

The status of care for persons with haemophilia registered within CNHP registry Annual Report 2018

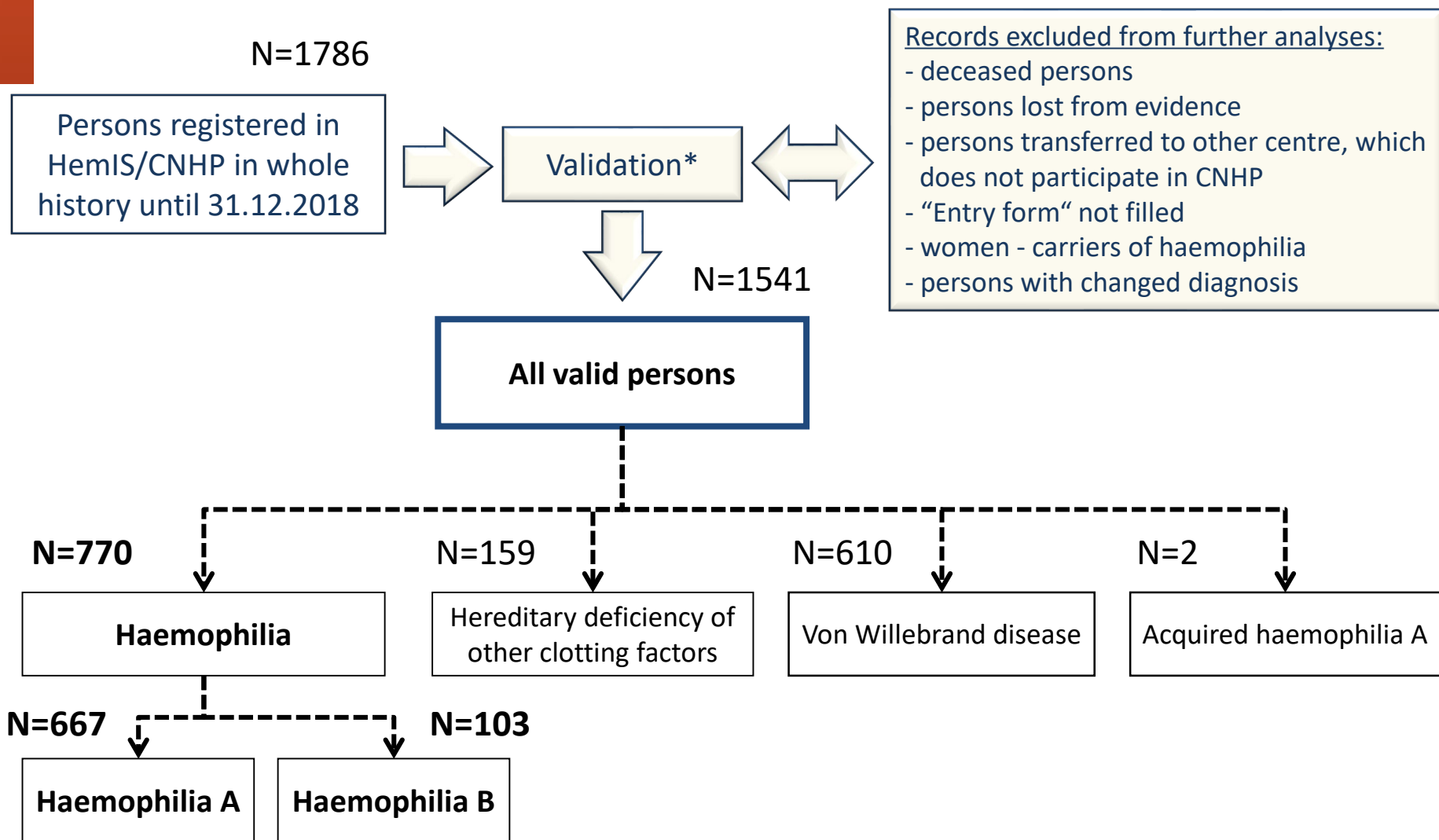
Jan Blatný, Petra Ovesná

on behalf of

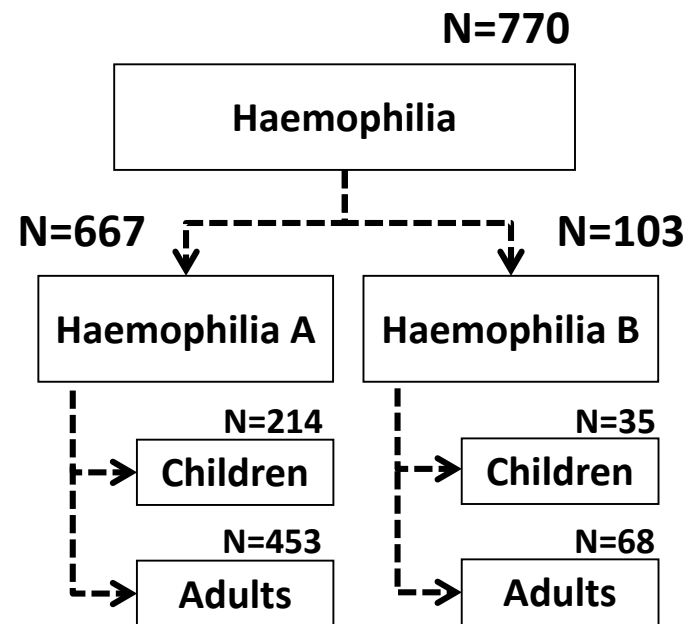
Centres contributing to CNHP registry
(Czech National Haemophilia Programme)

Export date: April 3, 2019

Sample size, valid records



Persons with haemophilia (PWH)



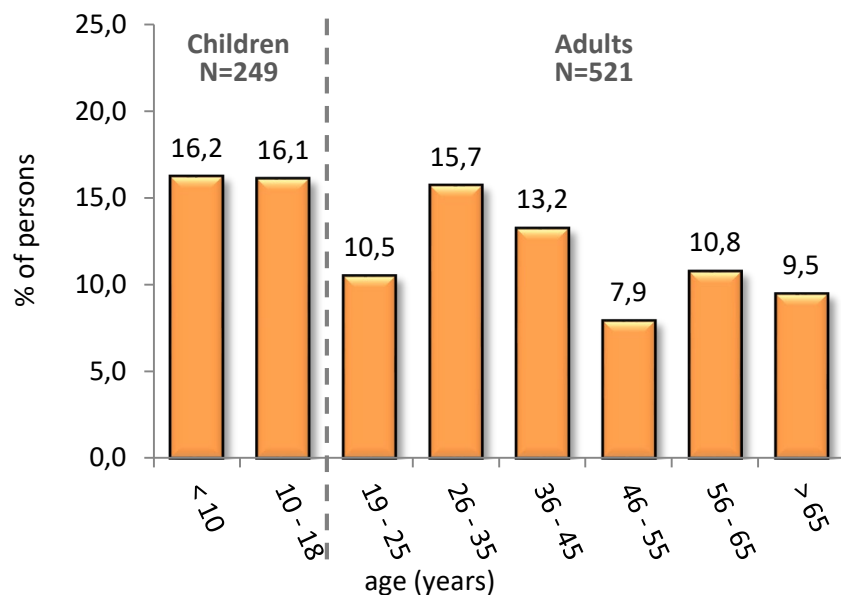
Centres participating in CNHP

| Paediatric centres | Valid persons | |
|---|---------------|------|
| | N | % |
| Prague – Dpt. of Pediatric Haematology and Oncology, CUH Motol | 89 | 11.6 |
| Brno – Dpt. of Pediatric Haematology, CUH Brno | 55 | 7.1 |
| Ústí n.L. – Pediatric Dpt. – Haematology, Masaryk Hospital | 28 | 3.6 |
| Hradec Králové – Dpt. of Pediatric Medicine, UH HK | 22 | 2.9 |
| Ostrava – Dpt. of Pediatric Medicine, UH Ostrava | 20 | 2.6 |
| Olomouc – Dpt. of Pediatric Medicine, UH Olomouc | 19 | 2.5 |
| Pilsen – Pediatric Dpt., UH Pilsen | 17 | 2.2 |
| České Budejovice – Pediatric Dpt., Hospital CB | 15 | 1.9 |

| Adult centres | Valid persons | |
|---|---------------|------|
| | N | % |
| Brno – Dpt. Of Clin Hematol, UH Brno | 152 | 19.7 |
| Ostrava – Blood centre, UH Ostrava | 76 | 9.9 |
| Hradec Králové – IV. Internal and Hematology Dpt., UH HK | 68 | 8.8 |
| Olomouc – Haemato-Oncology Dpt., UH Olomouc | 58 | 7.5 |
| Pilsen – Dpt. of Biochemistry and Hematology, UH Pilsen | 49 | 6.4 |
| Liberec – Dpt. Of Clin Hematol, Hospital Liberec | 37 | 4.8 |
| Ústí n.L. – Dpt. Of Clin Hematol, Masaryk Hospital | 29 | 3.8 |
| České Budějovice – Dpt. Of Clin Hematol, Hospital CB | 28 | 3.6 |
| Pilsen - Hemacentrum | 8 | 1.0 |

Basic demographics

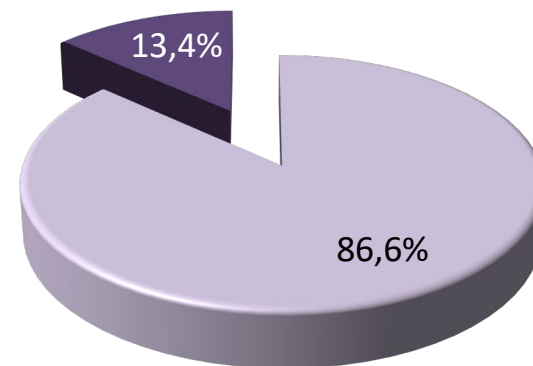
| | Actual age* (years) |
|---------------------------|---------------------|
| N | 770 |
| Mean | 32.8 |
| Median (min - max) | 29 (0 – 96) |



* age reached in year 2018

Type of haemophilia

- Haemophilia A (N=667)
- Haemophilia B (N=103)



Twelve children with haemophilia were born in 2018.

Persons with haemophilia and inhibitors in 2018

Active inhibitors were recorded in 21 persons in the end of 2018 (+cca 5 in another centre, not reported here)

- 3 inhibitors in children with severe HA newly developed in 2018

PWH with inhibitors:

- 13 children and 8 adults
- 20 haemophilia A and 1 haemophilia B
- 17 in severe, 2 in moderate and 2 in mild haemophilia
- 17 high-titre and 4 low-titre (<5BU),
- 11 high response and 6 low response inhibitors; this information not available in 4 PWH with inhibitors
- 4 patients were treated with rFVIIa, 7 patients with aPCC and 3 patients both with rFVIIa and aPCC
 - 2 patients were treated with emicizumab
 - 5 patients were without any „by-pass“ therapy and 2 patients were without any recorded treatment at all

ITT:

- Seven of above mentioned 21 persons (six children, one adult) started ITT in 2018
 - Out of them three children developed inhibitors in 2018, three children and one adult earlier
- Another 6 patients (of them 1 adult) have already been on-going ITT in 2018 (started earlier)

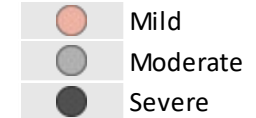
Eradication of inhibitor:

- One child finished ITI successfully in the beginning of January 2018 and for 2018 is considered as inhibitor free.
- Another one child finished ITT unsuccessfully during 2018 (than commenced on emicizumab)
- None of the ITIs started in 2018 led to eradication in 2018. All of them are on-going also in 2019

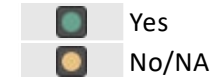
ABR and treatment regimens in patients with inhibitor

| | Type | Year of birth | Severity | ITT | By-pass/emi prophylaxis | Titre | Responder | ABR | Joint / other |
|----|------|---------------|----------|-------|-------------------------|-----------------|-----------|-----|---------------|
| 1 | HA | 2017 | Severe | Yes | Temporary | Low | LR | | 3 0/3 |
| 2 | HA | 2017 | Severe | Yes | Temporary | Low | LR | | 4 1/3 |
| 3 | HA | 2016 | Severe | Yes | OD | High (>5 BU/ml) | NA | | 0 0/0 |
| 4 | HA | 2016 | Severe | Yes | OD | High (>5 BU/ml) | LR | | 1 0/1 |
| 5 | HA | 2015 | Severe | Yes | OD | High (>5 BU/ml) | NA | | 1 0/1 |
| 6 | HA | 2015 | Severe | Yes | OD | Low | LR | | 1 0/1 |
| 7 | HA | 2015 | Severe | Yes | Temporary | High (>5 BU/ml) | HR | | 8 3/5 |
| 8 | HA | 2014 | Severe | Yes | OD | High (>5 BU/ml) | HR | | 1 0/1 |
| 9 | HA | 2011 | Moderate | Yes | Temporary | High (>5 BU/ml) | HR | | 14 3/11 |
| 10 | HA | 2004 | Severe | Yes | Temporary | High (>5 BU/ml) | HR | | 5 / 4 |
| 11 | HA | 2003 | Severe | No/NA | Permanent | High (>5 BU/ml) | HR | | 14 8/6 |
| 12 | HA | 2001 | Severe | Yes | Permanent | High (>5 BU/ml) | LR | | 4 2/2 |
| 13 | HA | 1988 | Mild | No/NA | OD | Low | NA | | 0 0/0 |
| 14 | HA | 1977 | Severe | No/NA | OD | High (>5 BU/ml) | HR | | 0 0/0 |
| 15 | HA | 1975 | Severe | Yes | Permanent | High (>5 BU/ml) | HR | | 11 11/0 |
| 16 | HA | 1971 | Severe | No/NA | OD | High (>5 BU/ml) | HR | | 1 0/1 |
| 17 | HA | 1971 | Severe | No/NA | OD | High (>5 BU/ml) | LR | | 0 0/0 |
| 18 | HA | 1956 | Severe | No/NA | Permanent | High (>5 BU/ml) | HR | | 0 0/0 |
| 19 | HA | 1949 | Mild | No/NA | OD | High (>5 BU/ml) | NA | | 6 / |
| 20 | HA | 1941 | Moderate | Yes | Permanent | High (>5 BU/ml) | HR | | 1 1/0 |
| 21 | HB | 2007 | Severe | No/NA | Temporary | High (>5 BU/ml) | HR | | 8 4/4 |

Severity



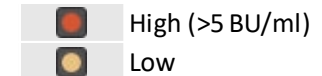
ITT



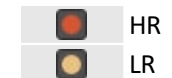
By-pass/emi prophylaxis



Titre



Responder



new in 2018

NA – not available

ABR according to treatment regimen in PWH with inhibitor

| Diagnosis | ITT | By-pass/emi prophylaxis | N | ABR (mean) | ABR (median, min-max) | Joint / other bleeds (median) |
|---------------|-----|-------------------------|---|------------|-----------------------|-------------------------------|
| Haemophilia A | Yes | Permanent | 3 | 5.3 | 4 (1-11) | 2 / 0 |
| | | Temporary | 5 | 6.8 | 5 (3-14) | 2 / 4 |
| | | OD | 5 | 0.8 | 1 (0-1) | 0 / 1 |
| | No | Permanent | 2 | 7.0 | 7 (0-14) | 4 / 3 |
| | | OD | 5 | 1.4 | 0 (0-6) | 0 / 0 |
| Haemophilia B | No | Temporary | 1 | 8.0 | 8 (8-8) | 4 / 4 |

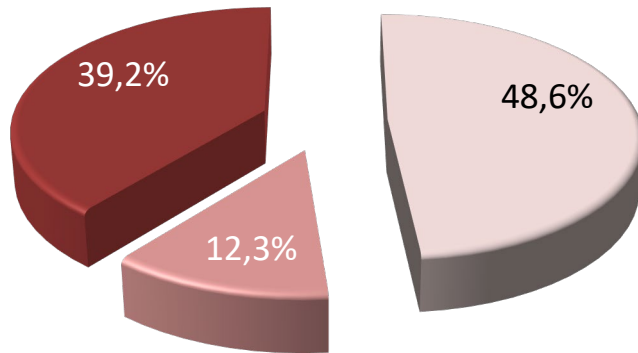
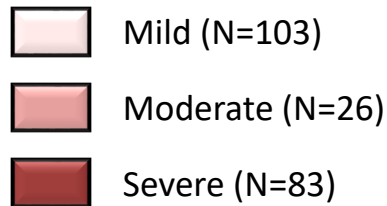
Demographic characteristics

Haemophilia A

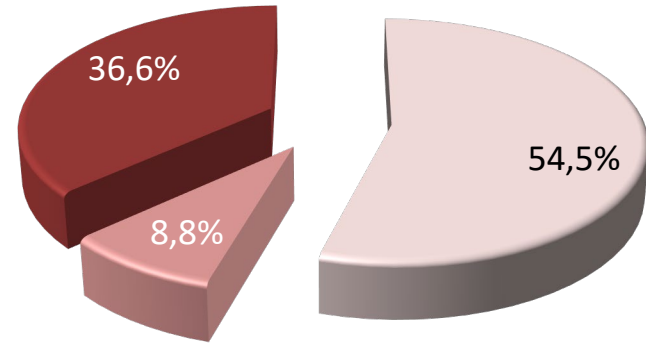
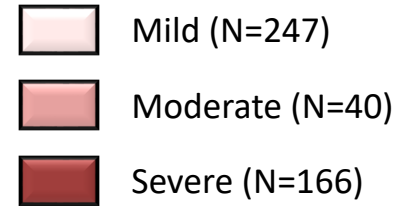


Severity of haemophilia A

Children (N=212*)



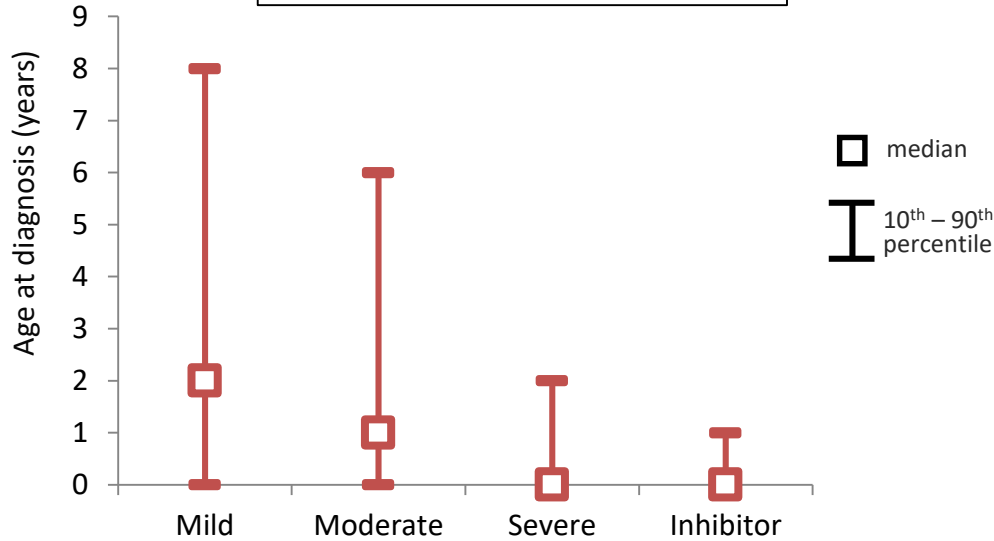
Adults (N=453)



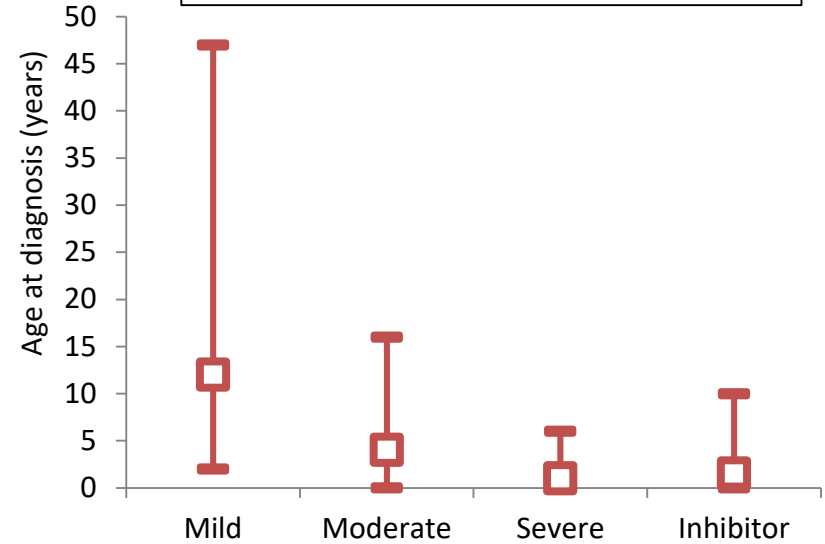
* severity of haemophilia not known in 2 newly born children with haemophilia A

Age at diagnosis according to severity of haemophilia A

Children (N=199¹)



Adults (N=356²)



| Mild* | Moderate* | Severe* | Inhibitor ⁺ | Age at diagnosis (years) | Mild* | Moderate* | Severe* | Inhibitor ⁺ |
|------------|------------|-----------|------------------------|---------------------------|-------------|------------|------------|------------------------|
| 98 | 25 | 76 | 12 | N valid | 204 | 29 | 123 | 8 |
| 2.9 | 2.1 | 0.6 | 0.6 | Mean | 18.9 | 6.0 | 2.4 | 3.3 |
| 2 (0 - 11) | 1 (0 - 11) | 0 (0 - 7) | 0 (0 - 4) | Median (min - max) | 12 (0 - 67) | 4 (0 - 32) | 1 (0 - 38) | 1.5 (0 - 10) |

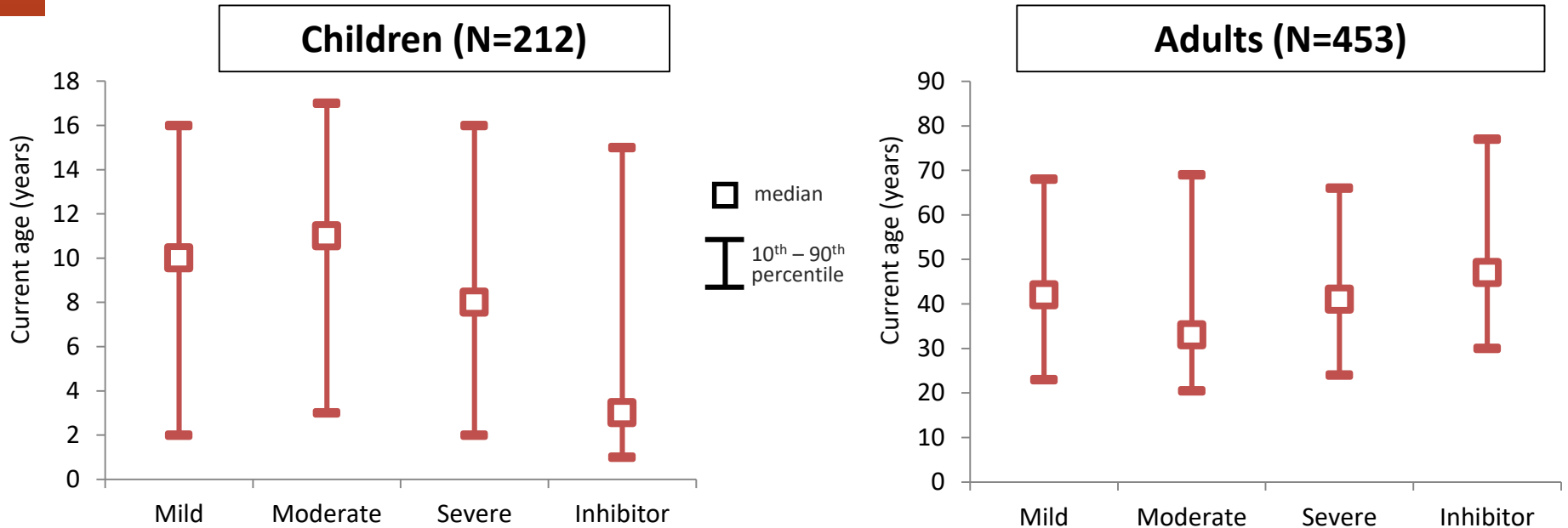
¹ Missing information on year of diagnosis in 13 children.

² Missing information on year of diagnosis in 97 adults.

