

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

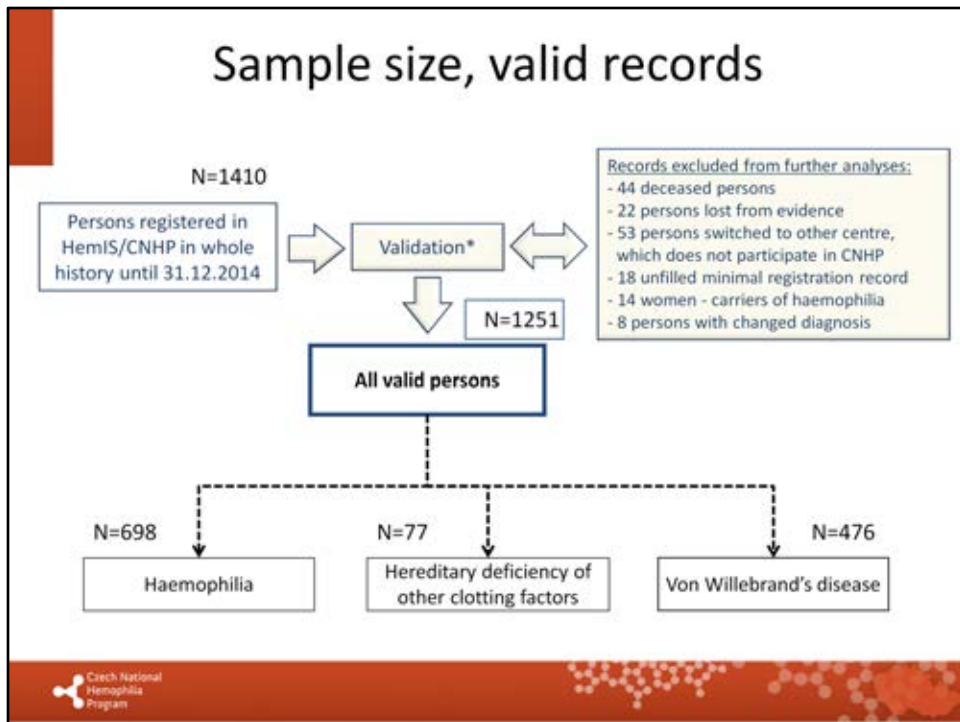
Jan Blatný, Petra Ovesná

on behalf of

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

*May 2015*

# Sample size, valid records

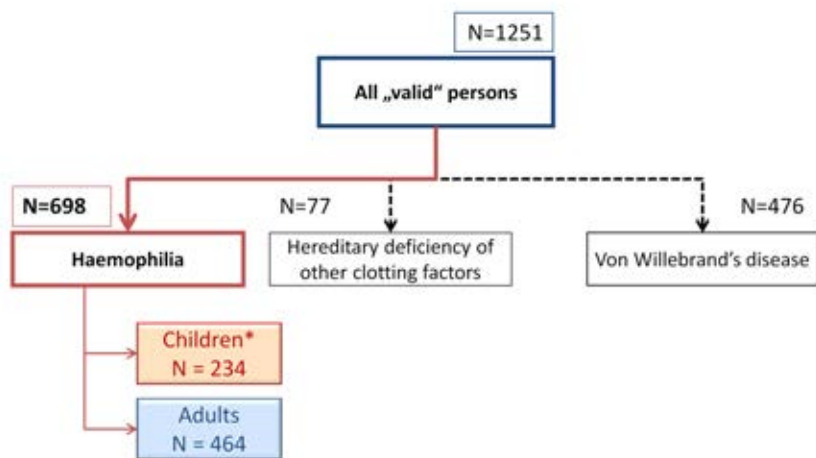


This slide describes the process of records' validation within the registry.

Part A

## Persons with haemophilia (PWH)

# Sample size



\* Persons under 19 years old in 2014

## Participating centres in CNHP

Paediatric centres	Valid persons	
	N	%
FN Motol – Dpt. of Pediatric Haematology and Oncology	86	12.3
FN Brno – DN – Dpt. of Pediatric Haematology	46	6.6
FNHK – Dpt. of Pediatric Medicine	27	3.9
FN Ostrava – Dpt. of Pediatric Medicine	27	3.9
UnL – Pediatric Dpt. – Haematology	27	3.9
CB – Pediatric Dpt.	13	1.9
FN Plzen – Pediatric Dpt.	13	1.9
FN Olomouc – Dpt. of Pediatric Medicine	12	1.7

Adult centres	Valid persons	
	N	%
FN Brno – OKH	138	19.8
FN Ostrava – Blood centre	67	9.6
FN Olomouc – Haemato-Oncology Dpt.	61	8.7
FN Plzen – UKBH	48	6.9
FN a LF HK – IV, IHK	39	5.6
KN Liberec – OKH	36	5.2
CB – OKH	29	4.2
UnL – OKH	20	2.9
Plzen - hemacentrum	9	1.3

Centres contributing to the CNHP registry.



Part A.1

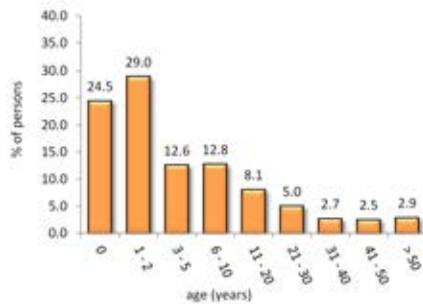
## **Demographic characteristics of persons with haemophilia**



# Age

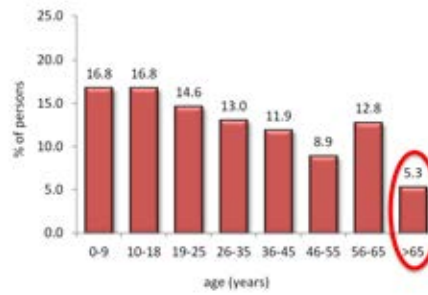
All  
N=698

Age at diagnosis (years)	
N	556*
Mean	8.1
Median (min - max)	2 (0 - 81)



\* Missing information on year of diagnosis in 142 persons.

Current age (years)	
N	698
Mean	31.2
Median (min - max)	27 (0 - 92)



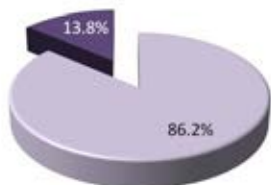
Please note gradually growing age of Czech PWH population!

# Type and severity of haemophilia I

All  
N=698

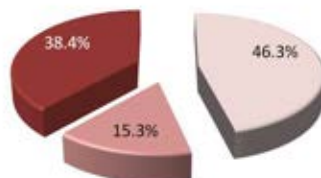
## Type of haemophilia

- Haemophilia A (N=602)
- Haemophilia B (N=96)



## Severity of haemophilia

- Mild (N=323)
- Moderate (N=107)
- Severe (N=268)



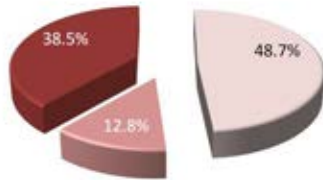


# Type and severity of haemophilia II

All  
N=698

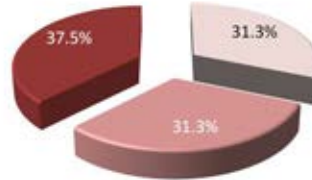
Haemophilia A (N=602)

- Mild (N=293)
- Moderate (N=77)
- Severe (N=232)



Haemophilia B (N=96)

- Mild (N=30)
- Moderate (N=30)
- Severe (N=36)

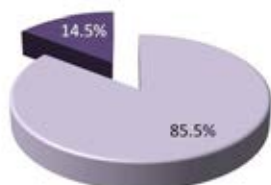


# Type and severity of haemophilia I

Children  
N=234

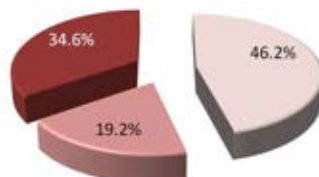
## Type of haemophilia

- Haemophilia A (N=200)
- Haemophilia B (N=34)



## Severity of haemophilia

- Mild (N=108)
- Moderate (N=45)
- Severe (N=81)

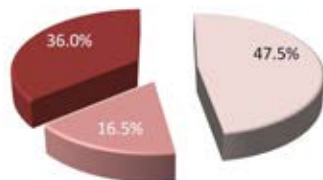


# Type and severity of haemophilia II

Children  
N=234

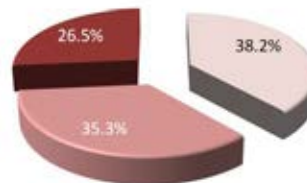
Haemophilia A (N=200)

- Mild (N=95)
- Moderate (N=33)
- Severe (N=72)



Haemophilia B (N=34)

- Mild (N=13)
- Moderate (N=12)
- Severe (N=9)

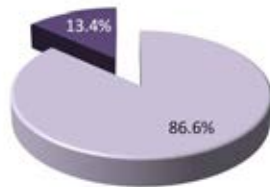


# Type and severity of haemophilia I

Adults  
N=464

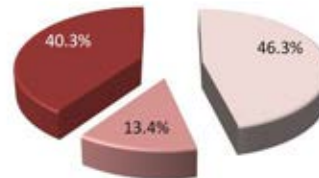
## Type of haemophilia

- Haemophilia A (N=402)
- Haemophilia B (N=62)



## Severity of haemophilia

- Mild (N=215)
- Moderate (N=62)
- Severe (N=187)

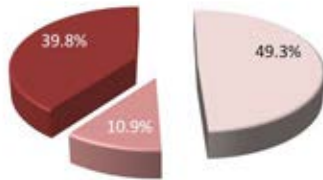


# Type and severity of haemophilia II

Adults  
N=464

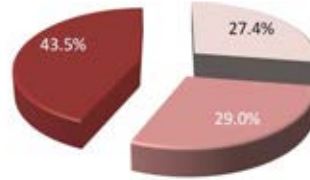
Haemophilia A (N=402)

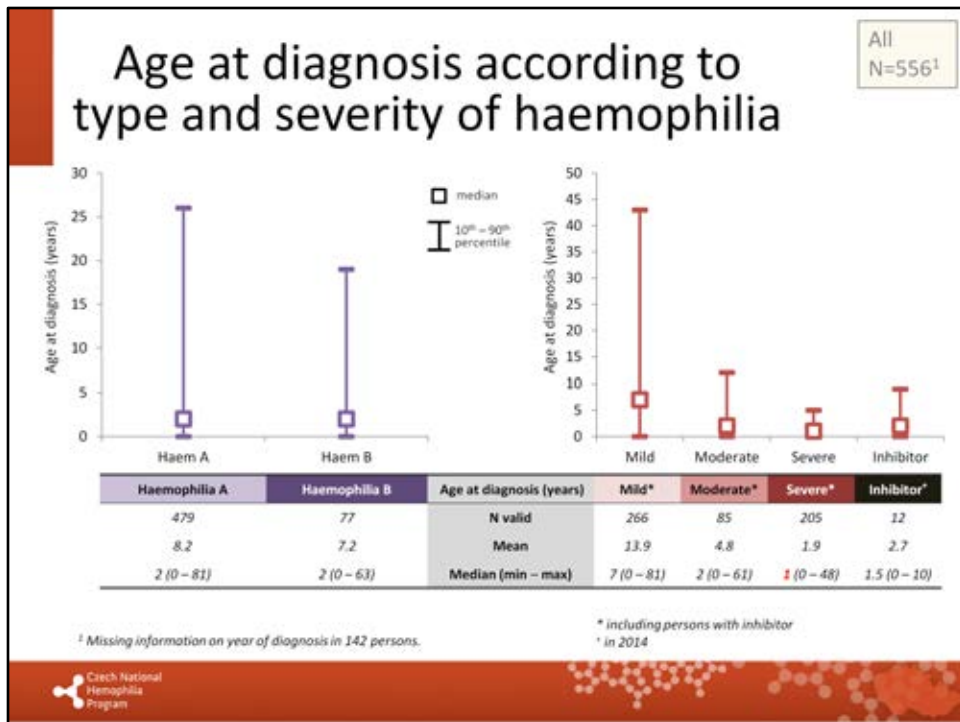
- Mild (N=198)
- Moderate (N=44)
- Severe (N=160)



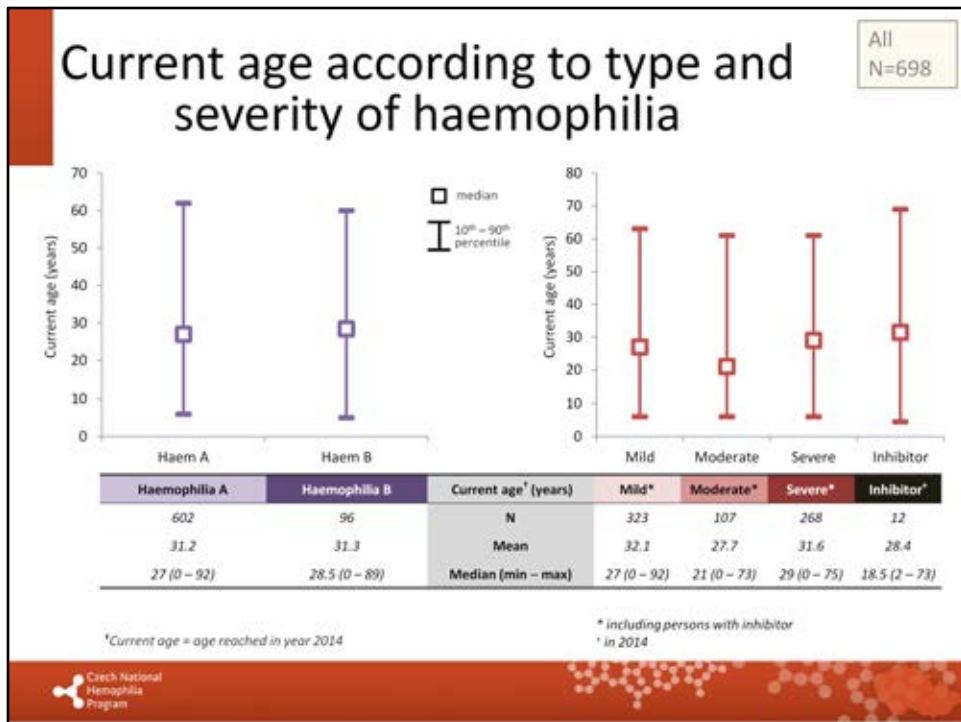
Haemophilia B (N=62)

