WAPPS-HEMO

McMaster University
HEALTH RESEARCH METHODS, EVIDENCE, AND IMPACT

Switching from standard to extended half-life FVIII prophylaxis in hemophilia A

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Disclosures

- PI of the WAPPS-Hemo project
- McMaster University receives research funds from:
  - Bayer, NovoNordisk, Pfizer, Takeda, Roche, Sobi
- Clinical research support from:
  - CSL-Behring, NovoNordisk, Pfizer, Spark, Sanofi
- Personal support:
  - none
- Support for participation to this meeting:
  - Biotest

Talk objectives

1) General considerations and lesson learned from switching to EHL
   A) Impact of switching at the population level
   B) Impact of switching at the individual level
   C) Impact of tailoring prophylaxis with EHL

2) How to maximize the gain when switching to EHL?
   A) What is the guidance, if any?
   B) Switching support tool in WAPPS-Hemo

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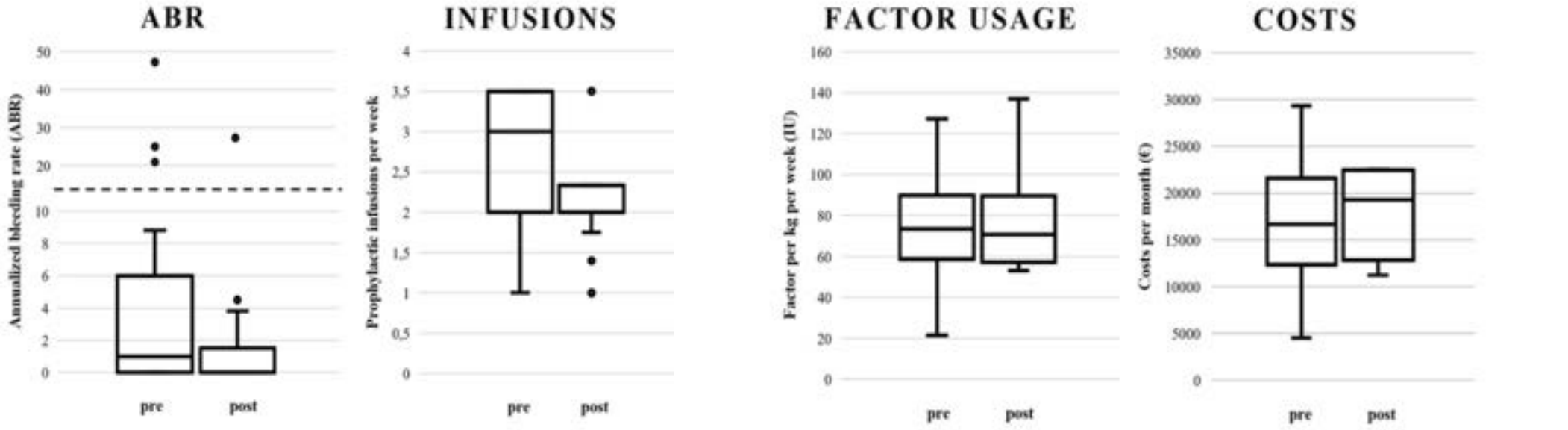
EHL benefits at the population level



	ABR	INFUSIONS	FACTOR USAGE	COSTS
Mean (±SD)	6.4 (12.2) vs. 2.3 (6.2)	2.7 (0.8) vs. 2.1 (0.6)	74 (25) IU vs. 77 (24) IU	17012 (6243) € vs. 18148 (4414) €
Median (range)	1 (0-47.2) vs. 0 (0-27.3)	3 (1-3.5) vs. 2 (1-3.5)	73 IU (22-127) vs. 71 IU (53-137)	16650 € (4543-29314) vs. 19286 € (11250-22500)

Ay, C., Feistritzer, C., Rettl, J., Schuster, G., Vavrovsky, A., Perschy, L., & Pabinger, I. Bleeding outcomes and factor utilization after switching to an extended half-life product for prophylaxis in haemophilia A in Austria. *Scientific Reports*, 2021, *11*(1), 12967. https://doi.org/10.1038/s41598-021-92245-5

Australian

TABLE 2 Factor usage comparin

			haemophilia A
			Eloctate n = 43
Prescribed no. of injections per week, median (LQ; UQ)			2.0 (1.9; 2.0)
Prescribed dose per injection (IU/kg), median (LQ; UQ)			52.6 (45.5; 58.8)
Expected factor usage per week (IU/kg/wk), median (LQ; UQ)			92.6 (79.9; 109.1)
Actual factor usage per week (IU/kg/wk), median (LQ; UQ),			94.5 (77.2; 120.1) n = 42

Abbreviations: LQ, lower quartile; SH

[a]Excludes patients who were on EHL

TABLE 3 Adherence and bleeding outcomes comparing last 6 mo of SHL prophylaxis to first 6 mo of EHL prophylaxis in patients with haemophilia A