* including persons with inhibitor

⁺ in 2018

Actual age according to severity of haemophilia A



| Mild* | Moderate* | Severe* | Inhibitor ⁺ | Current age ^{**} (years) | Mild* | Moderate* | Severe* | Inhibitor ⁺ |
|-------------|-------------|------------|------------------------|-----------------------------------|--------------|--------------|--------------|------------------------|
| 103 | 26 | 83 | 12 | N valid | 247 | 40 | 166 | 8 |
| 9.4 | 10.2 | 8.7 | 6.0 | Mean | 44.7 | 40.4 | 43.0 | 52.0 |
| 10 (0 – 18) | 11 (3 – 17) | 8 (0 – 18) | 3 (1 – 17) | Median (min – max) | 42 (19 – 96) | 33 (19 – 77) | 41 (19 – 79) | 47 (30 – 77) |

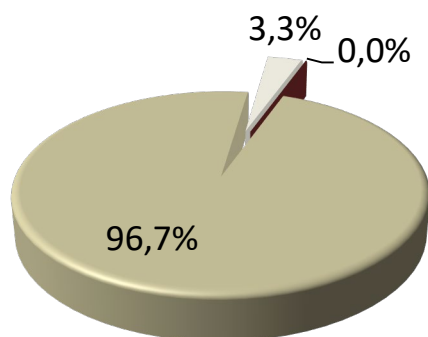
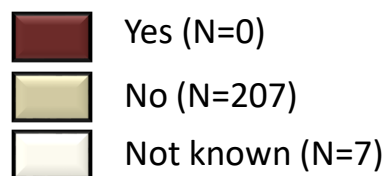
* including persons with inhibitor

⁺ in 2018

^{**} age reached in year 2018

Hepatitis (ever) experienced

Experienced hepatitis



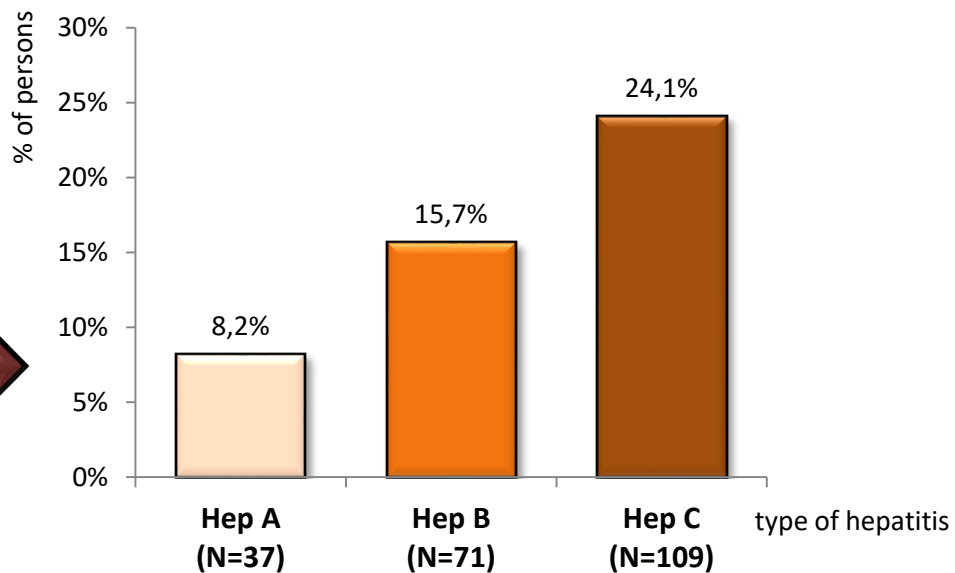
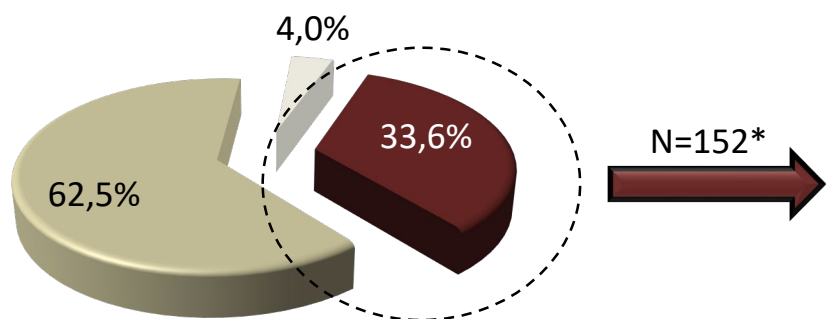
No child has hepatitis.

Data from last completed annual report of each person.

Hepatitis (ever) experienced

Experienced hepatitis

- Yes (N=152)
- No (N=283)
- Not known (N=18)






31 adults are HCV RNA positive

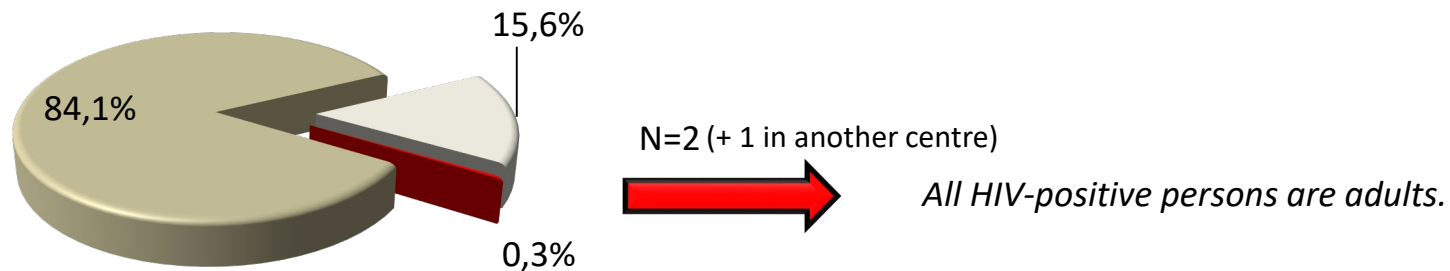
Data from last completed annual report of each person.

*Total of 217 cases of hepatitis in 152 persons. One person may have more types of hepatitis recorded.

HIV

HIV

-  Positive (N=2)
-  Negative (N=561)
-  Not known / not available (N=104)



Data from last completed annual report of each person.

Treatment outcomes and bleeding frequency

Haemophilia A



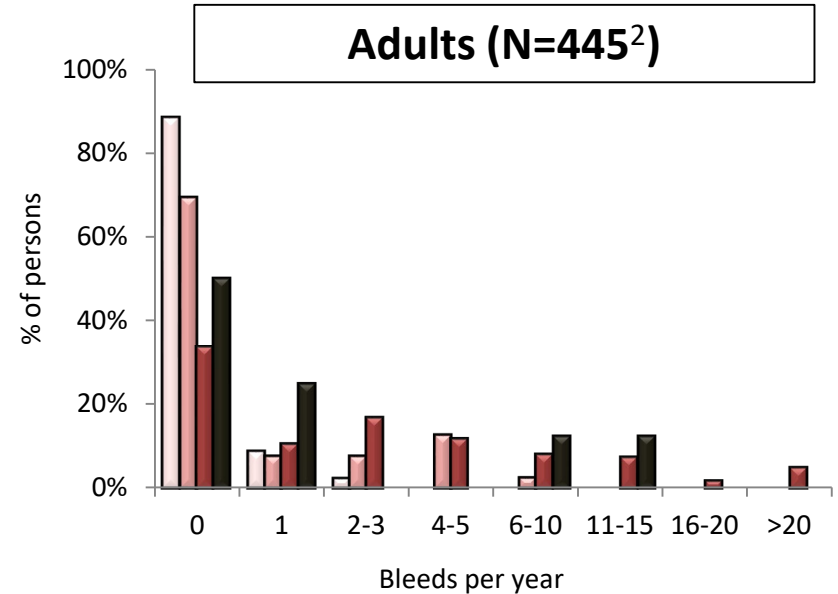
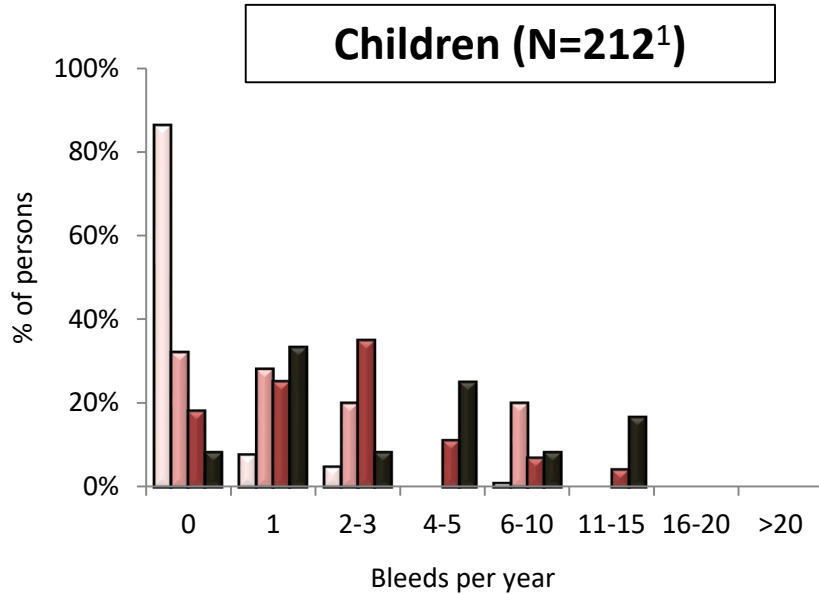
All
Haem A
N=667

Data from year 2018 – sample size

| | Valid persons | | → | Persons with <u>valid</u> annual report | | → | Persons <u>examined</u> | | → | Persons <u>treated</u> | |
|------------------------|---------------|------|---|---|-------|---|-------------------------|-------|---|------------------------|-------|
| | N | % | | N | % | | N | % | | N | % |
| All | 667 | 100% | → | 643 | 96.4% | → | 508 | 76.2% | → | 356 | 53.4% |
| of them with inhibitor | 20 | | | 20 | | | 19 | | | 18 | |
| Children | 214 | 100% | → | 208 | 97.2% | → | 186 | 86.9% | → | 122 | 57.0% |
| of them with inhibitor | 12 | | | 12 | | | 12 | | | 12 | |
| Adults | 453 | 100% | → | 435 | 96.0% | → | 322 | 71.1% | → | 234 | 51.7% |
| of them with inhibitor | 8 | | | 8 | | | 7 | | | 6 | |



Frequency of bleeding requiring treatment in 2018



| Mild* | Moderate* | Severe* | Inhibitor | Frequency of bleeding | Mild* | Moderate* | Severe* | Inhibitor |
|------------|-----------|------------|--------------|-----------------------|-------------|------------|------------|--------------|
| 103 | 25 | 72 | 12 | N valid | 245 | 39 | 153 | 8 |
| 0.3 | 2.2 | 2.7 | 4.7 | Mean | 0.2 | 1.1 | 4.5 | 2.4 |
| 0 (0 – 7) | 1 (0 – 9) | 2 (0 – 15) | 3.5 (0 – 14) | Median (min – max) | 0 (0 – 3) | 0 (0 – 10) | 2 (0 – 39) | 0.5 (0 – 11) |
| 89 (86.4%) | 8 (32%) | 13 (18.1%) | 1 (8.3%) | N (%) with no bleed | 217 (88.6%) | 27 (69.2%) | 54 (33.5%) | 4 (50%) |

* without inhibitor

¹ Missing severity in 2 children.

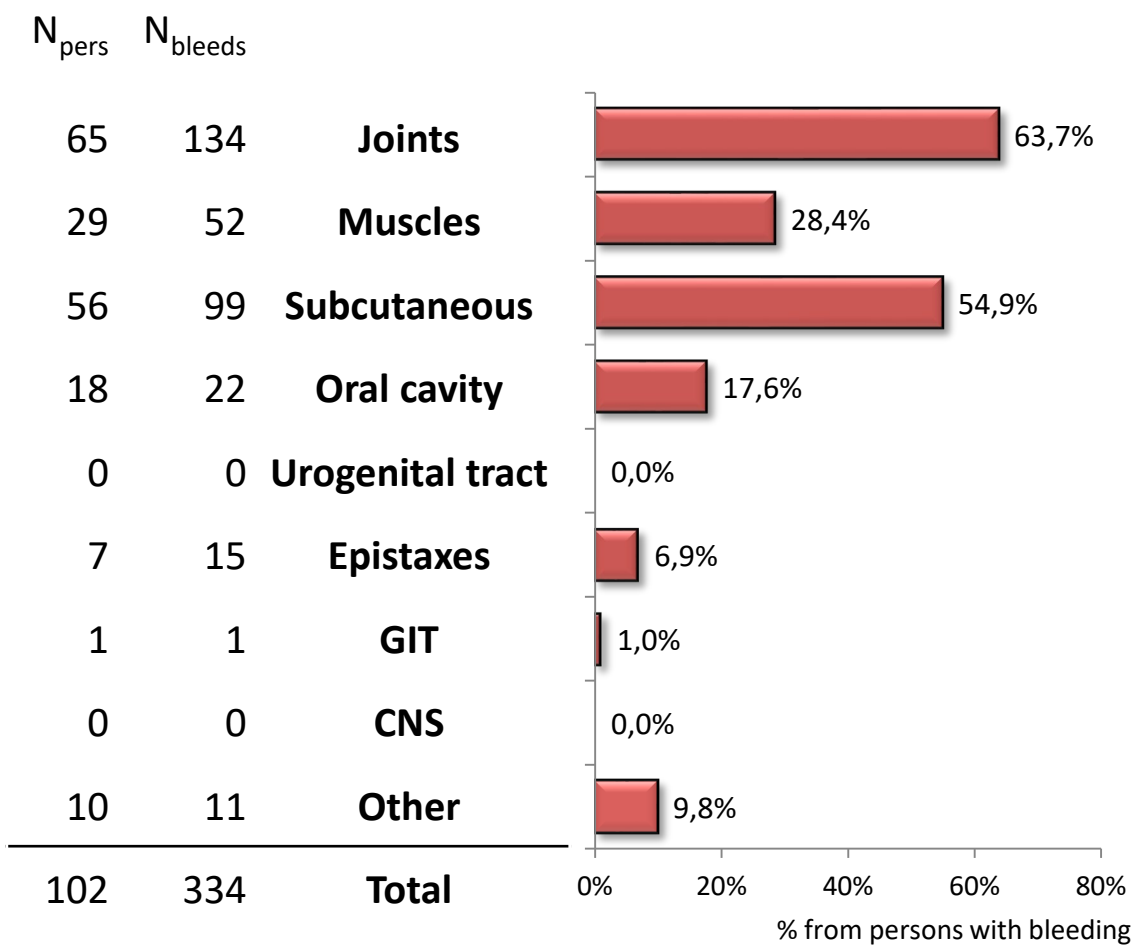
² Frequency of bleeding is missing in 8 adults.

Location of bleeds in 2018

102 (47.7%) children experienced bleeding requiring treatment at least once in year; 334 bleeds were recorded in total, 25 bleeds required hospitalization.

All of these 102 children have recorded location of their bleeds.

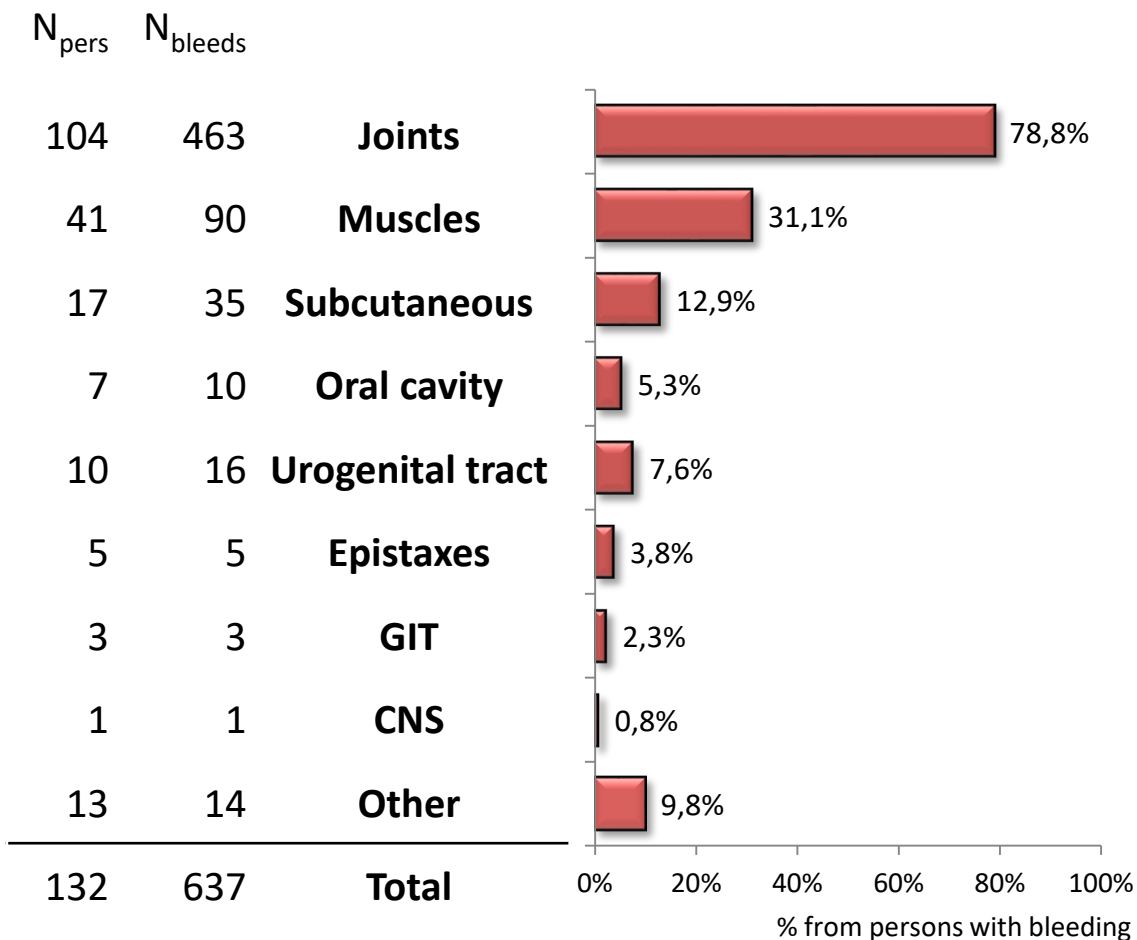
112 (52.3%) children recorded no bleed during year 2018.



Location of bleeds in 2018

143 (32.1%) adults experienced bleeding requiring treatment at least once in year; 788 bleeds were recorded in total, 24 bleeds required hospitalization.

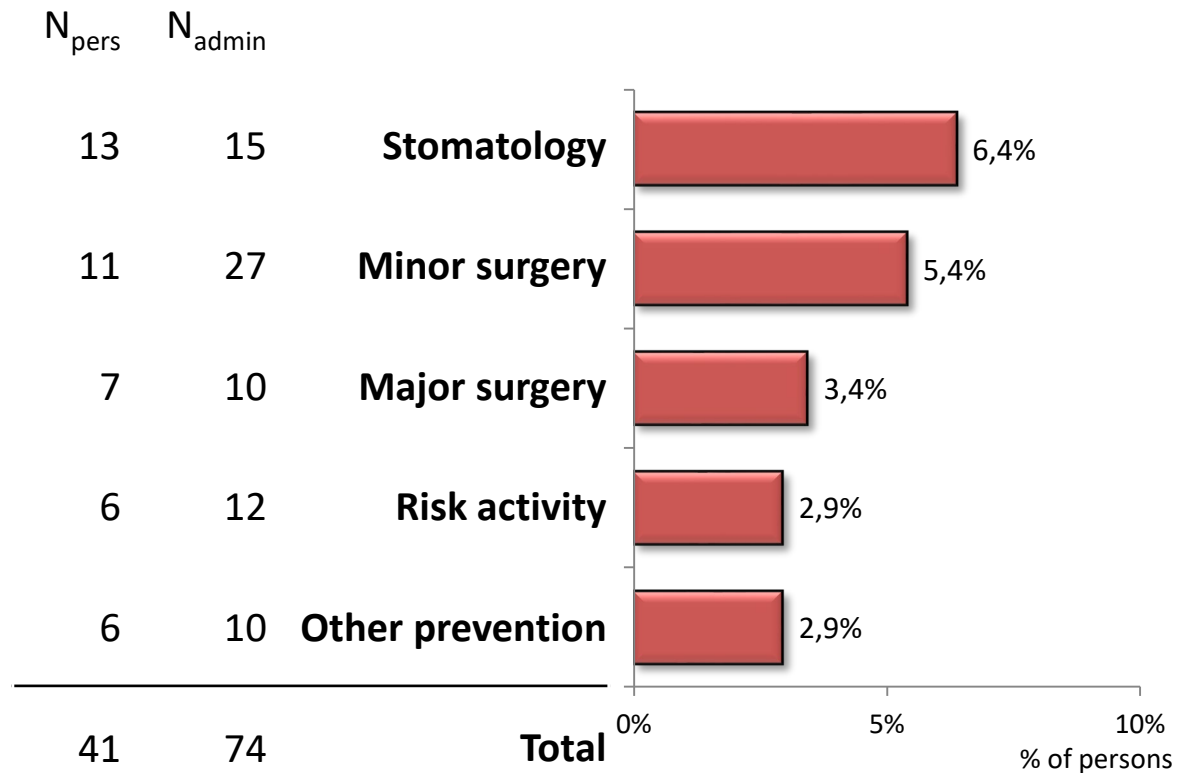
132 of these 143 adults have recorded location of their bleeds. Localization is not known in 11 adults. 302 (67.9%) adults have recorded no bleed during year 2018.



¹Frequency of bleeding is missing in 8 adults.

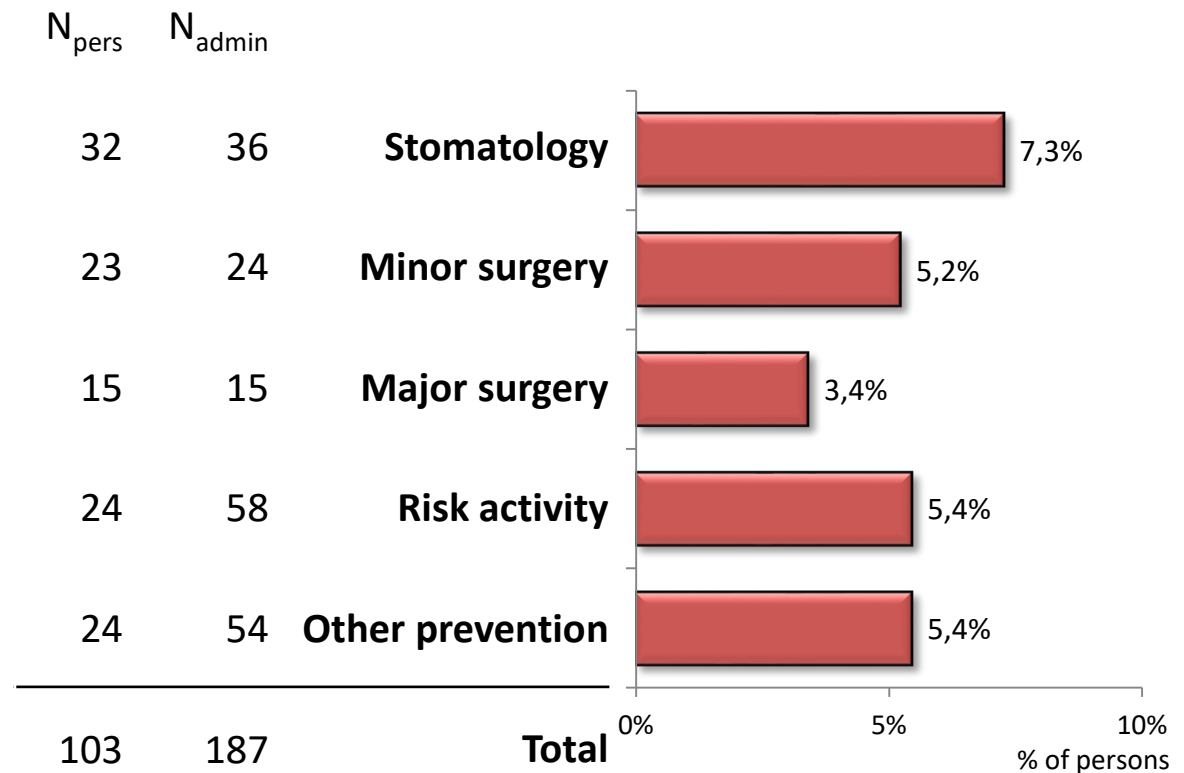
Preventive administration in 2018

41 (19.2%) children were given factor to prevent bleeding during/before risk situation.
74 preventive administrations were recorded in total.



Preventive administration in 2018

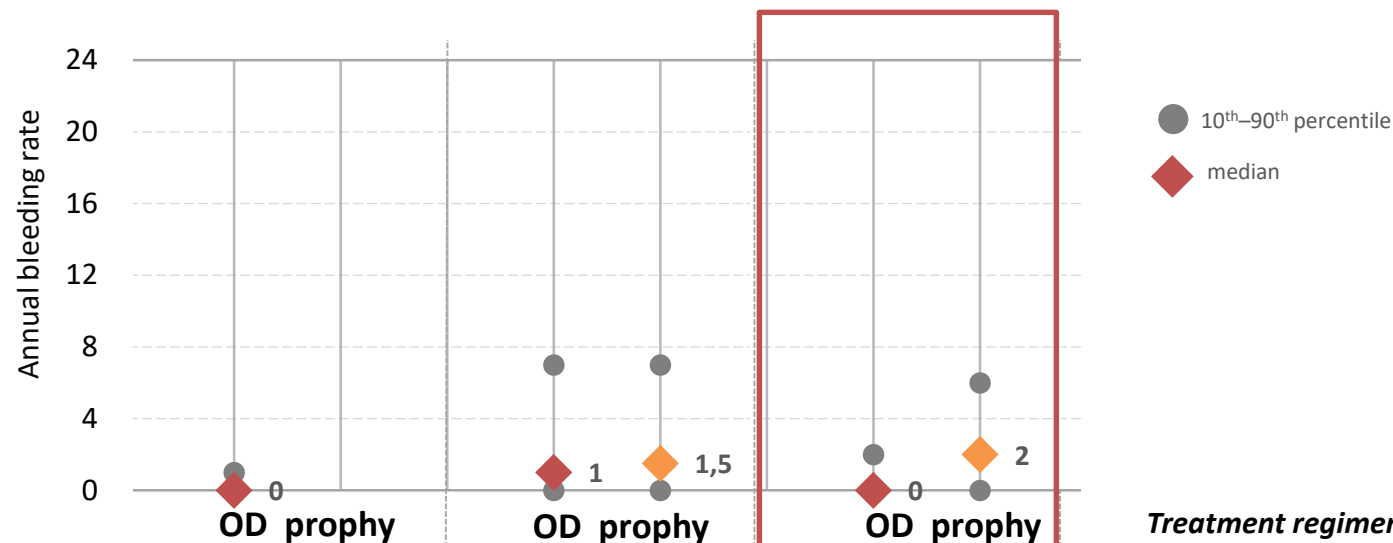
103 (22.7%) persons were given factor to prevent bleeding during/before risk situation.
187 preventive administrations were recorded in total.



