava	Severe	7	100.0%	7					1.5	1.5	0.4	0.0	0			
Č Budžiouico	Moderate	2	0.0%	0									2	0.0	0.0	
C. Budejovice	Severe	12	100.0%	12			74.3	73.6	1.4	1.4	0.2	0.0	0			
	Moderate	1	100.0%	1			61.4	61.4			0.0	0.0	0			
HIAGEC KIAIOVE	Severe	2	100.0%	2			91.5	91.5			1.0	1.0	0			
lístí nad Labem	Moderate	1	100.0%	1					2.2	2.2	1.0	1.0	0			
Usti nau Labern	Severe	3	100.0%	3			58.6	58.6	1.3	1.3	1.0	0.0	0			
Plzeň	Moderate	1	0.0%	0									1	4.0	4.0	
1 12011	Severe	4	100.0%	4			160.7	160.7	1.4	1.5	2.0	1.0	0			
Olomour	Moderate	3	33.3%	1					1.2	1.2	0.0	0.0	2	0.0	0.0	
Chonhouc	Severe	3	100.0%	3					1.5	1.5	0.7	1.0	0			



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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=175	

			PERMANENT PROPHYLAXIS										ON-DEMAND / TEMPORARY PROPHY					
Adult centre	Severity	Total N	% of patients	% of	% of N	Dosii prophyl	ng of axis SHL	Dosi prophyl	ng of axis EHL	Dosing propl	of EMI Nylaxis			Age	N			Age
					(IU/kg p Mean	er week) Median	(IU/kg p Mean	er week) Median	(mg/kg Mean	per week) Median	Mean	Median	Median		Mean	Median	Median	
	Moderate	15	13.3%	2			56.3	56.3	1.9	1.9	0.5	0.5	55	13	0.2	0.0	40	
Brno	Severe	42	81.0%	34	92.5	90.2	75.6	72.9	1.4	1.4	0.5	0.0	43	8	0.1	0.0	42	
Ostrous	Moderate	7	42.9%	3			72.1	64.5			2.0	1.0	72	4	0.0	0.0	32	
USLIdVd	Severe	29	89.7%	89.7% 26	79.6	76.2	77.2	77.6	1.5	1.5	0.7	0.0	38	3	0.7	0.0	61	
Moderate	3	0.0%	0										3	0.0	0.0	48		
Pizen	Severe	20	80.0%	16	52.5	52.5	65.6	59.1	1.4	1.4	0.1	0.0	46	4	4.5	3.0	60	
Liboroo	Moderate	3	66.7%	2					1.7	1.7	0.0	0.0	51	1	0.0	0.0	43	
Liberec	Severe	10	70.0%	7			76.4	73.9	1.5	1.5	0.6	0.0	40	3	5.3	1.0	25	
Olomour	Moderate	2	50.0%	1	73.2	73.2	72.5	72.5			1.0	1.0	25	1	3.0	3.0	29	
Ciolillouc	Severe	17	82.4%	14			55.0	52.2	2.2	2.2	0.5	0.0	37	3	17.5	17.5	64	
Úctín Labom	Moderate	3	0.0%	0										3	0.0	0.0	27	
USUIII. LADEIII	Severe	10	90.0%	9			37.9	42.9			0.4	0.0	45	1	0.0	0.0	40	
Č Rudčiovico	Moderate	2	0.0%	0										2	5.0	5.0	56	
c. buuejovice	Severe	9	33.3%	3			70.5	57.1			0.7	0.0	56	6	0.7	0.0	62	
Nymburk	Moderate	0	0.0%	0										0				
Trymbulk	Savara	3	100.0%	3			81 5	81.5	13	1.3	23	0.0	34	0				



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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 90% of children treated in 2024 took the advantage of home treatment. Over 85% of treated children were commenced on any type of prophylaxis a and 97% out of those on prophylaxis were on permanent prophy in 2024.





79% of adults treated in 2024 took the advantage of home treatment. 70% of treated adults were commenced on any type of prophylaxis and 90% out of those on prophylaxis were on permanent prophy in 2024.





This slide describe the population of HA patients treated with emicizumab in CZ. The total number of PWHs on emi increased from 76 in 2023 to 89 in 2024. It is seen, that in 2024 emi was used mainly for people with HA (currently) without inhibitors and its efficacy was very high for both children and adults.