- Mild (N=17)
- Moderate (N=18)
- Severe (N=27)

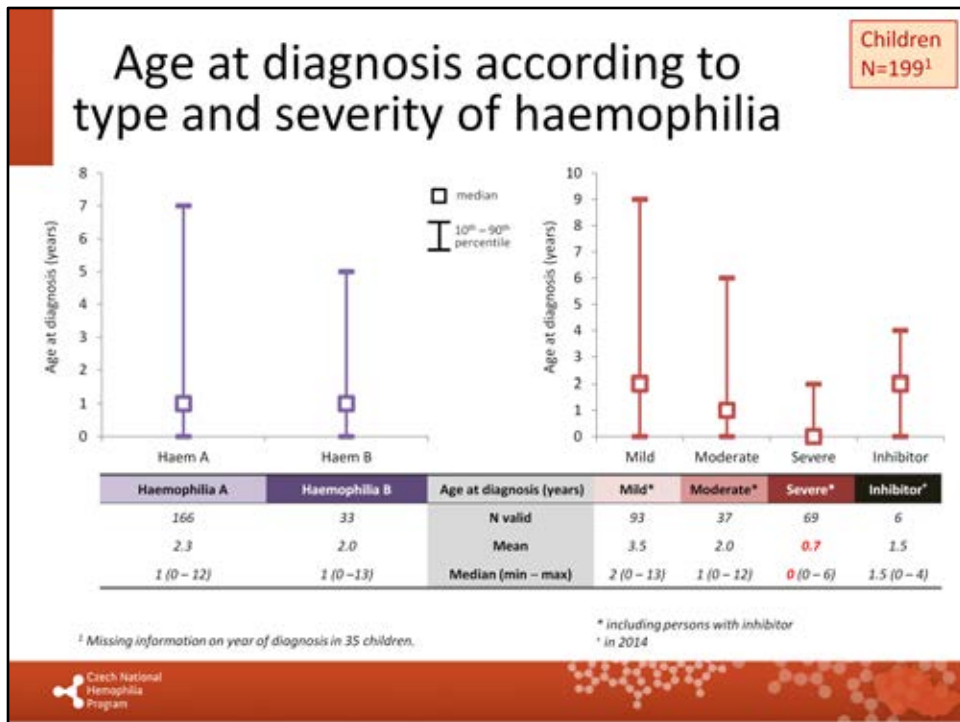




Median age at diagnosis of 1 year in severe haemophilia enables us to offer primary prophylaxis to our PUPs.

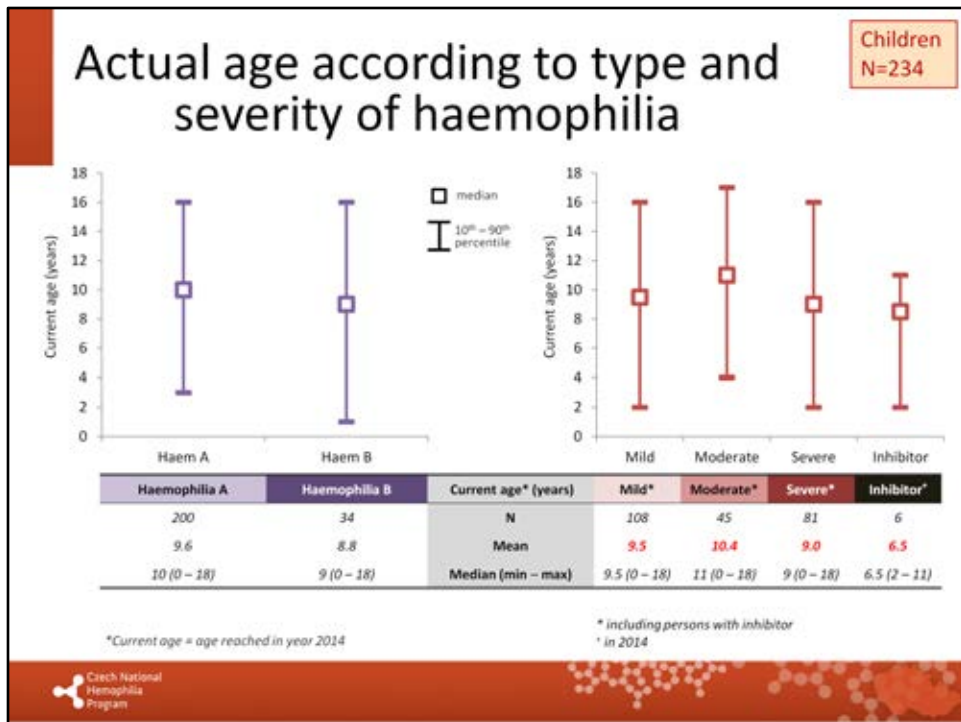


Our haemophilia population is relatively young.

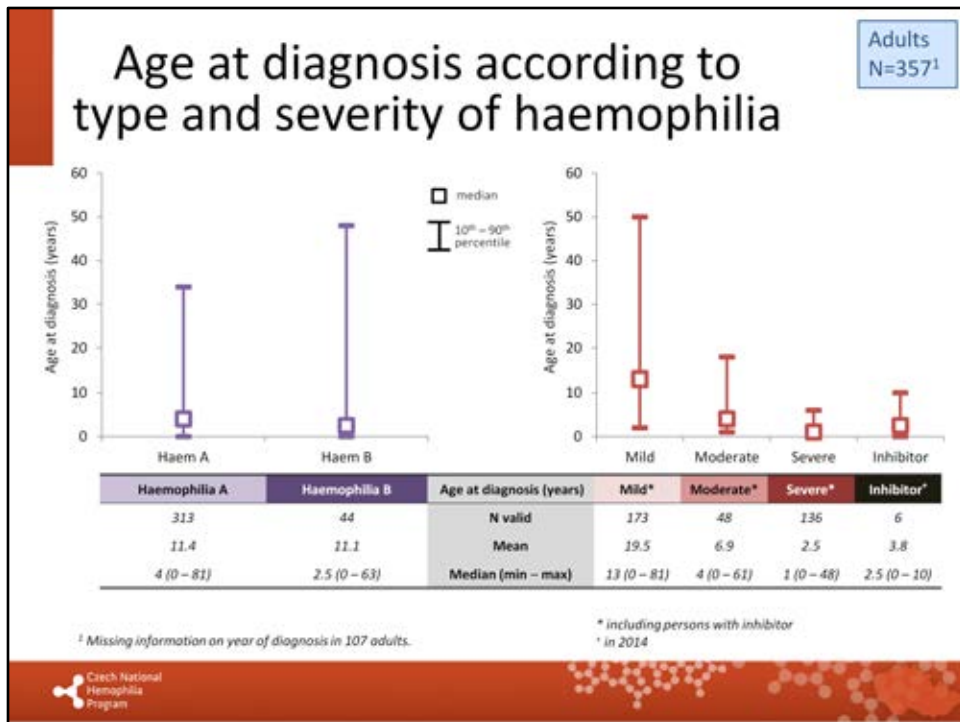


Median age at diagnosis below 1 year in severe haemophiliacs enables us to offer primary prophylaxis to our PUPs. Even better seen within paediatric population.

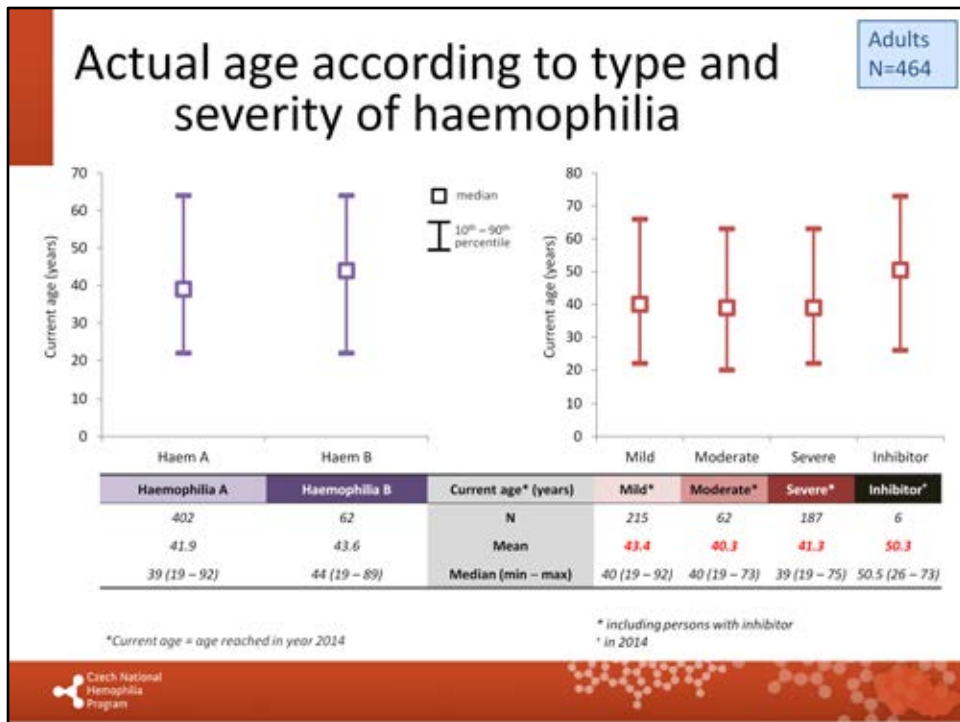




Mean age of Czech paediatric haemophilia population is around 10 years.



Even haemophiliacs who are adult in these days, were diagnosed early enough. However, for those, born before 1990, there was no chance for prophylaxis due to lack of concentrates behind the „iron curtain“. Though some of those, who are now adults were able to take advantage of prophylaxis, none of them had primary prophylaxis, which is a gold standard in these days This is the major reason for higher annual bleeding rates in adult haemophiliacs as their joints have been significantly impaired during childhood (before 1990, when factor concentrates became available in CZ).



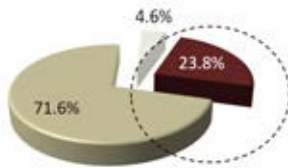
Mean age of Czech adult PWHs is around 40 years.

# Hepatitis experienced

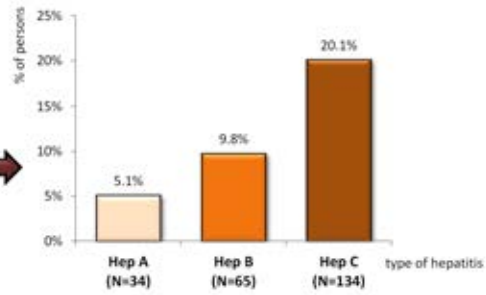
All  
N=698

## Experienced hepatitis

- Yes (N=166)
- No (N=500)
- Not known (N=32)



N=166\*



Data from last annual report of each person.

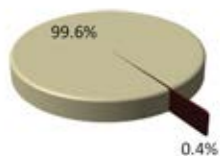
\*Total of 233 cases of hepatitis in 166 persons. One person may have more types of hepatitis recorded.

Relatively low prevalence of HepC compared to many other countries.

# Hepatitis experienced

Children  
N=234

## Experienced hepatitis



One child has hepatitis C.

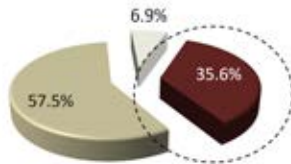
Data from last annual report of each person.

# Hepatitis experienced

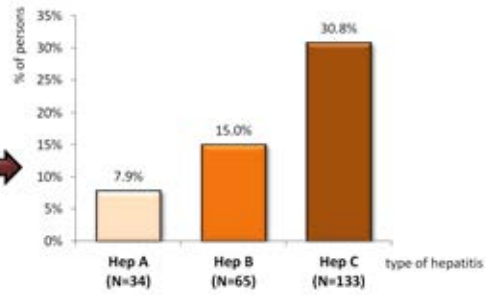
Adults  
N=464

## Experienced hepatitis

- Yes (N=165)
- No (N=267)
- Not known (N=32)

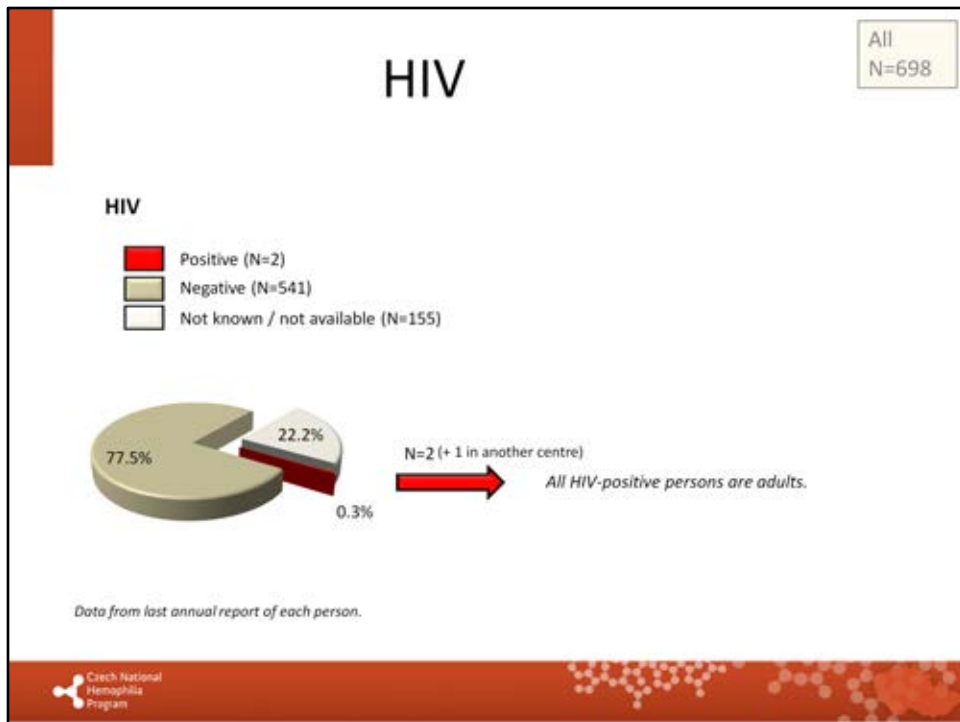


N=165\*



Data from last annual report of each person.