ABR according to treatment regimen Haemophilia A without inhibitor



Annual bleeding rate according to treatment regimen



| Frequency of bleeding | Mild* | | Moderate* | | Severe* | |
|---|-----------|---|-----------|-------------|------------|------------|
| N valid | 103 | 0 | 17 | 8 | 6 | 66 |
| Mean | 0.3 | | 1.8 | 3.0 | 0.5 | 2.9 |
| Median (min – max) | 0 (0 – 7) | | 1 (0 – 9) | 1.5 (0 – 7) | 0 (0 – 2) | 2 (0 – 15) |
| Total no of recorded bleeds | 27 | | 31 | 24 | 3 | 192 |
| children on permanent prophylaxis | 0 (0%) | | 8 (32%) | | 66 (91.7%) | |
| % of factor (FVIII) consumed by children on permanent prophylaxis | - | | 89.3% | | 99.9% | |

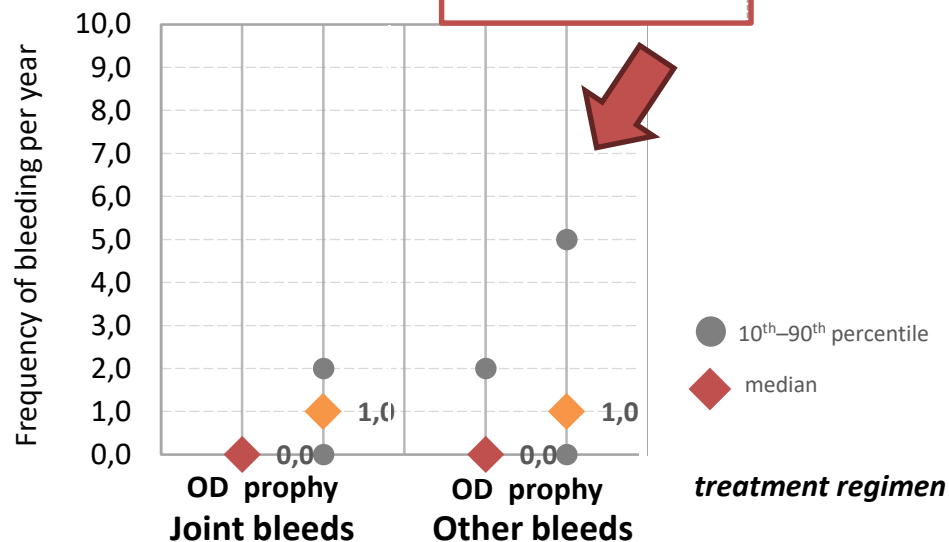
Treatment regimen:
OD = on demand and/or temporary prophylaxis
prophy = permanent prophylaxis

* without inhibitor,
missing severity in 2 children

Joint and other bleeds according to treatment regimen

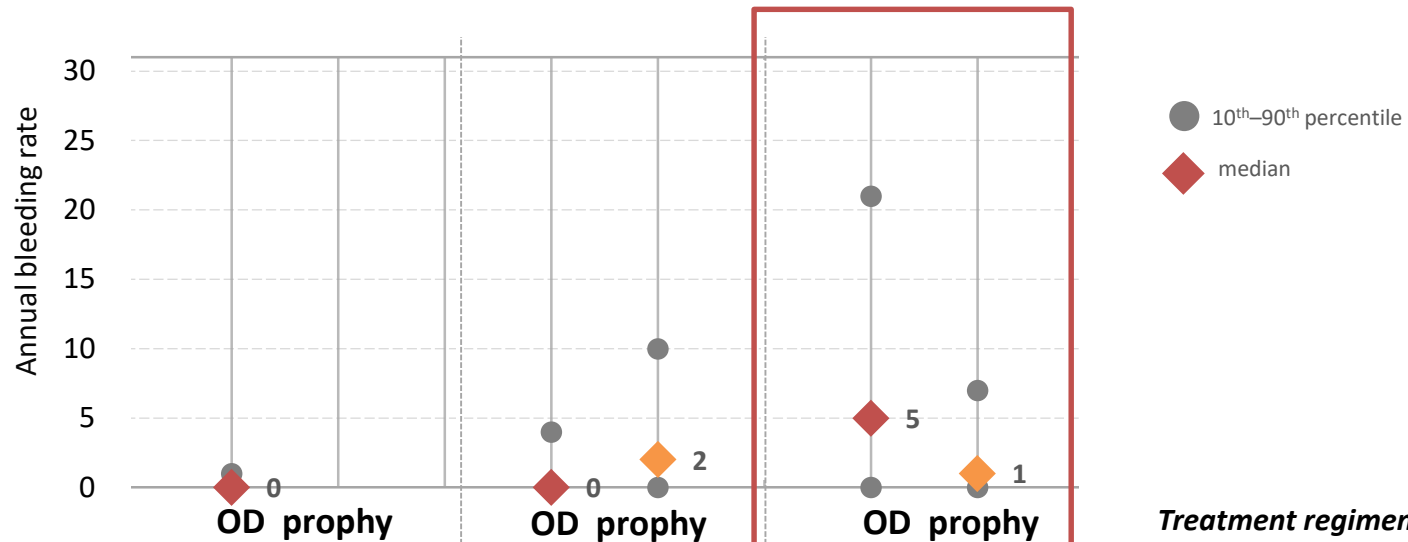
| Frequency of bleeding | Mild* | | Moderate* | | Severe* | |
|-----------------------------|---------|--------|-----------|-----------|---------|----------|
| | OD | prophy | OD | prophy | OD | prophy |
| Treatment regimen | OD | prophy | OD | prophy | OD | prophy |
| N valid | 103 | 0 | 17 | 8 | 6 | 66 |
| JOINT BLEEDS | | | | | | |
| Mean | 0.1 | | 0.6 | 1.5 | 0.0 | 1.3 |
| Median (range) | 0 (0-3) | | 0 (0-3) | 1 (0-6) | 0 (0-0) | 1 (0-10) |
| Total no of recorded bleeds | 7 | | 11 | 12 | 0 | 87 |
| OTHER BLEEDS | | | | | | |
| Mean | 0.2 | | 1.2 | 1.5 | 0.5 | 1.6 |
| Median (range) | 0 (0-6) | | 1 (0-7) | 0.5 (0-5) | 0 (0-2) | 1 (0-8) |
| Total no of recorded bleeds | 20 | | 20 | 12 | 3 | 105 |

* without inhibitor,
missing severity in 2 children



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

Annual bleeding rate according to treatment regimen



| Frequency of bleeding | Mild* | | Moderate* | | Severe* | |
|---|-----------|---|-----------|------------|------------|------------|
| N valid | 245 | 0 | 33 | 6 | 57 | 96 |
| Mean | 0.2 | | 0.7 | 3.2 | 7.3 | 2.9 |
| Median (min – max) | 0 (0 – 3) | | 0 (0 – 5) | 2 (0 – 10) | 5 (0 – 28) | 1 (0 – 39) |
| Total no of recorded bleeds | 37 | | 22 | 19 | 416 | 275 |
| adults on permanent prophylaxis | 0 (0%) | | 6 (15.4%) | | 96 (59.6%) | |
| % of factor (FVIII) consumed by adults on permanent prophylaxis | - | | 73.5% | | 87.0% | |

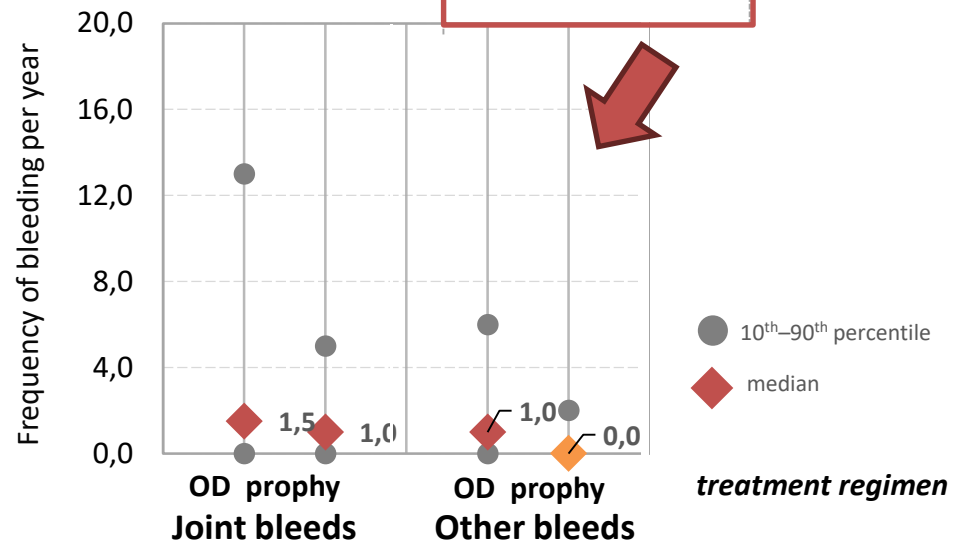
Treatment regimen:
OD = on demand and/or temporary prophylaxis
prophy = permanent prophylaxis

* without inhibitor;
 missing ABR in 8 adults

Joint and other bleeds according to treatment regimen

* without inhibitor; missing location of bleeds in 11 adults

| Frequency of bleeding | Mild* | | Moderate* | | Severe* | |
|-----------------------------|---------|--------|-----------|-----------|------------|----------|
| | OD | prophy | OD | prophy | OD | prophy |
| Treatment regimen | OD | prophy | OD | prophy | OD | prophy |
| N valid | 245 | 0 | 33 | 6 | 49 | 93 |
| JOINT BLEEDS | | | | | | |
| Mean | 0.0 | | 0.5 | 2.5 | 4.2 | 2.2 |
| Median (range) | 0 (0-1) | | 0 (0-4) | 1.5 (0-7) | 1.5 (0-22) | 1 (0-39) |
| Total no of recorded bleeds | 12 | | 17 | 15 | 203 | 204 |
| OTHER BLEEDS | | | | | | |
| Mean | 0.1 | | 0.2 | 0.7 | 1.6 | 0.7 |
| Median (range) | 0 (0-3) | | 0 (0-3) | 0 (0-3) | 1 (0-9) | 0 (0-14) |
| Total no of recorded bleeds | 25 | | 5 | 4 | 77 | 62 |



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

Adults
Haem A
N=437*

* without inhibitor;
missing ABR in 8 adults

ABR according to treatment regimen and age

| Frequency of bleeding | Mild* | | Moderate* | | Severe* | | |
|---|---------------|--------|------------------|------------|--------------------|-------------------|--|
| | OD | Prophy | OD | Prophy | OD | Prophy | |
| Treatment regimen | OD | Prophy | OD | Prophy | OD | Prophy | Adults (haem A) born <u>before 1990</u> N=328 |
| N valid | 187 | 0 | 19 | 4 | 53 | 65 | |
| Mean | 0.1 | | 0.5 | 4.3 | 7.7 | 2.9 | |
| Median (min – max) | 0 (0 – 3) | | 0 (0 – 5) | 3 (1 – 10) | 5 (0 – 28) | 1 (0 – 39) | |
| Total no of recorded bleeds | 27 | | 9 | 17 | 407 | 187 | |
| adults on permanent prophylaxis | 0 (0%) | | 4 (17.4%) | | 65 (52.4%) | | |
| % of factor (FVIII) consumed by adults on permanent prophylaxis | - | | 70.0% | | 81.8% | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | Adults (haem A) born in <u>1990 or later</u> N=109 |
| N valid | 58 | 0 | 14 | 2 | 4 | 31 | |
| Mean | 0.2 | | 0.9 | 1.0 | 2.3 | 2.8 | |
| Median (min – max) | 0 (0 – 2) | | 0 (0 – 5) | 1 (0 – 2) | 0.5 (0 – 8) | 1 (0 – 29) | |
| Total no of recorded bleeds | 10 | | 13 | 2 | 9 | 88 | |
| adults on permanent prophylaxis | 0 (0%) | | 2 (12.5%) | | 31 (83.8%) | | |
| % of factor (FVIII) consumed by adults on permanent prophylaxis | - | | 81.1% | | 98.8% | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |

Joint and other bleeds according to treatment regimen and age

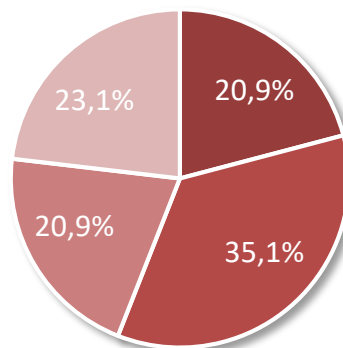
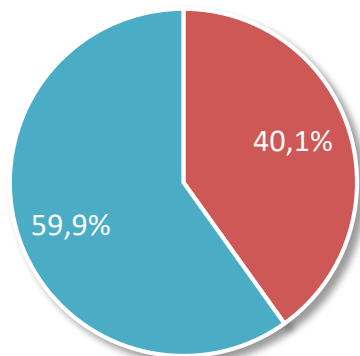
* without inhibitor; missing location of bleeds in 11 adults

| Frequency of bleeding | Mild* | | Moderate* | | Severe* | | Adults (haem A) born <u>before 1990</u> N=318 |
|-----------------------------|---------|--------|-----------|-----------|------------|----------|---|
| Treatment regimen | OD | prophy | OD | prophy | OD | prophy | |
| N valid | 187 | 0 | 19 | 4 | 45 | 63 | |
| JOINT BLEEDS | | | | | | | |
| Mean | 0.0 | | 0.4 | 3.3 | 4.5 | 2.5 | |
| Median (range) | 0 (0-1) | | 0 (0-4) | 2.5 (1-7) | 2.5 (0-22) | 1 (0-39) | |
| Total no of recorded bleeds | 9 | | 8 | 13 | 200 | 156 | |
| OTHER BLEEDS | | | | | | | |
| Mean | 0.1 | | 0.1 | 1.0 | 1.6 | 0.4 | |
| Median (range) | 0 (0-3) | | 0 (0-1) | 0.5 (0-3) | 1 (0-9) | 0 (0-5) | |
| Total no of recorded bleeds | 18 | | 1 | 4 | 71 | 27 | |

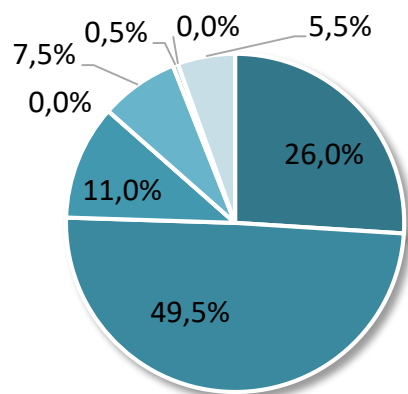
| Frequency of bleeding | Mild* | | Moderate* | | Severe* | | Adults (haem A) born in <u>1990 or later</u> N=108 |
|-----------------------------|---------|--------|-----------|---------|-----------|------------|--|
| Treatment regimen | OD | prophy | OD | prophy | OD | prophy | |
| N valid | 58 | 0 | 14 | 2 | 4 | 30 | |
| JOINT BLEEDS | | | | | | | |
| Mean | 0.1 | | 0.6 | 1.0 | 0.8 | 1.6 | |
| Median (range) | 0 (0-1) | | 0 (0-4) | 1 (0-2) | 0.5 (0-2) | 0.5 (0-14) | |
| Total no of recorded bleeds | 3 | | 9 | 2 | 3 | 48 | |
| OTHER BLEEDS | | | | | | | |
| Mean | 0.1 | | 0.3 | 0.0 | 1.5 | 1.2 | |
| Median (range) | 0 (0-2) | | 0 (0-3) | 0 (0-0) | 0 (0-6) | 0 (0-14) | |
| Total no of recorded bleeds | 7 | | 4 | 0 | 6 | 35 | |

Location and etiology of bleeds

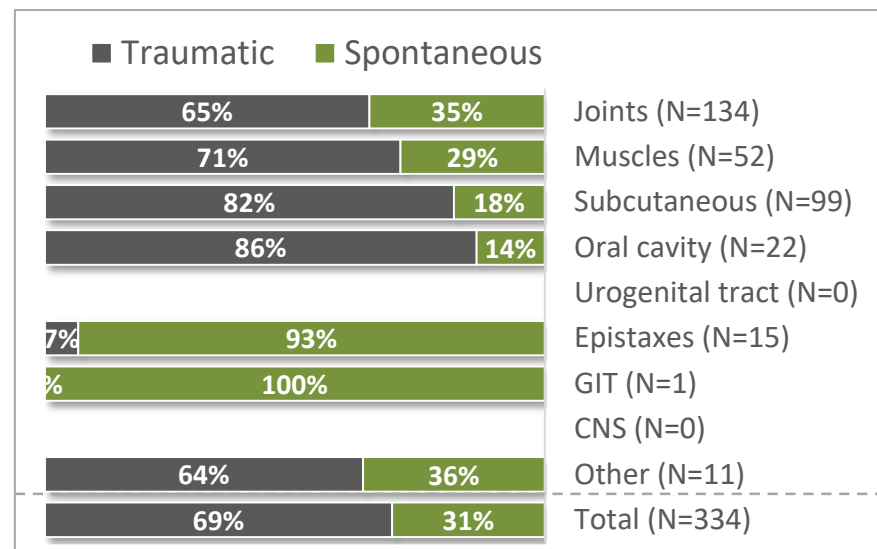
- Joints (N=134)
- Other (N=200)



- Knee (N=28)
- Ankle (N=47)
- Elbow (N=28)
- Other joint (N=31)



- Muscles (N=52)
- Subcutaneous (N=99)
- Oral cavity (N=22)
- Urogenital tract (N=0)
- Epistaxes (N=15)
- GIT (N=1)
- CNS (N=0)
- Other (N=11)



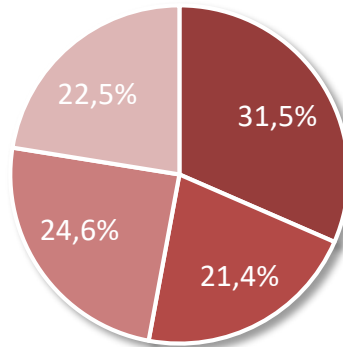
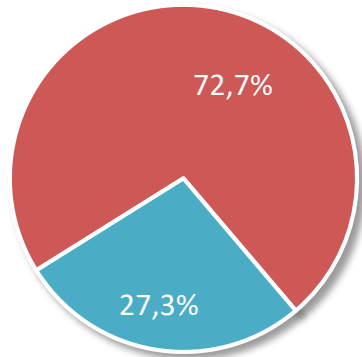
Detailed treatment of bleeds

| | Joints | Muscles | Subcutaneous | Oral cavity | Urogenital tract | Epistaxes | GIT | CNS | Other | Total |
|--|---------------|---------------|---------------|--------------|------------------|---------------|---------------|-----|---------------|-------------------|
| No. of bleeds | 134 | 52 | 99 | 22 | 0 | 15 | 1 | 0 | 11 | 334 |
| FVIII consumption per bleed (IU), valid N | 122 | 45 | 83 | 22 | | 15 | 1 | | 10 | 298 |
| geometric mean | 1740.5 | 2457.6 | 1005.4 | 1046.0 | | 815.4 | 3500.0 | | 2800.8 | 1485.8 |
| median | 1500.0 | 2000.0 | 1000.0 | 875.0 | | 1000.0 | 3500.0 | | 2750.0 | 1375.0 |
| min – max | 250–25000 | 500–130500 | 500–12000 | 500–20500 | | 500–2000 | 3500–3500 | | 500–20000 | 250–130500 |
| sum | 336250 | 421250 | 126000 | 51000 | | 13250 | 3500 | | 55500 | 1006550 |
| No. of doses per bleed | | | | | | | | | | |
| geometric mean | 1.7 | 2.4 | 1.5 | 1.8 | | 1.0 | 7.0 | | 4.4 | 1.8 |
| median | 1 | 2 | 1 | 1 | | 1 | 7 | | 4 | 1 |
| min – max | 1–112 | 1–60 | 1–44 | 1–20 | | 1–1 | 7–7 | | 1–56 | 1–112 |
| Duration of therapy per bleed, days | | | | | | | | | | |
| geometric mean | 1.7 | 2.3 | 1.5 | 2.2 | | 1.0 | 4.0 | | 6.1 | 1.8 |
| median | 1 | 2 | 1 | 2 | | 1 | 4 | | 8 | 1 |
| min – max | 1–56 | 1–66 | 1–31 | 1–16 | | 1–1 | 4–4 | | 1–59 | 1–66 |
| N (%) with hospitalization | 3 (2.2%) | 5 (9.6%) | 7 (7.1%) | 4 (18.2%) | | 0 (0%) | 1 (100%) | | 5 (45.5%) | 25 (7.5%) |
| N (%) with rebleeding | 8 (6%) | 0 (0%) | 0 (0%) | 4 (18.2%) | | 3 (20%) | 0 (0%) | | 1 (9.1%) | 16 (4.8%) |

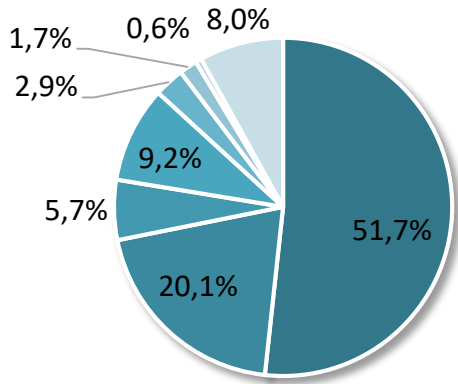
Location and etiology of bleeds

* number of bleeds

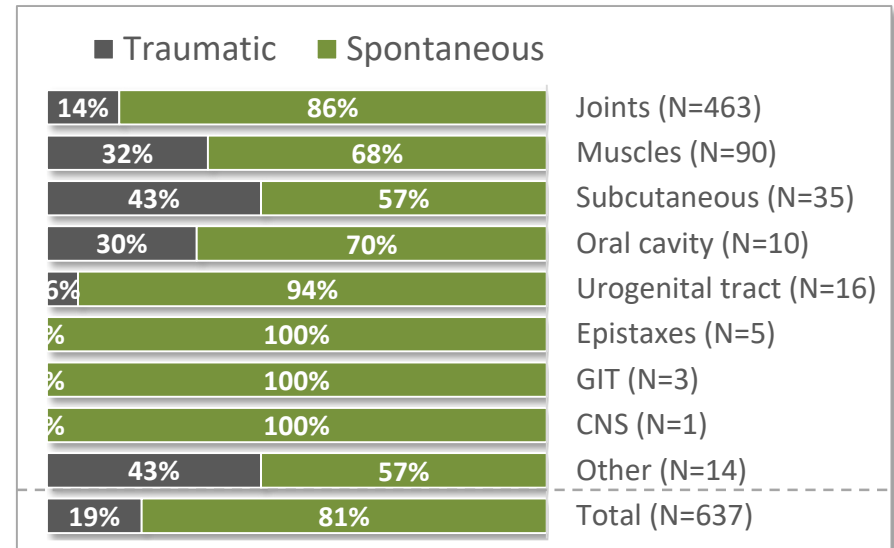
- Joints (N=463)
- Other (N=174)



- Knee (N=146)
- Ankle (N=99)
- Elbow (N=114)
- Other joint (N=104)



- Muscles (N=90)
- Subcutaneous (N=35)
- Oral cavity (N=10)
- Urogenital tract (N=16)
- Epistaxes (N=5)
- GIT (N=3)
- CNS (N=1)
- Other (N=14)



Detailed treatment of bleeds

* number of bleeds

| | Joints | Muscles | Subcutaneous | Oral cavity | Urogenital tract | Epistaxes | GIT | CNS | Other | Total |
|--|---------------|---------------|---------------|---------------|------------------|---------------|----------------|-----------------|---------------|-------------------|
| No. of bleeds | 463 | 90 | 35 | 10 | 16 | 5 | 3 | 1 | 14 | 637 |
| FVIII consumption per bleed (IU), valid N | 451 | 89 | 35 | 10 | 16 | 5 | 3 | 1 | 14 | 624 |
| geometric mean | 2004.6 | 3328.3 | 3307.6 | 1669.3 | 7838.4 | 2940.9 | 37755.6 | 467000.0 | 2997.0 | 2369.9 |
| median | 2000.0 | 3000.0 | 3000.0 | 1500.0 | 7750.0 | 2000.0 | 30000.0 | 467000.0 | 2000.0 | 2000.0 |
| min – max | 500–59000 | 500–44000 | 1000–23000 | 500–7000 | 500–140500 | 1000–10000 | 23000–78000 | | 1000–13000 | 500–467000 |
| sum | 1522500 | 457000 | 167000 | 23500 | 358500 | 20500 | 131000 | 467000 | 57000 | 3204000 |
| No. of doses per bleed | | | | | | | | | | |
| geometric mean | 1.7 | 2.5 | 1.7 | 1.2 | 5.2 | 2.4 | 27.3 | 226.0 | 1.9 | 1.9 |
| median | 1 | 2 | 1 | 1 | 4 | 2 | 20 | 226 | 2 | 1 |
| min – max | 1–55 | 1–30 | 1–20 | 1–3 | 1–95 | 1–10 | 13–78 | 226–226 | 1–7 | 1–226 |
| Duration of therapy per bleed, days | | | | | | | | | | |
| geometric mean | 1.6 | 2.3 | 1.6 | 1.2 | 4.2 | 1.8 | 13.8 | 147.0 | 1.8 | 1.7 |
| median | 1 | 2 | 1 | 1 | 4 | 2 | 11 | 147 | 2 | 1 |
| min – max | 1–120 | 1–33 | 1–16 | 1–3 | 1–34 | 1–5 | 7–34 | 147–147 | 1–6 | 1–147 |
| N (%) with hospitalization | 11 (2.4%) | 4 (4.4%) | 0 (0%) | 1 (10%) | 4 (25%) | 0 (0%) | 3 (100%) | 1 (100%) | 0 (0%) | 24 (3.8%) |
| N (%) with rebleeding | 21 (4.5%) | 2 (2.2%) | 2 (5.7%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 1 (7.1%) | 26 (4.1%) |

ABR according to centres Haemophilia A (PWHA)