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Demographic characteristics Haemophilia B











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



* including persons with inhibitor * in 2024 ** age reached in year 2024



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 2024

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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



Data from year 2024 – sample size

All	
Haem B	
N=105	

	Valid persons			Persons with <u>valid</u> annual report			Pe <u>exa</u>	rsons <u>mined</u>		Persons <u>treated</u>			
	Ν	%		Ν	%		Ν	%		Ν	%		
All	105	100%	\rightarrow	101	96.2%	\rightarrow	81	77.1%	\rightarrow	66	62.9%		
of them with inhibitor	1			1			1			1			
Children	36	100%	\rightarrow	36	100.0%	\rightarrow	32	88.9%	\rightarrow	22	61.1%		
of them with inhibitor	1			1			1			1			
Adults	69	100%	\rightarrow	65	94.2%	\rightarrow	49	71.0%	\rightarrow	44	63.8%		
of them with inhibitor	0			0			0			0			



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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) are similar to 2023

Location of bleeds in 2024

12

24

(33.3%)

hospitalization.

of their bleeds.

recorded no

during year 2024.





52

There was no CNS bleed in children with haemophilia B in 2024. 66.% of children had no bleed at all. Was 67,6% in 2023.

Location of bleeds in 2024

	N _{pers}	N _{bleeds}			Adults Haem B N=67 ¹
20 (29.9%) adults	14	32	Joints		70.0%
experienced bleeding	5	7	Muscles	25.0%	
requiring treatment at least once in year: 53	3	4	Subcutaneous	15.0%	
bleeds were recorded in	1	1	Oral cavity	5.0%	
total, 9 bleeds required	4	7	Urogenital tract	20.0%	
All of these 20 adults	0	0	Epistaxes	0.0%	
have recorded location	0	0	GIT	0.0%	
of their bleeds.	0	0	CNS	0.0%	
47 (70.1%) adults have	2	2	Other	10.0%	
during year 2024.	20	53	Total	0% 20% 40%	60% 80%
				76 II)	bleeding

¹Frequency of bleeding is missing in 2 adults.



Bleeding events in adults. 70.1% HB adults with no bleed (similar to 2023).





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





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

ABR according to treatment regimen Haemophilia B without inhibitor



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Annual bleeding rate according to treatment regimen



Frequency of bleeding	Mi	ld*	Mode	erate*	Sev	ere*	* without inhibitor
Treatment regimen	OD	prophy	OD	prophy	OD	prophy	
N valid	15	0	6	1	3	10	
Mean	0.1	0.0	1.5	0.0	1.7	2.4	
Median (min – max)	0 (0 – 1)	(-)	1 (0 – 4)	0 (0 – 0)	1 (0 – 4)	0 (0 – 15)	
Total no of recorded bleeds	1	0	9	0	5	24	
Children on permanent prophylaxis	n permanent O (0%) ohylaxis		1 (14	1.3%)	10 (7	6.9%)	Treatment regime
% of factor (FVIII) consumed by children on permanent prophylaxis	ned by nt 0.0%		64.	8%	98.	.8%	<u>ob</u> - on demand d temporary prophy <u>prophy</u> = permane
							propriyiaxis
Location of bleeding	Mi	ld*	Mode	rate*	Sev	ere*	
Location of bleeding Treatment regimen	Mi OD	ld* prophy	Mode OD	prophy	Sev OD	ere* prophy	
Location of bleeding Treatment regimen N valid	OD 15	ld* prophy 0	Mode OD 6	prophy	OD 3	ere* prophy 10	
Location of bleeding Treatment regimen N valid JOINT BLEEDS	Mi 0D 15	ld* prophy 0	Mode OD 6	prophy 1	OD 3	ere* prophy 10	
Location of bleeding Treatment regimen N valid JOINT BLEEDS Mean	0D 15 0.0	ld* prophy 0	Mode OD 6	prophy 1	Sev 0D 3 1.0	ere* prophy 10 0.7	
Location of bleeding Treatment regimen N valid JOINT BLEEDS Mean Median (range)	0.0 0.0 0 (0 - 0)	Id* prophy 0 0 (-)	0D 6 0.8 0 (0 - 3)	prophy 1 0.0 0 (0 - 0)	Sev <u>OD</u> 3 1.0 0 (0 - 3)	ere* prophy 10 0.7 0 (0 - 6)	
Location of bleeding Treatment regimen N valid JOINT BLEEDS Mean Median (range) Total no of recorded bleeds	0.0 0 (0 - 0) 0 (0 - 0)	ld* prophy 0 (-) 0	0.8 0 (0 – 3) 5	Prophy 1 0.0 0 (0 - 0) 0	Sev <u>OD</u> 3 1.0 0 (0-3) 3	ere* prophy 10 0.7 0(0-6) 7	
Location of bleeding Treatment regimen N valid JOINT BLEEDS Mean Median (range) Total no of recorded bleeds OTHER BLEEDS	Mi OD 15 0.0 0 (0 - 0) 0	ld* prophy 0 (-) 0	Mode OD 6 0.8 0 (0 - 3) 5	erate* prophy 1 0.0 0(0-0) 0	Sev <u>OD</u> 3 1.0 0 (0-3) 3	ere* prophy 10 0.7 0 (0 - 6) 7	
Location of bleeding Treatment regimen N valid JOINT BLEEDS Mean Median (range) Total no of recorded bleeds OTHER BLEEDS Mean	Mil OD 15 0.0 0 (0 - 0) 0 0.1	Id* prophy 0 (-) 0 0	Mode OD 6 0.8 0 (0 - 3) 5 0.7	rate* prophy 1 0.0 0 (0 - 0) 0 0.0 0.0	Sev OD 3 1.0 0 (0 - 3) 3 0.7	ere* prophy 10 0.7 0 (0 - 6) 7 1.7	
Location of bleeding Treatment regimen N valid JOINT BLEEDS Mean Median (range) Total no of recorded bleeds OTHER BLEEDS Mean Median (range)	Mil OD 15 0.0 0 (0 - 0) 0 0.1 0 (0 - 1)	Id* prophy 0 0 (-) 0 0 (-)	Mode OD 6 0.8 0 (0 - 3) 5 0.7 1 (0 - 1) 10	rate* prophy 1 0.0 0 (0 - 0) 0 0.0 0.0 0 (0 - 0)	Sev OD 3 1.0 0 (0-3) 3 0.7 1 (0-1)	ere* prophy 10 0.7 0(0-6) 7 1.7 0(0-14)	