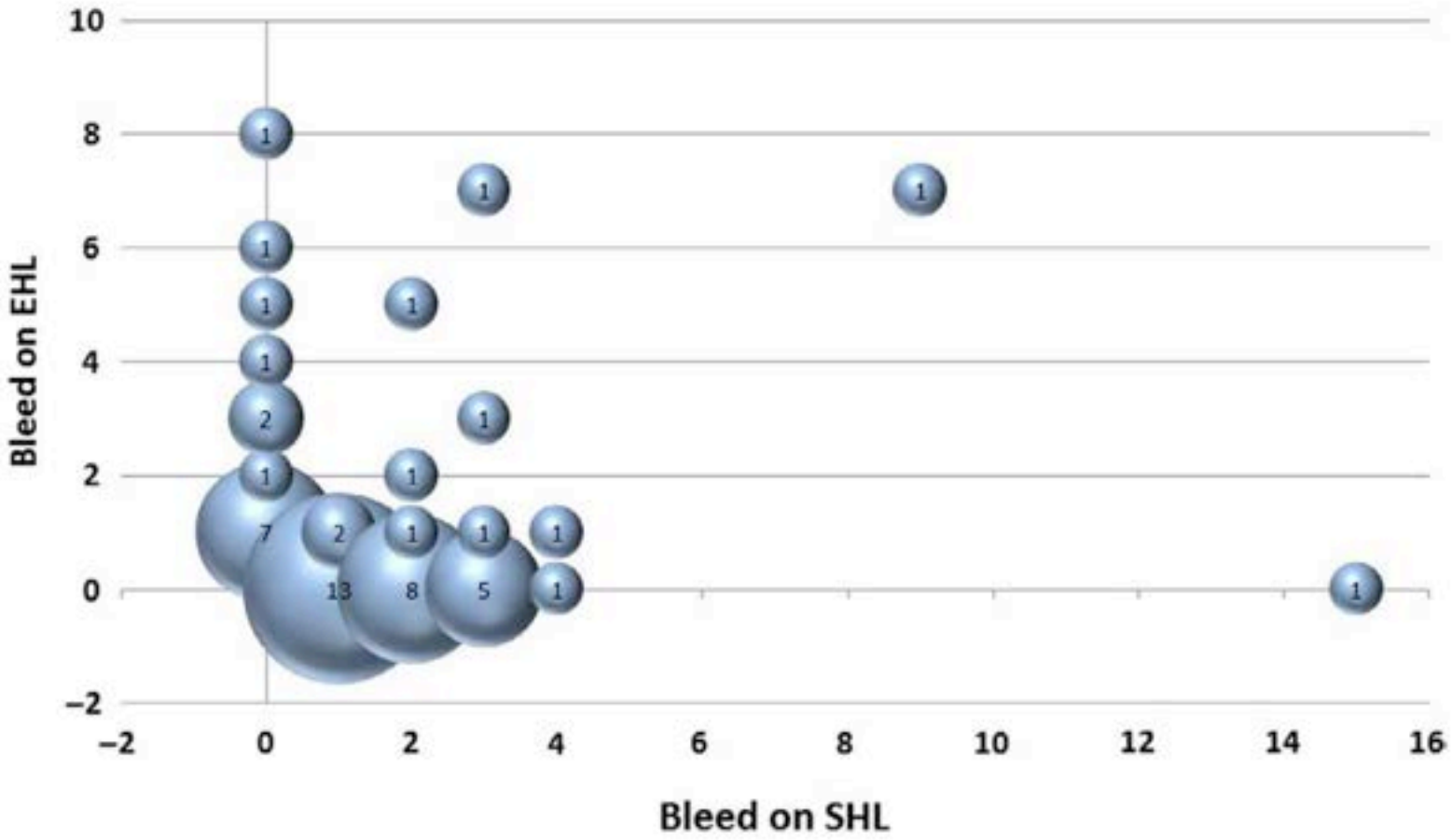
	SHL FVIII n = 61	EHL FVIII n = 127
Optimal adherence, n (%) (95% CI)	45 (74) (59.3-81.1)	110 (87) (79.6-91.5)
Reduced adherence, n (%) (95% CI)	11 (18) (10.0-28.6)	9 (7) (3.8-12.9)
ABR, median (LQ; UQ)	2.0 (0.0; 4.0)	0 (0; 2.0)
Zero bleeds, n (%) (95% CI)	27 (44) (32.5-56.7)	81 (64) (55.1-71.6)

Note: Of the 61 SHL patients analysed, 52 switched to Adynovate and 9 switched to Eloctate.

Abbreviations: ABR, annualized bleeding rate; CI, confidence interval; EHL, extended half-life; LQ, lower quartile; SHL, standard half-life; UQ, upper quartile.

Brennan, Y., Parikh, S., McRae, S., & Tran, H. (2020). The Australian experience with switching to extended half-life factor VIII and IX concentrates: On behalf of the Australian Haemophilia Centre Directors' Organisation. *Haemophilia*, *26*(3), 529–535. https://doi.org/10.1111/hae.13970

Australian real-world data



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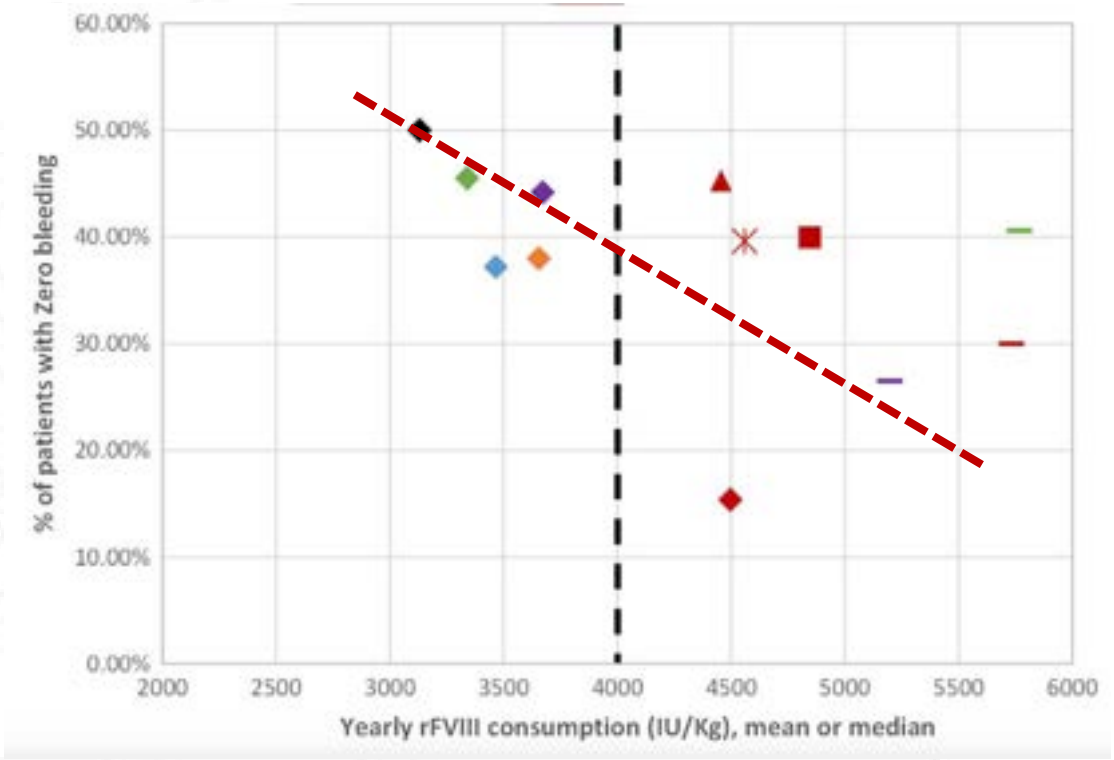
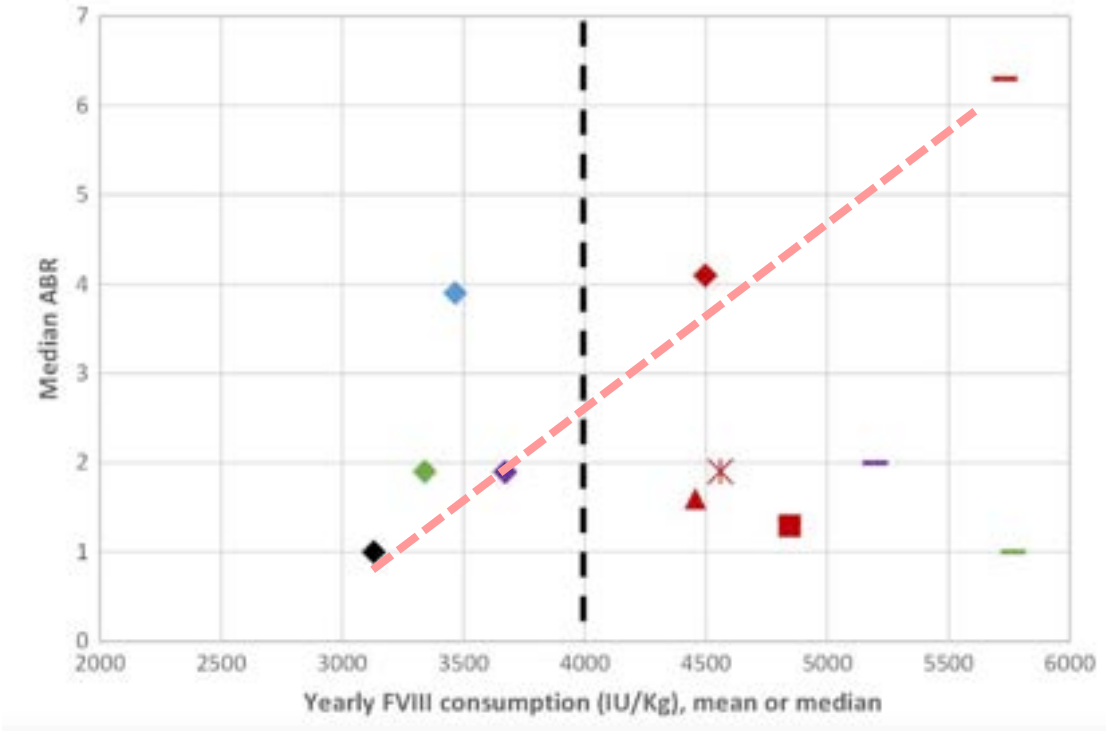
Hallucinations??