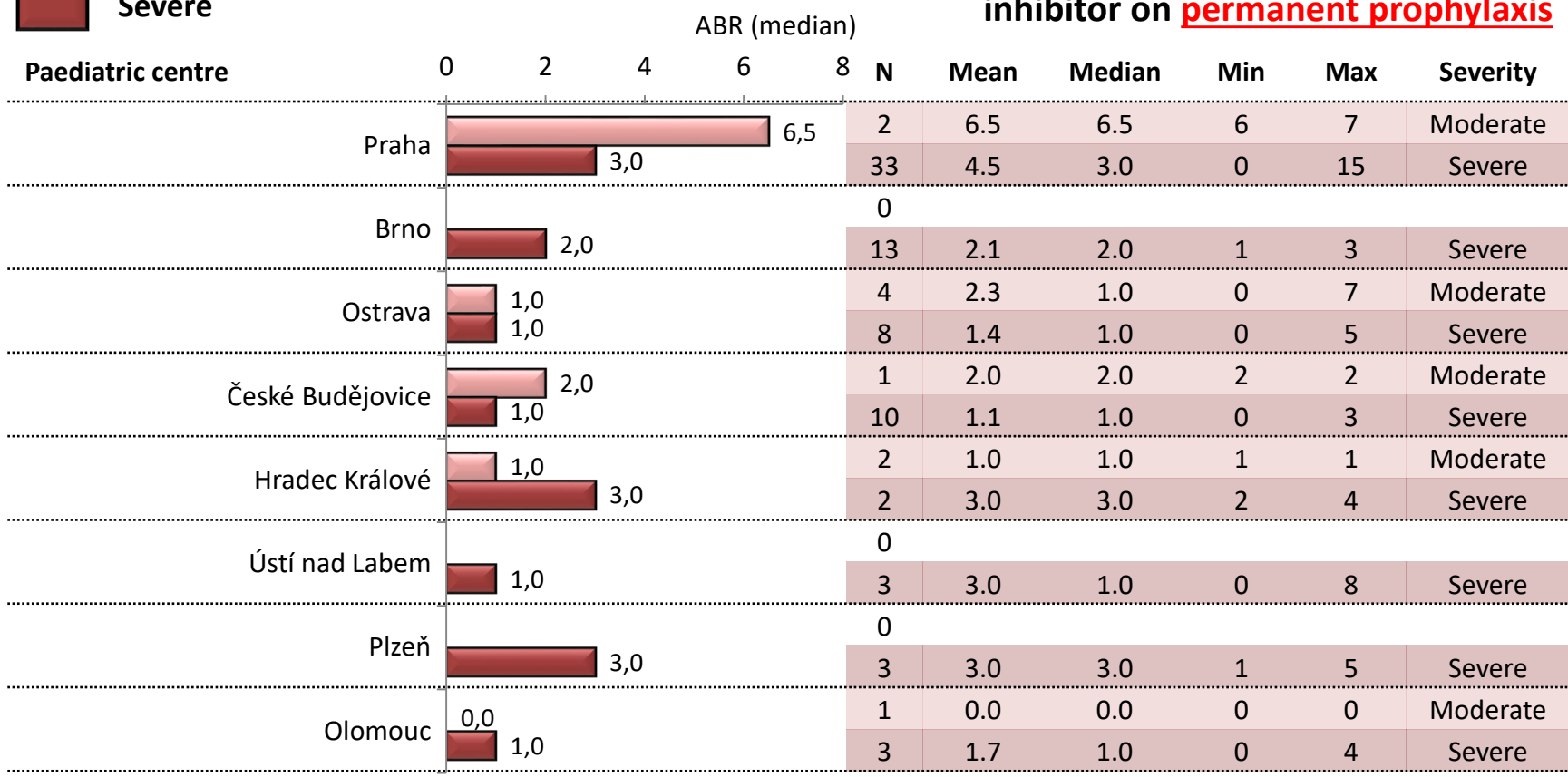


Annual bleeding rate on permanent prophylaxis

HaemA on prophylaxis
Paed. centres
N=85

 Moderate
 Severe

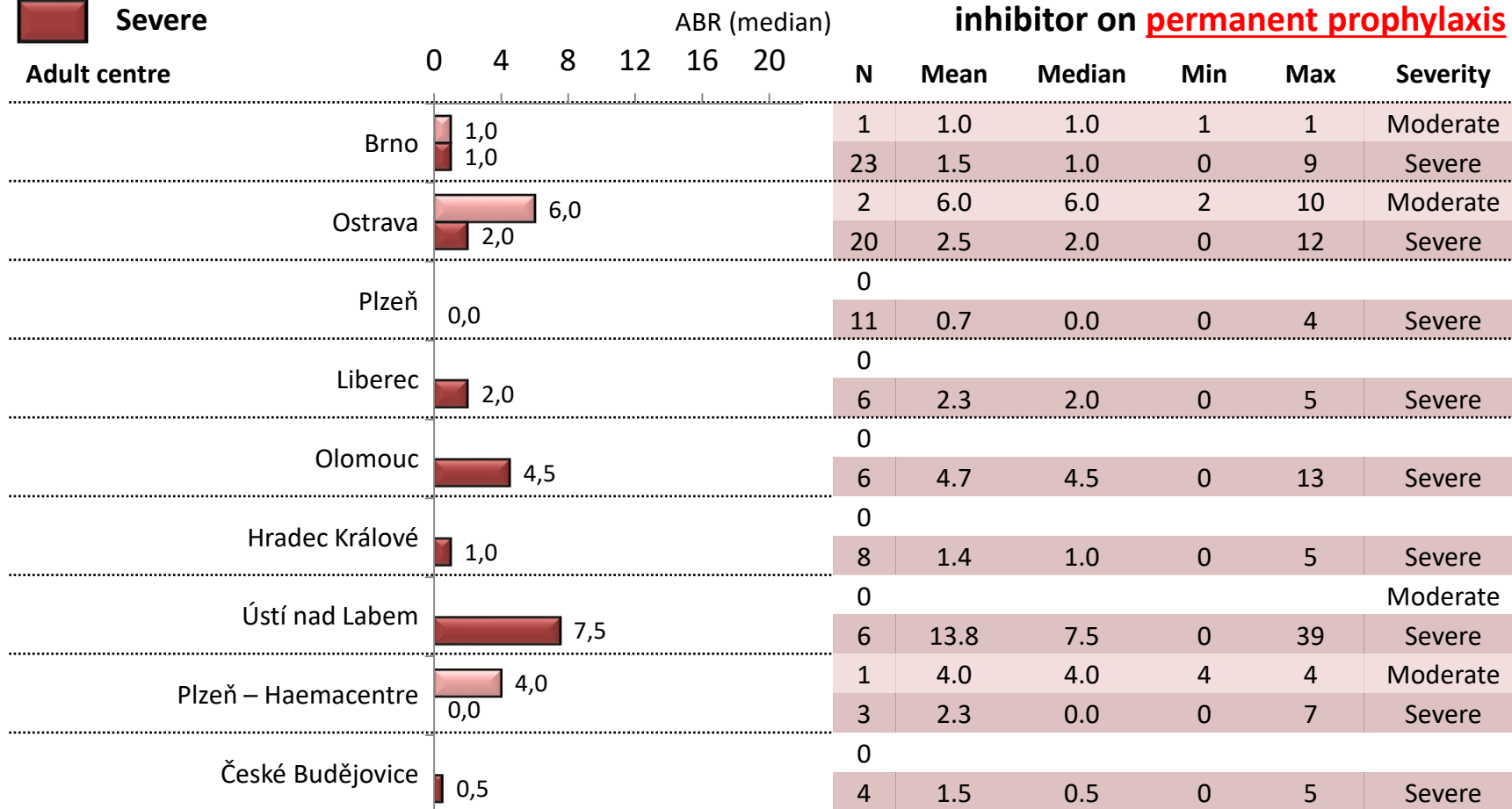
Frequency of bleeding in PWhA without inhibitor on **permanent prophylaxis**



Annual bleeding rate on permanent prophylaxis



Frequency of bleeding in PWhA without inhibitor on **permanent prophylaxis**

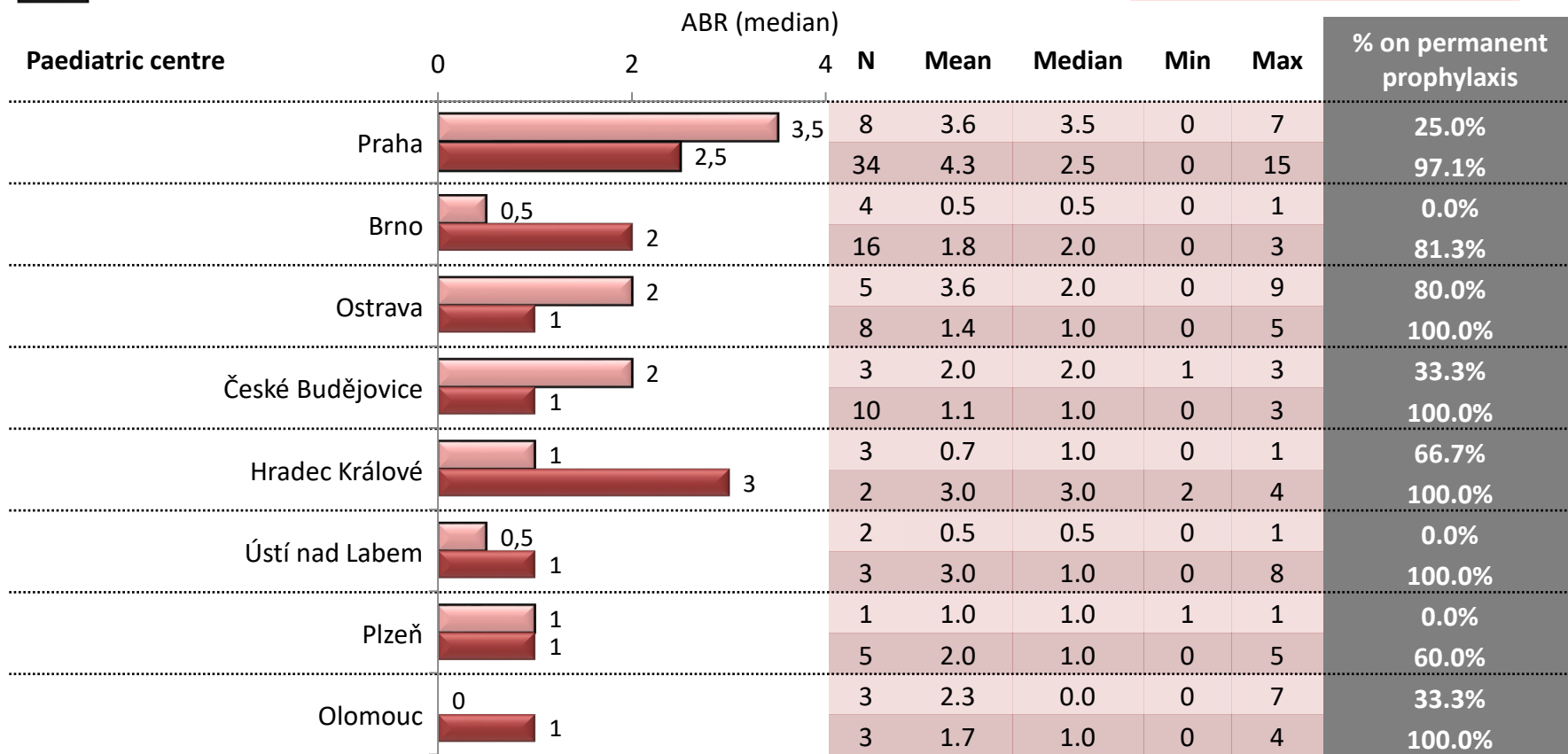


Annual bleeding rate regardless prophylaxis

Haema
Paed. centres
N=110



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



Annual bleeding rate regardless prophylaxis

HaemA
Adult centres
N=179*

* missing ABR in 8 adults



Frequency of bleeding in PWHA without inhibitor regardless of prophylaxis

| Adult centre | ABR (median) | | | | | N* | Mean | Median | Min | Max | % on permanent prophylaxis |
|---------------------|--------------|---|----|----|----|----|------|--------|-----|-----|----------------------------|
| | 0 | 5 | 10 | 15 | 20 | | | | | | |
| Brno | 0,0 | | | | | 12 | 0.1 | 0.0 | 0 | 1 | 8.3% |
| | 1,0 | | | | | 34 | 2.0 | 1.0 | 0 | 18 | 63.9% |
| Ostrava | 3,0 | | | | | 6 | 3.7 | 3.0 | 0 | 10 | 33.3% |
| | 2,0 | | | | | 27 | 2.7 | 2.0 | 0 | 12 | 74.1% |
| Plzeň | 0,0 | | | | | 3 | 0.0 | 0.0 | 0 | 0 | 0.0% |
| | 1,0 | | | | | 18 | 6.9 | 1.0 | 0 | 28 | 55.0% |
| Liberec | 0,0 | | | | | 0 | | | | | |
| | 4,5 | | | | | 10 | 6.1 | 4.5 | 0 | 26 | 60.0% |
| Olomouc | 1,0 | | | | | 1 | 1.0 | 1.0 | 1 | 1 | 0.0% |
| | 9,0 | | | | | 18 | 8.8 | 9.0 | 0 | 21 | 30.0% |
| Hradec Králové | 0,0 | | | | | 5 | 0.0 | 0.0 | 0 | 0 | 0.0% |
| | 1,0 | | | | | 13 | 2.0 | 1.0 | 0 | 13 | 53.3% |
| Ústí nad Labem | 0,0 | | | | | 4 | 0.0 | 0.0 | 0 | 0 | 0.0% |
| | 10,0 | | | | | 9 | 13.7 | 10.0 | 0 | 39 | 66.7% |
| Plzeň – Haemacentre | 4,0 | | | | | 1 | 4.0 | 4.0 | 4 | 4 | 100.0% |
| | 0,0 | | | | | 3 | 2.3 | 0.0 | 0 | 7 | 100.0% |
| České Budějovice | 0,0 | | | | | 3 | 0.7 | 0.0 | 0 | 2 | 0.0% |
| | 0,5 | | | | | 12 | 1.6 | 0.5 | 0 | 5 | 33.3% |

Prophylactic regimens and treatment outcomes

HaemA
Paed. centres
N=110

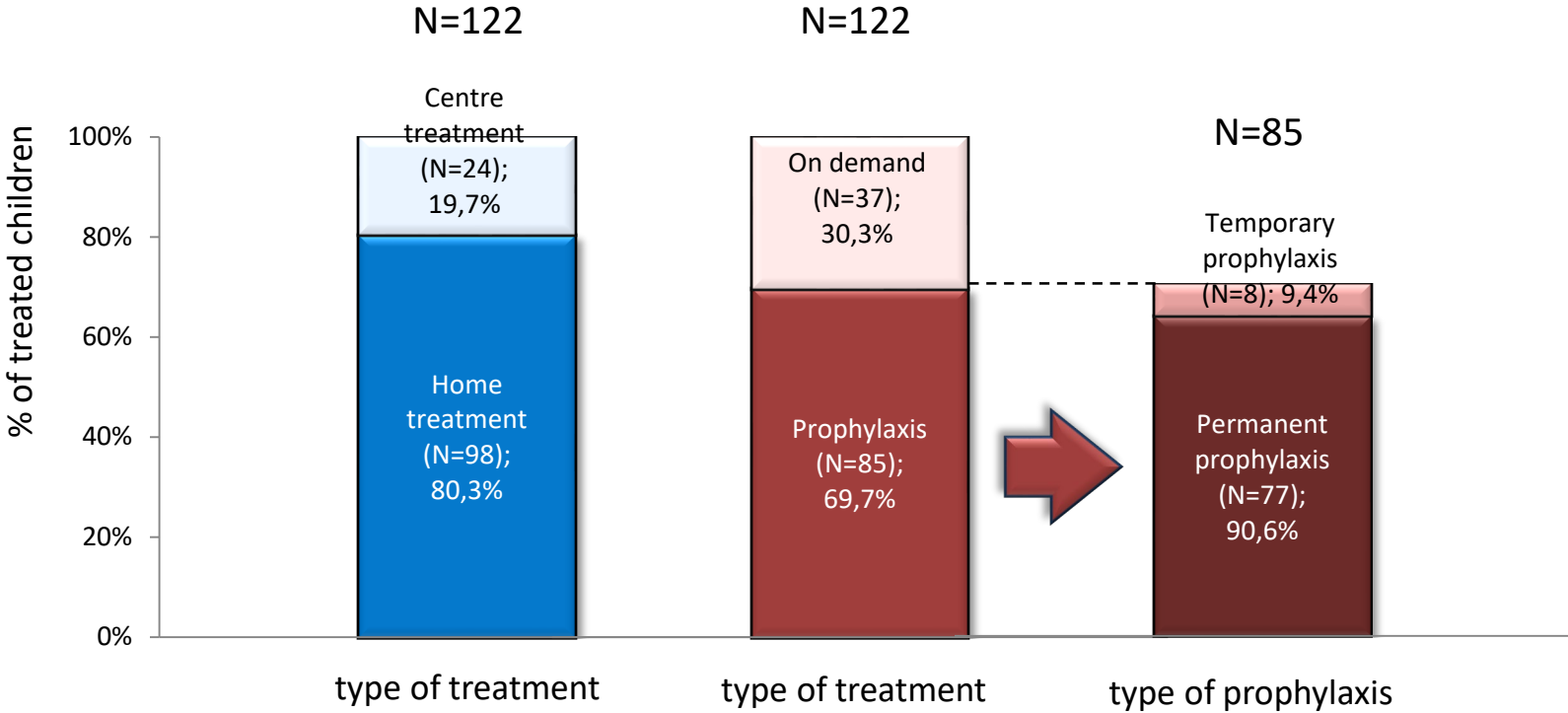
| Paediatric centre | Severity | Total N | PERMANENT PROPHYLAXIS | | | | | | | | ON-DEMAND / TEMPORARY PROPHY | | | |
|-------------------|----------|---------|-----------------------|----|--|-------------|------|-------|------|-------------|------------------------------|------|--------|--|
| | | | % of patients | N | Dosing of prophylaxis (IU/kg per week) | | | | ABR | | N | ABR | | |
| | | | | | Mean | Median | Min | Max | Mean | Median | | Mean | Median | |
| Praha | Moderate | 8 | 25.0% | 2 | 49.7 | 49.7 | 49.4 | 50.0 | 96.8 | 96.8 | 6 | 6.0 | 8.0 | |
| | Severe | 34 | 97.1% | 33 | 79.1 | 78.5 | 22.8 | 121.5 | 0.0 | 0.0 | 1 | 1.0 | 3.0 | |
| Brno | Moderate | 4 | 0.0% | 0 | | | | | | | 4 | 4.0 | 1.0 | |
| | Severe | 16 | 81.3% | 13 | 92.9 | 83.3 | 65.2 | 140.0 | 17.9 | 17.9 | 3 | 3.0 | 2.0 | |
| Ostrava | Moderate | 5 | 80.0% | 4 | 68.5 | 65.9 | 52.6 | 89.7 | 0.0 | 0.0 | 1 | 1.0 | 0.0 | |
| | Severe | 8 | 100.0% | 8 | 90.4 | 98.6 | 52.6 | 115.6 | 0.0 | 0.0 | 0 | 0.0 | 3.0 | |
| Č. Budějovice | Moderate | 3 | 33.3% | 1 | 34.3 | 34.3 | 34.3 | 34.3 | 58.8 | 58.8 | 2 | 2.0 | 1.0 | |
| | Severe | 10 | 100.0% | 10 | 55.5 | 50.1 | 20.8 | 109.6 | 0.0 | 0.0 | 0 | 0.0 | 0.0 | |
| Hradec Králové | Moderate | 3 | 66.7% | 2 | 54.8 | 54.8 | 12.9 | 96.8 | 0.0 | 0.0 | 1 | 1.0 | 1.0 | |
| | Severe | 2 | 100.0% | 2 | 76.9 | 76.9 | 70.1 | 83.7 | 0.0 | 0.0 | 0 | 0.0 | 0.0 | |
| Ústí nad Labem | Moderate | 2 | 0.0% | 0 | | | | | | | 2 | 2.0 | 0.0 | |
| | Severe | 3 | 100.0% | 3 | 57.4 | 61.6 | 46.6 | 64.0 | 0.0 | 0.0 | 0 | 0.0 | 1.0 | |
| Plzeň | Moderate | 1 | 0.0% | 0 | | | | | | | 1 | 1.0 | 1.0 | |
| | Severe | 5 | 60.0% | 3 | 60.1 | 58.1 | 55.2 | 66.8 | 0.0 | 0.0 | 2 | 2.0 | 1.0 | |
| Olomouc | Moderate | 3 | 33.3% | 1 | 26.3 | 26.3 | 26.3 | 26.3 | 0.0 | 0.0 | 2 | 2.0 | 1.0 | |
| | Severe | 3 | 100.0% | 3 | 28.4 | 26.3 | 19.2 | 39.7 | 0.0 | 0.0 | 0 | 0.0 | 0.0 | |

Prophylactic regimens and treatment outcomes

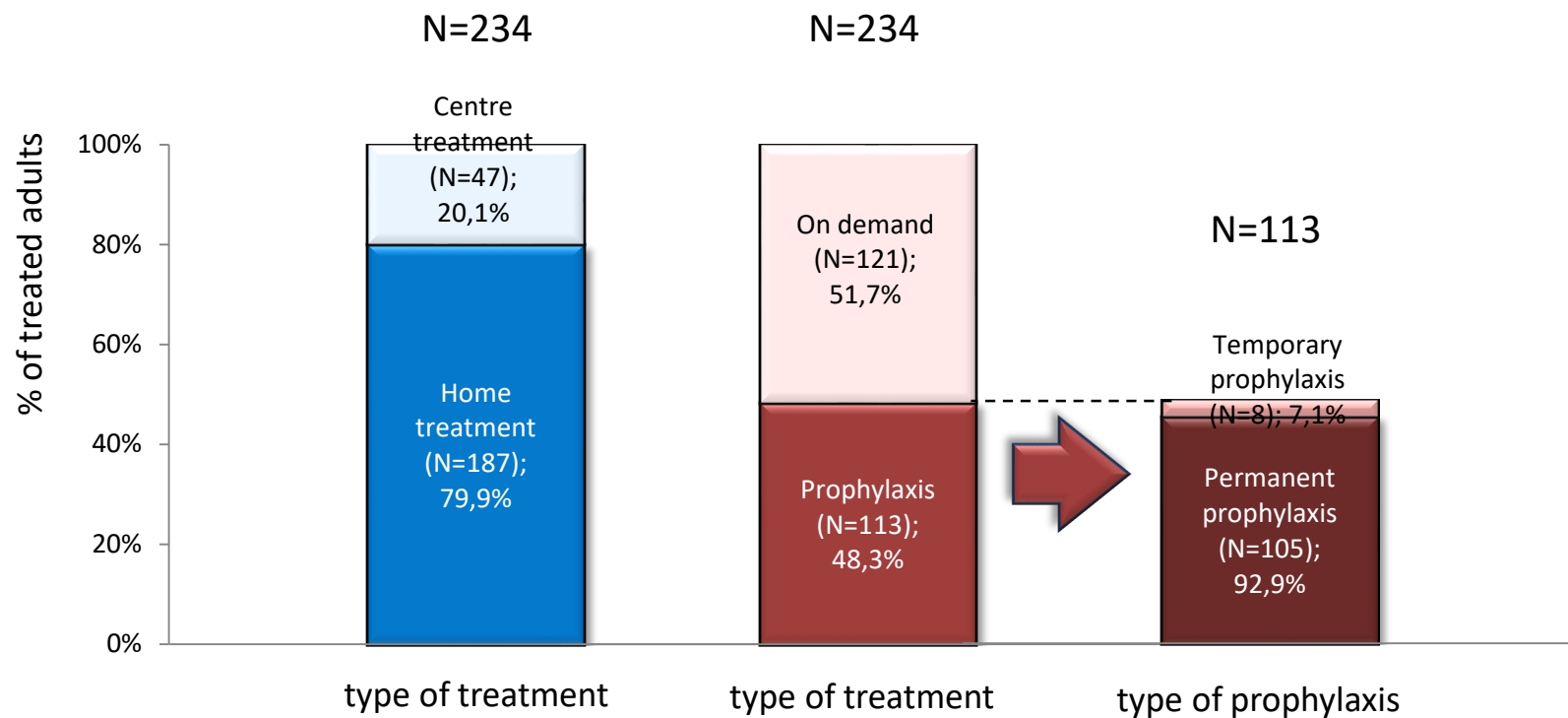
| Adult centre | Severity | Total N | PERMANENT PROPHYLAXIS | | | | | | | | | ON-DEMAND / TEMPORARY PROPHY | | | | |
|------------------------|----------|---------|-----------------------|----|---|--------|------|-------|-------|--------|--------|---------------------------------|------|--------|--------|----|
| | | | % of patients | N | Dosing of prophylaxis (IU/kg per week) | | | | ABR* | | Age | N | ABR* | | Age | |
| | | | | | Mean | Median | Min | Max | Mean | Median | Median | | Mean | Median | Median | |
| Brno | Moderate | 12 | 8.3% | 1 | 42.9 | 42.9 | 42.9 | 42.9 | 42.9 | 1.0 | 1.0 | 29 | 11 | 0.0 | 0.0 | 47 |
| | Severe | 36 | 63.9% | 23 | 54.8 | 44.9 | 19.0 | 100.0 | 100.0 | 1.5 | 1.0 | 37 | 13 | 3.0 | 1.0 | 46 |
| Ostrava | Moderate | 6 | 33.3% | 2 | 71.8 | 71.8 | 52.7 | 90.9 | 90.9 | 6.0 | 6.0 | 68 | 4 | 2.5 | 2.5 | 53 |
| | Severe | 27 | 74.1% | 20 | 58.6 | 53.8 | 35.1 | 96.8 | 96.8 | 2.5 | 2.0 | 39 | 7 | 3.1 | 3.0 | 61 |
| Plzeň | Moderate | 3 | 0.0% | 0 | | | | | | | | | 3 | 0.0 | 0.0 | 42 |
| | Severe | 20 | 55.0% | 11 | 42.2 | 39.5 | 14.3 | 107.4 | 107.4 | 0.7 | 0.0 | 44 | 9 | 16.6 | 20.0 | 51 |
| Liberec | Moderate | 0 | | | | | | | | | | | | | | |
| | Severe | 10 | 60.0% | 6 | 63.1 | 61.0 | 40.9 | 96.2 | 96.2 | 2.3 | 2.0 | 37 | 4 | 11.8 | 8.0 | 64 |
| Olomouc | Moderate | 1 | 0.0% | 0 | | | | | | | | | 1 | 1.0 | 1.0 | 23 |
| | Severe | 20 | 30.0% | 6 | 37.8 | 36.3 | 20.0 | 62.5 | 62.5 | 4.7 | 4.5 | 29 | 14 | 10.8 | 11.0 | 52 |
| Hradec Králové | Moderate | 5 | 0.0% | 0 | | | | | | | | | 5 | 0.0 | 0.0 | 23 |
| | Severe | 15 | 53.3% | 8 | 63.5 | 63.0 | 45.5 | 90.0 | 90.0 | 1.4 | 1.0 | 29 | 7 | 3.0 | 1.0 | 32 |
| Ústí n. Labem | Moderate | 4 | 0.0% | 0 | | | | | | | | | 4 | 0.0 | 0.0 | 24 |
| | Severe | 9 | 66.7% | 6 | 47.6 | 32.5 | 13.9 | 100.5 | 100.5 | 13.8 | 7.5 | 31 | 3 | 13.3 | 10.0 | 43 |
| Plzeň - Haemacentre | Moderate | 1 | 100.0% | 1 | 24.9 | 24.9 | 24.9 | 24.9 | 24.9 | 4.0 | 4.0 | 49 | 0 | | | |
| | Severe | 3 | 100.0% | 3 | 62.8 | 73.2 | 31.0 | 84.3 | 84.3 | 2.3 | 0.0 | 45 | 0 | | | |
| Č. Budějovice | Moderate | 3 | 0.0% | 0 | | | | | | | | | 3 | 0.7 | 0.0 | 72 |
| | Severe | 12 | 33.3% | 4 | 51.8 | 52.1 | 33.3 | 69.8 | 69.8 | 1.5 | 0.5 | 51 | 8 | 1.6 | 0.5 | 52 |