atment regimen: = on demand and/or nporary prophylaxis p<u>phy</u> = permanent phylaxis



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The data on bleeding rate in children with HB. Median ABR in children with severe haemophilia B on prophylaxis decreased from 3 to 0 in 2024. Keep in mind low numbers of children with HB, though

Almost no joint bleeds in HB children in 2024.

Annual bleeding rate according to treatment regimen



inequency of biccomig	1411	u	wouerate		3600		
Treatment regimen	OD	prophy	OD	prophy	OD	prophy	
N valid	17	0	22	5	5	18	
Mean	0.1	0.0	1.0	0.8	1.6	1.1	
Median (min – max)	0 (0 – 1)	(-)	0 (0 – 8)	0 (0 – 4)	0 (0 – 5)	0 (0 – 7)	
Total no of recorded bleeds	1	0	21	4	8	19	
Adults on permanent prophylaxis	0 (0)%)	5 (18	8.5%)	19 (76%)		
% of factor (FVIII) consumed by children on permanent prophylaxis	0.0)%	51.	5%	92.9%		
Location of bleeding	Mi	ld*	Mode	rate*	Severe*		
Treatment regimen	OD	prophy	OD	prophy	OD	prophy	
N valid	17	0	22	5	5	18	
JOINT BLEEDS							
Mean	0.1	0	0.5	0.4	1.4	0.7	
Mean Median (range)	0.1 0 (0 - 1)	0 (—)	0.5 0 (0 – 6)	0.4 0 (0 – 2)	1.4 0 (0 - 4)	0.7 0 (0 – 4)	
Mean Median (range) Total no of recorded bleeds	0.1 0 (0 - 1) 1	0 (–) 0	0.5 0 (0 – 6) 10	0.4 0 (0 – 2) 2	1.4 0 (0 - 4) 7	0.7 0 (0 - 4) 12	
Mean Median (range) Total no of recorded bleeds OTHER BLEEDS	0.1 0 (0 - 1) 1	0 (-) 0	0.5 0 (0 – 6) 10	0.4 0 (0 – 2) 2	1.4 0 (0 - 4) 7	0.7 0 (0 - 4) 12	
Mean Median (range) Total no of recorded bleeds OTHER BLEEDS Mean	0.1 0 (0 - 1) 1 0.0	0 (-) 0	0.5 0 (0 - 6) 10 0.5	0.4 0 (0 – 2) 2 0.4	1.4 0 (0 - 4) 7 0.2	0.7 0 (0 - 4) 12 0.4	
Mean Median (range) Total no of recorded bleeds OTHER BLEEDS Mean Median (range)	0.1 0 (0 - 1) 1 0.0 0 (0 - 0)	0 (-) 0 (-)	0.5 0 (0 - 6) 10 0.5 0 (0 - 4)	0.4 0 (0 - 2) 2 0.4 0 (0 - 2)	1.4 0 (0 - 4) 7 0.2 0 (0 - 1)	0.7 0 (0 - 4) 12 0.4 0 (0 - 3)	

out inhibitor; missing ency of bleeding in 2

ment regimen: on demand and/or orary prophylaxis 1<u>y</u> = permanent 1ylaxis



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As well as in HA, adults with severe haemophilia B, who bleed frequently should be commenced on prophylaxis. Median ABR in adults with severe haemophilia B on prophylaxis decreased from 1 to 0 in 2024 for both ABR and JABR.