Mannucci, P. M., Cortesi, P. A., di Minno, M. N. D., Sanò, M., Mantovani, L. G., & di Minno, G. Comparative analysis of the pivotal studies of extended half-life recombinant FVIII products for treatment of haemophilia A. *Haemophilia*, 2021, *27*(4), e422–e433. https://doi.org/10.1111/hae.14313

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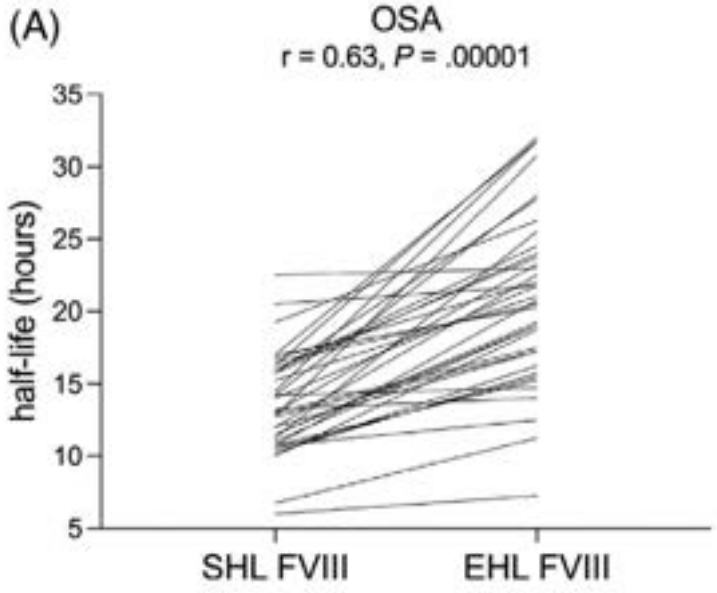
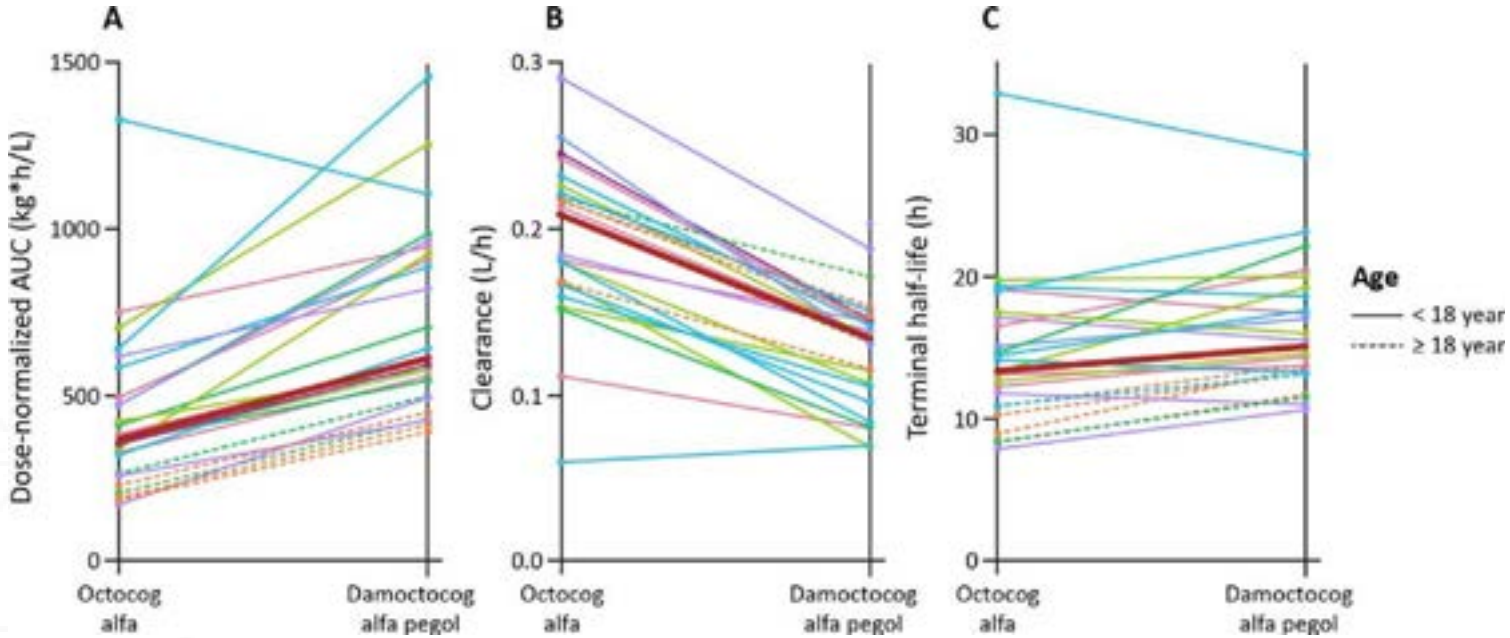
Not everyone gains (and for sure not to the same extent…)