* missing ABR in 8 adults

Type of treatment (subgroup of treated patients)



Type of treatment (subgroup of treated patients)



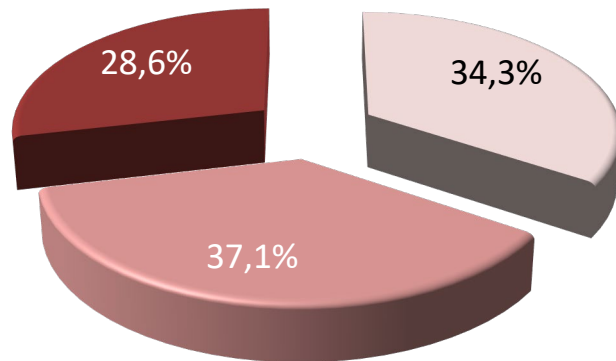
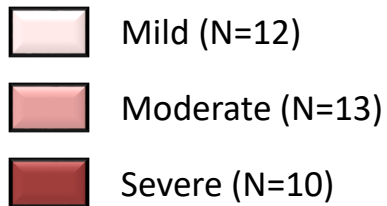
Demographic characteristics

Haemophilia B

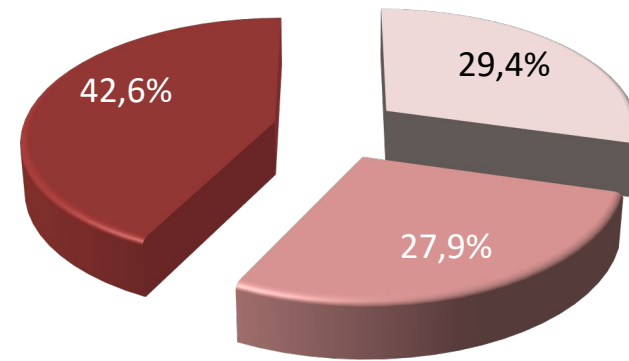
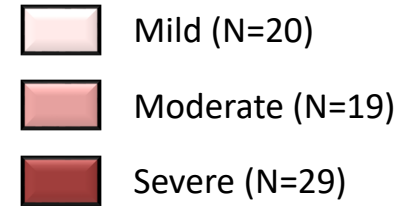


Severity of haemophilia B

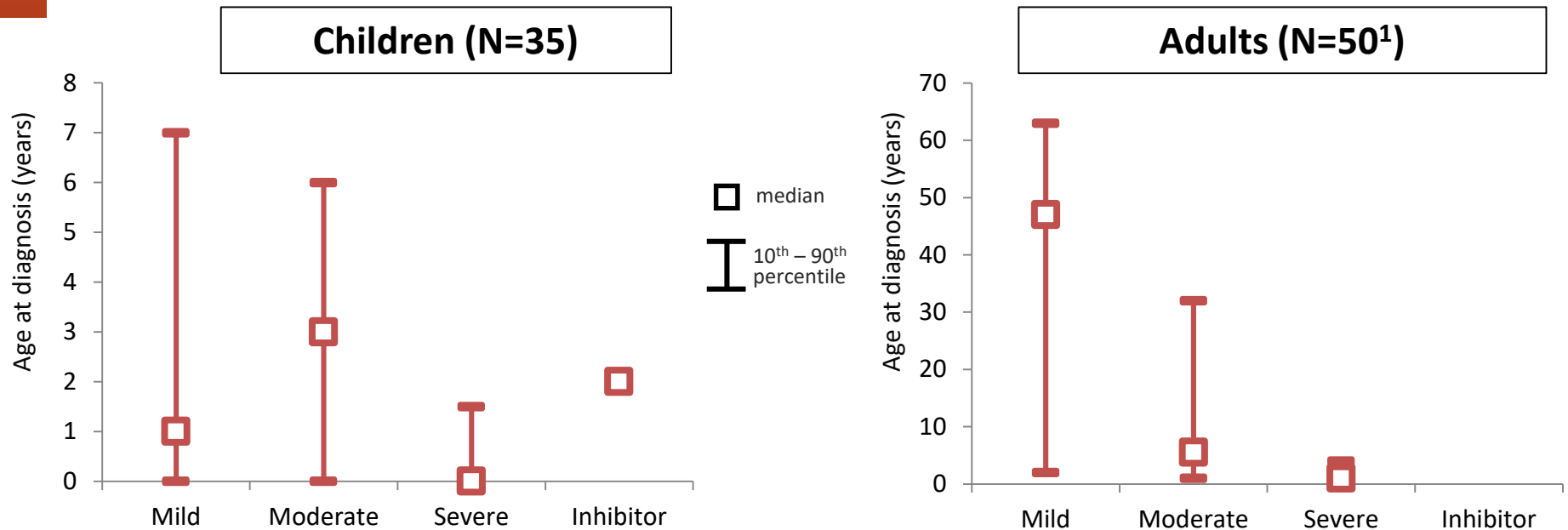
Children (N=35)



Adults (N=68)



Age at diagnosis according to severity of haemophilia B

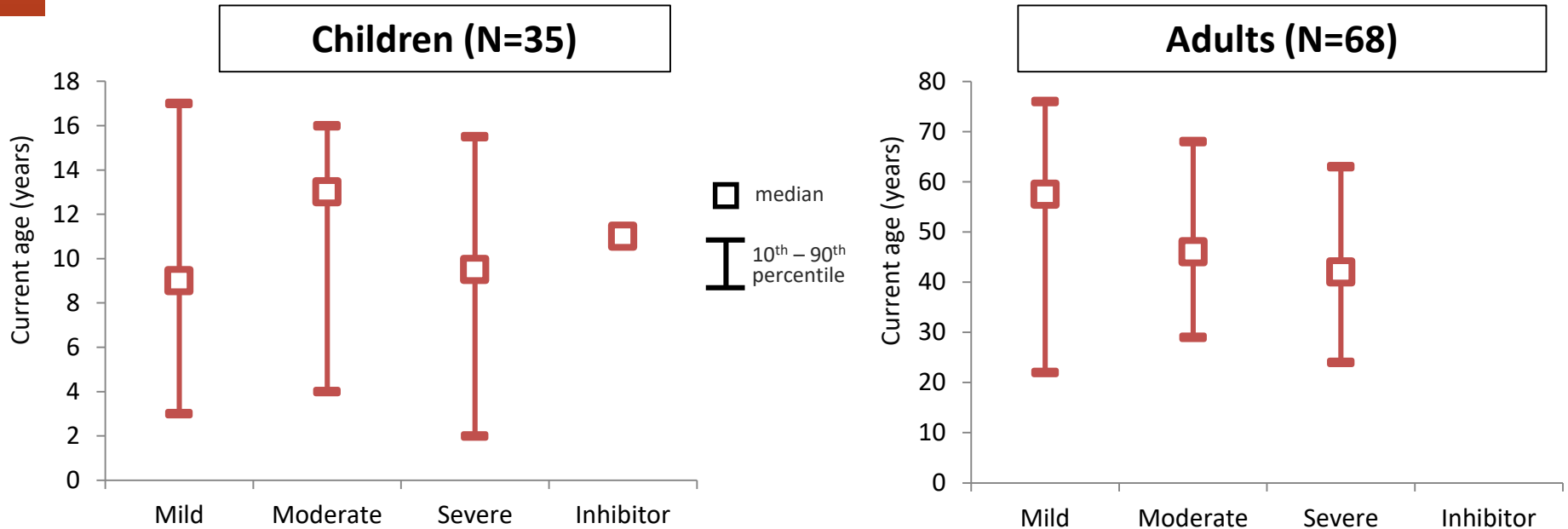


| Mild* | Moderate* | Severe* | Inhibitor ⁺ | Age at diagnosis (years) | Mild* | Moderate* | Severe* | Inhibitor ⁺ |
|------------|-----------|-----------|------------------------|---------------------------|-------------|--------------|-----------|------------------------|
| 12 | 13 | 10 | 1 | N valid | 13 | 14 | 23 | 0 |
| 2.3 | 2.7 | 0.5 | 2.0 | Mean | 33.5 | 10.5 | 1.7 | |
| 1 (0 – 11) | 3 (0 – 8) | 0 (0 – 2) | 2 (2 – 2) | Median (min – max) | 47 (0 – 67) | 5.5 (0 – 61) | 1 (0 – 8) | |

¹ Missing information on year of diagnosis in 18 adults.

* including persons with inhibitor
+ in 2018

Actual age according to severity of haemophilia B



| Mild* | Moderate* | Severe* | Inhibitor ⁺ | Current age ⁺⁺ (years) | Mild* | Moderate* | Severe* | Inhibitor ⁺ |
|------------|-------------|--------------|------------------------|-----------------------------------|----------------|--------------|--------------|------------------------|
| 12 | 13 | 10 | 1 | N valid | 20 | 19 | 29 | 0 |
| 8.7 | 10.2 | 8.8 | 11.0 | Mean | 51.8 | 47.8 | 43.1 | |
| 9 (1 – 18) | 13 (1 – 17) | 9.5 (1 – 16) | 11 (11 – 11) | Median (min – max) | 57.5 (20 – 93) | 46 (19 – 69) | 42 (20 – 67) | |

* including persons with inhibitor

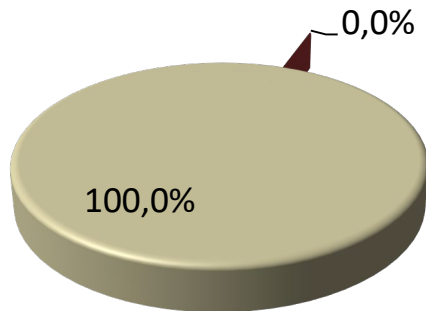
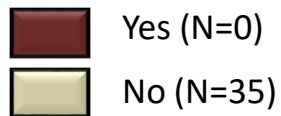
⁺ in 2018

⁺⁺ age reached in year 2018

Hepatitis (ever) experienced

Children
Haem B
N=35

Experienced hepatitis



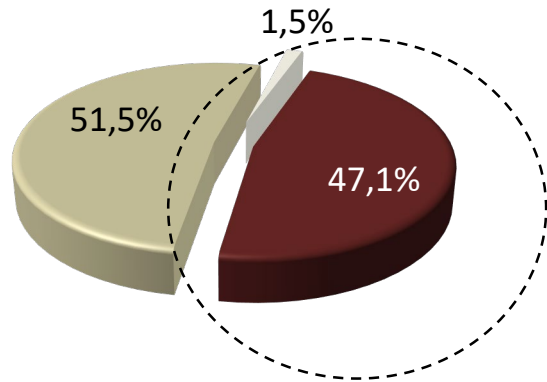
No child has hepatitis C.

Data from last completed annual report of each person.

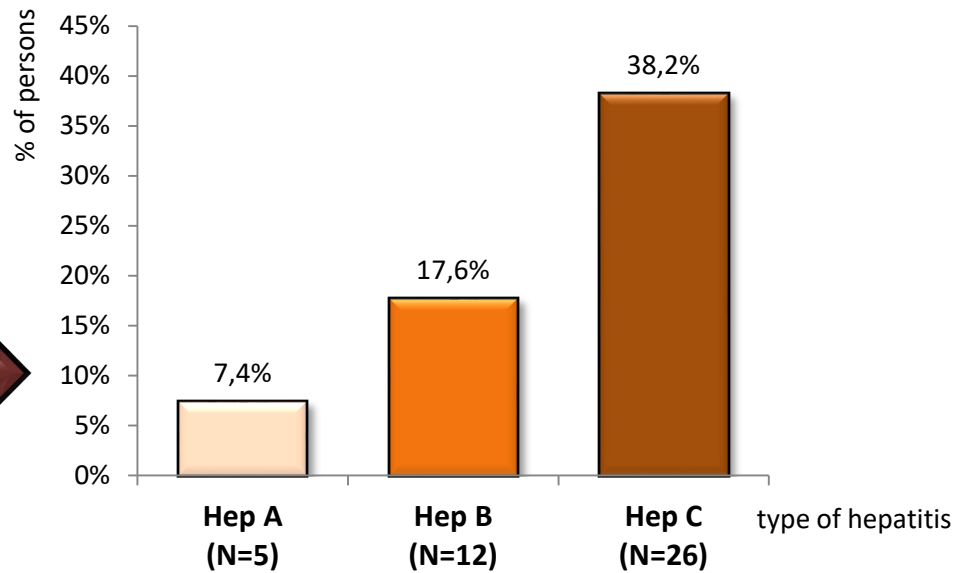
Hepatitis (ever) experienced

Experienced hepatitis

- Yes (N=32)
- No (N=35)
- Not known (N=1)



N=32* →



Data from last completed annual report of each person.

*Total of 43 cases of hepatitis in 32 persons. One person may have more types of hepatitis recorded.

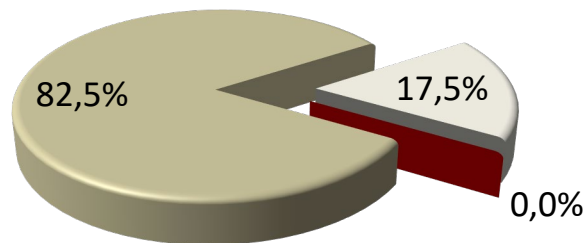
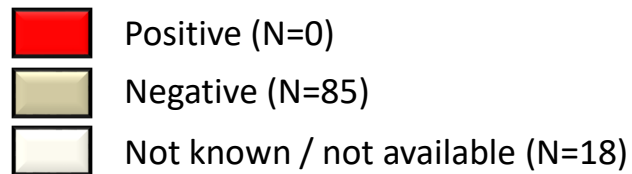


11 adults are HCV RNA positive

HIV

All
Haem B
N=103

HIV



No HIV-positive person.

Data from last completed annual report of each person.

Treatment outcomes and bleeding frequency

Haemophilia B



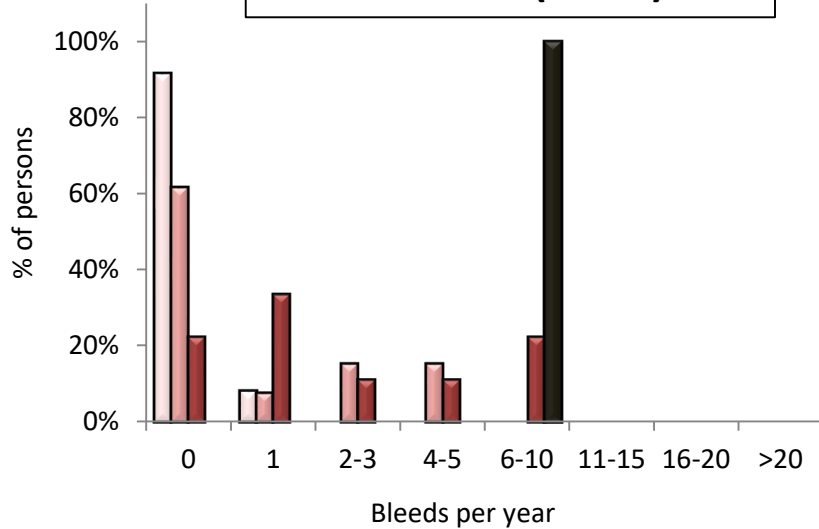
All
Haem B
N=103

Data from year 2018 – sample size

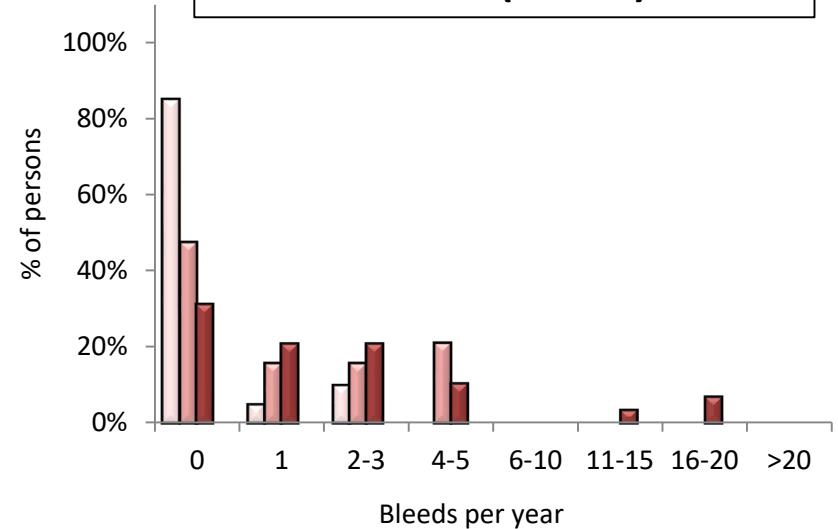
| | Valid persons | | | Persons with <u>valid</u> annual report | | | Persons <u>examined</u> | | | Persons <u>treated</u> | |
|------------------------|---------------|------|---|---|--------|---|-------------------------|-------|---|------------------------|-------|
| | N | % | | N | % | | N | % | | N | % |
| All | 103 | 100% | → | 100 | 97.1% | → | 83 | 80.6% | → | 63 | 61.2% |
| of them with inhibitor | 1 | | | 1 | | | 1 | | | 1 | |
| Children | 35 | 100% | → | 35 | 100.0% | → | 29 | 82.9% | → | 17 | 48.6% |
| of them with inhibitor | 1 | | | 1 | | | 1 | | | 1 | |
| Adults | 68 | 100% | → | 65 | 95.6% | → | 54 | 79.4% | → | 46 | 67.6% |
| of them with inhibitor | 0 | | | 0 | | | 0 | | | 0 | |

Frequency of bleeding requiring treatment in 2018

Children (N=35)



Adults (N=66¹)



| Mild* | Moderate* | Severe* | Inhibitor | Frequency of bleeding | Mild* | Moderate* | Severe* | Inhibitor |
|------------|-----------|------------|-----------|-----------------------|-----------|-----------|------------|-----------|
| 12 | 13 | 9 | 1 | N valid | 20 | 19 | 27 | 0 |
| 0.1 | 1.1 | 3.3 | 8.0 | Mean | 0.3 | 1.4 | 3.0 | |
| 0 (0 – 1) | 0 (0 – 5) | 1 (0 – 10) | 8 (8 – 8) | Median (min – max) | 0 (0 – 2) | 1 (0 – 4) | 1 (0 – 18) | |
| 11 (91.7%) | 8 (61.5%) | 2 (22.2%) | 0 (0%) | N (%) with no bleed | 17 (85%) | 9 (47.4%) | 9 (31%) | |

* without inhibitor

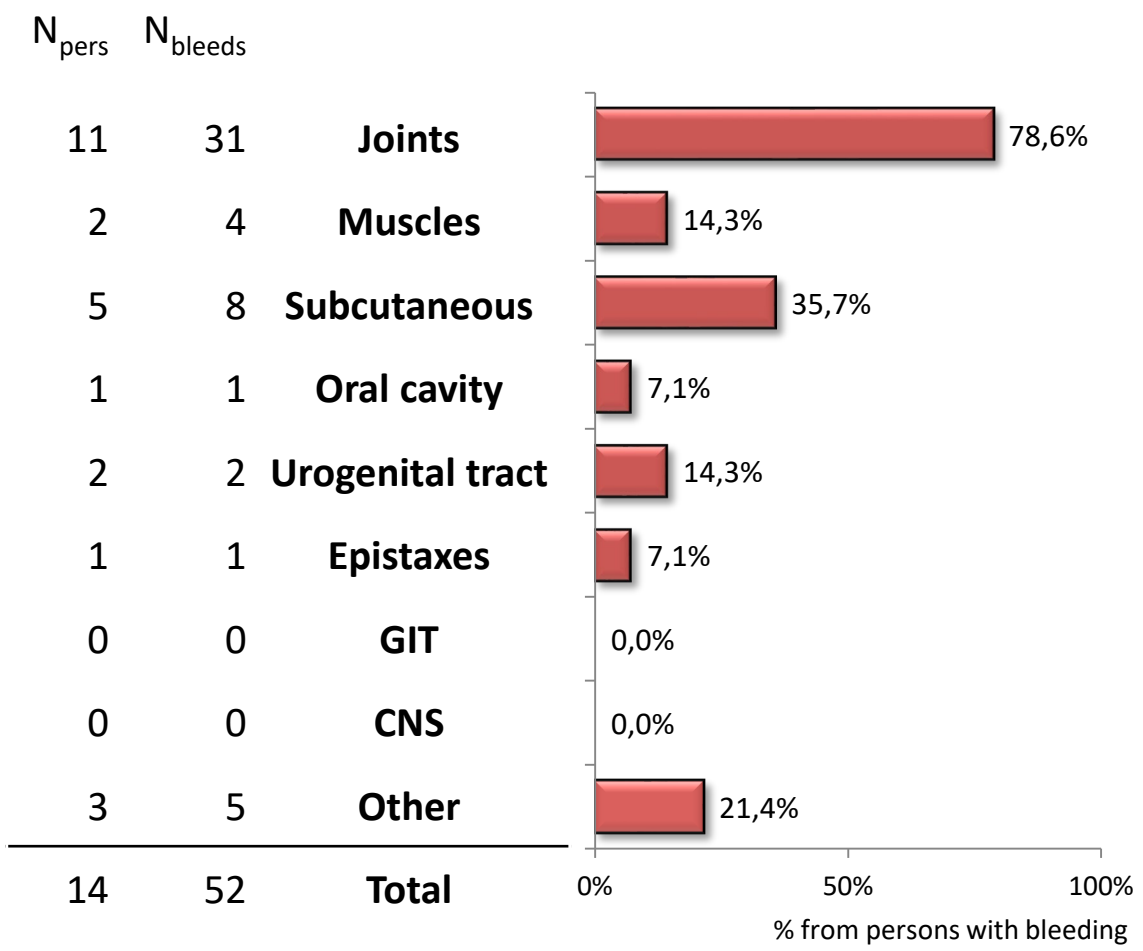
¹Frequency of bleeding is missing in 2 adults.

Location of bleeds in 2018

14 (40%) children experienced bleeding requiring treatment at least once in year; 53 bleeds were recorded in total, 4 bleeds required hospitalization.

All of these children have recorded location of their bleeds except of one bleed.

21 (60%) children recorded no bleed during year 2018.