In contrary to HA, joint bleeds are relatively more frequent in children with HB. 57,4% of all bleeds and 61,5% of joint bleeds are traumatic.

Detailed treatment of bleeds



	Joints	Muscles	Subcuta- neous	Oral cavity	Urogenital tract	Epistaxes	GIT	CNS	Other	Total
No. of bleeds	26	0	9	2	0	14	0	0	3	54
FIX consumption per bleed (IU), valid N	13		5	2		7			3	30
geometric mean	2790.5		1974.4	1500.0		1059.6			1651.0	1913.1
median	3000.0		2000.0	1500.0		1000.0			1500.0	1750.0
min – max	1000-16000		1000-7500	1500-1500		500-2000			1000-3000	500-16000
sum	49 500		13 500	3 000		8 000			5 500	79 500
No. of doses per bleed										
geometric mean	2.1		1.5	1.7		1.2			1.3	1.7
median	2		1	2		1			1	1
min – max	0–8		0–5	1–3		0–3			1–2	0-8
Duration of therapy per bleed, days										
geometric mean	2.3		2.1	3.2		2.9			1.3	2.3
median	2		1	4		3			1	2
min – max	1–13		1–19	2–5		1–4			1–2	1–19
N (%) with hospitalization	2 (7.7%)		1 (11.1%)	1 (50%)		0 (0%)			0 (0%)	4 (7.4%)
N (%) with rebleeding	4 (15.4%)		3 (33.3%)	0 (0%)		2 (14.3%)			0 (0%)	9 (16.7%)



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MUNI

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Joint bleeds in children were treated with median dose of 3000 IU FIX administered in23 infusions in two days. There was no muscle bleed in 2024.





No major difference between HA and HB bleeding. Most of bleeds are spontaneous joint bleeds, most frequently elbow.

Detailed treatment of bleeds

	Adults
	Haem B
	N=53*
r n	umber of bleed

	Joints	Muscles	Subcuta- neous	Oral cavity	Urogenital tract	Epistaxes	GIT	CNS	Other	Total
No. of bleeds	32	7	4	1	7	0	0	0	2	53
FIX consumption per bleed (IU), valid N	31	7	4	1	7				2	52
geometric mean	5042.3	7416.1	4000.0	4000.0	10998.5				6324.6	5819.6
median	4000.0	8000.0	3000.0	4000.0	10000.0				7000.0	4000.0
min – max	2000-69000	2000-42000	2000-16000	4000-4000	2000-60000				4000-10000	2000–69000
sum	273 000	87 000	24 000	4 000	157 000				14 000	559 000
No. of doses per bleed										
geometric mean	3.2	3.1	1.2	2.0	3.0				1.0	2.8
median	1	2	1	2	2				1	1
min – max	0–2000	1–48	1–2	2–2	1–15				1–1	0–2000
Duration of therapy per bleed, days										
geometric mean	1.7	2.8	1.2	4.0	2.4				1.0	1.8
median	1	2	1	4	1				1	1
min – max	1-80	1–47	1-2	4–4	1–12				1-1	1–80
N (%) with hospitalization	3 (9.4%)	2 (28.6%)	0 (0%)	1 (100%)	3 (42.9%)				0 (0%)	9 (17%)
N (%) with rebleeding	1 (3.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)				0 (0%)	1 (1.9%)

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In adults, joint bleeds are treated with median of 4000 IU FIX in total, administered in one infusion in most of the cases. Muscle bleeds needed in median 8000 IU mostly in two infusion.

ABR according to centres Haemophilia B (PWHB)



Annual bleeding rate on permanent prophylaxis

HaemB on prophy Paed. centres N=10

Moderate Severe					F	requeno inhit	cy of blee pitor on <mark>p</mark>	ding in <mark>erman</mark>	PWHB ent pro	without phylaxis
Paediatric centre	0	ABR (2	median) 4	6	N	Mean	Median	Min	Max	Severity
Droh		1	1		1	0.0	0.0	0	0	Moderate
Prana	0.0				5	4.2	0.0	0	15	Severe
Dura	-				0					
Brno	0.5				2	0.5	0.5	0	1	Severe
0-1	-				0					
Ostrava	0.0				2	0.0	0.0	0	0	Severe
Ústí as dustas	-				0					
Usti nad Laben	0.0				0					



Not all centres treat children with HB. The median ABR is similar to HA.