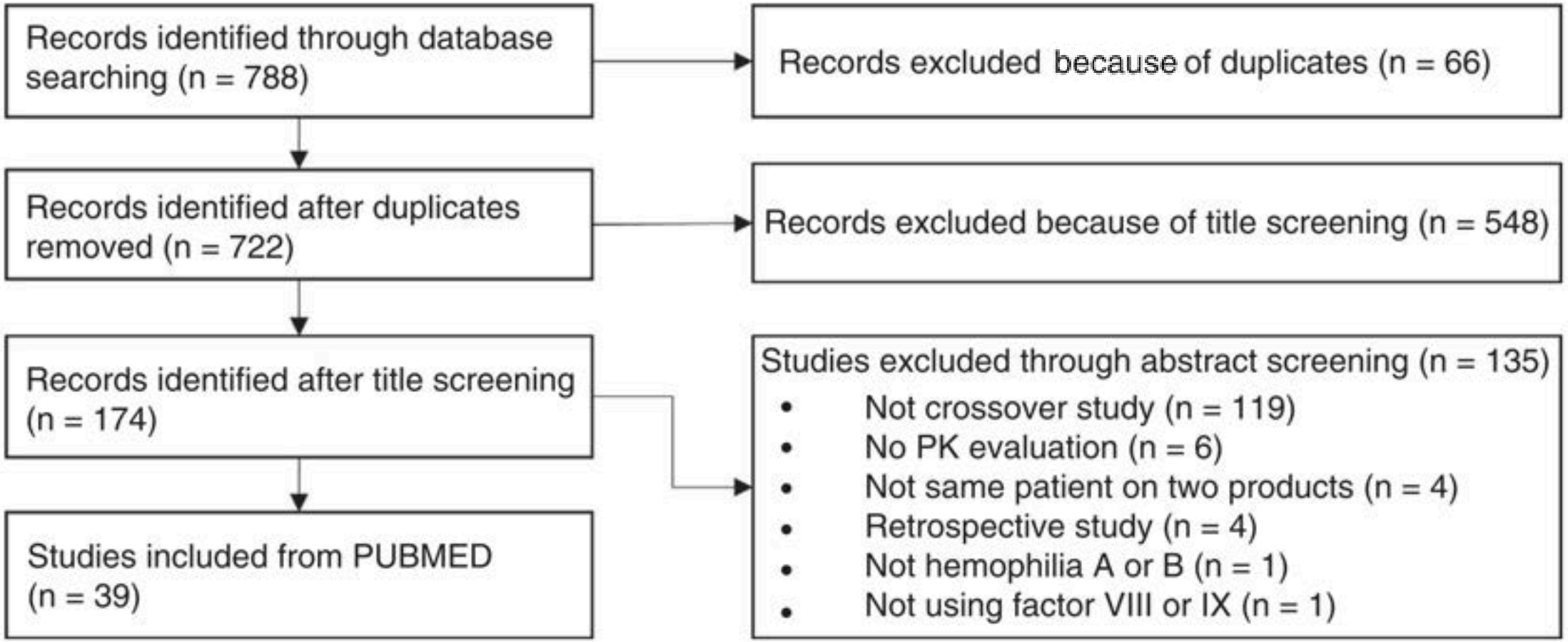
- A-long kids study.
  - No increase in terminal half-life in 5% of children under 6 (n = 19; CI: 0%-26%) and 12% of children aged 6–12 (n = 27; CI: 7%-19%).





Young G et al. J Thromb Haemost. 2015;13:967–977; **Nummi, V** et al. *Haemophilia*, 2022;*28*(6), 237–244.; **Matino D** et al. under review

Why did not we realize this sooner?



Yu, J. K., Iorio, A., & Edginton, A. N. Using pharmacokinetics for tailoring prophylaxis in people with hemophilia switching between clotting factor products: A scoping review. *Research and Practice in Thrombosis and Haemostasis*, 2019, *March*, 1–14. https://doi.org/10.1002/rth2.12204

Most common switching study aims

Biosimilarity or comparative PK and inhibitor development studies						
Abshire[38]	(1) Kogenate (2) rFVIII-FS	50	35	-	4	Compare PK and safety of Kogenate and rFVIII-FS
Coyle[39]	(1) rFVIII-FS (2) BAY 94-9027	25/50 25/60	14	21-58 (36.1)	3	Assess PK and safety of BAY 94-9027
Kulkarni[40]	(1) Prior FVIII product (2) Turoctocog alfa	- 25-60	69	1-11 (6.1)	3	Investigate safety, efficacy, and PK properties of turoctocog alfa
Mahlangu[29]	(1) Advate (2) rFVIIIFc	50	30	12-65 [29]	-	Evaluate safety, efficacy, and PK of rFVIIIFc
Meunier[41]	(1) Prior FVIII product (2) N8-GP	- 60	24	0-11 (6.0)	-	Assess safety, efficacy, and PK of N8-GP
Mullins[42]	(1) Advate (2) BAX855	60 ± 5	31	1-11 (6) [6]	-	Determine immunogenicity, PK, efficacy, safety, and quality of life using BAX855

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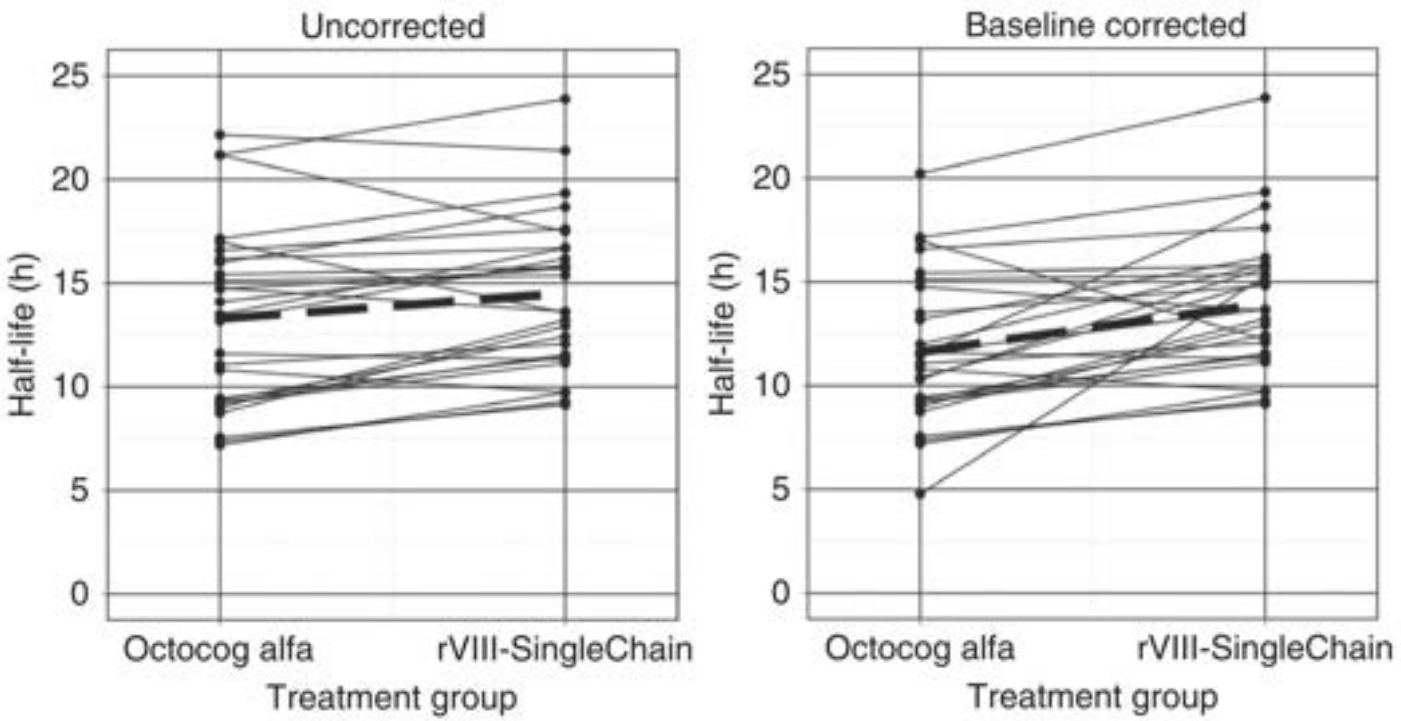
Switching studies characteristics