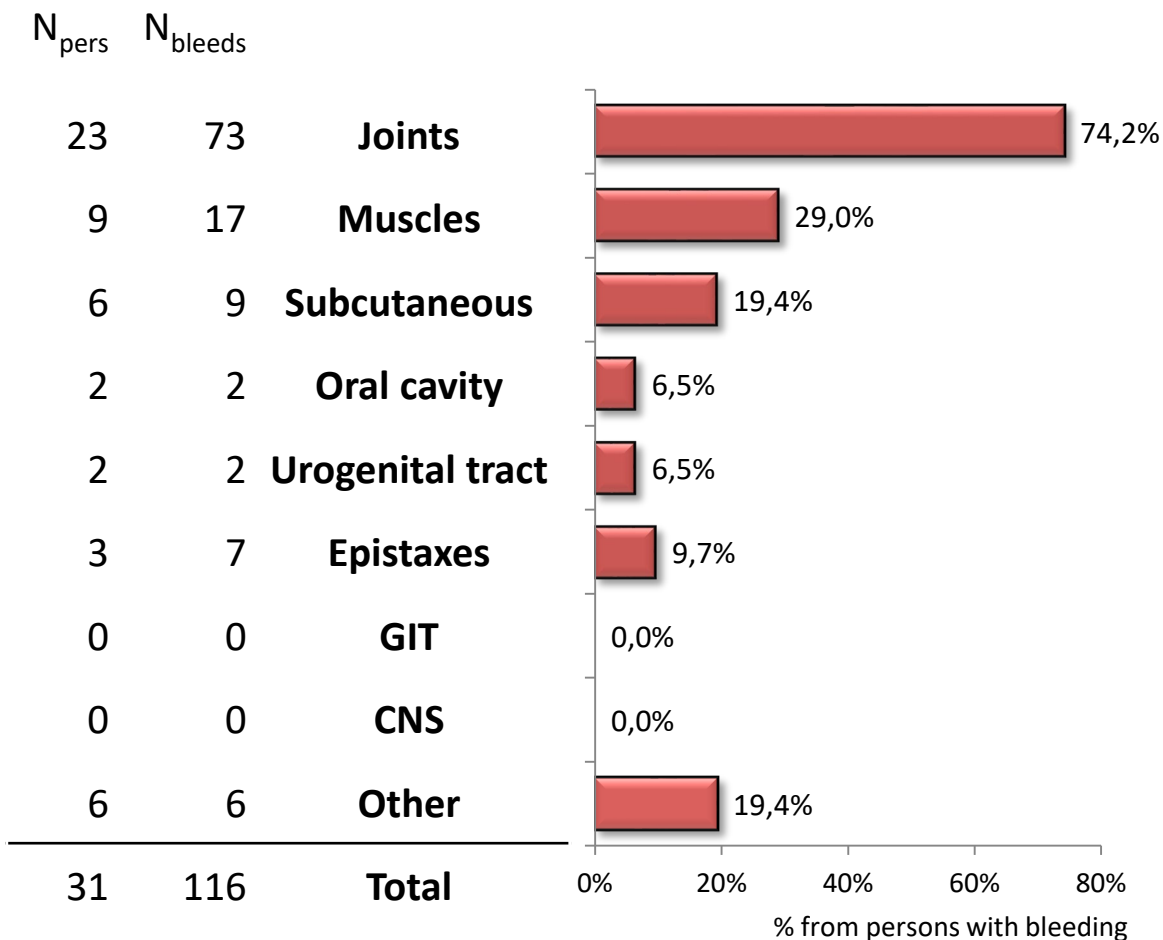


Location of bleeds in 2018

31 (47%) adults experienced bleeding requiring treatment at least once in year; 116 bleeds were recorded in total, 6 bleeds required hospitalization.

All of these 33 adults have recorded location of their bleeds.

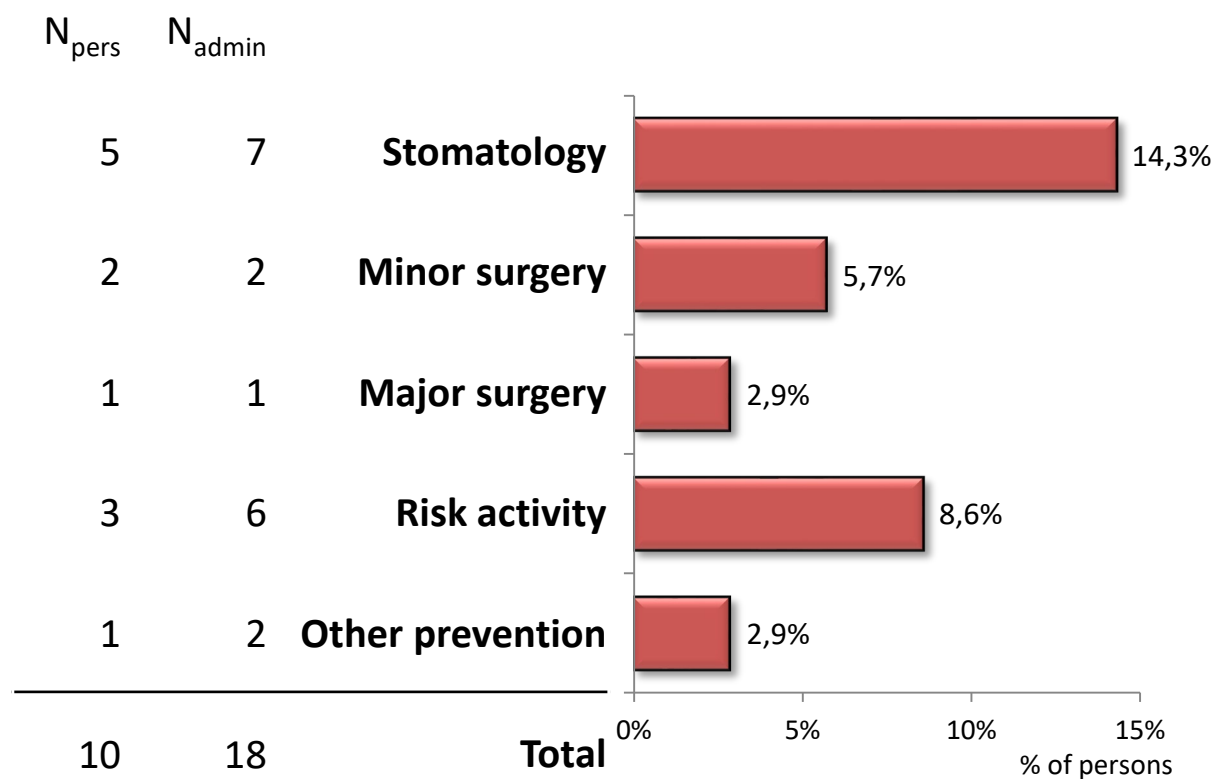
35 (53%) adults have recorded no bleed during year 2018.



¹Frequency of bleeding is missing in 2 adults.

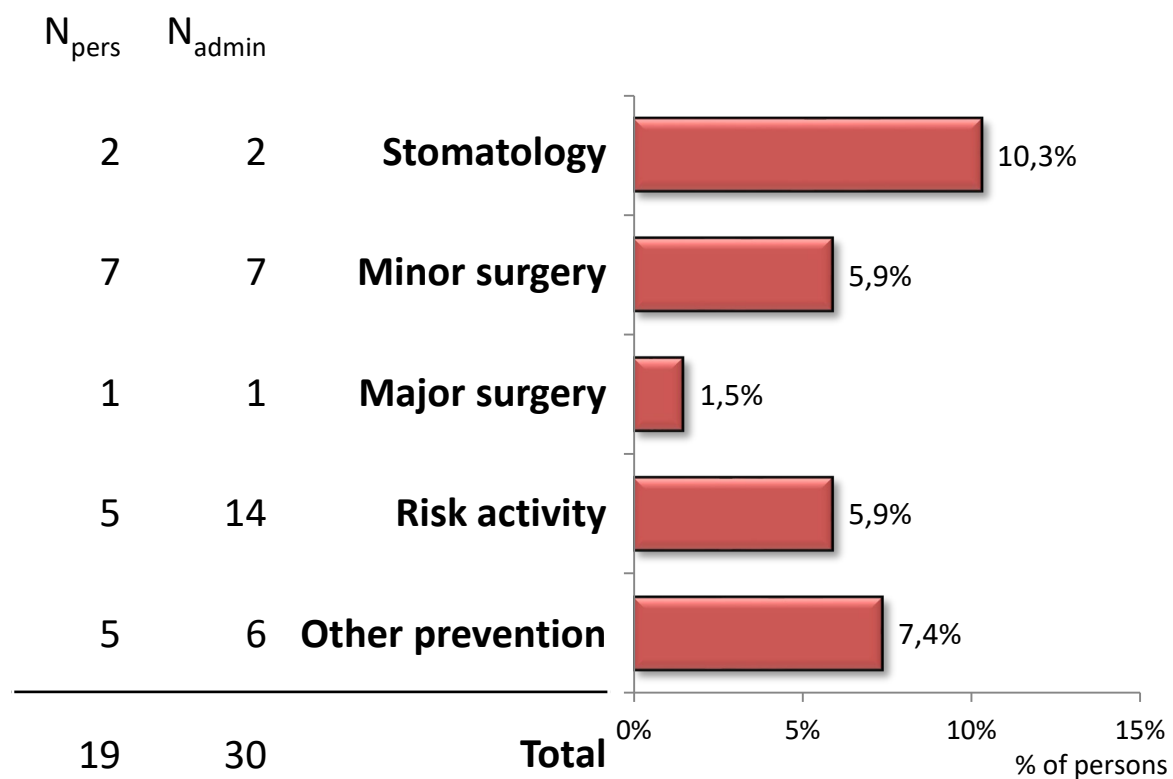
Preventive administration in 2018

10 (28.6%) children were given factor to prevent bleeding during/before risk situation.
18 preventive administrations were recorded in total.



Preventive administration in 2018

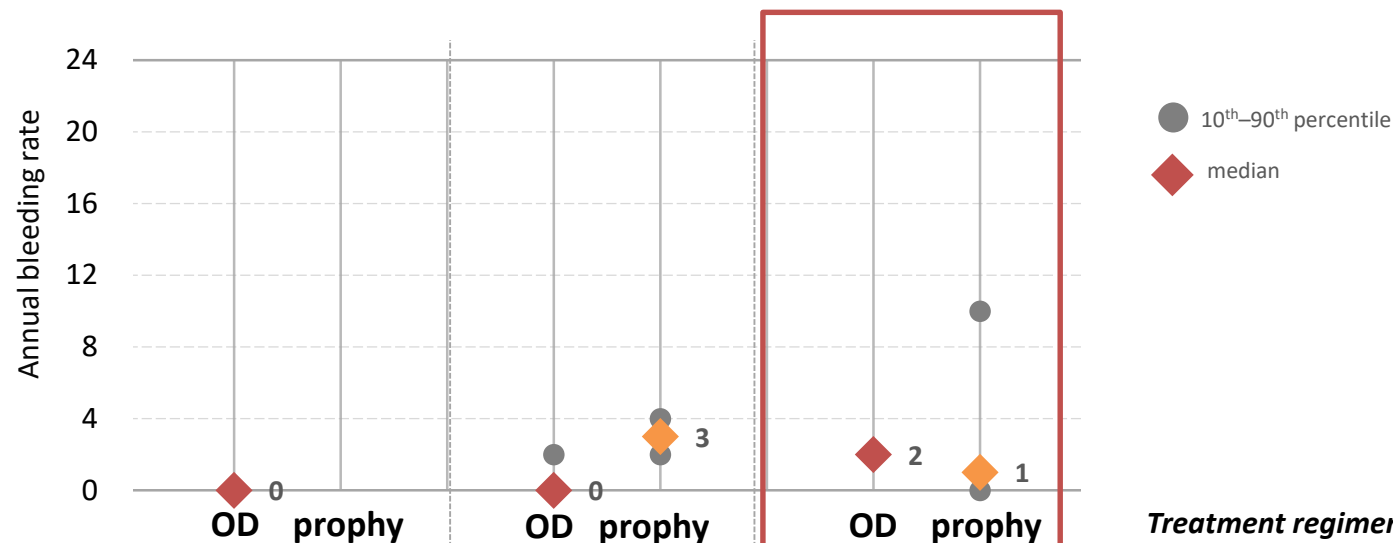
19 (27.9%) persons were given factor to prevent bleeding during/before risk situation.
30 preventive administrations were recorded in total.



ABR according to treatment regimen Haemophilia B without inhibitor



Annual bleeding rate according to treatment regimen



| Frequency of bleeding | Mild* | | Moderate* | | Severe* | |
|---|---------------|---|------------------|-----------|------------------|-------------------|
| N valid | 12 | 0 | 11 | 2 | 1 | 8 |
| Mean | 0.1 | | 0.7 | 3.0 | 2.0 | 3.5 |
| Median (min – max) | 0 (0 – 1) | | 0 (0 – 5) | 3 (2 – 4) | 2 (2 – 2) | 1 (0 – 10) |
| Total no of recorded bleeds | 1 | | 8 | 6 | 2 | 28 |
| children on permanent prophylaxis | 0 (0%) | | 2 (15.4%) | | 8 (88.9%) | |
| % of factor (FIX) consumed by children on permanent prophylaxis | - | | 90.5% | | 99.8% | |

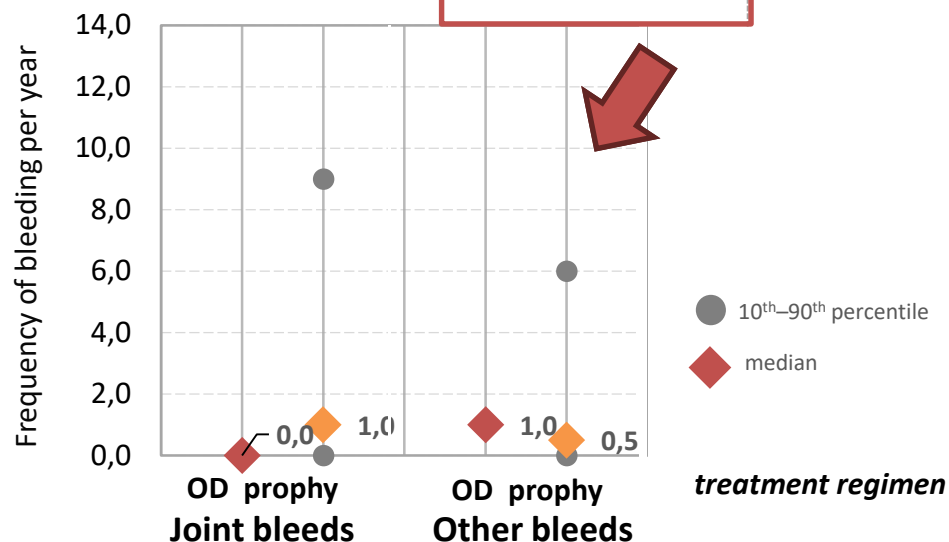
Treatment regimen:
OD = on demand and/or temporary prophylaxis
prophy = permanent prophylaxis

* without inhibitor

Joint and other bleeds according to treatment regimen

* without inhibitor

| Frequency of bleeding | Mild* | | Moderate* | | Severe* | |
|-----------------------------|---------|--------|-----------|---------|---------|-----------|
| | OD | prophy | OD | prophy | OD | prophy |
| Treatment regimen | OD | prophy | OD | prophy | OD | prophy |
| N valid | 12 | 0 | 11 | 2 | 1 | 8 |
| JOINT BLEEDS | | | | | | |
| Mean | 0.0 | | 0.4 | 3.0 | 0.0 | 2.1 |
| Median (range) | 0 (0-0) | | 0 (0-2) | 3 (2-4) | 0 (0-0) | 1 (0-9) |
| Total no of recorded bleeds | 0 | | 4 | 6 | 0 | 17 |
| OTHER BLEEDS | | | | | | |
| Mean | 0.1 | | 0.4 | 0.0 | 1.0 | 1.4 |
| Median (range) | 0 (0-1) | | 0 (0-3) | 0 (0-0) | 1 (1-1) | 0.5 (0-6) |
| Total no of recorded bleeds | 1 | | 4 | 0 | 1 | 11 |

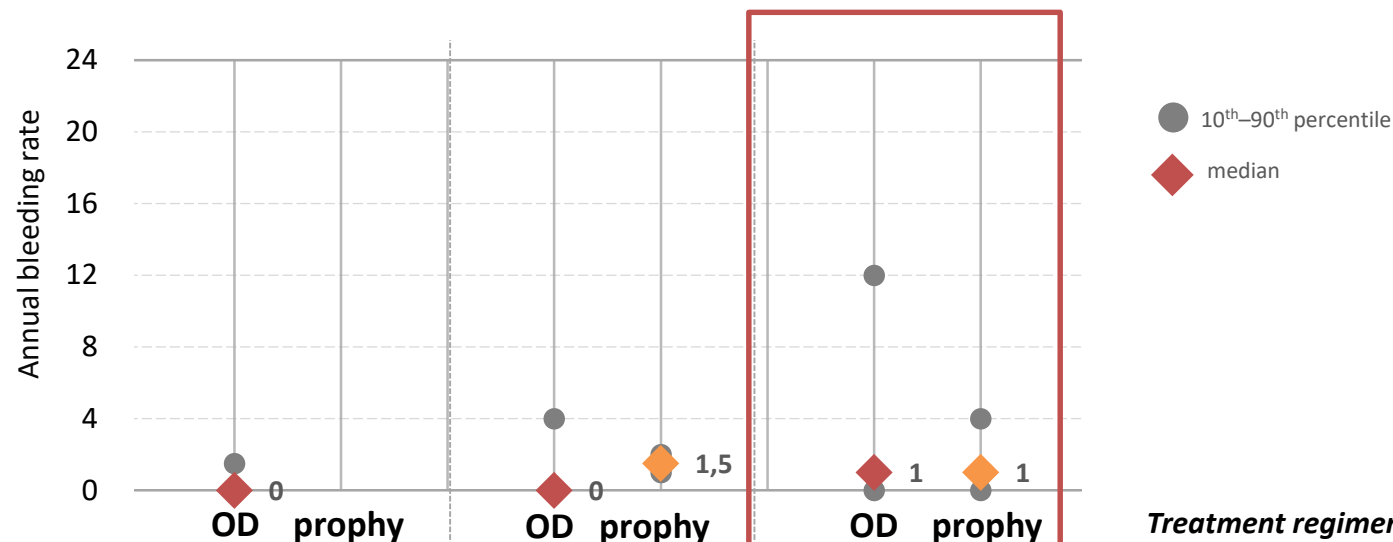


Treatment regimen:

OD = on demand and/or temporary prophylaxis

prophy = permanent prophylaxis

Annual bleeding rate according to treatment regimen



| Frequency of bleeding | Mild* | | Moderate* | | Severe* | |
|---|-----------|---|-----------|-------------|------------|------------|
| N total | 20 | 0 | 17 | 2 | 12 | 15 |
| Mean | 0.3 | | 1.4 | 1.5 | 3.6 | 2.5 |
| Median (min – max) | 0 (0 – 2) | | 0 (0 – 4) | 1.5 (1 – 2) | 1 (0 – 18) | 1 (0 – 17) |
| Total no of recorded bleeds | 5 | | 23 | 3 | 43 | 37 |
| adults on permanent prophylaxis | 0 (0%) | | 2 (10.5%) | | 16 (55.2%) | |
| % of factor (FIX) consumed by adults on permanent prophylaxis | - | | 23.7% | | 91.0% | |

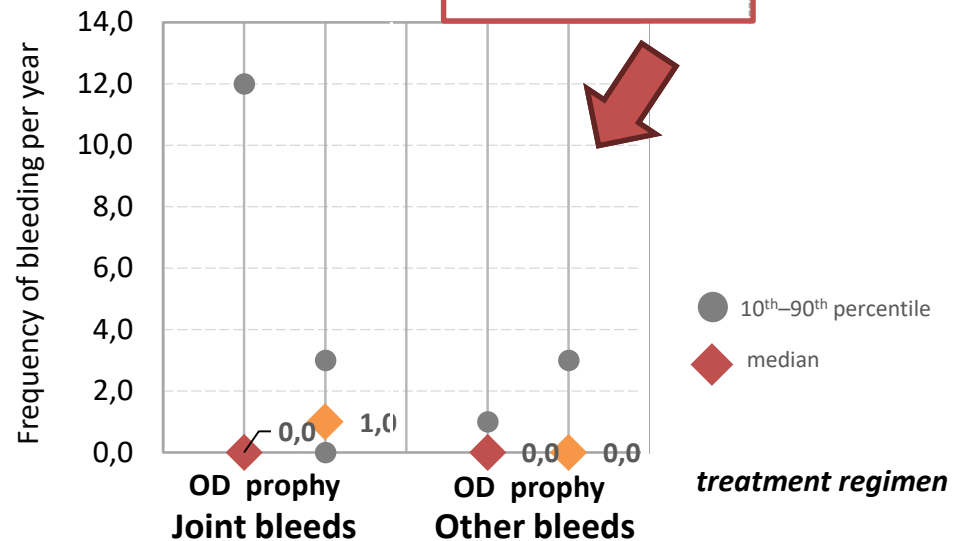
Treatment regimen:
OD = on demand and/or temporary prophylaxis
prophy = permanent prophylaxis

* without inhibitor;
 missing ABR in 2 adults

Joint and other bleeds according to treatment regimen

| Frequency of bleeding | Mild* | | Moderate* | | Severe* | |
|-----------------------------|---------|--------|-----------|-----------|-----------------|-----------------|
| | OD | prophy | OD | prophy | OD | prophy |
| Treatment regimen | OD | prophy | OD | prophy | OD | prophy |
| N valid | 20 | 0 | 17 | 2 | 12 | 15 |
| JOINT BLEEDS | | | | | | |
| Mean | 0.1 | 0 | 0.6 | 1.5 | 2.8 | 1.3 |
| Median (range) | 0 (0-1) | (-) | 0 (0-4) | 1.5 (1-2) | 0 (0-13) | 1 (0-7) |
| Total no of recorded bleeds | 2 | 0 | 11 | 3 | 34 | 19 |
| OTHER BLEEDS | | | | | | |
| Mean | 0.2 | 0 | 0.7 | 0.0 | 0.8 | 1.3 |
| Median (range) | 0 (0-2) | (-) | 0 (0-4) | 0 (0-0) | 0 (0-5) | 0 (0-10) |
| Total no of recorded bleeds | 3 | 0 | 12 | 0 | 9 | 19 |

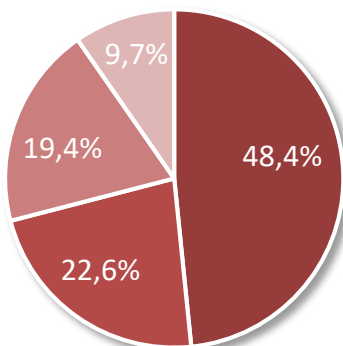
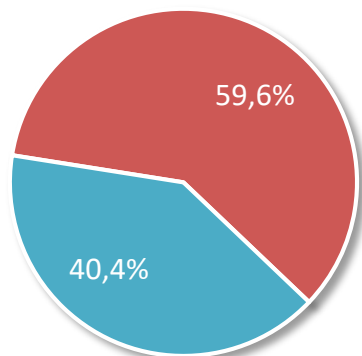
* without inhibitor; missing location of bleeds in 2 adults



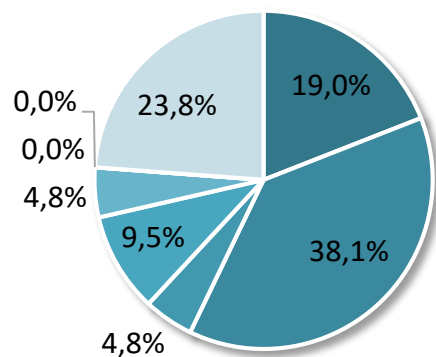
Treatment regimen:
OD = on demand and/or temporary
prophylaxis
prophy = permanent prophylaxis

Location and etiology of bleeds

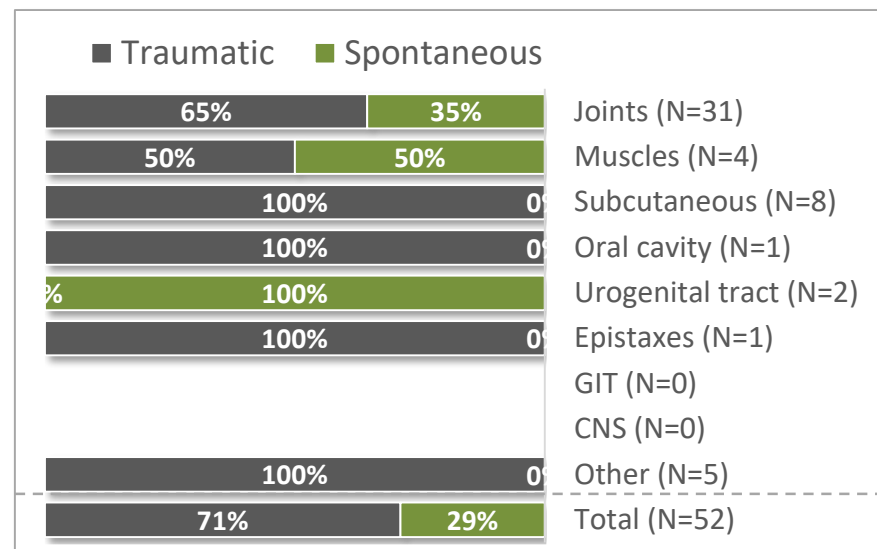
- Joints (N=31)
- Other (N=21)



- Knee (N=15)
- Ankle (N=7)
- Elbow (N=6)
- Other joint (N=3)



- Muscles (N=4)
- Subcutaneous (N=8)
- Oral cavity (N=1)
- Urogenital tract (N=2)
- Epistaxes (N=1)
- GIT (N=0)
- CNS (N=0)
- Other (N=5)



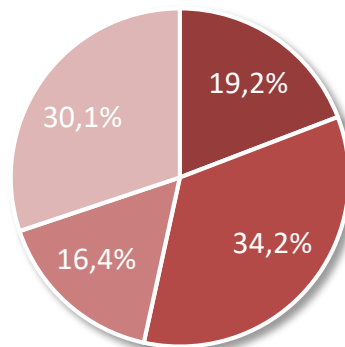
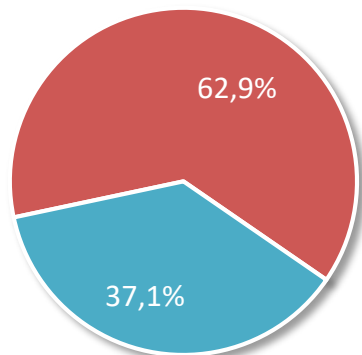
Detailed treatment of bleeds

| | Joints | Muscles | Subcutaneous | Oral cavity | Urogenital tract | Epistaxes | GIT | CNS | Other | Total |
|--|---------------|---------------|---------------|---------------|------------------|--------------|-----|-----|---------------|------------------|
| No. of bleeds | 31 | 4 | 8 | 1 | 2 | 1 | 0 | 0 | 5 | 52 |
| FIX consumption per bleed (IU), valid N | 27 | 3 | 6 | 1 | 1 | 1 | | | 5 | 44 |
| geometric mean | 2712.7 | 2381.1 | 1505.4 | 4000.0 | 1500.0 | 500.0 | | | 1745.4 | 2260.5 |
| median | 2500.0 | 2000.0 | 1578.0 | 4000.0 | 1500.0 | 500.0 | | | 1500.0 | 1828.0 |
| min – max | 500–52000 | 1500–4500 | 500–2500 | 4000–4000 | 1500–1500 | 500–500 | | | 1000–7200 | 500–52000 |
| sum | 140483 | 8000 | 10155 | 4000 | 1500 | 500 | | | 12200 | 176838 |
| No. of doses per bleed | | | | | | | | | | |
| geometric mean | 1.9 | 1.6 | 1.1 | 4.0 | 3.7 | 1.0 | | | 1.2 | 1.7 |
| median | 2 | 2 | 1 | 4 | 8 | 1 | | | 1 | 1 |
| min – max | 1–14 | 1–3 | 1–2 | 4–4 | 1–14 | 1–1 | | | 1–3 | 1–14 |
| Duration of therapy per bleed, days | | | | | | | | | | |
| geometric mean | 2.2 | 1.6 | 1.2 | 4.0 | 3.6 | 1.0 | | | 1.8 | 2.0 |
| median | 2 | 2 | 1 | 4 | 7 | 1 | | | 1 | 1 |
| min – max | 1–36 | 1–3 | 1–2 | 4–4 | 1–13 | 1–1 | | | 1–20 | 1–36 |
| N (%) with hospitalization | 2 (6.5%) | 0 (0%) | 1 (12.5%) | 0 (0%) | 1 (50%) | 0 (0%) | | | 0 (0%) | 4 (7.7%) |
| N (%) with rebleeding | 3 (9.7%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | | | 0 (0%) | 3 (5.8%) |