Annual bleeding rate on permanent prophylaxis

HaemB on prophy Adult centres N=23

	Moderate					F	requen	cy of blee	ding in	PWHB	without
	Severe		ABR	(median)			inhit	pitor on p	erman	ent pro	ophylaxis
Adult c	entre	0	2	4	6	N	Mean	Median	Min	Max	Severity
	Br		_			0					
	DI		1 .0			6	1.2	1.0	0	3	Severe
	Octra	<u>_</u>				1	0.0	0.0	0	0	Moderate
	Ustra	va 📄	1 .0			5	2.0	1.0	0	7	Severe
	Plzeň		0.0			2	0.0	0.0	0	0	Moderate
			0.0			3	0.0	0.0	0	0	Severe
	Libo					0					
	Liber		0.0			1	0.0	0.0	0	0	Severe
	Olomo	0	.0			1	0.0	0.0	0	0	Moderate
	Olomo	uc Č	.Ō			1	0.0	0.0	0	0	Severe
	Ústí nad Labo	_				0					
		''' C	0.0			1	0.0	0.0	0	0	Severe
	Čoská Budělov				1.0	1	4.0	4.0	4	4	Moderate
	Ceske Budejov		2.0				2.0	2.0	2	2	Severe
	Numer	-				0					
	Nymbu	IK				0					



Similar situation for adults with HB.

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Annual bleeding rate regardless prophylaxis

HaemB
Paed. centres
N=22

	Moderate			Frequency of bleeding in PWHB without									
	Severe			inhibitor <u>regardless of prophylaxis</u>									
Paediat	ric centre	0 2 ^{ABR (median)}	6 1	l Mea	ın Median	Min	Max	% on permanent prophylaxis					
	Braha	0.0	(5 0.3	0.0	0	1	16.7%					
	Pidild	0 .5	6	5 3.7	0.5	0	15	83.3%					
	Brno	3.0		3.0	3.0	3	3	0.0%					
BITIO		0.0		0.3	0.0	0	1	66.7%					
Ostrava		-	()									
		0.0		0.0	0.0	0	0	100.0%					
	České Budějovice		()									
			0	4.0	4.0	4	4	0.0%					
	Hradec Králové	4.	0)									
	Ú-16	1	()									
	Usti nad Labem	4.	0 :	4.0	4.0	4	4	0.0%					
	Direž	00	:	0.0	0.0	0	0	0.0%					
	Pizen	2.0		2.0	2.0	2	2	100.0%					
	Olamaua	1	()									
Ulomoi			()									



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

Annual bleeding rate regardless prophylaxis

HaemB Adult centres N=48*
* missing ABR in 2 adults

Moderate Severe				I	Freque ir	ncy of bl hibitor <mark>I</mark>	eedin egard	g in P\ <mark>lless o</mark>	WHB without f prophylaxis
Adult centre	(O ABR (median)	5	N*	Mean	Median	Min	Max	% on permanent prophylaxis
	Brno	1.0		5	0.6	1.0	0	1	0.0%
		2.0		7	1.7	2.0	0	5	85.7%
0	ctrovo	0.0		3	1.3	0.0	0	4	33.3%
0	stiava	1 .0		7	1.4	1.0	0	7	71.4%
	Dizoň			3	0.0	0.0	0	0	66.7%
	FIZEII	0.0		3	0.0	0.0	0	0	100.0%
	iboroc	0.0		3	0.7	0.0	0	2	0.0%
L	iberec	0.0		1	0.0	0.0	0	0	100.0%
	mour	0.0		8	1.5	0.0	0	8	12.5%
UI	Jinouc	0.0		2	0.0	0.0	0	0	33.3%
Úctí pod l	lahom			0					
USUITAU	Labelli	1.5		2	1.5	1.5	0	3	50.0%
Čocká Budž	lovico	0.0		3	1.3	0.0	0	4	33.3%
Ceske buue	Jovice	2.0		1	2.0	2.0	2	2	100.0%
Nha	mhurk			0					
iny	mourk			0					