\*Total of 232 cases of hepatitis in 165 persons. One person may have more types of hepatitis recorded.



Very low number of HIV+ PWHs 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+ PWHs reported since late 90s.



Part A.2

## **Persons with haemophilia with inhibitor**






All  
N=698

## Persons with haemophilia with inhibitors in year 2014

- Active inhibitors were recorded in **12 persons** in year 2014 (+ 6 in another centre)
  - 6 children and 6 adults
  - 11 haemophilia A and 1 haemophilia B
  - 9 severe, 1 moderate and 2 mild haemophilia
  - 10 HR and 2 LR
  - 4 patients were treated with rFVIIa, 2 patients with aPCC, other 2 patients with both rFVIIa and aPCC
  - 2 patients were without „by-pass“ therapy and 2 patients were without any recorded treatment
- ITT
  - Two of above mentioned 12 persons (1 child, 1 adult) finished ITT in 2014 as „unsuccessful“ (adult PWH started in 2014, child in 2011)
  - Two children started ITT in 2013 and continued in 2014
  - ITT was successfully finished in another 1 child during 2014, this child is inhibitor free now

 Czech National Hemophilia Program

Summary description of the PWHs with inhibitors within registry. There are six other PWHs with inhibitor in the center not participating in CNHP registry.

All  
N=10

## Persons with inhibitor

	1	2	3	4	5	6	7	8	9	10	11	12	13
Age group	child	child	child	child	child	child	adult	adult	adult	adult	adult	adult	child
Year of birth	2012	2011	2008	2007	2004	2003	1988	1977	1971	1956	1949	1941	2013
Type of haemophilia	A	A	A	B	A	A	A	A	A	A	A	A	A
Severity	sev	sev	sev	sev	sev	sev	mild	sev	sev	sev	mild	mod	sev
Year of inhibitor development	<b>2014</b>	2012	2013	2009	2009	2005	2013	2001	1988	1972	2012	2013	2011
HR/LR	HR	HR	HR	HR	HR	HR	LR	HR	HR	HR	LR	HR	LR
„By-pass” treatment in 2014	w/o by-pass therapy	-	-	rFVIIa	rFVII + aPCC	rFVIIa	w/o any treatment	w/o any treatment	rFVII + aPCC	aPCC	aPCC	rFVIIa	-
ITT	Planned for 2015	Since 2013	Since 2013	-	2011-2014, unsuccessful	-	-	-	-	-	-	in 2014, unsuccessful	2013-2014, <u>successful</u>

Information about PWHs with inhibitors and their treatment. Information reflects situation in December 2014.

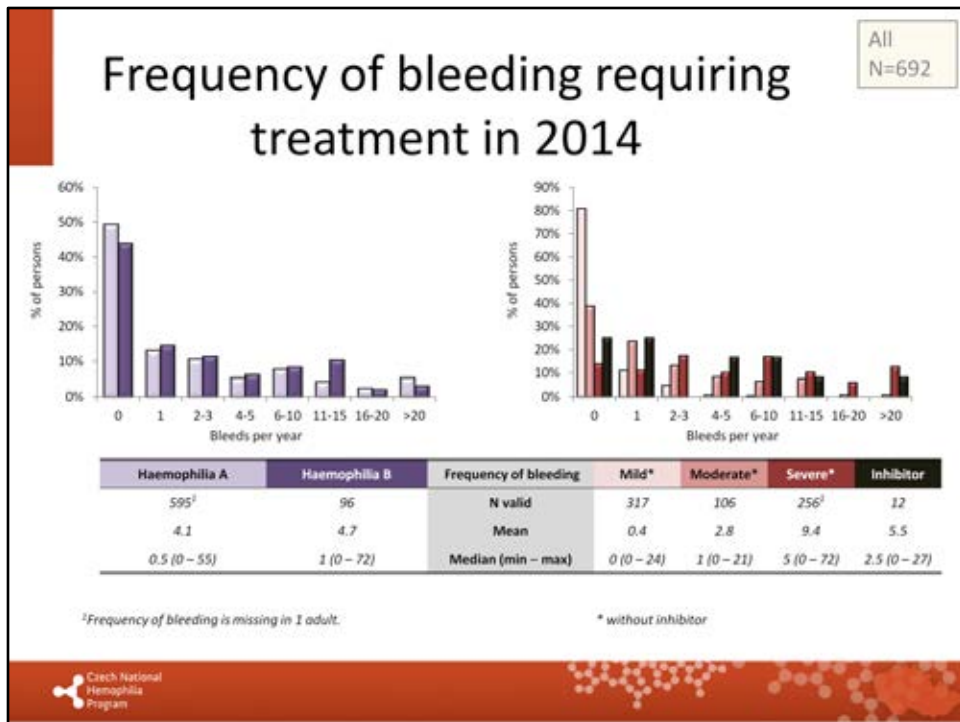
Part A.3

**Treatment outcomes including bleeding  
frequency in persons with haemophilia  
2014 data**

## Data from year 2014 – sample size

	Valid persons		Persons with annual report in 2014		Persons examined in 2014		Persons treated in 2014	
	N	%	N	%	N	%	N	%
<b>All</b>	698	100%	→ 692	99.1%	→ 536	76.8%	→ 402	57.6%
of them with inhibitor			12		9		9	
<b>Children</b>	234	100%	→ 231	98.7%	→ 211	90.2%	→ 138	59.0%
of them with inhibitor			6		6		6	
<b>Adults</b>	464	100%	→ 461	99.4%	→ 325	70.0%	→ 264	56.9%
of them with inhibitor			6		3		3	

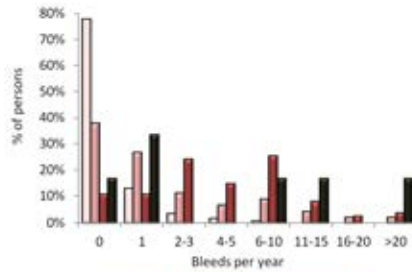
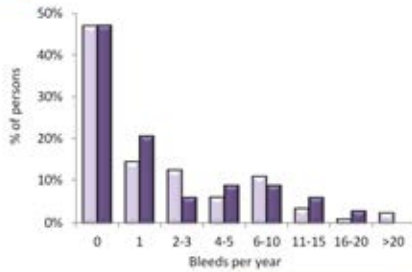
There are records of nearly 80% of all Czech haemophiliacs in total within the CNHP registry. As for paediatric population, ALL children are recorded. CNHP registry also houses records of over two thirds of adult haemophiliacs in Czech Republic. Further slides display analyses performed only on records, which were updated during 2014. Not all patients came to the centre (especially adults) and not all centres fully reported data in 2014. Thus not all records have been updated and used for further analyses. Though the data completeness is still improving, it is our task to get as close as possible to 100% in future years. ( Ideally, percentage of PWHs with annual report should be equal to PWHs examined and both should be 100%).



Data shown strongly support the positive effect of prophylaxis in Czech PWHs, no matter what age category they are. Mean number of bleedings per year 9,4 in the whole severe haemophilia population regardless of prophylaxis.

# Frequency of bleeding requiring treatment in 2014

Children  
N=231



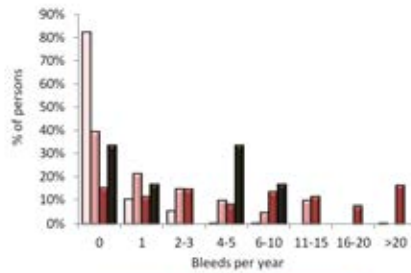
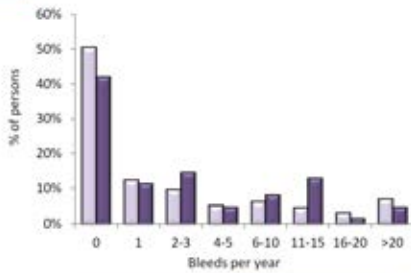
Haemophilia A	Haemophilia B	Frequency of bleeding	Mild*	Moderate*	Severe*	Inhibitor
197	34	N valid	105	45	75	6
2.8	2.7	Mean	0.4	3.0	5.7	8.2
1 (0 - 31)	1 (0 - 18)	Median (min - max)	0 (0 - 9)	1 (0 - 21)	4 (0 - 31)	4 (0 - 27)

\* without inhibitor

Median bleeding rate (all bleeds) in children with haemophilia is 4 per year, regardless of prophylaxis.

# Frequency of bleeding requiring treatment in 2014

Adults  
N=461



Haemophilia A	Haemophilia B	Frequency of bleeding	Mild*	Moderate*	Severe*	Inhibitor
398 <sup>2</sup>	62	N valid	212	61	181 <sup>2</sup>	6
4.7	5.8	Mean	0.4	2.7	10.9	2.8
0 (0 - 55)	1 (0 - 72)	Median (min - max)	0 (0 - 24)	1 (0 - 15)	5 (0 - 72)	2.5 (0 - 7)

<sup>2</sup>Frequency of bleeding is missing in 1 adult.

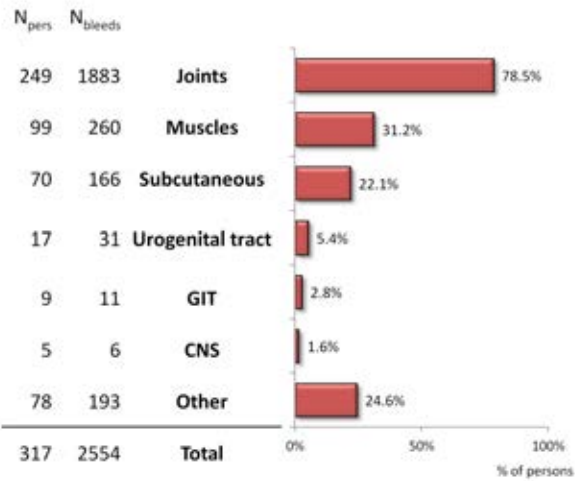
\* without inhibitor

The same information for adult PWHs,.

# Location of bleeds in 2014

All  
N=692

353 (51%) persons experienced bleeding requiring treatment at least once per year; 2889 bleeds were recorded in total, 86 bleeds required hospitalization.  
317 of these 353 persons have recorded location of their bleeds. Localization is not known in 36 persons.  
339 (49%) persons recorded no bleed during year 2014.



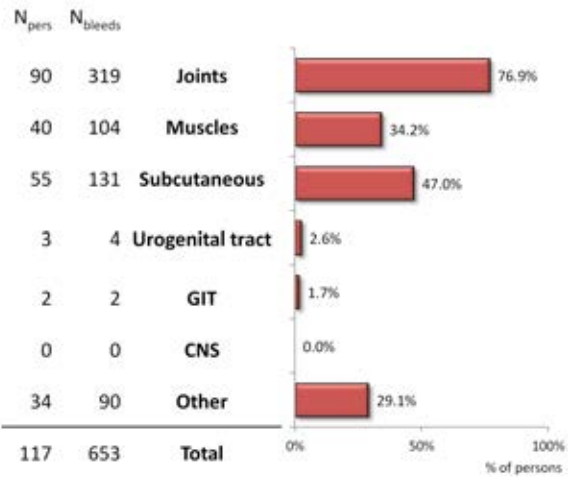
Almost one half of all Czech PWHs did not experience any bleeding in 2014. Our aim should be to avoid CNS bleeds, though!



# Location of bleeds in 2014

Children  
N=231

121 (52.4%) children experienced bleeding requiring treatment at least once in year; 651 bleeds were recorded in total, 28 bleeds required hospitalization. 117 of these 121 children have recorded location of their bleeds. Localization is not known in 4 children. 110 (47.6%) children recorded no bleed during year 2014.

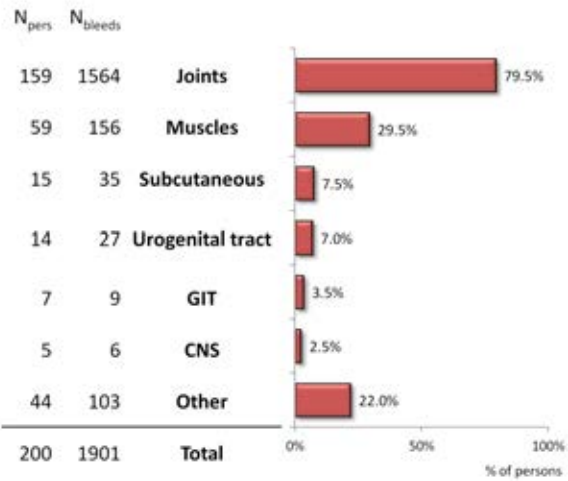


There was NO CNS bleed in children with Haemophilia in 2014. Half of children had no bleed at all.

# Location of bleeds in 2014

Adults  
N=461

232 (50.3%) adults experienced bleeding requiring treatment at least once in year; 2238 bleeds were recorded in total, 58 bleeds required hospitalization. 200 of these 232 adults have recorded location of their bleeds. Localization is not known in 32 adults. 229 (49.7%) adults have recorded no bleed during year 2014.