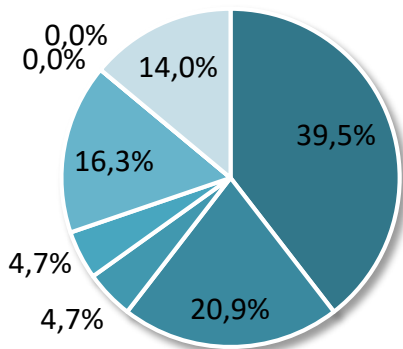
Location and etiology of bleeds

* number of bleeds

- Joints (N=73)
- Other (N=43)



- Knee (N=14)
- Ankle (N=25)
- Elbow (N=12)
- Other joint (N=22)



- Muscles (N=17)
- Subcutaneous (N=9)
- Oral cavity (N=2)
- Urogenital tract (N=2)
- Epistaxes (N=7)
- GIT (N=0)
- CNS (N=0)
- Other (N=6)

| | Traumatic | Spontaneous | |
|------------------------|------------|-------------|--|
| Joints (N=73) | 42% | 58% | |
| Muscles (N=17) | 18% | 82% | |
| Subcutaneous (N=9) | 67% | 33% | |
| Oral cavity (N=2) | 0% | 100% | |
| Urogenital tract (N=2) | 0% | 100% | |
| Epistaxes (N=7) | 14% | 86% | |
| GIT (N=0) | | | |
| CNS (N=0) | | | |
| Other (N=6) | 33% | 67% | |
| Total (N=116) | 37% | 63% | |

Detailed treatment of bleeds

* number of bleeds

| | Joints | Muscles | Subcutaneous | Oral cavity | Urogenital tract | Epistaxes | GIT | CNS | Other | Total |
|--|---------------|---------------|---------------|----------------|------------------|---------------|-----|-----|---------------|-------------------|
| No. of bleeds | 73 | 17 | 9 | 2 | 2 | 7 | 0 | 0 | 6 | 116 |
| FIX consumption per bleed (IU), valid N | 73 | 17 | 9 | 2 | 2 | 7 | | | 6 | 116 |
| geometric mean | 3430.9 | 4257.3 | 5163.2 | 9219.5 | 4024.9 | 5858.2 | | | 3911.8 | 3876.9 |
| median | 3000.0 | 3600.0 | 3000.0 | 11000.0 | 5400.0 | 4200.0 | | | 5100.0 | 3550.0 |
| min – max | 1000–81000 | 1200–31000 | 1500–45000 | 5000–17000 | 1800–9000 | 1800–68500 | | | 1200–8000 | 1000–81000 |
| sum | 425200 | 98600 | 95800 | 22000 | 10800 | 93100 | | | 27800 | 773300 |
| No. of doses per bleed | | | | | | | | | | |
| geometric mean | 1.9 | 2.4 | 2.5 | 12.2 | 2.8 | 3.3 | | | 1.8 | 2.1 |
| median | 2 | 2 | 1 | 13 | 3 | 3 | | | 2 | 2 |
| min – max | 1–43 | 1–15 | 1–15 | 10–15 | 2–4 | 1–26 | | | 1–6 | 1–43 |
| Duration of therapy per bleed, days | | | | | | | | | | |
| geometric mean | 1.6 | 2.0 | 2.3 | 8.4 | 2.0 | 2.5 | | | 1.5 | 1.8 |
| median | 1 | 2 | 1 | 10 | 2 | 2 | | | 1 | 2 |
| min – max | 1–31 | 1–11 | 1–14 | 5–14 | 2–2 | 1–19 | | | 1–5 | 1–31 |
| N (%) with hospitalization | 1 (1.4%) | 1 (5.9%) | 1 (11.1%) | 1 (50%) | 0 (0%) | 1 (14.3%) | | | 1 (16.7%) | 6 (5.2%) |
| N (%) with rebleeding | 3 (4.1%) | 0 (0%) | 0 (0%) | 1 (50%) | 0 (0%) | 0 (0%) | | | 0 (0%) | 4 (3.4%) |

ABR according to centres Haemophilia B (PWHB)

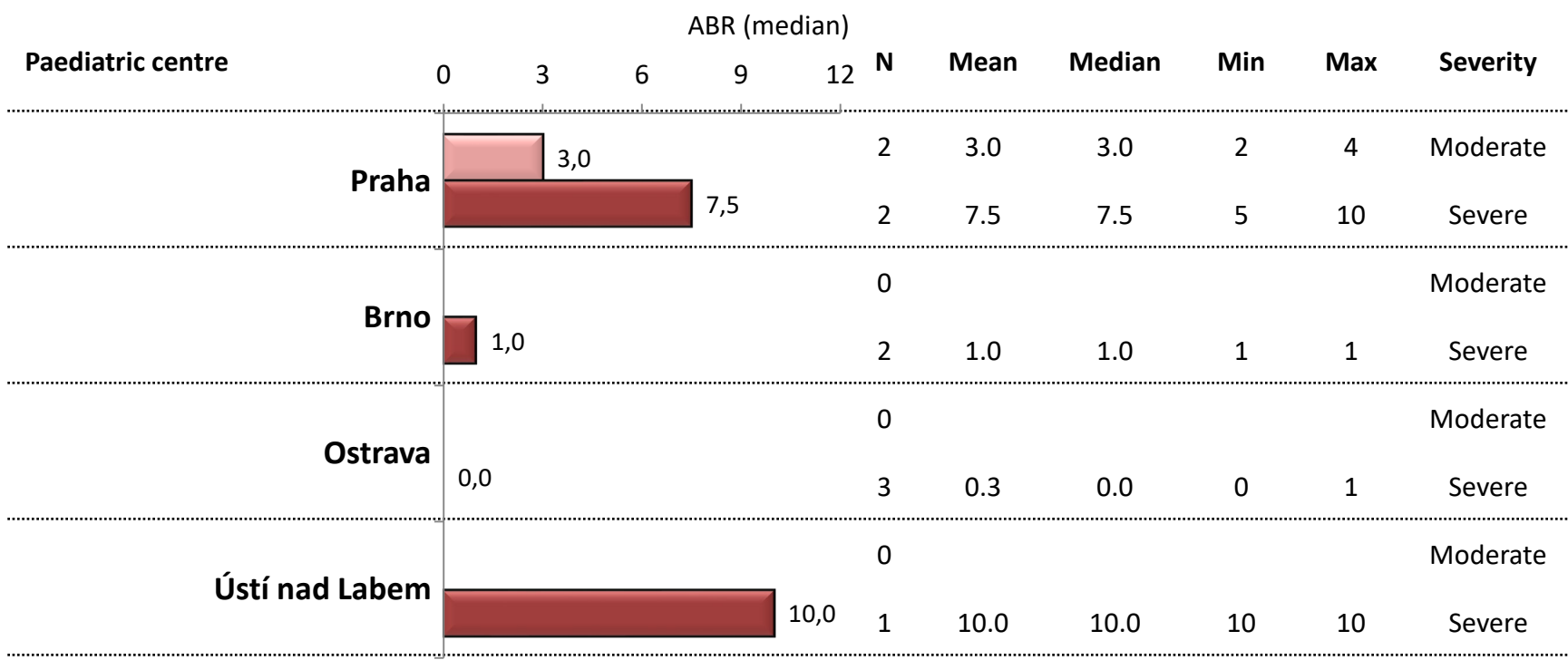


Annual bleeding rate on permanent prophylaxis

HaemB on prophylaxis
Paed. centres
N=10

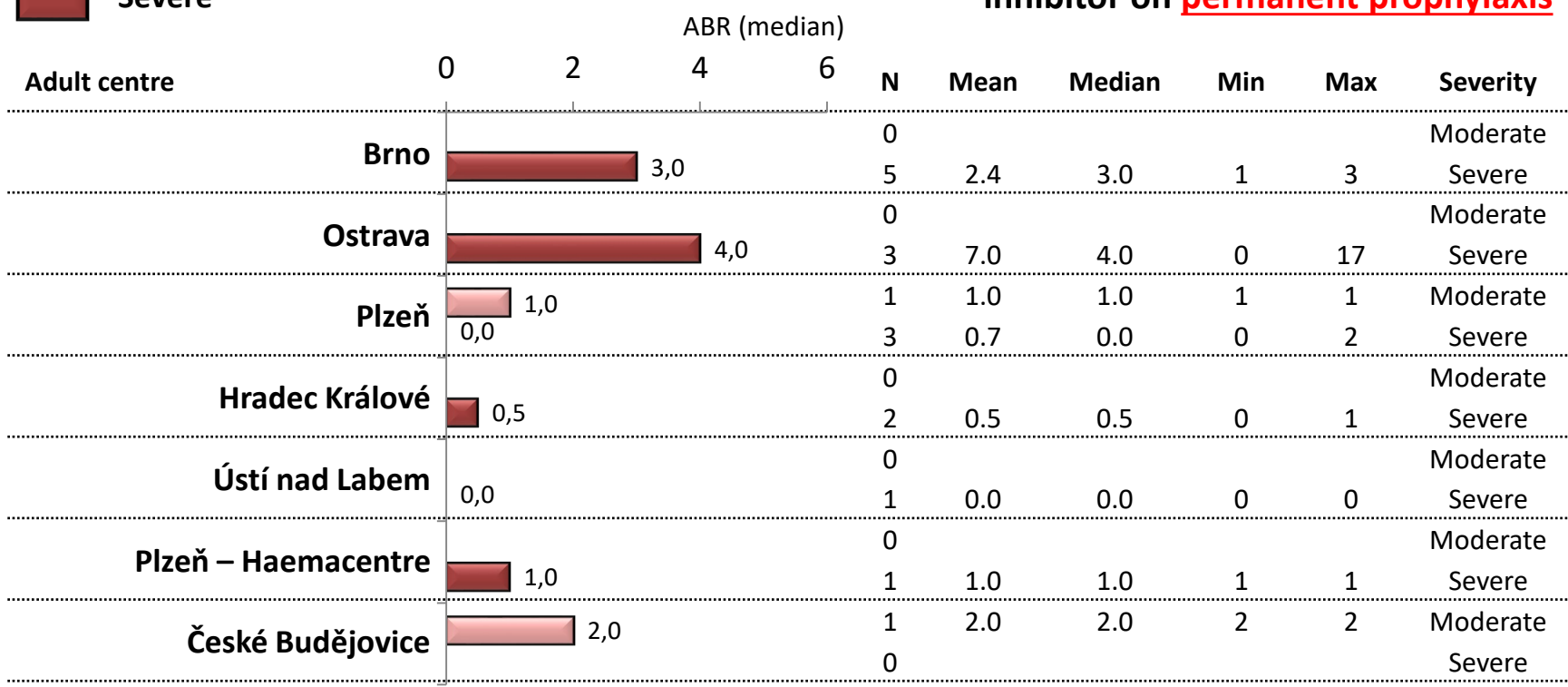
 Moderate
 Severe

Frequency of bleeding in PWHB without inhibitor on **permanent prophylaxis**



Annual bleeding rate on permanent prophylaxis

Frequency of bleeding in PWHB without inhibitor on **permanent prophylaxis**



Annual bleeding rate regardless prophylaxis

HaemB
Paed. centres
N=23



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

| Paediatric centre | ABR (median) | | | | N | Mean | Median | Min | Max | % on permanent prophylaxis |
|-------------------|--------------|-----|------|----|---|------|--------|-----|-----|----------------------------|
| | 0 | 5 | 10 | 15 | | | | | | |
| Praha | 0,5 | | | | 8 | 1.5 | 0.5 | 0 | 5 | 25.0% |
| | | 5,0 | | | 3 | 5.3 | 5.0 | 1 | 10 | 66.7% |
| Brno | 0,0 | | | | 1 | 0.0 | 0.0 | 0 | 0 | 0.0% |
| | | 1,0 | | | 2 | 1.0 | 1.0 | 1 | 1 | 100.0% |
| Ostrava | | | | | 0 | | | | | |
| | 0,0 | | | | 3 | 0.3 | 0.0 | 0 | 1 | 100.0% |
| České Budějovice | 0,0 | | | | 1 | 0.0 | 0.0 | 0 | 0 | 0.0% |
| | | | | | 0 | | | | | |
| Hradec Králové | | 2,0 | | | 1 | 2.0 | 2.0 | 2 | 2 | 0.0% |
| | | | | | 0 | | | | | |
| Ústí nad Labem | | | | | 0 | | | | | |
| | | | 10,0 | | 1 | 10.0 | 10.0 | 10 | 10 | 100.0% |
| Plzeň | 0,0 | | | | 1 | 0.0 | 0.0 | 0 | 0 | 0.0% |
| | | 2,0 | | | 1 | 2.0 | 2.0 | 2 | 2 | 0.0% |
| Olomouc | 0,0 | | | | 1 | 0.0 | 0.0 | 0 | 0 | 0.0% |
| | | | | | 0 | | | | | |

Annual bleeding rate regardless prophylaxis

HaemB
Adult centres
N=45

* missing ABR in 2 adults



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

| Adult centre | ABR (median) | | N* | Mean | Median | Min | Max | % on permanent prophylaxis |
|---------------------|--------------|--------|----|------|--------|-----|-----|----------------------------|
| | Moderate | Severe | | | | | | |
| Brno | 2,0 | 3,0 | 4 | 2.0 | 2.0 | 0 | 4 | 0.0% |
| | | | 5 | 2.4 | 3.0 | 1 | 3 | 100.0% |
| Ostrava | 3,0 | 1,0 | 2 | 3.0 | 3.0 | 2 | 4 | 0.0% |
| | | | 6 | 3.8 | 1.0 | 0 | 17 | 50.0% |
| Plzeň | 0,0 | 0,5 | 3 | 0.3 | 0.0 | 0 | 1 | 33.3% |
| | | | 4 | 0.8 | 0.5 | 0 | 2 | 75.0% |
| Liberec | 0,0 | 18,0 | 1 | 0.0 | 0.0 | 0 | 0 | 0.0% |
| | | | 1 | 18.0 | 18.0 | 18 | 18 | 0.0% |
| Olomouc | 0,0 | 6,5 | 7 | 1.1 | 0.0 | 0 | 4 | 0.0% |
| | | | 2 | 6.5 | 6.5 | 1 | 12 | 25.0% |
| Hradec Králové | 1,0 | 0,0 | 1 | 1.0 | 1.0 | 1 | 1 | 0.0% |
| | | | 3 | 0.3 | 0.0 | 0 | 1 | 66.7% |
| Ústí nad Labem | | 2,0 | 0 | | | | | |
| | | | 2 | 2.0 | 2.0 | 0 | 4 | 50.0% |
| Plzeň – Haemacentre | | 1,0 | 0 | | | | | |
| | | | 1 | 1.0 | 1.0 | 1 | 1 | 100.0% |
| České Budějovice | 2,0 | 2,0 | 1 | 2.0 | 2.0 | 2 | 2 | 100.0% |
| | | | 2 | 2.0 | 2.0 | 0 | 4 | 0.0% |

Prophylactic regimens and treatment outcomes

HaemB
Paed. centres
N=23

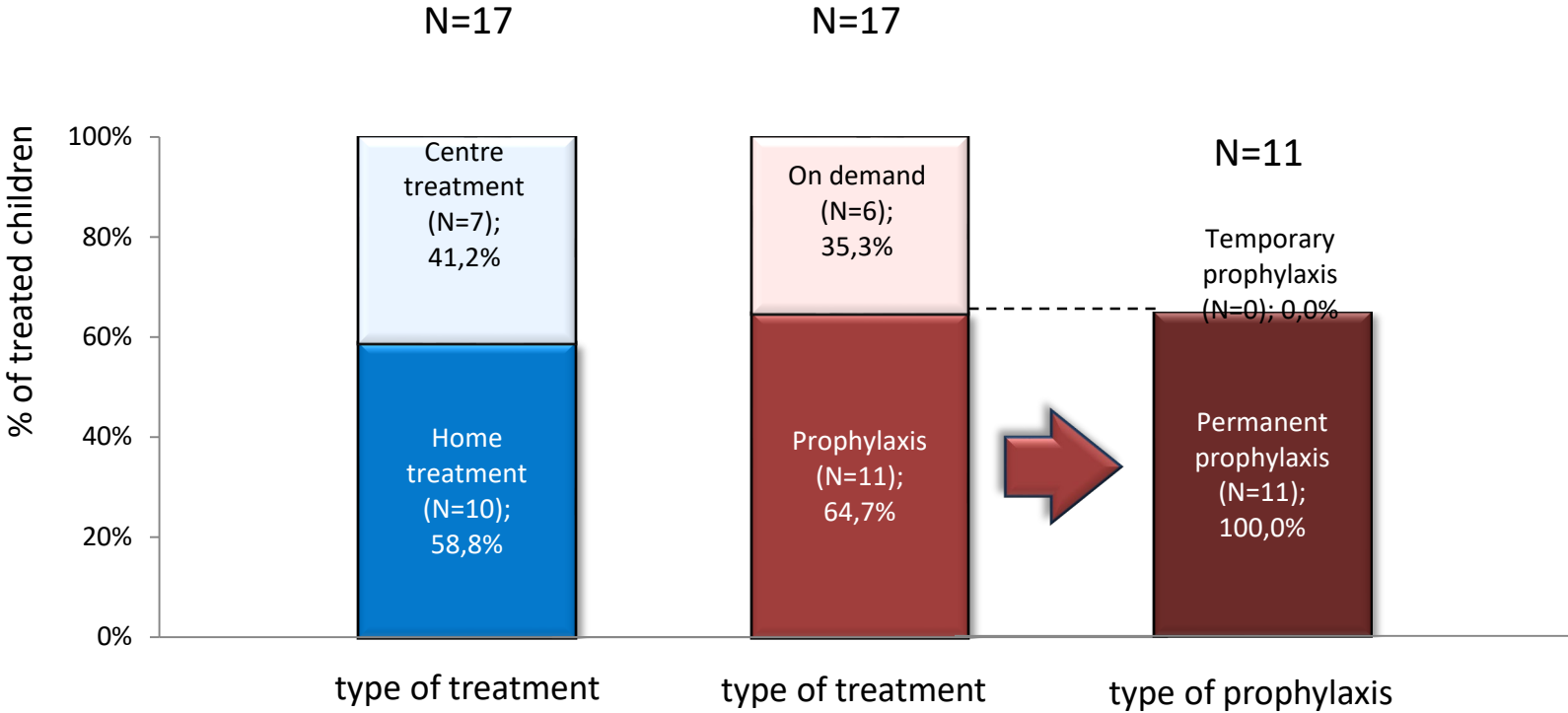
| Paediatric centre | Severity | Total N | PERMANENT PROPHYLAXIS | | | | | | | | ON-DEMAND / TEMPORARY PROPHY | | | |
|-------------------|----------|---------|-----------------------|---|--|-------------|------|------|-------|--------------|------------------------------|------|--------|--|
| | | | % of patients | N | Dosing of prophylaxis (IU/kg per week) | | | | ABR | | N | ABR | | |
| | | | | | Mean | Median | Min | Max | Mean | Median | | Mean | Median | |
| Praha | Moderate | 8 | 25.0% | 2 | 75.6 | 75.6 | 71.4 | 79.8 | 0.0 | 0.0 | 6 | 6.0 | 16.0 | |
| | Severe | 3 | 66.7% | 2 | 31.1 | 31.1 | 30.3 | 31.9 | 115.4 | 115.4 | 1 | 1.0 | 37.0 | |
| Brno | Moderate | 1 | 0.0% | 0 | | | | | | | 1 | 1.0 | 5.0 | |
| | Severe | 2 | 100.0% | 2 | 34.8 | 34.8 | 33.9 | 35.7 | 0.0 | 0.0 | 0 | | | |
| Ostrava | Moderate | 0 | 0.0% | 0 | | | | | | | 0 | | | |
| | Severe | 3 | 100.0% | 3 | 48.2 | 46.9 | 29.6 | 68.2 | 0.0 | 0.0 | 0 | | | |
| Č. Budějovice | Moderate | 1 | 0.0% | 0 | | | | | | | 1 | 1.0 | 4.0 | |
| | Severe | 0 | 0.0% | 0 | | | | | | | 0 | | | |
| Hradec Králové | Moderate | 1 | 0.0% | 0 | | | | | | | 1 | 1.0 | 4.0 | |
| | Severe | 0 | 0.0% | 0 | | | | | | | 0 | | | |
| Ústí nad Labem | Moderate | 0 | 0.0% | 0 | | | | | | | 0 | | | |
| | Severe | 1 | 100.0% | 1 | 62.7 | 62.7 | 62.7 | 62.7 | 0.0 | 0.0 | 0 | | | |
| Plzeň | Moderate | 1 | 0.0% | 0 | | | | | | | 1 | 1.0 | 2.0 | |
| | Severe | 1 | 0.0% | 0 | | | | | | | 1 | 1.0 | 6.0 | |
| Olomouc | Moderate | 1 | 0.0% | 0 | | | | | | | 1 | 1.0 | 4.0 | |
| | Severe | 0 | | | | | | | | | | | | |

Prophylactic regimens and treatment outcomes

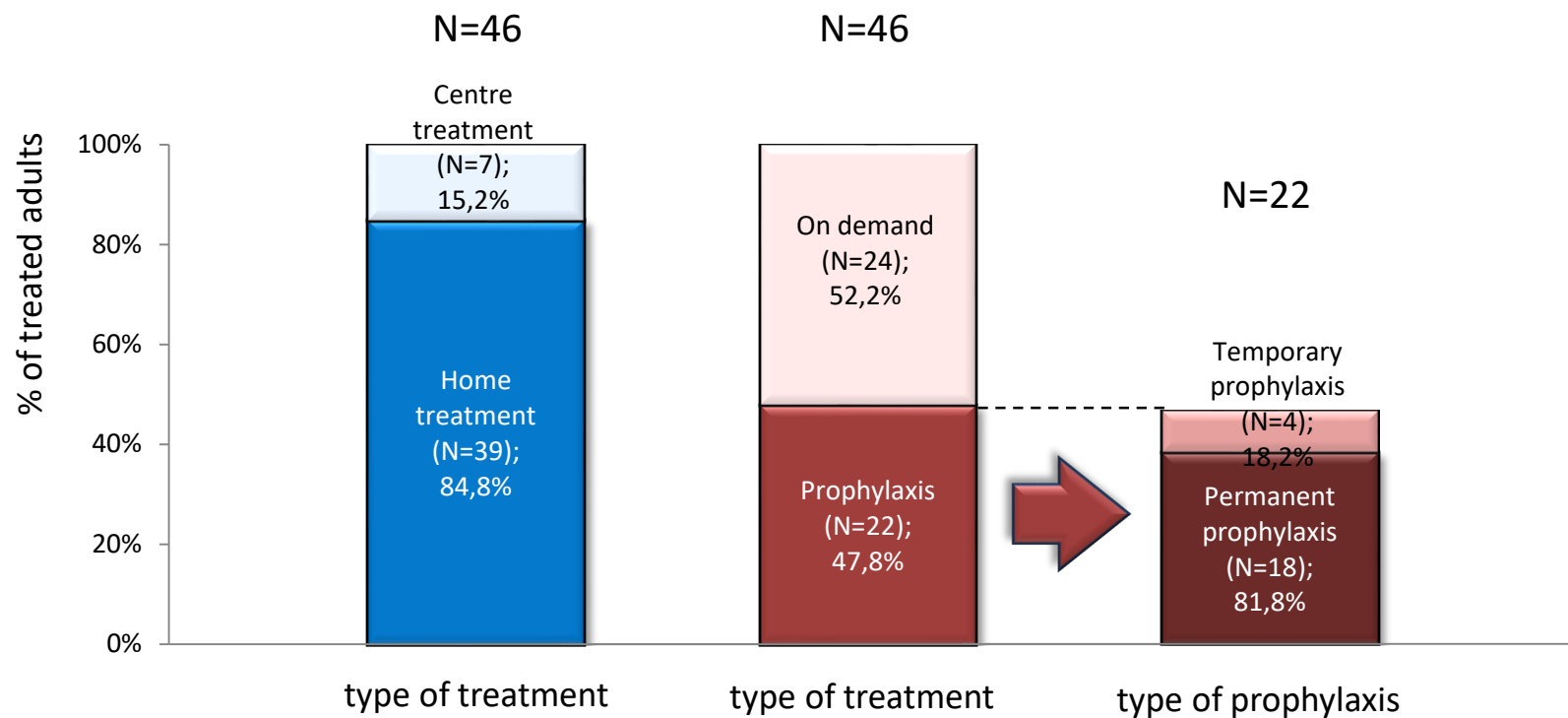
| Adult centre | Severity | Total N | PERMANENT PROPHYLAXIS | | | | | | | | | ON-DEMAND / TEMPORARY PROPHY | | | |
|---------------------|----------|---------|-----------------------|---|--|--------|------|------|------|--------|--------|------------------------------|------|--------|--------|
| | | | % of patients | N | Dosing of prophylaxis (IU/kg per week) | | | | ABR* | | Age | N | ABR* | | Age |
| | | | | | Mean | Median | Min | Max | Mean | Median | Median | | Mean | Median | Median |
| Brno | Moderate | 4 | 0.0% | 0 | | | | | | | | 4 | 2.0 | 2.0 | 49 |
| | Severe | 5 | 100.0% | 5 | 54.3 | 54.5 | 43.8 | 73.2 | 2.4 | 3.0 | 31 | 0 | | | |
| Ostrava | Moderate | 2 | 0.0% | 0 | | | | | | | | 2 | 3.0 | 3.0 | 27 |
| | Severe | 6 | 50.0% | 3 | 44.9 | 46.2 | 38.6 | 50.0 | 7.0 | 4.0 | 51 | 3 | 0.7 | 0.0 | 59 |
| Plzeň | Moderate | 3 | 33.3% | 1 | 6.1 | 6.1 | 6.1 | 6.1 | 1.0 | 1.0 | 35 | 2 | 0.0 | 0.0 | 62 |
| | Severe | 4 | 75.0% | 3 | 11.6 | 11.8 | 10.5 | 12.6 | 0.7 | 0.0 | 42 | 1 | 1.0 | 1.0 | 36 |
| Liberec | Moderate | 1 | 0.0% | 0 | | | | | | | | 1 | 0.0 | 0.0 | 45 |
| | Severe | 1 | 0.0% | 0 | | | | | | | | 1 | 18.0 | 18.0 | 26 |
| Olomouc | Moderate | 7 | 0.0% | 0 | | | | | | | | 7 | 1.1 | 0.0 | 45 |
| | Severe | 4 | 25.0% | 1 | 26.7 | 26.7 | 26.7 | 26.7 | 0.0 | 0.0 | 52 | 3 | 6.5 | 6.5 | 49 |
| Hradec Králové | Moderate | 1 | 0.0% | 0 | | | | | | | | 1 | 1.0 | 1.0 | 64 |
| | Severe | 3 | 66.7% | 2 | 36.4 | 36.4 | 21.1 | 51.7 | 0.5 | 0.5 | 40 | 1 | 0.0 | 0.0 | 62 |
| Ústí n. Labem | Moderate | 0 | | | | | | | | | | | | | |
| | Severe | 2 | 50.0% | 1 | 52.5 | 52.5 | 52.5 | 52.5 | 0.0 | 0.0 | 23 | 1 | 4.0 | 4.0 | 47 |
| Plzeň - Haemacentre | Moderate | 0 | | | | | | | | | | | | | |
| | Severe | 1 | 100.0% | 1 | 46.9 | 46.9 | 46.9 | 46.9 | 1.0 | 1.0 | 37 | 0 | | | |
| Č. Budějovice | Moderate | 1 | 100.0% | 1 | 22.1 | 22.1 | 22.1 | 22.1 | 2.0 | 2.0 | 52 | 0 | | | |
| | Severe | 2 | 0.0% | 0 | | | | | | | | 2 | 2.0 | 2.0 | 50 |