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

Prophylactic regimens and treatment outcomes

HaemB Paed. centres N=22

Paediatric centre						PERI	ON-DEMAND / TEMPORARY PROPHY						
	Severity	Total N	% of	N	Dosing propt (IU/kg p	g of SHL hylaxis er week)	Dosing proph (IU/kg p	; of EHL nylaxis er week)		BR	N		BR
			patients		Mean	Median	Mean	Median	Mean	Median		Mean	Median
Draha	Moderate	6	16.7%	1			17.9	17.9	0.0	0.0	5	0.4	0.0
Prana	Severe	6	83.3%	5			45.2	55.6	4.2	0.0	1	1.0	1.0
Brno	Moderate	1	0.0%	0							1	3.0	3.0
	Severe	3	66.7%	2			44.3	44.3	0.5	0.5	1	0.0	0.0
Ostrous	Moderate	0	0.0%	0							0		
Ostrava	Severe	2	100.0%	2			18.7	18.7	0.0	0.0	0		
	Moderate	0	0.0%	0							0		
C. Budejovice	Severe	0	0.0%	0							0		
Hradoc Králová	Moderate	1	0.0%	0							1	4.0	4.0
HIAUEC KIAIOVE	Severe	0	0.0%	0							0		
Úctí nad Labom	Moderate	0	0.0%	0							0		
Usti nau Labern	Severe	1	0.0%	0							1	4.0	4.0
Dizoň	Moderate	1	0.0%	0							1	0.0	0.0
Pizen	Severe	1	100.0%	1			44.8	44.8	2.0	2.0	0		
Olemana	Moderate	0	0.0%	0							0		
Olomouc	C	0	0.0%	0							0		



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More detailed description of prophylactic dosing/regimens used by different paediatric centres within CNHP and its correlation with annual bleeding rates in respective centres. All children with HB are treated with EHL FIX in 2024.

Prophylactic regimens and treatment outcomes

HaemB Adult centres N=50

Adult centre					PE	ON-DEMAND / TEMPORARY PROPHY									
	Severity	Total N	% of patients	N	Dosing proph (IU/kg p	Dosing of SHL prophylaxis (IU/kg per week)		Dosing of EHL prophylaxis (IU/kg per week)		ABR		N	AI	BR	Age
					Mean	Median	Mean	Median		Median	Median			Median	Median
Press	Moderate	5	0.0%	0								5	0.6	1.0	52
Brno	Severe	7	85.7%	6			37.5	34.2	1.2	1.0	35	1	5.0	5.0	22
Ostrava	Moderate	3	33.3%	1			29.6	29.6	0.0	0.0	25	2	2.0	2.0	63
	Severe	7	71.4%	5	50.6	50.6	47.6	45.2	2.0	1.0	57	2	0.0	0.0	54
Dizoň	Moderate	3	66.7%	2			23.5	23.5	0.0	0.0	58	1	0.0	0.0	62
Fizeli	Severe	4	100.0%	4			29.3	29.6	0.0	0.0	45	0			
Liborac	Moderate	3	0.0%	0								3	0.7	0.0	42
Adult centre S Brno M Ostrava M Liberec M Olomouc M Ústí n. Labem N Č. Budějovice M	Severe	1	100.0%	1			76.9	76.9	0.0	0.0	32	0			
Olomour	Moderate	8	12.5%	1			20.2	20.2	0.0	0.0	45	7	1.7	0.0	56
Clonioue	Severe	3	33.3%	1			19.2	19.2	0.0	0.0	55	2	0.0	0.0	45
lístí n Lahom	Moderate	0	0.0%	0								0			
Usti II. Labelli	Severe	2	50.0%	1			19.2	19.2	0.0	0.0	29	1	3.0	3.0	53
	Moderate	3	33.3%	1			93.2	93.2	4.0	4.0	58	2	0.0	0.0	49
Aduit centre Se Brno Se Ostrava Mo Se Liberec Mo Se Olomouc Se Ústí n. Labem Mo Se Ústí n. Labem Se	Sovoro	1	100.0%	1			17.9	17.9	2.0	2.0	51	0			



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





Similar numbers of children on prophylaxis as in 2024. All of them on permanent prophy.





No major change compared to 2023. More adults are, however, taking the advantage of home treatment.

Treatment data and factor consumption Haemophilia A and B






Majority of PWH are now treated with EHL concentrates. Only less than 20 persons were treated with plasma-derived factor concentrates. Some of PWH were treated with more concentrates/brands over the year (i.e. switch from concentrate A to B). The number of PWHs on emicizumab further increased (was 76 in 2023).