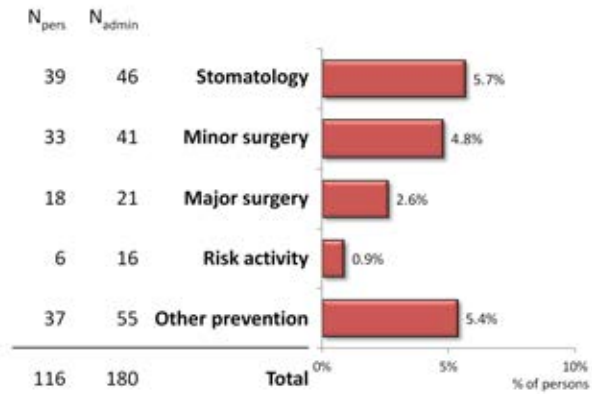


Bleeding events in adults.

# Preventive administration in 2014

All  
N=692

116 (16.8%) persons were given factor to prevent bleeding during/before risk situation.  
180 preventive administrations were recorded in total.

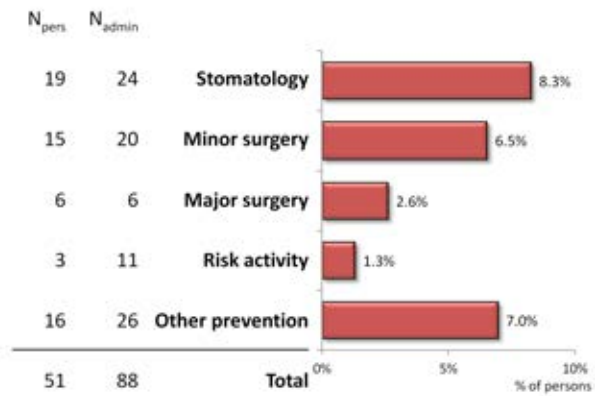


Some PWHs were given factor not to treat bleeding, but to prevent bleeding during risk situations (i.e. surgeries, dental extractions, risk activities/sports etc...). These event were NOT counted/analyzed as bleeding episodes.

# Preventive administration in 2014

Children  
N=231

51 (22.2%) children were given factor to prevent bleeding during/before risk situation. 88 preventive administrations were recorded in total.

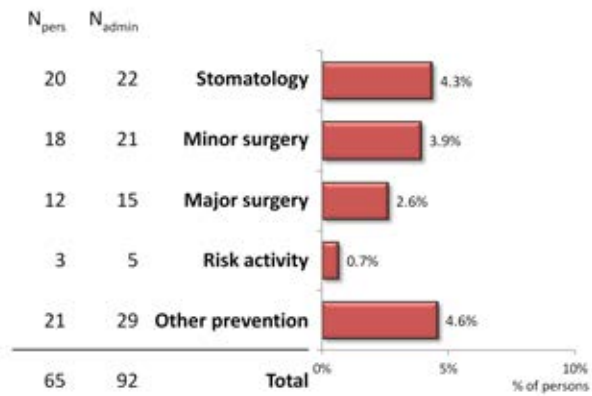


See comments on previous slide for explanation. This figure refers to paediatric population.

# Preventive administration in 2014

Adults  
N=461

65 (14.1%) persons were given factor to prevent bleeding during/before risk situation. 92 preventive administrations were recorded in total.

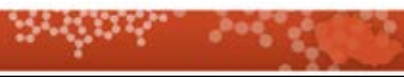


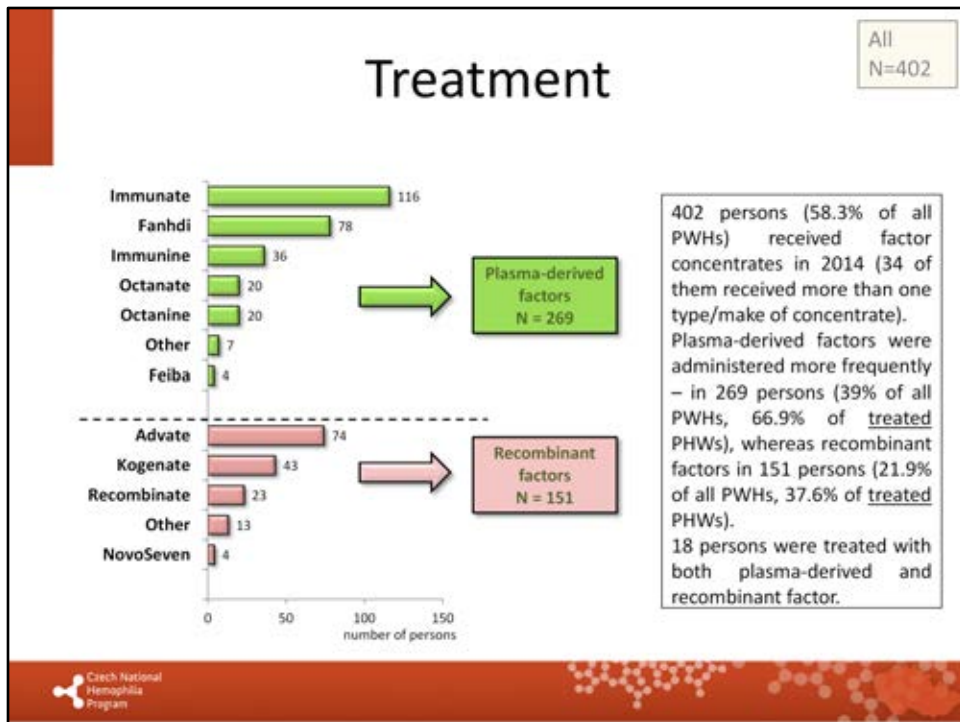
See comments on previous slide for explanation. This figure refers to adult population.



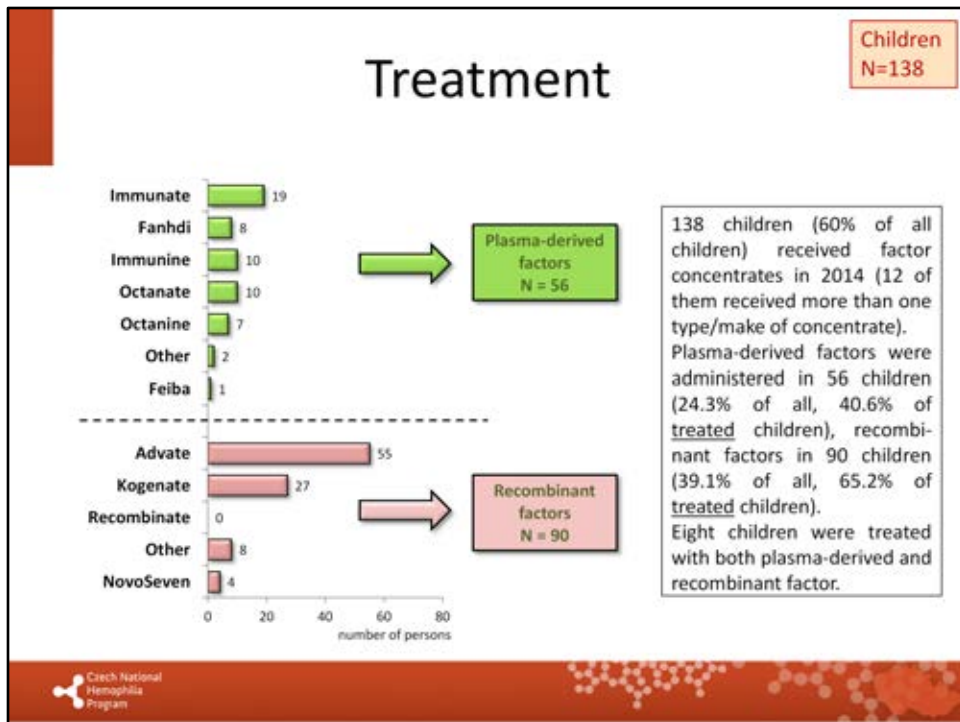
Part A.4

## **Treatment data and factor consumption 2014 data**



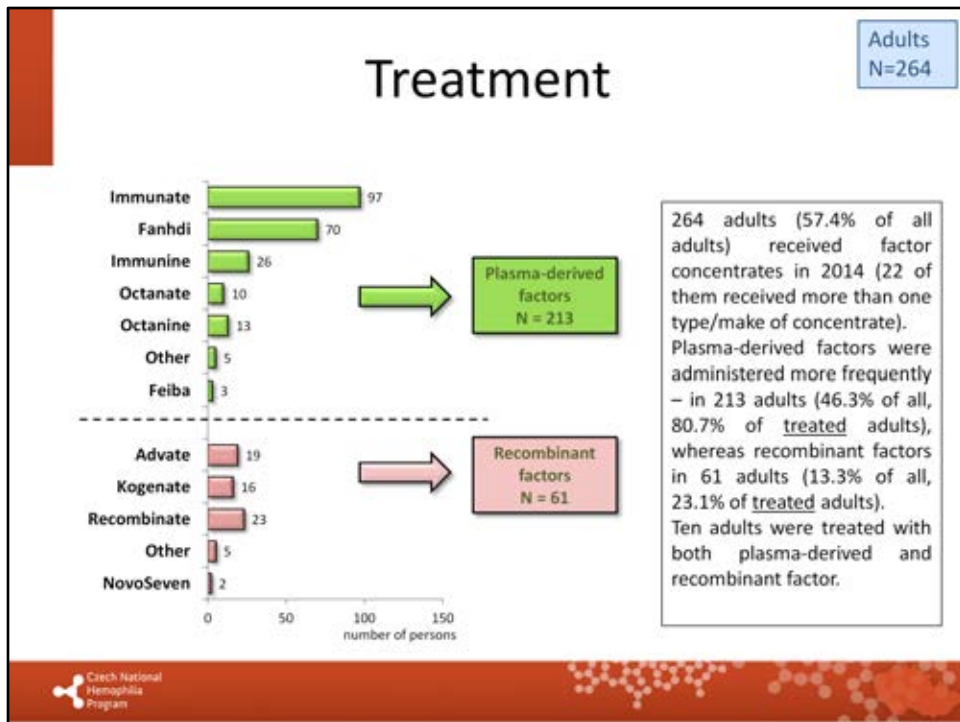


Over one third of PWHs registered in CNHP registry and treated with any factor concentrate. were treated with recombinants in 2014.



Almost two thirds of children, who were given factor concentrate in 2014 were treated with recombinants.





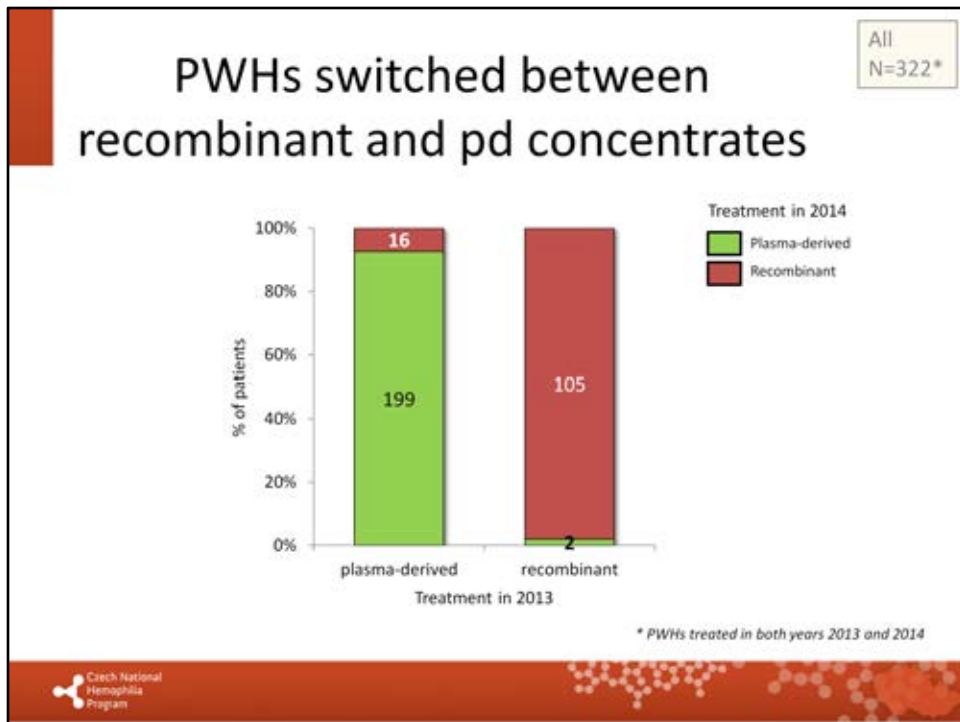
Number of adult PWHs treated with recombinants is increasing (currently 23% of those treated with factor concentrate in 2014 and registered within CNHP registry).