- Most studies
  - do not report individual data or ”spaghetti plots”
  - plot geometric means and standard errors
  - use non-compartmental PK estimation



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WAPPS data base analysis

- 688 participants (2174 infusions)
  - SHL: 1073;
  - EHL: 1101
- 121 HTC in 43 countries.







Versloot, O., Iserman, E., Chelle, P., Germini, F., Edginton, A. N., Schutgens, R. E. G., Iorio, A., & Fischer, K. (2022). Predicting Individual Changes in Terminal Half-Life After Switching to Extended Half-Life Concentrates in Patients With Severe Hemophilia. *HemaSphere*, *6*(4), e694.

SHL-EHL switching study dataset

N=688	Hemophilia A	
	Children (0-17)	Adults (≥18)
N	259 (42%)	353 (58%)
Age (y)	10 (6-14)	35 (26-47)
Blood group O	47%	43%
Terminal Half-life		
SHL (h)	9 (8-11)	12 (10-15)
EHL (h)	13 (10-16)	17 (13-21)
THL_ratio $\left(\frac{EHL}{SHL}\right)$	1.4 (1.2-1.7)	1.4 (1.2-1.7)

Versloot, O., Iserman, E., Chelle, P., Germini, F., Edginton, A. N., Schutgens, R. E. G., Iorio, A., & Fischer, K. (2022). Predicting Individual Changes in Terminal Half-Life After Switching to Extended Half-Life Concentrates in Patients With Severe Hemophilia. *HemaSphere*, *6*(4), e694.

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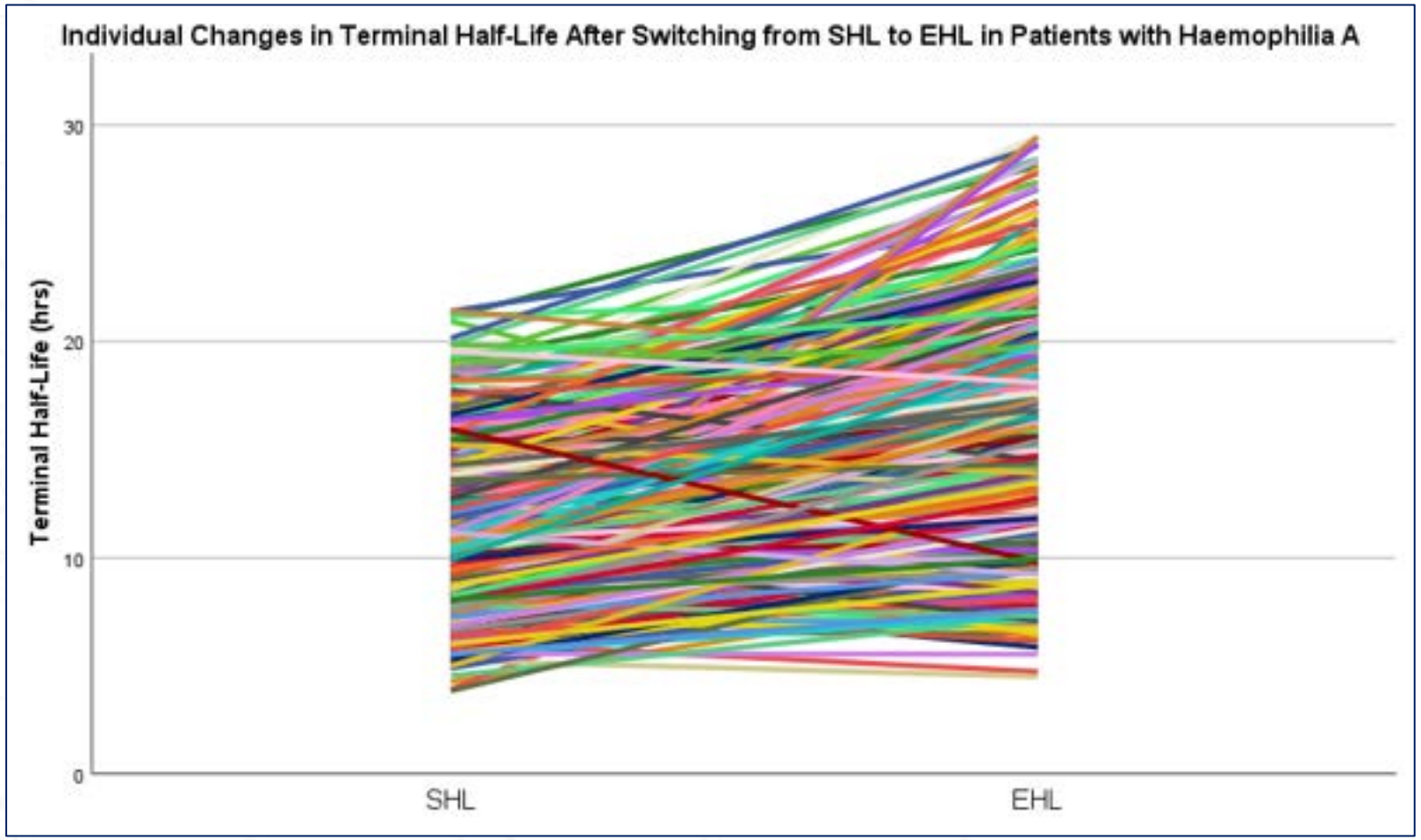

- Improvement: 4,1 hrs
  - 1.4 fold
- 551/612 (90%): longer THL

However:

- 61/612 (10%): shorter THL
- 181/612 (30%): less than 1.3 fold improvement

=> Clinical decision making?

Versloot, O., Iserman, E., Chelle, P., Germini, F., Edginton, A. N., Schutgens, R. E. G., Iorio, A., & Fischer, K. (2022). Predicting Individual Changes in Terminal Half-Life After Switching to Extended Half-Life Concentrates in Patients With Severe Hemophilia. *HemaSphere*, *6*(4), e694.

Determinants of switching benefit

Participant Characteristics According to Relevant FVIII-THL Extension After Switching From SHL to EHL Concentrates.