* missing ABR in 2 adults

Type of treatment (subgroup of treated patients)



Type of treatment (subgroup of treated patients)

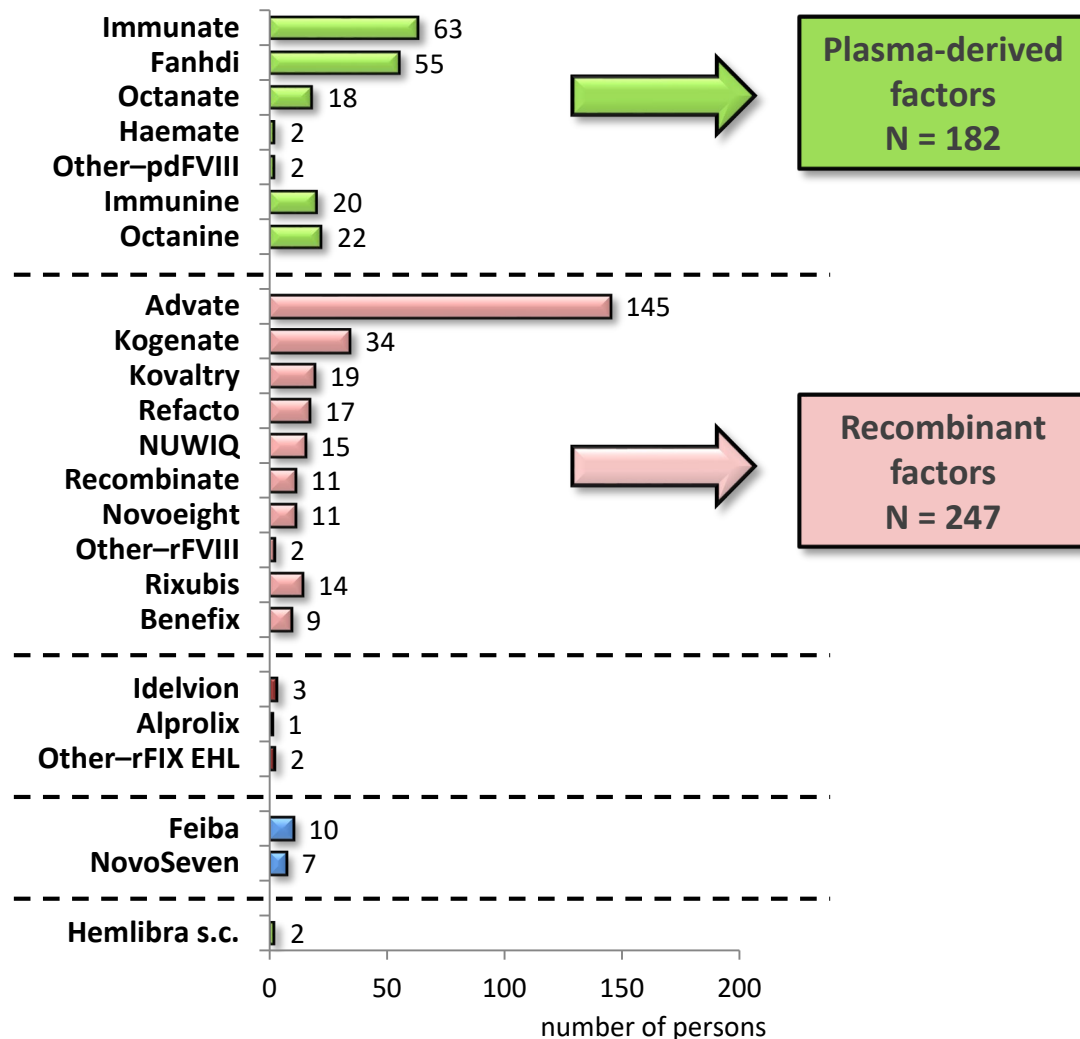


Treatment data and factor consumption

Haemophilia A and B



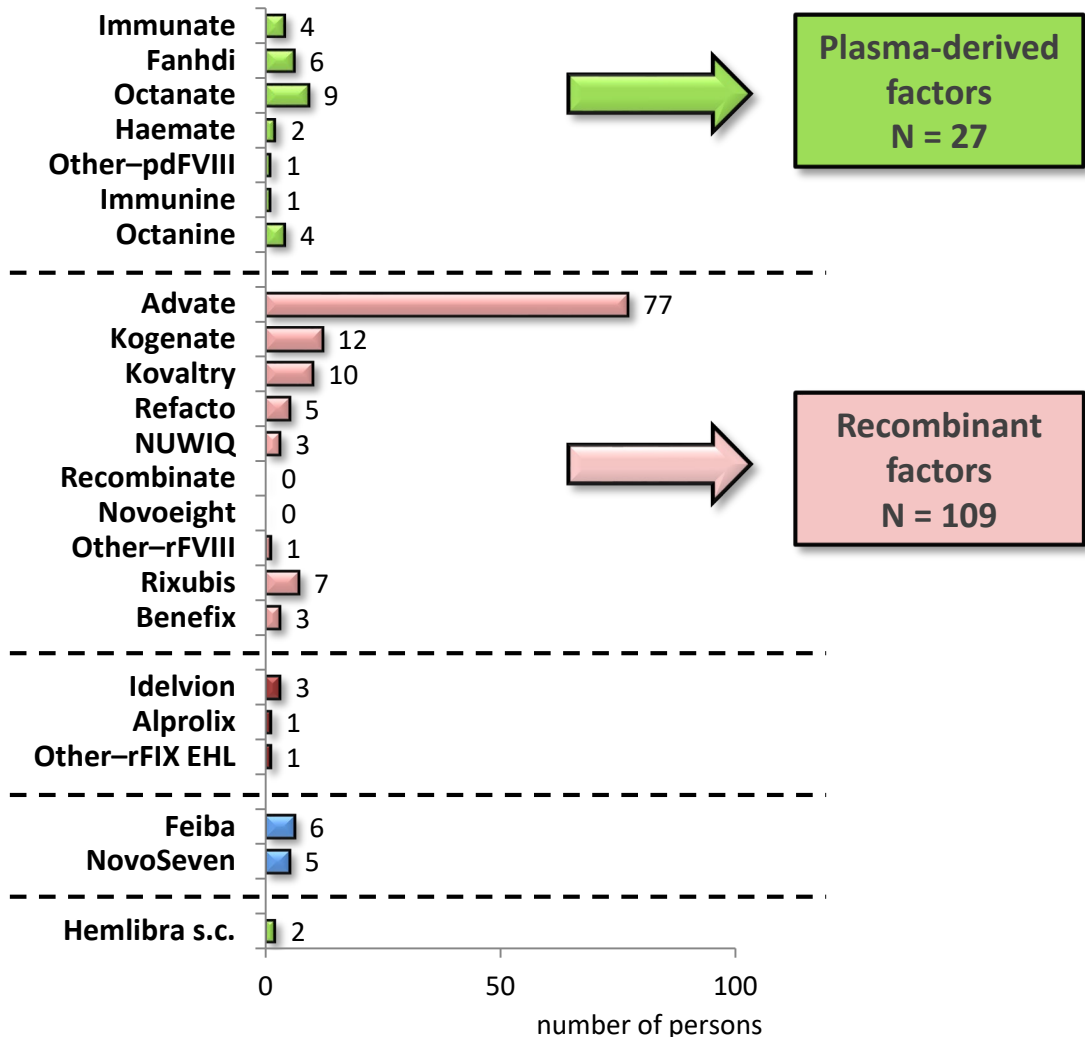
Treatment



419 persons (54.4% of all PWH) were treated in 2018 (**404 persons received standard factor concentrates**, another 9 persons EHL factors, by-pass therapy or emicizumab and in 6 data are not available; 34 persons received more than one type/brand of concentrate). Plasma-derived factors were administered in 182 persons (23.6% of all PWH, 45% of 404 PHWs treated with factor), whereas recombinant factors in 247 persons (32.1% of all PWH, 61.1% of 404 factor treated PHWs). 25 persons were treated with both plasma-derived and recombinant factor.

¹ missing type of treatment in 5 adults and 1 child

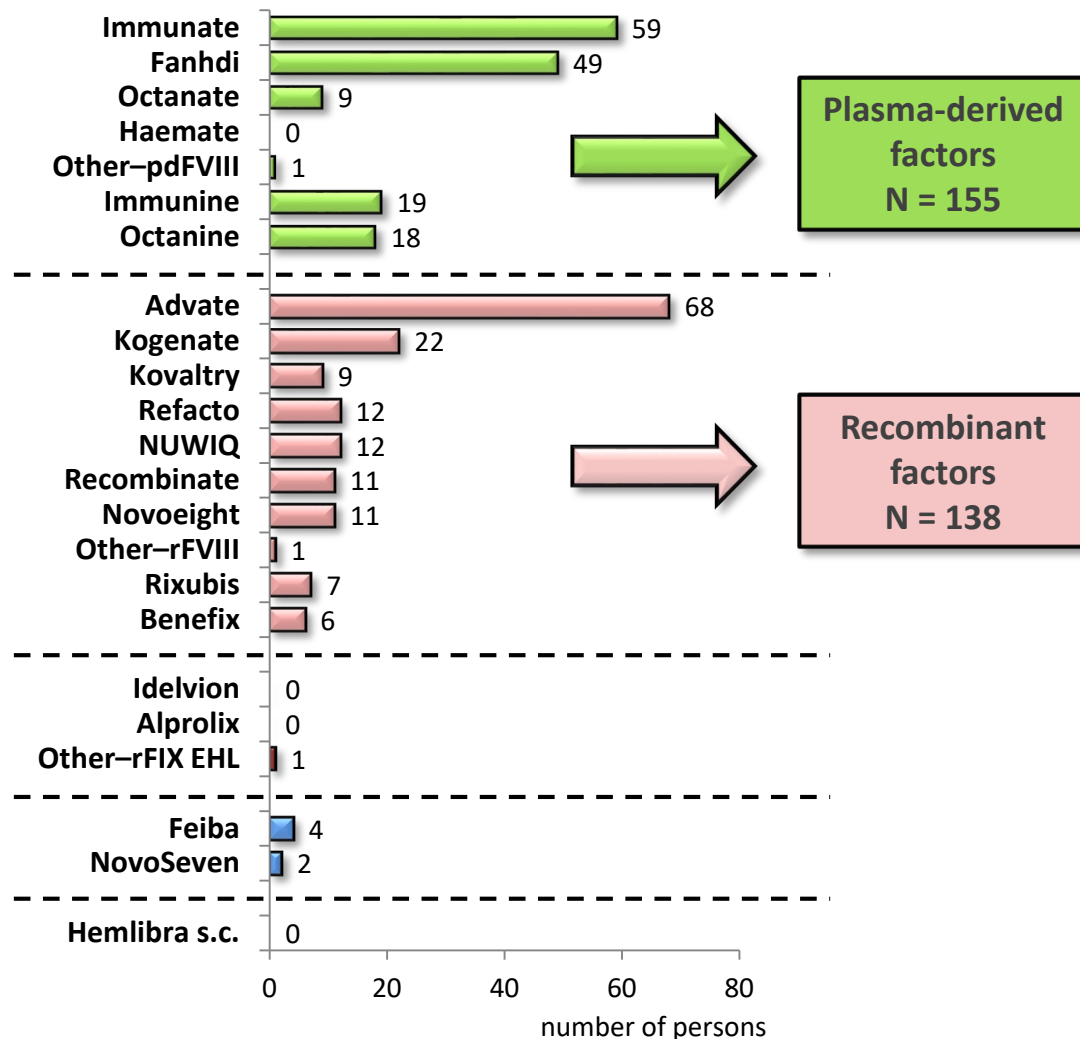
Treatment



139 children (55.8% of all PWH) were treated in 2018 (**133 children received standard factor concentrates**, another 5 children EHL factors, by-pass therapy or emicizumab and in 1 data are not available; 11 persons received more than one type/brand of concentrate). Plasma-derived factors were administered in 27 children (10.8% of all PWH, 20.3% of 133 PHWs treated with factor), whereas recombinant factors in 109 children (43.8% of all PWH, 82% of 133 factor treated PHWs). Three children were treated with both plasma-derived and recombinant factor.

¹ missing type of treatment in 1 child

Treatment



280 adults (53.7% of all PWH) were treated in 2018 (**271 adults received standard factor concentrates**, another 4 adults EHL factors or by-pass therapy only and in 5 data are not available; 23 adults received more than one type/brand of concentrate).

Plasma-derived factors were administered in 155 adults (29.8% of all PWH, 57.2% of 271 PHWs treated with factor), whereas recombinant factors in 138 adults (26.5% of all PWH, 50.9% of 271 factor treated PHWs).

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

¹ missing type of treatment in 5 adults

Comparison of treatment in years 2018 and 2017

| | 2018 | | | 2017 | | |
|--|------------|--------------|---------------|------------|--------------|---------------|
| | N | % of all PWH | % treated PWH | N | % of all PWH | % treated PWH |
| All persons treated with factor concentrates | 404 | 52.5 | 100.0 | 404 | 54.4 | 100.0 |
| <i>Plasma-derived factor</i> | 157 | 20.4 | 38.9 | 204 | 27.5 | 50.5 |
| <i>Recombinant factor</i> | 247 | 32.1 | 61.1 | 200 | 26.9 | 49.5 |
| Without treatment | 366 | 47.5 | - | 339 | 45.6 | - |
| Total | 770 | 100.0 | - | 743 | 100.0 | - |

Comparison of treatment in years 2018 and 2017

| | 2018 | | | 2017 | | |
|---|------------|--------------|---------------|------------|--------------|---------------|
| | N | % of all PWH | % treated PWH | N | % of all PWH | % treated PWH |
| All children treated with factor concentrates | 133 | 53.4 | 100.0 | 134 | 56.5 | 100.0 |
| <i>Plasma-derived factor</i> | 24 | 9.6 | 18.0 | 28 | 11.8 | 20.9 |
| <i>Recombinant factor</i> | 109 | 43.8 | 82.0 | 106 | 44.7 | 79.1 |
| Without treatment | 116 | 46.6 | - | 103 | 43.5 | - |
| Total | 249 | 100.0 | - | 237 | 100.0 | - |

Comparison of treatment in years 2018 and 2017

| | 2018 | | | 2017 | | |
|---|------------|--------------|---------------|-----------|--------------|---------------|
| | N | % of all PWH | % treated PWH | N | % of all PWH | % treated PWH |
| All adults treated with factor concentrates | 271 | 52.0 | 100.0 | 270 | 53.4 | 100.0 |
| <i>Plasma-derived factor</i> | 133 | 25.5 | 49.1 | 176 | 34.8 | 65.2 |
| <i>Recombinant factor</i> | 138 | 26.5 | 50.9 | 94 | 18.6 | 34.8 |
| Without treatment | 250 | 48.0 | - | 236 | 46.6 | - |
| Total | 521 | 100.0 | - | 506 | 100.0 | - |

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 |
|-------------------|-----------------------------|--------------------------|---------------------------|---|-------------------------|---|
| FVIII (IU) | <i>Immunate</i> | 5 423 500 | 63 | 86 087.3 | | |
| | <i>Fanhdi</i> | 8 648 000 | 55 | 157 236.4 | | |
| | <i>Octanate</i> | 1 874 500 | 18 | 104 138.9 | | |
| | <i>Haemate P</i> | 1 798 500 | 2 | 899 250.0 | | |
| | <i>Other plasma-derived</i> | 307 000 | 2 | 153 500.0 | | |
| | FVIII PD total | 18 051 500 | 140 | 128 939.3 | | |
| | <i>Advate</i> | 21 264 650 | 145 | 146 652.8 | | |
| | <i>Kogenate</i> | 5 123 250 | 34 | 150 683.8 | | |
| | <i>Kovaltry</i> | 1 128 250 | 19 | 59 381.6 | | |
| | <i>Refacto</i> | 1 363 000 | 17 | 80 176.5 | | |
| | <i>NUWIQ</i> | 1 137 500 | 15 | 75 833.3 | | |
| | <i>Recombinate</i> | 1 119 000 | 11 | 101 727.3 | | |
| | <i>Novoeight</i> | 993 000 | 11 | 90 272.7 | | |
| | <i>Other recombinant</i> | 421 500 | 2 | 210 750.0 | | |
| | FVIII REC total | 32 550 150 | 225 | 144 667.3 | | |
| | FVIII total | 50 601 650 | 347 | 145 826.1 | 667 | 75 864.5 |
| FIX (IU) | <i>Immunine</i> | 1 140 800 | 20 | 57 040.0 | | |
| | <i>Octanine</i> | 1 126 500 | 22 | 51 204.5 | | |
| | FIX PD total | 2 267 300 | 42 | 53 983.3 | | |
| | <i>Rixubis</i> | 2 026 250 | 14 | 144 732.1 | | |
| | <i>Benefix</i> | 666 500 | 9 | 74 055.6 | | |
| | FIX REC total | 2 692 750 | 22 | 122 397.7 | | |
| | FIX total | 4 960 050 | 57 | 87 018.4 | 103 | 48 155.8 |
| EHL (IU) | <i>Idelvion</i> | 443 850 | 3 | 147 950.0 | | |
| | <i>Alprolix</i> | 10 200 | 1 | 10 200.0 | | |
| | <i>Other FIX EHL</i> | 5 466 | 1 | 5 466.0 | | |
| by-pass | <i>Feiba (U)</i> | 3 440 750 | 10 | 344 075.0 | | |
| | <i>NovoSeven (mg)</i> | 5 180.0 | 7 | 740.0 | | |
| emicizumab | <i>Hemlibra s.c. (mg)</i> | 1 620 | 2 | 810.0 | | |

Consumption of drugs

Children

| 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 |
|-----------------------------|--------------------------|---------------------------|---|-------------------------|---|
| FVIII (IU) | | | | | |
| <i>Immunate</i> | 202 000 | 4 | 50 500.0 | | |
| <i>Fanhdi</i> | 1 586 500 | 6 | 264 416.7 | | |
| <i>Octanate</i> | 1 169 000 | 9 | 129 888.9 | | |
| <i>Haemate P</i> | 1 798 500 | 2 | 899 250.0 | | |
| <i>Other plasma-derived</i> | 298 000 | 1 | 298 000.0 | | |
| FVIII PD total | 5 054 000 | 22 | 229 727.3 | | |
| <i>Advate</i> | 11 133 150 | 77 | 144 586.4 | | |
| <i>Kogenate</i> | 1 574 250 | 12 | 131 187.5 | | |
| <i>Kovaltry</i> | 547 750 | 10 | 54 775.0 | | |
| <i>Refacto</i> | 491 000 | 5 | 98 200.0 | | |
| <i>NUWIQ</i> | 322 000 | 3 | 107 333.3 | | |
| <i>Recombinate</i> | 0 | 0 | - | | |
| <i>Novoeight</i> | 0 | 0 | - | | |
| <i>Other recombinant</i> | 262 500 | 1 | 262 500.0 | | |
| FVIII REC total | 14 330 650 | 100 | 143 306.5 | | |
| FVIII total | 19 384 650 | 120 | 161 538.8 | 214 | 90 582.5 |
| FIX (IU) | | | | | |
| <i>Immunine</i> | 7 200 | 1 | 7 200.0 | | |
| <i>Octanine</i> | 88 000 | 4 | 22 000.0 | | |
| FIX PD total | 95 200 | 5 | 19 040.0 | | |
| <i>Rixubis</i> | 643 250 | 7 | 91 892.9 | | |
| <i>Benefix</i> | 82 000 | 3 | 27 333.3 | | |
| FIX REC total | 725 250 | 9 | 80 583.3 | | |
| FIX total | 820 450 | 13 | 63 111.5 | 35 | 23 441.4 |
| EHL (IU) | | | | | |
| <i>Idelvion</i> | 443 850 | 3 | 147 950.0 | | |
| <i>Alprolix</i> | 10 200 | 1 | 10 200.0 | | |
| <i>Other FIX EHL</i> | 5 466 | 1 | 5 466.0 | | |
| by-pass | | | | | |
| <i>Feiba (U)</i> | 1 952 750 | 6 | 325 458.3 | | |
| <i>NovoSeven (mg)</i> | 1 955.0 | 5 | 391.0 | | |
| emicizumab | | | | | |
| <i>Hemlibra s.c. (mg)</i> | 1 620 | 2 | 810.0 | | |

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 |
|-----------------------------|--------------------------|---------------------------|---|-------------------------|---|
| FVIII (IU) | | | | | |
| <i>Immunate</i> | 5 221 500 | 59 | 88 500.0 | | |
| <i>Fanhdi</i> | 7 061 500 | 49 | 144 112.2 | | |
| <i>Octanate</i> | 705 500 | 9 | 78 388.9 | | |
| <i>Haemate P</i> | 0 | 0 | - | | |
| <i>Other plasma-derived</i> | 9 000 | 1 | 9 000.0 | | |
| FVIII PD total | 12 997 500 | 118 | 110 148.3 | | |
| <i>Advate</i> | 10 131 500 | 68 | 148 992.6 | | |
| <i>Kogenate</i> | 3 549 000 | 22 | 161 318.2 | | |
| <i>Kovaltry</i> | 580 500 | 9 | 64 500.0 | | |
| <i>Refacto</i> | 872 000 | 12 | 72 666.7 | | |
| <i>NUWIQ</i> | 815 500 | 12 | 67 958.3 | | |
| <i>Recombinate</i> | 1 119 000 | 11 | 101 727.3 | | |
| <i>Novoeight</i> | 993 000 | 11 | 90 272.7 | | |
| <i>Other recombinant</i> | 159 000 | 1 | 159 000.0 | | |
| FVIII REC total | 18 219 500 | 125 | 145 756.0 | | |
| FVIII total | 31 217 000 | 227 | 137 519.8 | 453 | 68 911.7 |
| FIX (IU) | | | | | |
| <i>Immunine</i> | 1 133 600 | 19 | 59 663.2 | | |
| <i>Octanine</i> | 1 038 500 | 18 | 57 694.4 | | |
| FIX PD total | 2 172 100 | 37 | 58 705.4 | | |
| <i>Rixubis</i> | 1 383 000 | 7 | 197 571.4 | | |
| <i>Benefix</i> | 584 500 | 6 | 97 416.7 | | |
| FIX REC total | 1 967 500 | 13 | 151 346.2 | | |
| FIX total | 4 139 600 | 44 | 94 081.8 | 68 | 60 876.5 |
| EHL (IU) | | | | | |
| <i>Idelvion</i> | 0 | 0 | - | | |
| <i>Alprolix</i> | 0 | 0 | - | | |
| <i>Other FIX EHL</i> | 0 | 0 | - | | |
| by-pass | | | | | |
| <i>Feiba (U)</i> | 1 488 000 | 4 | 372 000.0 | | |
| <i>NovoSeven (mg)</i> | 3 225.0 | 2 | 1 612.5 | | |
| emicizumab | | | | | |
| <i>Hemlibra s.c. (mg)</i> | 0 | 0 | - | | |