## Comparison of treatment in years 2013 and 2014

All  
N=692

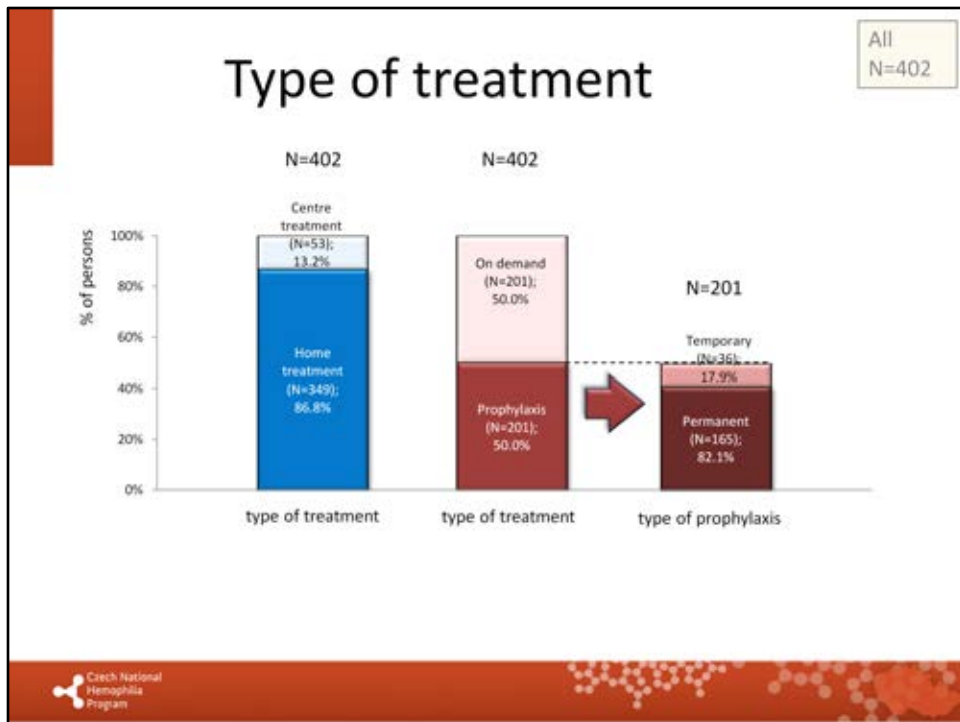
	2014			2013		
	N	% of all PWs	% treated PWs	N	% of all PWs	% treated PWs
All persons with treatment	402	58.1	100.0	383	60.4	100.0
<i>Plasma-derived factor</i>	255	36.8	63.4	276	43.5	72.1
<i>Recombinant factor</i>	<b>147</b>	<b>21.2</b>	<b>36.6</b>	<b>107</b>	<b>16.9</b>	<b>27.9</b>
Without treatment	290	41.9	-	251	39.6	-
Total	692	100.0	-	634	100.0	-

This table compares data between 2013 and 2014. E.g you can see, that percentage of patients treated with recombinant concentrates and registered within CNHP registry changed from 28% in 2013 to 37% in 2014.

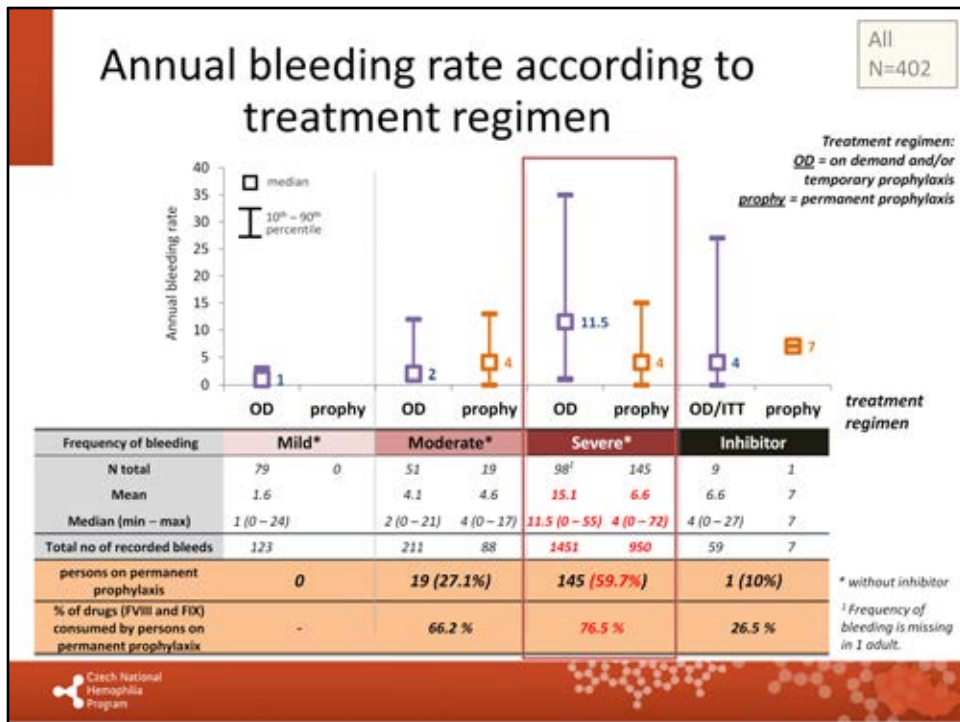


This table compares data between 2013 and 2014. E.g you can see, that 16 PWHs within CNHP registry were switched from pdFVIII to rFVIII in 2014.

NB Please note the difference between slide 43 and 42. Data on slide 43 refer to switched patients ONLY !



Almost 90% of PWHs treated in 2014 took the advantage of home treatment. Half of treated PWHs were commenced on any type prophylaxis and 82% out of those on prophylaxis were on permanent prophylaxis in 2014.

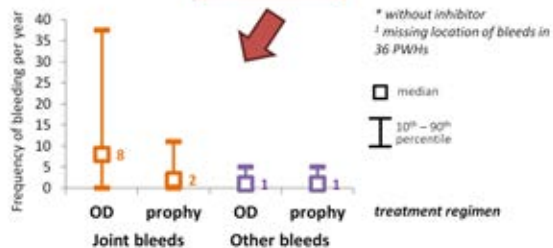


These data strongly support the positive effect of prophylaxis in Czech PWHs, no matter what age category they are. Mean number of bleedings per year in severe haemophiliacs can be decreased from 15.1 in those without prophylaxis to 6.6 in those, who are taking the advantage of prophylactic factor application. It also shows, that, in general, consumption of factors is not significantly increased by prophylaxis as 59.7% of treated persons with severe form of haemophilia were on permanent prophylaxis and they consumed 76.5% of total factor consumption for that particular group. Difference is thus rather small.

# Joint and other bleeds according to treatment regimen

All  
N=366<sup>1</sup>

Frequency of bleeding	Mild*		Moderate*		Severe*		Inhibitor	
	OD	prophy	OD	prophy	OD	prophy	OD/TTT	prophy
<b>Treatment regimen</b>	OD	prophy	OD	prophy	OD	prophy	OD/TTT	prophy
N valid	72	0	48	19	80	138	8	1
<b>JOINT BLEEDS</b>								
Mean	0.6		2.2	3.2	12.6	4.6	3.6	2.0
Median (range)	0 (0-5)		0 (0-14)	2 (0-13)	8 (0-55)	2 (0-64)	1 (0-16)	2
Total no of recorded bleeds	41		103	61	1009	638	29	2
<b>OTHER BLEEDS</b>								
Mean	0.9		2.1	1.4	2.0	2.1	3.3	5.0
Median (range)	0 (0-22)		0 (0-17)	1 (0-7)	1 (0-19)	1 (0-31)	2 (0-12)	5
Total no of recorded bleeds	66		98	26	159	287	26	5

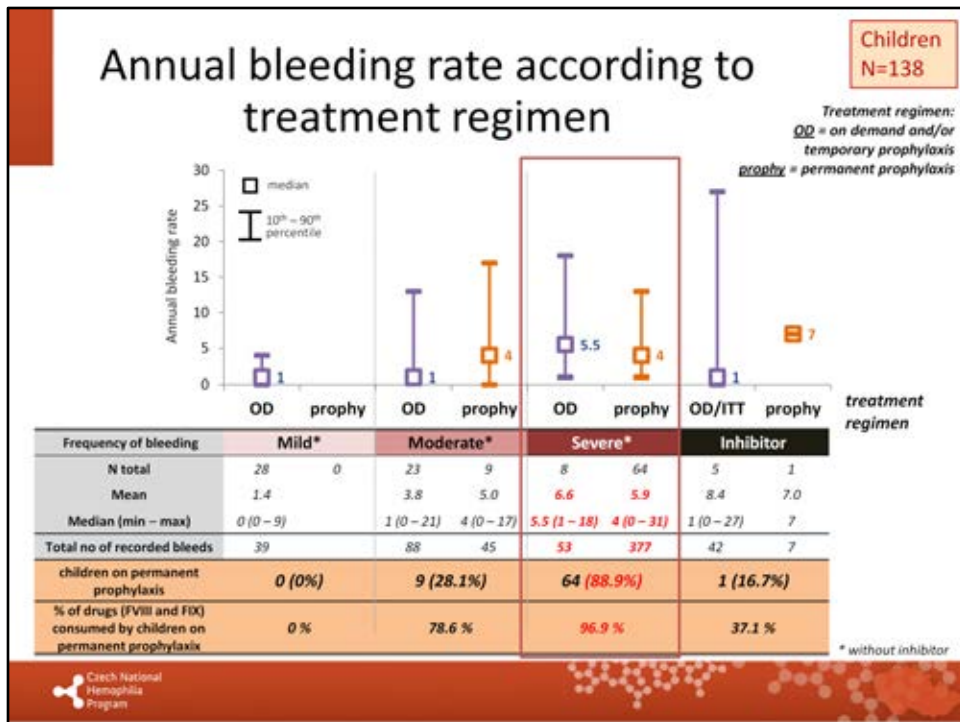


**Treatment regimen:**  
 OD = on demand and/or temporary prophylaxis  
 prophy = permanent prophylaxis



This important table shows, that the vast majority of bleeds in Czech PWHs which are influenced/diminished by prophylaxis are JOINT bleeds. The benefit of prophylaxis, leading to decrease of annual joint-bleeding rate from 8 to 2 (median) is undoubted.

On the other hand, it is alarming to see, that vast majority of bleeds in Czech PWHs are still joint bleeds (up to 4/5)  
 If PWH has >1 joint bleed per year in a long term prospective, the locomotory apparatus deteriorates progressively.



This slide supports good effect of permanent prophylaxis in children. Children with severe haemophilia, who are not on permanent prophylaxis yet shall be encouraged to do so.

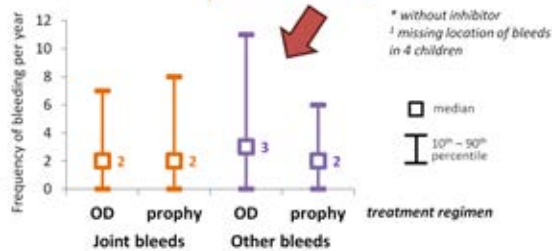
Number of bleeds per year (median) in severe haemophilacs on prophylaxis decreased compared to 2013 from 6 to 4. This is probably partially due to better data recording (some preventive factor applications were probably recorded as bleedings in past), but also by the reflection of 2013 data by respective centres.

We should, however, still bear in mind, that over 2 bleeds/year 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, regardless of their prophylaxis status in 2014.

# Joint and other bleeds according to treatment regimen

Children  
N=134<sup>1</sup>

Frequency of bleeding	Mild*		Moderate*		Severe*		Inhibitor	
Treatment regimen	OD	prophy	OD	prophy	OD	prophy	OD/TTT	prophy
N valid	26	0	22	9	7	64	5	1
<b>JOINT BLEEDS</b>								
Mean	0.6		1.6	3.0	3	3.0	5.2	2.0
Median (range)	0 (0 - 3)		0 (0 - 8)	1 (0 - 13)	2 (0 - 7)	2 (0 - 13)	1 (0 - 16)	2
Total no of recorded bleeds	15		34	27	21	194	26	2
<b>OTHER BLEEDS</b>								
Mean	0.8		2.6	1.9	4.4	2.9	3.4	5.0
Median (range)	0 (0 - 6)		1.5 (0 - 13)	1 (0 - 7)	3 (0 - 11)	2 (0 - 31)	1 (0 - 12)	5
Total no of recorded bleeds	20		58	17	31	183	17	5

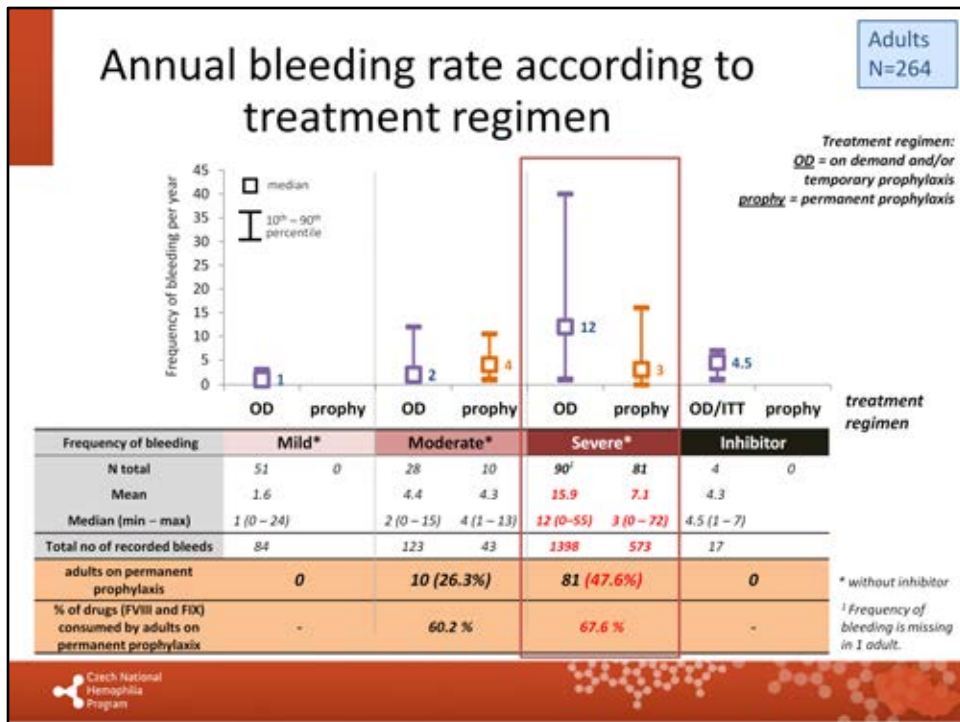


This table shows, that in contrary to adult population, children with haemophilia in CZ do not have so many joint bleeds and its annual median rate is 2. We, however, shall work together to get the median number of joint bleeds in children on prophylaxis below 2!!!

Perhaps, those children with severe haemophilia, who were not on prophylaxis in 2014, could have even 0 ABR when commenced on prophylaxis??