	<30% Increase	≥30% Increase	*P*
	Median (IQR) or % (95% CI)		
Number	242	370	
Age (y)	26 (12-40)	20 (11-35)	0.06
Children (%)	39% (33-45)	45% (40-50)	0.13
BMI[a]	22 (20-25)	22 (18-25)	0.13
Weight (kg)	67 (46-80)	65 (40-80)	0.44
Blood Group O (%)[a]	53% (45-60)	40% (34-46)	**0.01**
Inhibitor Status (%)[a]	14% (10-19)	11% (8-15)	0.47
Baseline THL_SHL (h)	11.9 (9.9-14.4)	9.5 (7.9-11.9)	**<0.01**

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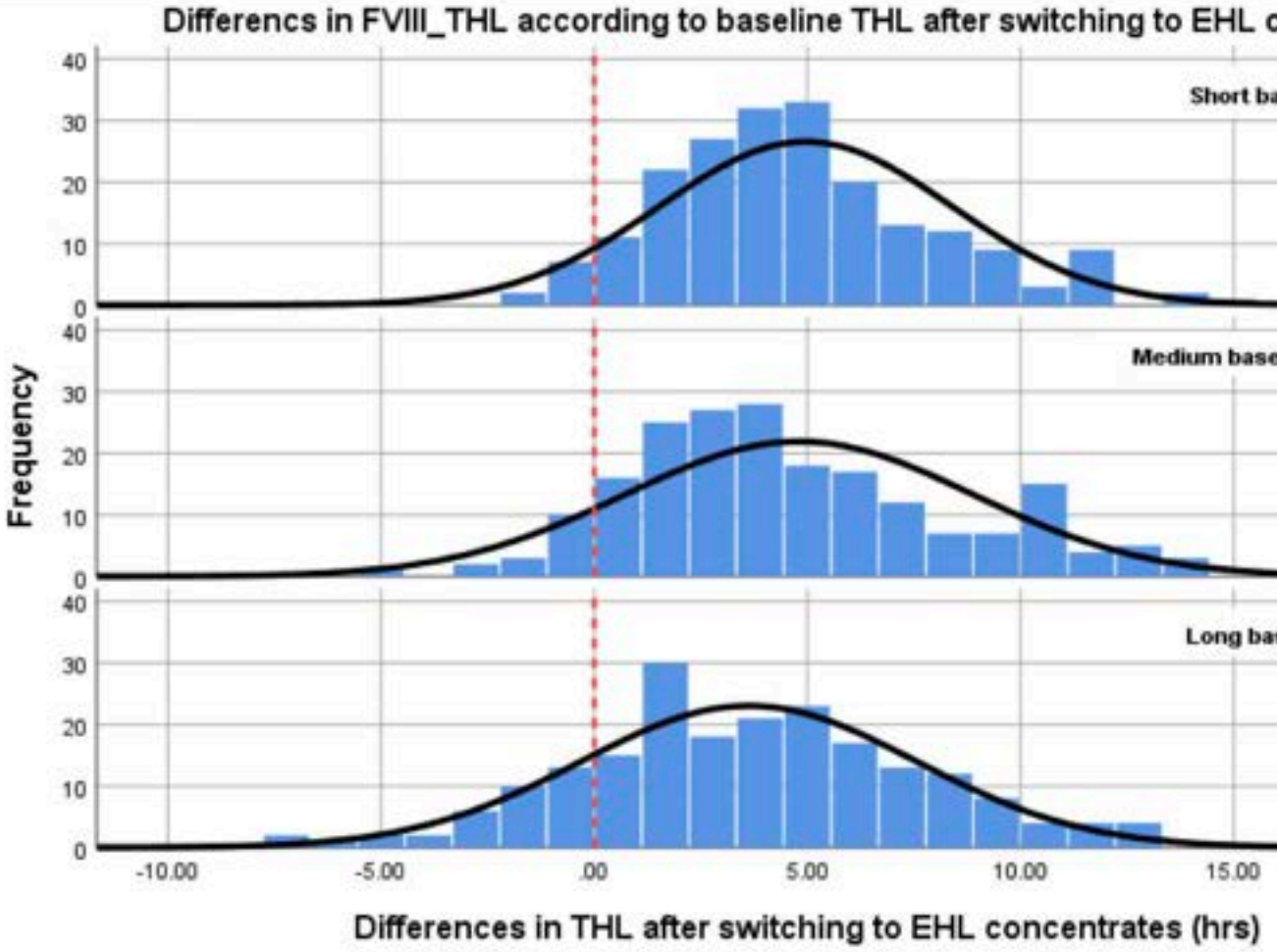

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Probability of >30% Increase in THL for Children (0–18) With Hemophilia A.

THL on SHL-FVIII	Blood Group	Probability of a Clinically Relevant Increase in THL on EHL_FVIII (%)
Short (<8 h)	Non-O	96
	O	69
Middle (8–10 h)	Non-O	81
	O	27
Long (>10 h)	Non-O	55
	O	10

Versloot, O., Iserman, E., Chelle, P., Germini, F., Edginton, A. N., Schutgens, R. E. G., Iorio, A., & Fischer, K. (2022). Predicting Individual Changes in Terminal Half-Life After Switching to Extended Half-Life Concentrates in Patients With Severe Hemophilia. *HemaSphere*, *6*(4), e694.