Only 1 childr registered in CNHP registry was treated with plasma-derived concentrates in 2024. Most children were switched to EHL, mainly Elocta. Majority of those treated with emicizumab (regardless of inhibitors) were children. Their number further increased (from 53 to 59)





Only 16 adults registered in CNHP registry were treated still with plasma derived concentrates in 2024 (was 23 in 2023). The number of adults treated with recombinants is furter increasing over last years with most of them being treated with EHLs. Number of adults on emi increaswed from 23 to 30 in 2024

Comparison of treatment in years 2024 and 2023

	2024			2023		
	N	% of all PWHs	% treated PWHs	N	% of all PWHs	% treated PWHs
All treated persons *	402	53.5	100.0	395	53.0	100.0
Plasma-derived factor	17	2.3	4.2	28	3.8	7.1
Recombinant factor	66	8.8	16.4	105	14.1	26.6
Recombinant f. EHL	262	34.8	65.2	238	31.9	60.3
Emicizumab	89	11.8	22.1	76	10.2	19.2
Without treatment	350	46.5	-	350	47.0	-
Total	752	100.0	-	745	100.0	-

* One patient could have more type of factor concentrates and/or emicizumab.

All



This table compares data between 2023 and 2024. Mainly you can see, further move from pdF to rF, mainly to EHLs

Comparison of treatment in years 2024 and 2023



	2024			2023		
	N	% of all PWHs	% treated PWHs	N	% of all PWHs	% treated PWHs
All treated persons *	148	53.4	100.0	154	54.2	100.0
Plasma-derived factor	1	0.4	0.7	5	1.8	3.2
Recombinant factor	18	6.5	12.2	36	12.7	23.4
Recombinant f. EHL	88	31.8	59.5	83	29.2	53.9
Emicizumab	59	21.3	39.9	53	18.7	34.4
Without treatment	129	46.6	-	130	45.8	-
Total	277	100.0	-	284	100.0	-

* One patient could have more type of factor concentrates and/or emicizumab.



This table compares data between 2023 and 2024. E.g. you can see, that percentage of children treated with recombinant EHL concentrates and registered within CNHP registry changed from 53,9% in 2023 to 59,5% in 2024. Seen is also further increase of those treated with emicizumab.

Comparison of treatment in years 2024 and 2023

Adults

	2024			2023		
	N	% of all PWHs	% treated PWHs	N	% of all PWHs	% treated PWHs
All treated persons *	254	53.5	100.0	241	52.3	100.0
Plasma-derived factor	16	3.4	6.3	23	5.0	9.5
Recombinant factor	48	10.1	18.9	69	15.0	28.6
Recombinant f. EHL	174	36.6	68.5	155	33.6	64.3
Emicizumab	30	6.3	11.8	23	5.0	9.5
Without treatment	221	46.5	-	220	47.7	-
Total	475	100.0	-	461	100.0	-

* One patient could have more type of factor concentrates and/or emicizumab.



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This table compares data between 2023 and 2024. E.g. you can see, that percentage of adults treated with recombinant EHL concentrates and registered within CNHP registry changed from 64,3% in 202 to 68,5% in 2024. 7 more PWHs were treated with emi in 2023 compared to 2024

Comparison of treatment in years



* One patient could have more type of treatments

All



This slide describes in graphical form the changes of treatment used during last 10 years in CZ. Switch from pdF to SHL rFVIII and EHL rF is clearly seen as well as the continuing boom of emicizumab.



* One patient could have more type of treatments



Trends in children.

Comparison of treatment in years

Adults



* One patient could have more type of treatments



Same information for adults.

Consumption of drugs

All

	D	Total annual	Number of treated	Average annual consumption
	Drug (IU)	consumption	persons	per treated person
FVIII (IU)	Fanhdi	1 379 150	14	98 510.7
	Octanate	215 000	2	107 500.0
	PD FVIII total	1 594 150	16	99 634.4
	Advate	1 940 267	49	39 597.3
	NUWIQ	1 282 950	6	213 825.0
	NovoEight	247 500	4	61 875.0
	Afstyla	607 500	3	202 500.0
	Kovaltry	5 500	2	2 750.0
	SHL REC FVIII total	4 083 717	64	63 808.1
	Standard FVIII total	5 677 867	79	71 871.7
	Elocta	21 014 066	124	169 468.3
	Adynovi	8 663 561	47	184 331.1
	Esperoct	3 252 800	20	162 640.0
	Jivi	3 158 995	16	197 437.2
	Altuvoct (Altuviiio)	579 150	10	57 915.0
	Other-recFVIII EHL	213 900	1	213 900.0
	EHL REC FVIII total	36 882 472	202	182 586.5
	FVIII total	42 560 339	272	156 471.8
FIX (IU)	Immunine	0	0	
	Octanine	187 000	1	187 000.0
	FIX PD total	187 000	1	187 000.0
	Rixubis	112 000	2	56 000.0
	FIX REC total	112 000	2	56 000.0
	Standard FIX total	299 000	3	99 666.7
	Alprolix	4 719 447	45	104 876.6
	Refixia	1 032 640	15	68 842.7
	EHL REC FIX total	5 752 087	60	95 868.1
	FIX total	6 051 087	63	96 049.0
By-pass	NovoSeven (mg)	1 626	2	813.0
Emicizumab	Hemlibra s.c. (mg)	291 127	89	3 271.1



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Absolute numbers of respective concentrates in this figure refer ONLY to the records within CNHP registry, which have been updated in 2023. 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 with respective type of the concentrate.