NB: Please note low joint - ABR in a patient with inhibitors on permanent prophylaxis with „by-pass“ agents.



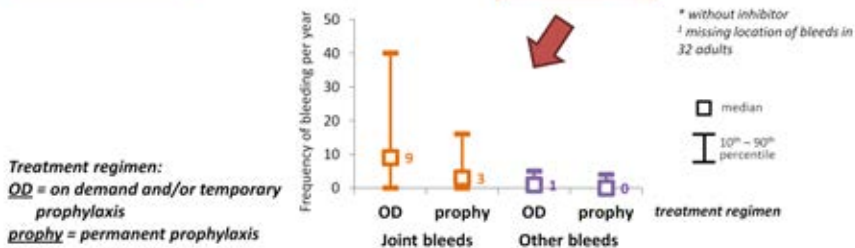


Prophylaxis works very well in Czech adult PWHs! It is able to decrease bleedings from 16 to 7 (mean numbers). It will certainly increase the factor consumption in adults, but the benefit - shown as far less bleedings - is undoubted.

# Joint and other bleeds according to treatment regimen

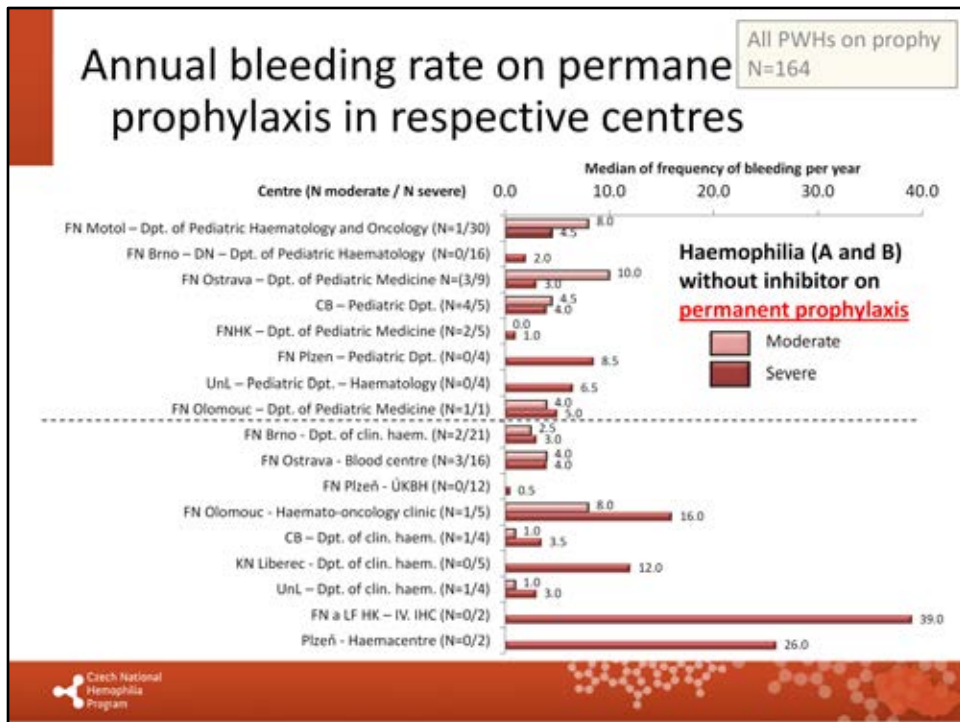
Adults  
N=232<sup>1</sup>

Frequency of bleeding	Mild*		Moderate*		Severe*		Inhibitor	
	OD	prophy	OD	prophy	OD	prophy	OD	prophy
Treatment regimen	46	0	26	10	73	74	3	0
N valid								
<b>JOINT BLEEDS</b>								
Mean	0.6		2.8	3.4	13.5	6.0	1.0	
Median (range)	0 (0-5)		1 (0-14)	3 (0-8)	9 (0-55)	3 (0-64)	1 (1-1)	
Total no of recorded bleeds	26		69	34	988	444	3	
<b>OTHER BLEEDS</b>								
Mean	1.1		1.7	0.9	1.8	1.4	3.0	
Median (range)	0 (0-22)		1 (0-17)	0.5 (0-5)	1 (0-19)	0 (0-17)	3 (0-6)	
Total no of recorded bleeds	46		40	9	128	104	9	



This table shows, that the vast majority of bleeds in Czech adult PWHs which are influenced/diminished by prophylaxis are JOINT bleeds. The benefit of prophylaxis, leading to decrease of annual joint-bleeding rate in adults from 9 to 3 (median) is undoubted.

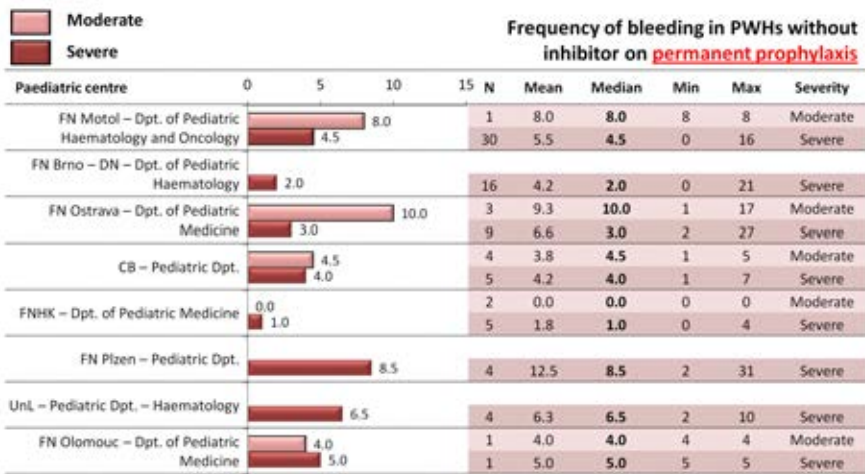
On the other hand, it is alarming to see, that vast majority of bleeds in Czech adult PWHs are joint bleeds (around 8/10)  
 If PWH has >1 joint bleed per year in a long term prospective, the locomotory apparatus deteriorates progressively. Prophylaxis in adults, can decrease the annual joint-bleeding rate down to 3 (median)!



Please note different bleeding rates in different centres. Though it may be influenced by relatively small patient numbers in respective centres, the differences are present. There are centres with median annual bleeding rate around 2 in severe haemophiliacs as well as centres with annual bleeding rate of over 6. On the other hand, the differences are less apparent, than in past years. This probably reflects the better data recoding (some preventive factor administrations were probably recorded as bleeding episodes in the past) but perhaps also the changed approach based on feed-back provided through past CNHP registry annual reports.

# Annual bleeding rate on permanent prophylaxis in paediatric centres

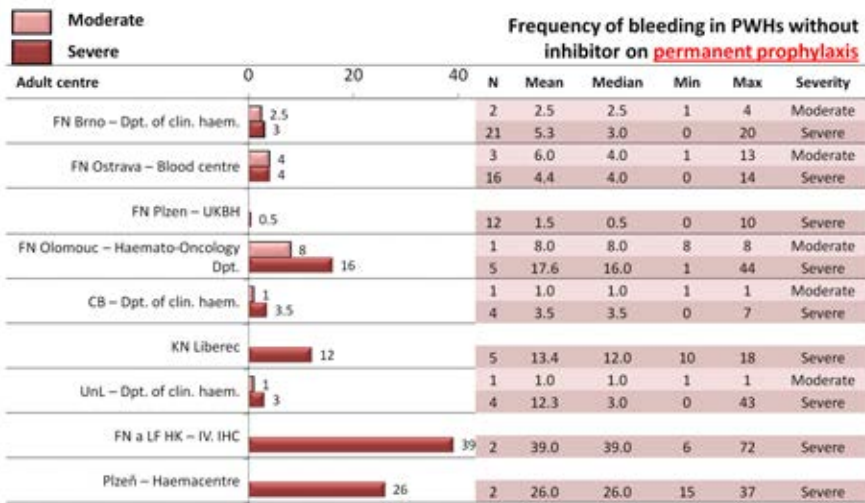
PWHs on prophylaxis in paed. centres  
N=85



In vast majority of paediatric centres, severe haemophiliacs on prophylaxis bleed not more, than 5 times per year (median). We should continue in our focus on individualized/tailored prophylaxis and shall offer it to all, who may benefit from this approach. Though the situations improved since 2013, it is still an important challenge for all paediatric centres.

# Annual bleeding rate on permanent prophylaxis in adult centres

PWHs on prophylaxis in adult centres  
N=79



Good news is, that there are adults with severe haemophilia, who have no bleed per year on permanent prophylaxis. This should encourage us to promote further prophylaxis in more adult PWHs.

# Annual bleeding rate regardless prophylaxis in paediatric centres

PWHs in  
paed. centres  
N=140



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

Paediatric centre	0	5	10	N	Mean	Median	Min	Max	% on permanent prophylaxis
FN Motol – Dpt. of Pediatric Haematology and Oncology	2.0	5.0		14	4.4	2.0	0	21	7.1
				40	6.0	5.0	0	18	75.0
FN Brno – DN – Dpt. of Pediatric Haematology	0.5	2.0		6	0.7	0.5	0	2	0.0
				17	3.8	2.0	0	21	94.1
FN Ostrava – Dpt. of Pediatric Medicine	2.0	3.0		9	5.9	2.0	0	17	33.3
				10	5.9	3.0	0	27	90.0
CB – Pediatric Dpt.	1.0	4.0		7	2.3	1.0	0	5	57.1
				5	4.2	4.0	1	7	100.0
FNHK – Dpt. of Pediatric Medicine	1.0	1.0		7	1.0	1.0	0	3	28.6
				5	1.8	1.0	0	4	100.0
FN Pízen – Pediatric Dpt.	0.0	5.0		1	0.0	0.0	0	0	0.0
				5	10.2	5.0	1	31	80.0
UnL – Pediatric Dpt. – Haematology	0.0	6.0		2	0.0	0.0	0	0	0.0
				5	5.2	6.0	1	10	80.0
FN Olomouc – Dpt. of Pediatric Medicine	1.0	5.0		3	2.0	1.0	1	4	33.3
				2	5.0	5.0	5	5	50.0

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 lower 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.

# Annual bleeding rate regardless prophylaxis in adult centres

PWHs in adult centres  
N=227



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

Adult centre	0.0	10.0	20.0	N	Mean	Median	Min	Max	% on permanent prophylaxis
FN Brno – Dpt. of clin. haem.	1.0	4.0		21	2.5	1.0	0	15	9.5
				41	5.9	4.0	0	25	51.2
FN Ostrava – Blood centre	1.0	5.0		9	3.4	1.0	0	13	33.3
				29	7.3	5.0	0	27	55.2
FN Pízen – UKBH	0.0	2.0		5	3.2	0.0	0	15	0.0
				25	10.8	2.0	0	40	48.0
FN Olomouc – Haemato-Oncology Dpt.	1	13.5		8	2.5	1.0	0	8	12.5
				24	18.3	13.5	0	55	20.8
CB – Dpt. of clin. haem.	0.0	1.0		4	0.3	0.0	0	1	25.0
				13	3.0	1.0	0	19	30.8
XN Liberec	0.5	16.0		2	0.5	0.5	0	1	0.0
				11	15.6	16.0	5	30	45.5
UnL – Dpt. of clin. haem.	1.0	14.0		4	3.3	1.0	0	11	25.0
				10	22.4	14.0	0	55	40.0
FN a LF HK – IV. IHC	2.0	17.0		3	1.7	2.0	0	3	0.0
				12	23.6	17.0	0	72	16.7
Pízeň – Haemacentre	12.0	15.0		1	12.0	12.0	12	12	0.0
				5	16.2	15.0	2	37	40.0

Similar information for adults.

# Prophylactic regimens and treatment outcomes in paediatric centres

PWHs in paed. centres  
N=140

Paediatric centre	Severity	Total N	% on perm prophy	% w/o perm prophy	Dosing of prophylaxis (IU/kg per week)					Annual bleeding rate ON permanent prophylaxis		Annual bleeding rate WITHOUT perm prophy	
					N	Mean	Median	Min	Max	Mean	Median	Mean	Median
FN Motol	Moderate	14	7.1	92.9	1	90.6	90.6			8.0	8.0	4.2	2.0
	Severe	40	75.0	25.0	30	81.4	81.0	45.1	148.9	5.5	4.5	8.1	7.5
FN Brno – DN	Moderate	6	0.0	100.0	-					-	-	0.8	1.0
	Severe	17	94.1	5.9	16	65.1	67.7	22.5	115.1	4.2	2.0	0.5	0.5
FN Ostrava – Ped. Dpt.	Moderate	9	33.3	66.7	3	57.0	46.0	41.7	83.3	9.3	10.0	4.2	1.0
	Severe	10	90.0	10.0	9	83.5	75.0	48.3	130.4	6.6	3.0	0.0	0.0
CB – Ped. Dpt.	Moderate	7	57.1	42.9	4	53.3	52.6	31.3	76.9	3.8	4.5	0.3	0.0
	Severe	5	100.0	0.0	5	64.3	61.5	49.8	88.2	4.2	4.0	-	-
FNHK – Ped. Dpt.	Moderate	7	28.6	71.4	0	na				0.0	0.0	2.0	2.0
	Severe	5	100.0	0.0	0	na				1.8	1.0	-	-
FN Plzen – Ped. Dpt.	Moderate	1	0.0	100.0	-	-				-	-	0.0	0.0
	Severe	5	80.0	20.0	4	46.2	48.8	22.7	64.2	12.5	8.5	1.0	1.0
UnL – Ped. Dpt.	Moderate	2	0.0	100.0	-	-				-	-	0.0	0.0
	Severe	5	80.0	20.0	4	45.8	39.9	17.9	85.7	6.3	6.5	1.0	1.0
FN Olomouc – Ped. Dpt.	Moderate	3	33.3	66.7	1	34.5	34.5			4.0	4.0	1.0	1.0
	Severe	2	50.0	50.0	0	na				5.0	5.0	na	na