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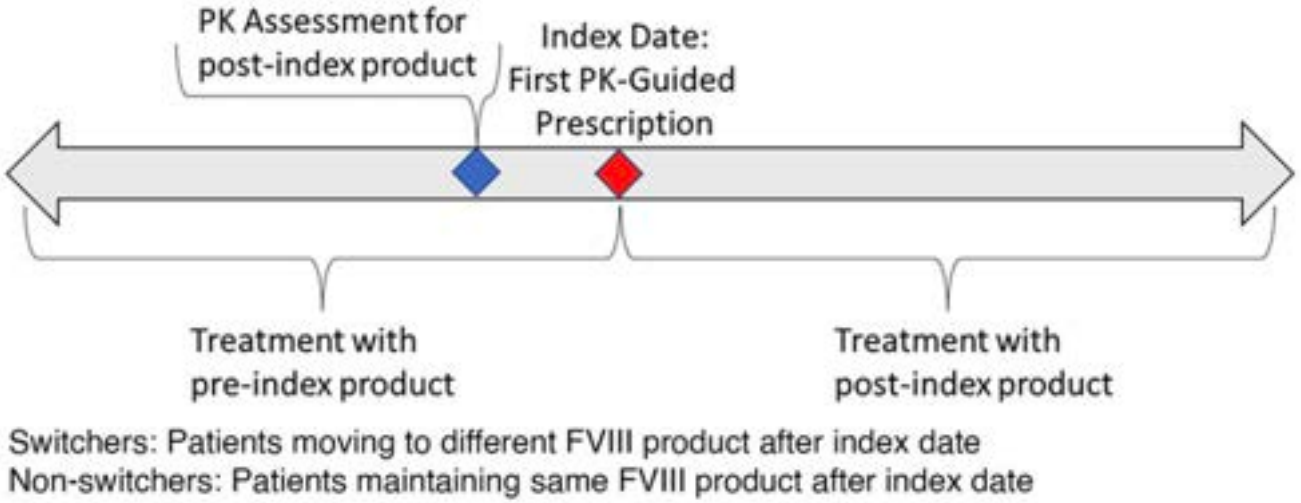
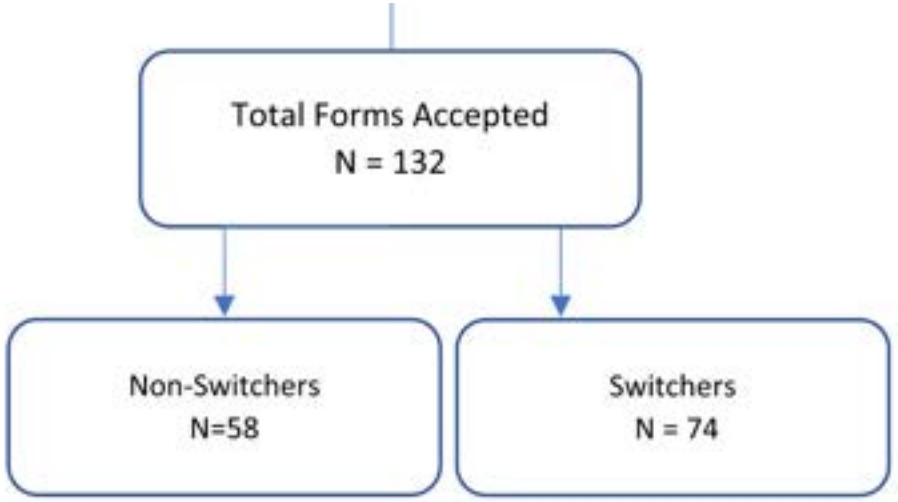
PK guided prophylaxis impact





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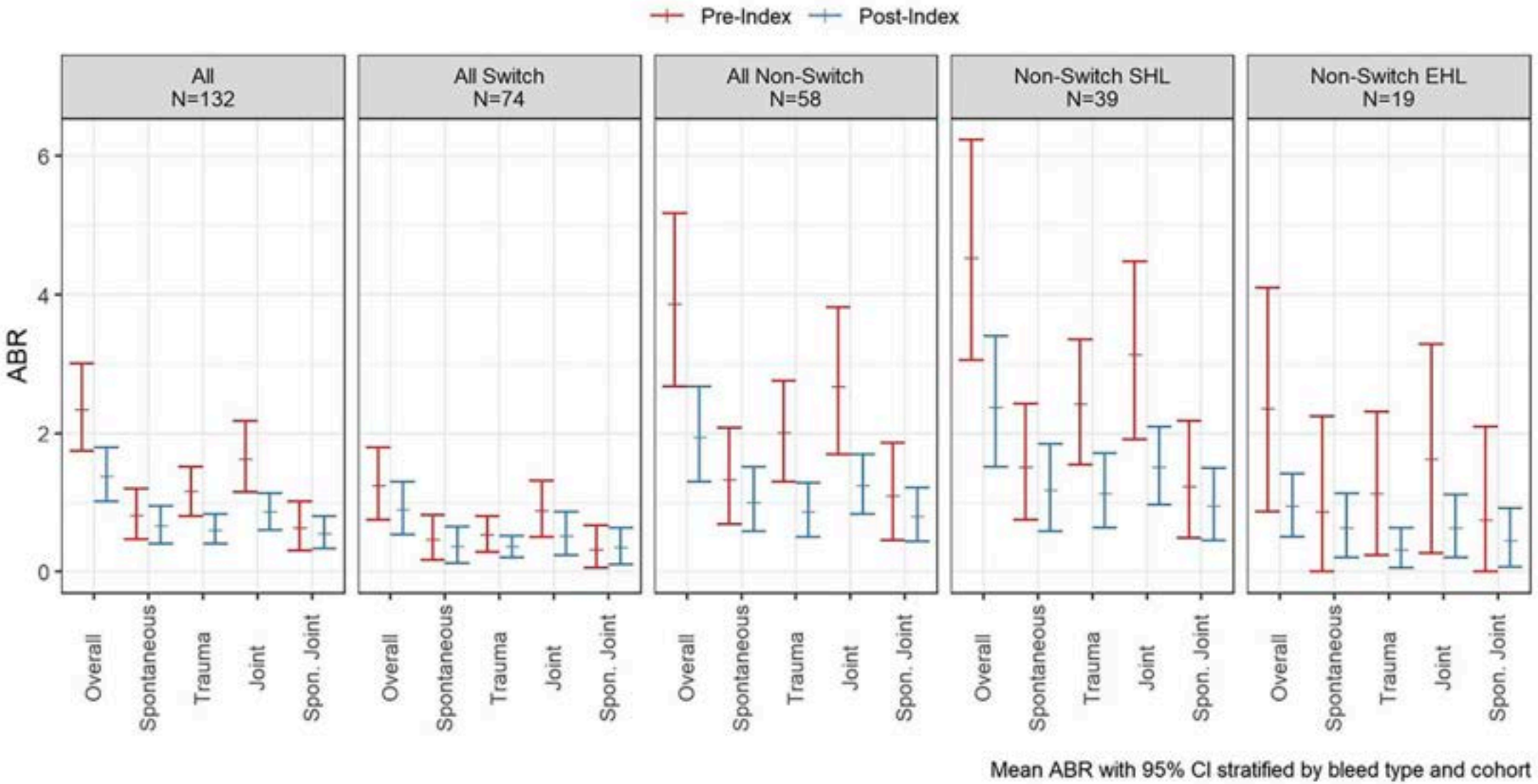
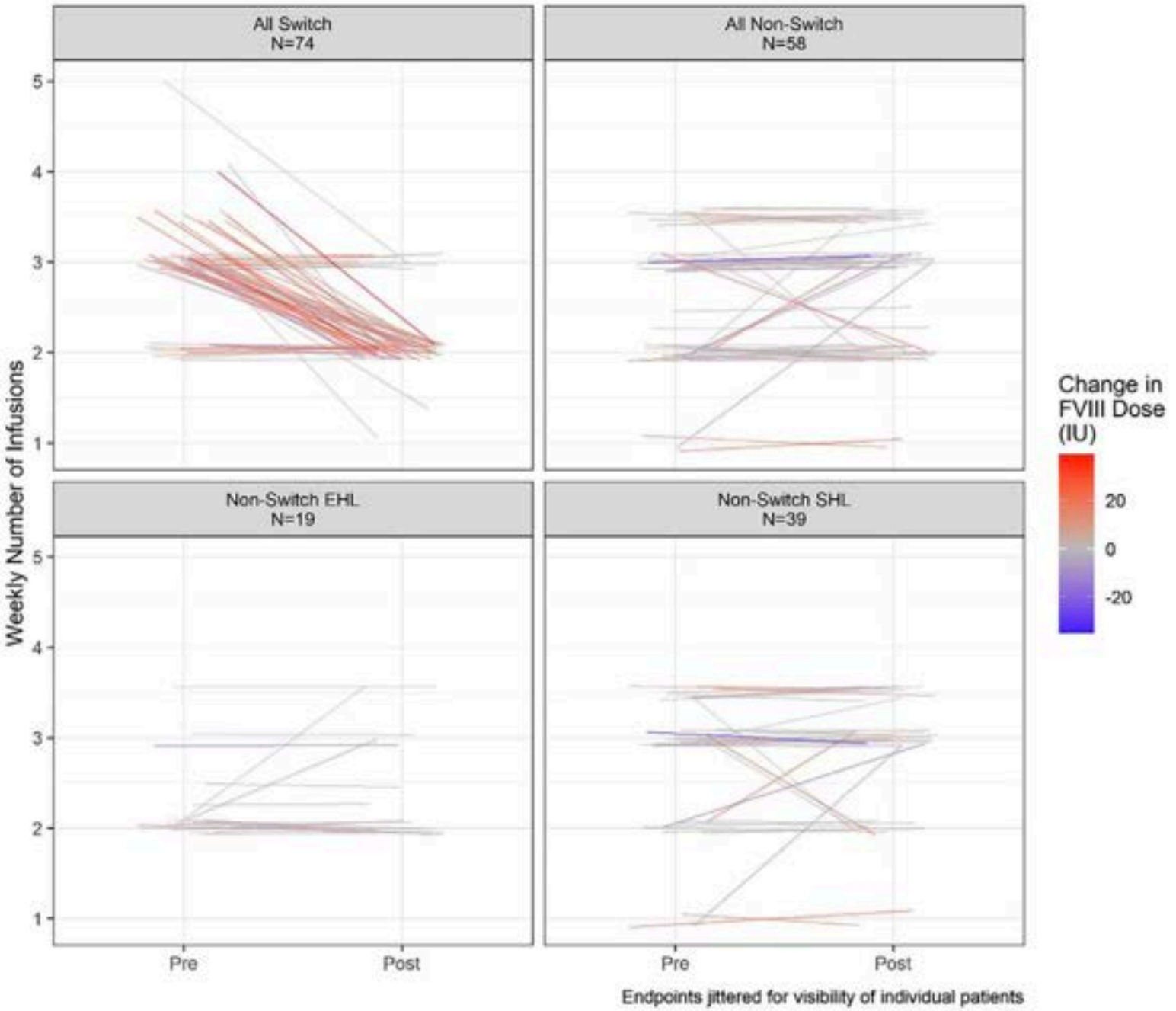
PK guided prophylaxis impact