Consumption of drugs

Childre n

	Drug (IU)	Total annual consumption	Number of treated persons	Average annual consumption per treated person
FVIII (IU)	Fanhdi	0	0	
	Octanate	205 000	1	205 000.0
	PD FVIII total	205 000	1	205 000.0
	Advate	306 500	11	27 863.6
	NUWIQ	28 000	1	28 000.0
	NovoEight	0	0	
	Afstyla	607 500	3	202 500.0
	Kovaltry	5 500	2	2 750.0
	SHL REC FVIII total	947 500	17	55 735.3
	Standard FVIII total	1 152 500	18	64 027.8
	Elocta	6 542 400	57	114 778.9
	Adynovi	1 140 500	7	162 928.6
	Esperoct	374 000	4	93 500.0
	Jivi	535 000	2	267 500.0
	Altuvoct (Altuviiio)	147 000	4	36 750.0
	Other-recFVIII EHL	0	0	
	EHL REC FVIII total	8 738 900	68	128 513.2
	FVIII total	9 891 400	85	116 369.4
FIX (IU)	Immunine	0	0	
	Octanine	0	0	
	FIX PD total	0	0	
	Rixubis	8 000	1	8 000.0
	FIX REC total	8 000	1	8 000.0
	Standard FIX total	8 000		8 000.0
	Alprolix	652 000	17	38 352.9
	Refixia	169 000	3	56 333.3
	EHL REC FIX total	821 000	20	41 050.0
	FIX total	829 000	21	39 476.2
By-pass	NovoSeven (mg)	1 626.0	2	813.0
Emicizumab	Hemlibra s.c. (mg)	102 306	59	1 734.0



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Absolute numbers of respective concentrates in this figure refer ONLY to the records within CNHP registry, which have been updated in 2023. 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.

Consumption of drugs

Adults

	Drug (IU)	Total annual consumption	Number of treated persons	Average annual consumption per treated person
FVIII (IU)	Fanhdi	1 379 150	14	98 510.7
	Octanate	10 000	1	10 000.0
	PD FVIII total	1 389 150	15	92 610.0
	Advate	1 633 767	38	42 993.9
	NUWIQ	1 254 950	5	250 990.0
	NovoEight	247 500	4	61 875.0
	Afstyla	0	0	
	Kovaltry	0	0	
	SHL REC FVIII total	3 136 217	47	66 728.0
	Standard FVIII total	4 525 367	61	74 186.3
	Elocta	14 471 666	67	215 995.0
	Adynovi	7 523 061	40	188 076.5
	Esperoct	2 878 800	16	179 925.0
	Jivi	2 623 995	14	187 428.2
	Altuvoct (Altuviiio)	432 150	6	72 025.0
	Other-recFVIII EHL	213 900	1	213 900.0
	EHL REC FVIII total	28 143 572	134	210 026.7
	FVIII total	32 668 939	187	174 700.2
FIX (IU)	Immunine	0	0	
	Octanine	187 000	1	187 000.0
	FIX PD total	187 000	1	187 000.0
	Rixubis	104 000	1	104 000.0
	FIX REC total	104 000	1	104 000.0
	Standard FIX total	291 000	2	145 500.0
	Alprolix	4 067 447	28	145 266.0
	Refixia	863 640	12	71 970.0
	EHL REC FIX total	4 931 087	40	123 277.2
	FIX total	5 222 087	42	124 335.4
By-pass	NovoSeven (mg)	0.0	0	
Emicizumab	Hemlibra s.c. (mg)	188 821	30	6 294.0



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Absolute numbers of respective concentrates in this figure refer ONLY to the records within CNHP registry, which have been updated in 2023. 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.

Though in rFVIII SHLs the dosing is almost identical for children and adults, in rFVIII EHLs it is significantly different, reflecting the difference in body weight between adults and children. Thus it seems, that EHLs are doses well in both adults and children, but adults with SHLs are still underdosed.