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 in adult centres

PWHs in adult centres  
N=227

Adult centre	Severity	Total N	% on perm prophy	% w/o perm prophy	Dosing of prophylaxis (IU/kg per week)					Annual bleeding rate ON permanent prophylaxis			Annual bleeding rate WITHOUT perm prophy			W/O perm prophy
					N	Mean	Median	Min	Max	Mean	Median	Median age	Mean	Median	Median age	
FN Brno – DCH	Moderate	21	9.5	90.5	2	51.9	51.9	50.0	53.9	2.5	2.5	23	3.6	2.0	43	
	Severe	41	51.2	48.8	21	41.8	38.9	14.7	70.7	5.3	3.0	32	6.7	5.0	51	
FN Ostrava – Blood centre	Moderate	9	33.3	66.7	3	41.6	50.0	23.8	50.9	6.0	4.0	62	4.0	2.0	61	
	Severe	29	55.2	44.8	16	44.9	48.1	15.9	67.2	4.4	4.0	33	10.9	9.0	57	
FN Pízen – UKBH	Moderate	5	0.0	100.0	-	-	-	-	-	-	-	-	3.2	0.0	38	
	Severe	25	48.0	52.0	11	22.2	13.7	5.3	40.0	1.5	0.5	42	20.9	25.0	50	
FN Olomouc – HOC	Moderate	8	12.5	87.5	1	22.7	22.7	-	-	8.0	8.0	24	1.7	1.0	41	
	Severe	24	20.8	79.2	5	42.1	42.9	28.2	54.1	17.6	16.0	24	23.4	15.0	48	
CB – DCH	Moderate	4	25.0	75.0	0	na	-	-	-	1.0	1.0	48	na	-	-	
	Severe	13	30.8	69.2	0	na	-	-	-	3.5	3.5	45	4.2	1.0	49	
KN Liberec	Moderate	2	0.0	100.0	-	-	-	-	-	-	-	-	1.0	1.0	41	
	Severe	11	45.5	54.5	5	37.5	35.7	15.6	69.4	13.4	12.0	30	17.5	16.5	60	
UnL – DCH	Moderate	4	25.0	75.0	1	25.0	25.0	-	-	1.0	1.0	22	6.0	6.0	25	
	Severe	10	40.0	60.0	4	32.3	21.3	6.9	79.6	12.3	3.0	27	30.6	35.0	39	
FN a LF HK – IV, IHC	Moderate	3	0.0	100.0	-	-	-	-	-	-	-	-	1.7	2.0	19	
	Severe	12	16.7	83.3	2	47.0	47.0	42.9	51.1	39.0	39.0	36	22.8	22.5	37	
Pízeň - Haemacentre	Moderate	1	0.0	100.0	-	-	-	-	-	-	-	-	12.0	12.0	45	
	Severe	5	40.0	60.0	2	33.7	33.7	16.7	50.7	26.0	26.0	48	9.7	5.0	33	



Czech National Hemophilia Program

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

# Consumption of drugs

All

Drug (IU)	Total annual consumption	Number of treated persons	Average annual consumption per treated person	Number of valid persons	Average annual consumption per valid person
<i>Immunate</i>	8 858 600	116	76 367.2		14 715.3
<i>FanhdI</i>	6 622 350	78	84 901.9		11 000.6
<i>Octanate</i>	2 304 000	20	115 200.0		3 827.2
<i>Other plasma-derived</i>	2 130 850	7	304 407.1		3 539.6
<b>FVIII</b>				<b>602</b>	
<i>Advate</i>	6 517 104	74	88 069.0		10 825.8
<i>Kogenate</i>	3 950 750	43	91 877.9		6 562.7
<i>Recombinate</i>	1 817 500	23	79 021.7		3 019.1
<i>Other recombinant</i>	1 885 050	9	209 450.0		3 131.3
<b>FVIII total (IU)</b>	<b>34 086 204</b>	<b>340</b>	<b>100 253.5</b>		<b>56 621.6</b>
<i>Immunine</i>	1 892 700	36	52 575.0		19 715.6
<i>Octanine</i>	2 922 000	20	146 100.0		30 437.5
<i>Other recombinant</i>	600 820	4	150 205.0		6 258.5
<b>FIX total (IU)</b>	<b>5 415 520</b>	<b>58</b>	<b>93 371.0</b>	<b>96</b>	<b>56 411.7</b>
aPCC <i>Feiba</i>	252 000	4	63 000.0		
rFVIIa <i>NovoSeven (mg)</i>	1 715 mg	6	285.8 mg		
<b>Plasma-derived factors - TOTAL*</b>	<b>24 730 500</b>	<b>266</b>	<b>92 971.8</b>		<b>35 430.5</b>
<b>Recombinant factors - TOTAL*</b>	<b>14 771 224</b>	<b>145</b>	<b>101 870.5</b>	<b>698</b>	<b>21 162.2</b>
<b>TOTAL CONSUMPTION (IU)*</b>	<b>39 501 724</b>	<b>398</b>	<b>99 250.6</b>		<b>56 592.7</b>

\*plasma-derived factors = Immunate, FanhdI, Octanate, Immunine, Octanine, Other plasma-derived

\*recombinant factors = Advate, Kogenate, Recombinate, BAX 326, Other recombinant

\*TOTAL CONSUMPTION = all mentioned drugs excluding Feiba and NovoSeven



Czech National Hemophilia Program

Absolute numbers of respective concentrates in this figure refer ONLY to the records within CNHP registry, which have been updated in 2014. The most important information on this slide is „Average annual consumption per treated person“ This reflects nation-wide consumption of factor concentrate per treated haemophiliac.

“Average annual consumption per valid person“ gives us an information on the consumption per patient, regardless of his treatment status. It also enables us to estimate the national-wide consumption of FVIII. As we do know, that there were 930 haemophilia A patients in 2014 (WFH survey 2014) the total consumption will be approximately 52 657 530 IU of FVIII/year in the Czech Republic. In other words, it means, that the total consumption was about 5 IU/capita of FVIII in 2014.

# Consumption of drugs

Drug (IU)	Total annual consumption	Number of treated persons	Average annual consumption per treated child	Number of valid persons	Average annual consumption per valid person
<i>Immunate</i>	1 110 500	19	58 447.4		5 552.5
<i>Fanhdi</i>	1 215 000	8	151 875.0		6 075.0
<i>Octanate</i>	1 851 500	10	185 150.0		9 257.5
<i>Other plasma-derived</i>	181 000	2	90 500.0		905.0
<b>FVIII</b>				200	
<i>Advate</i>	4 356 604	55	79 211.0		21 783.0
<i>Kogenate</i>	1 605 250	27	59 453.7		8 026.3
<i>Recombinate</i>					
<i>Other recombinant</i>	1 106 802	5	221 360.4		5 534.0
<b>FVIII total (IU)</b>	<b>11 426 656</b>	<b>116</b>	<b>98 505.7</b>		<b>57 133.3</b>
<i>Immunine</i>	558 200	10	55 820.0		16 417.6
<i>Octanine</i>	272 000	7	38 857.1		8 000.0
<i>Other recombinant</i>	309 534	3	103 178.0	34	9 103.9
<b>FIX total (IU)</b>	<b>1 139 734</b>	<b>20</b>	<b>56 986.7</b>		<b>33 521.6</b>
aPCC <i>Feiba</i>	5 000	1	5 000.0		
rFVIIa <i>NovoSeven (mg)</i>	1 338 mg	4	334.5 mg		
<b>Plasma-derived factors - TOTAL*</b>	<b>5 188 200</b>	<b>55</b>	<b>94 330.9</b>		<b>22 171.8</b>
<b>Recombinant factors - TOTAL*</b>	<b>7 378 190</b>	<b>86</b>	<b>85 792.9</b>	234	<b>31 530.7</b>
<b>TOTAL CONSUMPTION (IU)*</b>	<b>12 566 390</b>	<b>136</b>	<b>92 399.9</b>		<b>53 702.5</b>

\*plasma-derived factors = Immunate, Fanhdi, Octanate, Immunine, Octanine, Other plasma-derived  
 \*recombinant factors = Advate, Kogenate, Recombinate, BAX 326, Other recombinant  
 \*TOTAL CONSUMPTION = all mentioned drugs excluding Feiba and NovoSeven



Absolute numbers of respective concentrates in this figure refer ONLY to the records within CNHP registry, which have been updated in 2014. The most important information on this slide is „Average annual consumption per treated child“ This reflects nation wide consumption of factor concentrate per treated child.

“Average annual consumption per valid child“ gives us an information of the consumption per child, regardless of his treatment status. It also enables us to estimate the national-wide consumption of FVIII in paediatrics. As we do know, that there were 200 boys (age 0-18 years) with haemophilia A in 2014 (WFH survey 2014) the total consumption will be approximately 11 426 600 IU of FVIII/year for children with haemophilia A in the Czech Republic. This represents around 21,7% of total national consumption, when children represent around 21,5 % of haemophilia population.

This information also suggests, that - in absolute numbers - prophylaxis in children does not cost more, than OD treatment in adults (Please note the difference in body weight between children and adults, though)

# Consumption of drugs

Adults

Drug (IU)	Total annual consumption	Number of treated persons	Average annual consumption per treated person	Number of valid persons	Average annual consumption per valid person
<i>Immunate</i>	7 748 100	97	79 877.3		19 273.9
<i>FanhdI</i>	5 407 350	70	77 247.9		13 451.1
<i>Octanate</i>	452 500	10	45 250.0		1 125.6
<i>Other plasma-derived</i>	1 949 850	5	389 970.0		4 850.4
<b>FVIII</b>				402	
<i>Advate</i>	2 160 500	19	113 710.5		5 374.4
<i>Kogenate</i>	2 345 500	16	146 593.8		5 834.6
<i>Recombinate</i>	1 817 500	23	79 021.7		4 521.1
<i>Other recombinant</i>	778 248	4	194 562.0		1 935.9
<b>FVIII total (IU)</b>	<b>22 659 548</b>	<b>224</b>	<b>101 158.7</b>		<b>56 367.0</b>
<i>Immunine</i>	1 334 500	26	51 326.9		21 524.2
<i>Octanine</i>	2 650 000	13	203 846.2		42 741.9
<i>Other recombinant</i>	291 285	1	291 285.0	62	4 698.2
<b>FIX total (IU)</b>	<b>4 275 786</b>	<b>38</b>	<b>112 520.7</b>		<b>68 964.3</b>
aPCC <i>Feiba</i>	247 000	3	82 333.3		
rFVIIa <i>NovoSeven (mg)</i>	1 715 mg	6	285.8 mg		
<b>Plasma-derived factors - TOTAL*</b>	<b>19 542 300</b>	<b>211</b>	<b>92 617.5</b>		<b>42 117.0</b>
<b>Recombinant factors - TOTAL*</b>	<b>7 393 034</b>	<b>59</b>	<b>125 305.7</b>	464	<b>15 933.3</b>
<b>TOTAL CONSUMPTION (IU)*</b>	<b>26 935 334</b>	<b>262</b>	<b>102 806.6</b>		<b>58 050.3</b>

\*plasma-derived factors = Immunate, FanhdI, Octanate, Immunine, Octanine, Other plasma-derived

\*recombinant factors = Advate, Kogenate, Recombinate, BAX 326, Other recombinant

\*TOTAL CONSUMPTION = all mentioned drugs excluding Feiba and NovoSeven



Czech National Hemophilia Program

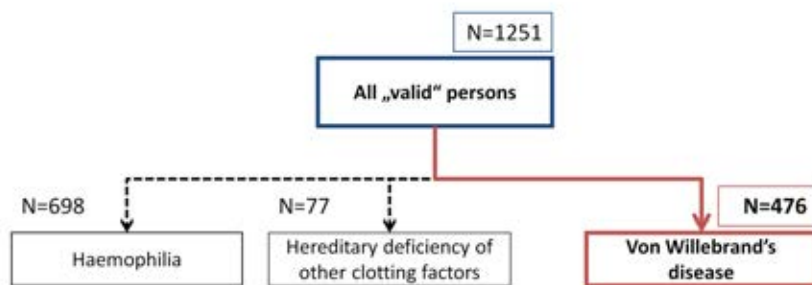
Absolute numbers of respective concentrates in this figure refer ONLY to the records within CNHP registry, which have been updated in 2014. The most important information on this slide is „Average annual consumption per treated person“ This reflects nation wide consumption of factor concentrate per treated adult.

“Average annual consumption per valid person“ gives us an information of the consumption per adult patient, regardless of his treatment status. It also enables us to estimate the national-wide consumption of FVIII in adults. As we do know, that there were 730 adult haemophiliacs A (over 18 years of age) in 2014 (WFH survey 2014) the total consumption will be approximately 41 147 910 IU of FVIII/year for adults with haemophilia A in the Czech Republic.

Part B

## Persons with Von Willebrand's disease

# Sample size



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

# Number of patients in participating centres

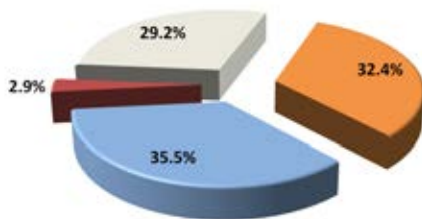
N=476

Paediatric centres	Valid patients	
	N	%
FN Brno – DN – Dpt. of Pediatric Haematology	32	6.7
FN Plzen – Pediatric Dpt.	24	5.0
FN Motol – Dpt. of Pediatric Haematology and Oncology	18	3.8
FNHK – Dpt. of Pediatric Medicine	14	2.9
FN Ostrava – Dpt. of Pediatric Medicine	13	2.7
UnL – Pediatric Dpt. – Haematology	8	1.7
FN Olomouc – Dpt. of Pediatric Medicine	1	0.2

Adult centres	Valid patients	
	N	%
FN Brno – OKH	203	42.6
FN Plzen – UKBH	66	13.9
FN Ostrava – Blood centre	59	12.4
KN Liberec – OKH	24	5.0
FN Olomouc – Haemato-Oncology Dpt.	12	2.5
CB – OKH	1	0.2
FNHK – IV. IHK	1	0.2

# Type of Von Willebrand's disease

N=476



Type of disease	Patients	
	N	%
Type 1	154	32.4
Type 2	169	35.5
Type 2A	71	14.9
Type 2B	10	2.1
Type 2M	24	5.0
Type 2N	11	2.3
Type 2 (not specified)	53	11.1
Type 3	14	2.9
Type not determined / unfilled	139	29.2
Total	476	100.0

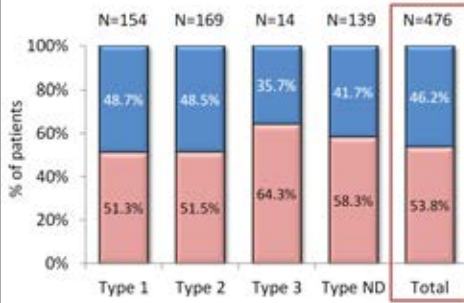


# Sex and current age of patients

N=476

## Sex

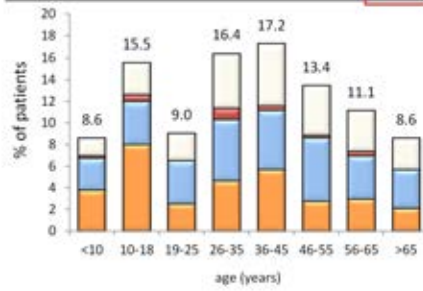
Men (N=220)  
Women (N=256)



Type ND = not determined or unfilled

## Current age\*

	Type 1	Type 2	Type 3	Type ND	Total
N	154	169	14	139	476
Mean	31.5	38.0	32.6	39.8	36.3
Median	30.5	38	32.5	39	36
min - max	2 - 86	1 - 77	7 - 63	3 - 88	1 - 88

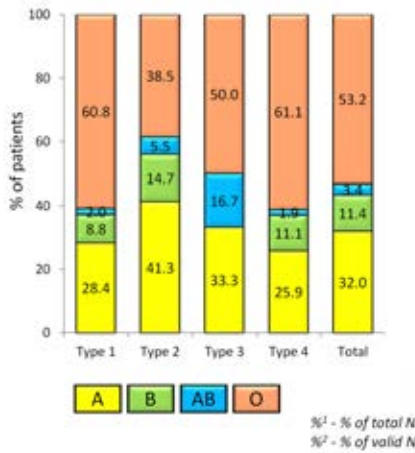


\* age reached in year 2014

Median age of Czech vWDs is below 40 years.

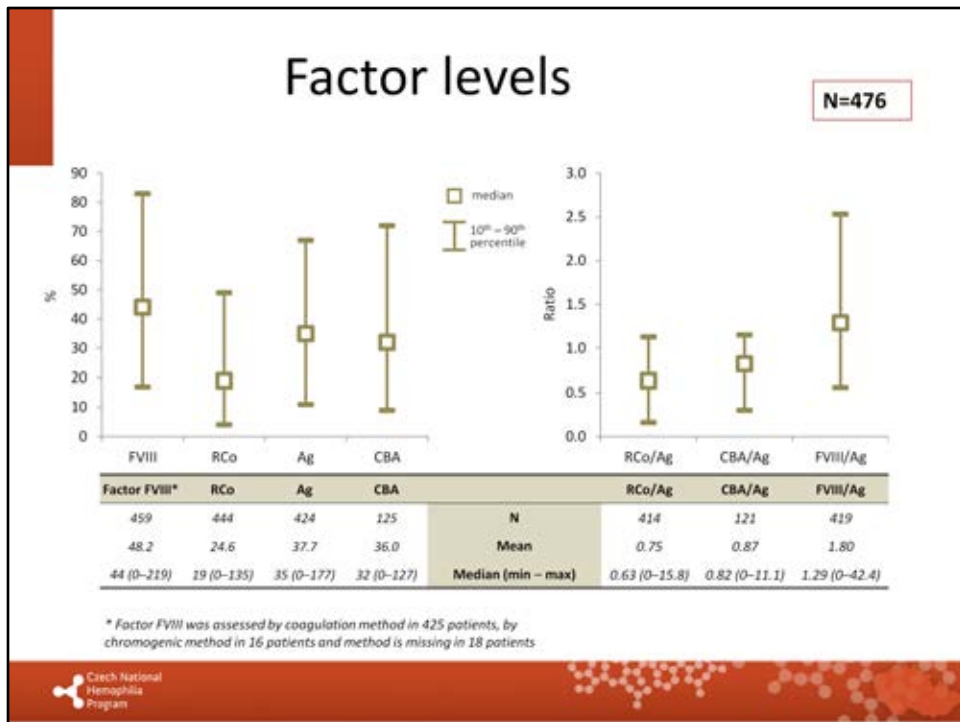
# Blood group

N=476



Blood group	A	B	AB	O	ND	Valid N	Total N
<b>Type 1</b>	N 29	9	2	62	52	102	154
	% <sup>1</sup> 18.8	5.8	1.3	40.3	33.8		100.0
	% <sup>2</sup> 28.4	8.8	2.0	60.8		100.0	
<b>Type 2</b>	N 45	16	6	42	60	109	169
	% <sup>1</sup> 26.6	9.5	3.6	24.9	35.5		100.0
	% <sup>2</sup> 41.3	14.7	5.5	38.5		100.0	
<b>Type 3</b>	N 2	0	1	3	8	6	14
	% <sup>1</sup> 14.3	0.0	7.1	21.4	57.1		100.0
	% <sup>2</sup> 33.3	0.0	16.7	50.0		100.0	
<b>Type ND</b>	N 28	12	2	66	31	108	139
	% <sup>1</sup> 20.1	8.6	1.4	47.5	22.3		100.0
	% <sup>2</sup> 25.9	11.1	1.9	61.1		100.0	
<b>Total</b>	N 104	37	11	173	151	325	476
	% <sup>1</sup> 21.8	7.8	2.3	36.3	31.7		100.0
	% <sup>2</sup> 32.0	11.4	3.4	53.2		100.0	

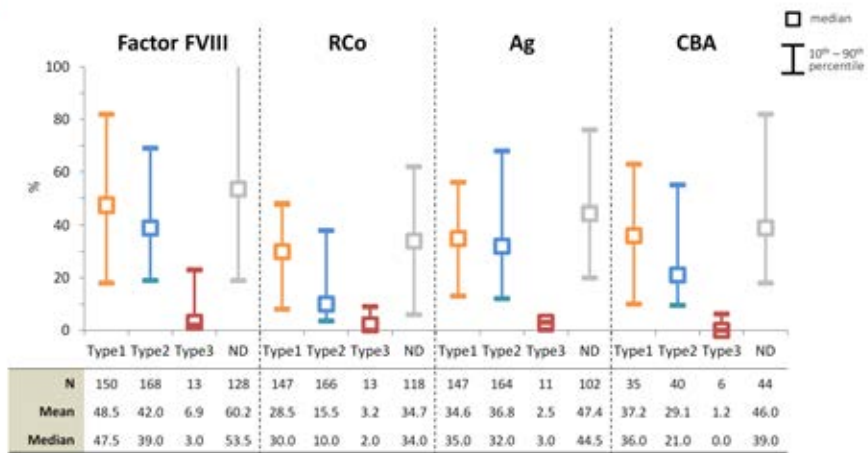
Well known predominance of BG O is confirmed within the registry.



This slide is giving just general overview as it is not linked to different vWD subtypes.

# Factor levels according to type of VWD disease I.

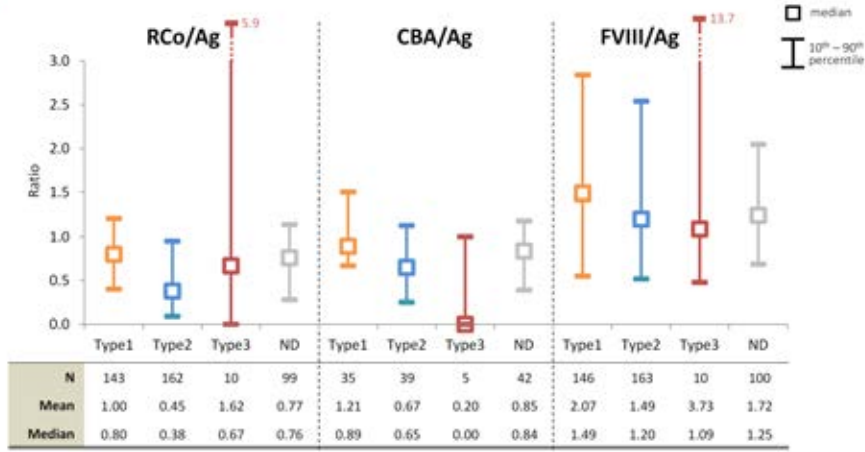
N=476



This and further slides show factor levels in accord with respective vWD subtypes and correlate well with published data.

# Factor levels according to type of VWD disease II.

N=476

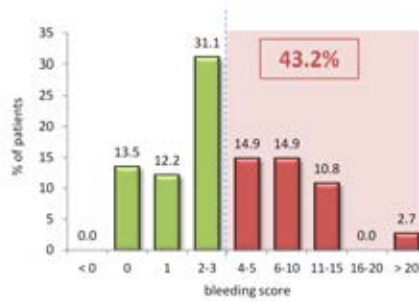


# Bleeding score<sup>1</sup> according to sex

N=167<sup>2</sup>

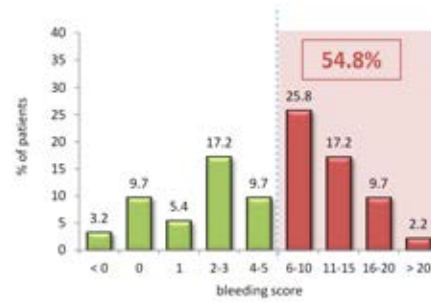
## Men

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



## Women

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



<sup>1</sup> Adult and Pediatric Vincenzo VWD Bleeding Questionnaire and Scoring System

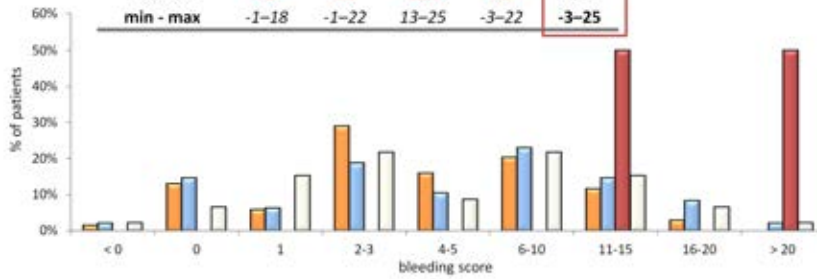
<sup>2</sup> Missing information on bleeding score in 309 patients.

# Bleeding score<sup>1</sup> according to type of disease

N=167<sup>2</sup>

Bleeding score

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



<sup>1</sup> Adult and Pediatric Vincenzo VWD Bleeding Questionnaire and Scoring System

<sup>2</sup> Missing information on bleeding score in 309 patients.

Type 3 has obviously the most heavy bleeding score.

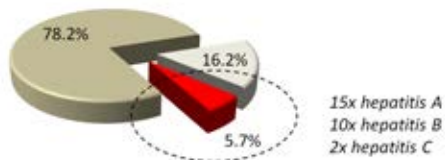
# Other diseases

N=476

## Experienced hepatitis

- Yes (N=27)
- No (N=372)
- Not known (N=77)

None of the patients is HIV positive.



Hepatitis and/or HIV prevalence in vWD patients within CNHP registry



## Consumption of drugs in year 2014

N=476

	Number of treated patients total (type1/type2/type3/typeND)	Total annual consumption (IU)	Average annual consumption per treated patient (IU)
<b>Fanhdi</b>	<b>21 (14/4/2/1)</b>	<b>99 250</b>	<b>4 726.2</b>
<i>of them on prophylaxis</i>	<i>6 (4/2/0/0)</i>	<i>47 000</i>	<i>7 833.3</i>
<b>Haemate P</b>	<b>81 (16/38/7/20)</b>	<b>1 128 500</b>	<b>13 932.1</b>
<i>of them on prophylaxis</i>	<i>12 (4/5/3/0)</i>	<i>419 000</i>	<i>34 916.7</i>
<b>Wilate</b>	<b>2 (0/1/0/1)</b>	<b>28 650</b>	<b>14 325.0</b>
<b>Willfact</b>	<b>1 (0/0/1/0)</b>	<b>215 000</b>	<b>215 000.0</b>
<i>of them on prophylaxis</i>	<i>1 (0/0/1/0)</i>	<i>215 000</i>	<i>215 000.0</i>
<b>Total</b>	<b>105 (30/43/10/22)</b>	<b>1 471 400</b>	<b>14 013.3</b>
<i>of them on prophylaxis</i>	<i>19 (8/7/4/0)</i>	<i>681 000</i>	<i>35 842.1</i>
Total - type 1	30	175 750	5 858.3
Total - type 2	43	449 600	10 455.8
Total - type 3	10	599 000	59 900.0
Total - type ND	22	247 050	11 229.5

Absolute numbers of respective concentrates consumption in this figure refer ONLY to the records within CNHP registry, which have been updated in 2014. The most important information on this slide is „Average annual consumption per treated person“ This aims to reflect nation wide consumption of factor concentrate per treated patient. Shows well the highest consumption in type 3 vWD. Please note, that the numbers of treated patients are relatively small and do vary significantly between different concentrates. This is a source of potential bias. To increase the data validity, we have to increase the number of treated patients recorded within CNHP registry. On the other hand, for vWD treated patients (excluding type 3 patients) the annual consumption per treated patient should reflect the real situation (around 14 000 IU/year) relatively well.