Mean ABR with 95% CI stratified by bleed type and cohort

Young, G., Callaghan, M. U., Balasa, V., Soni, A., Ahuja, S., Roberts, J. C., Simpson, M. L., Kizilocak, H., Frick, A., Mokdad, A. G., Xing, S., & Caicedo, J. Effects of PK-guided prophylaxis on clinical outcomes and FVIII consumption for patients with moderate to severe Haemophilia A. *Haemophilia*, 2023, *29*(5), 1234–1242. https://doi.org/10.1111/hae.14826



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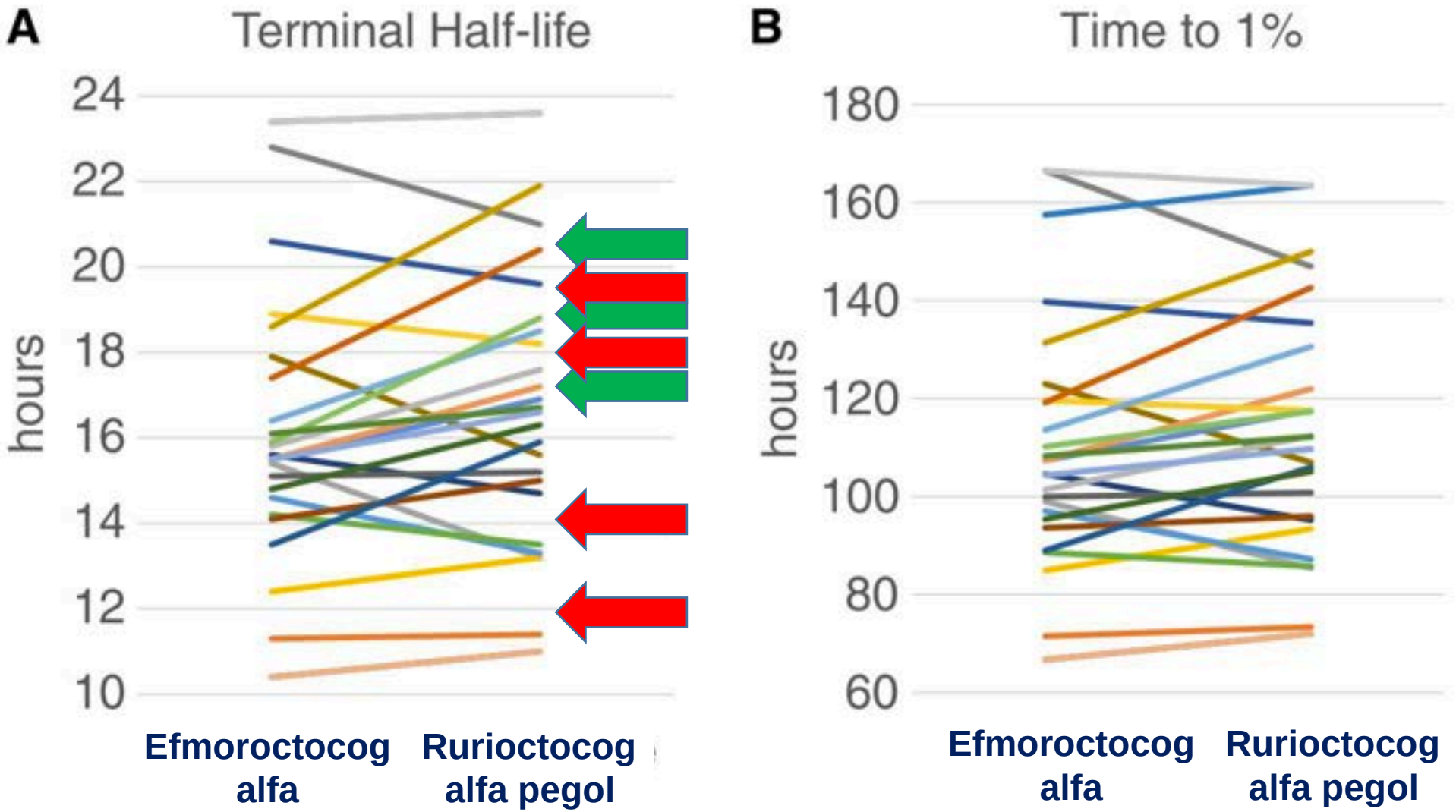
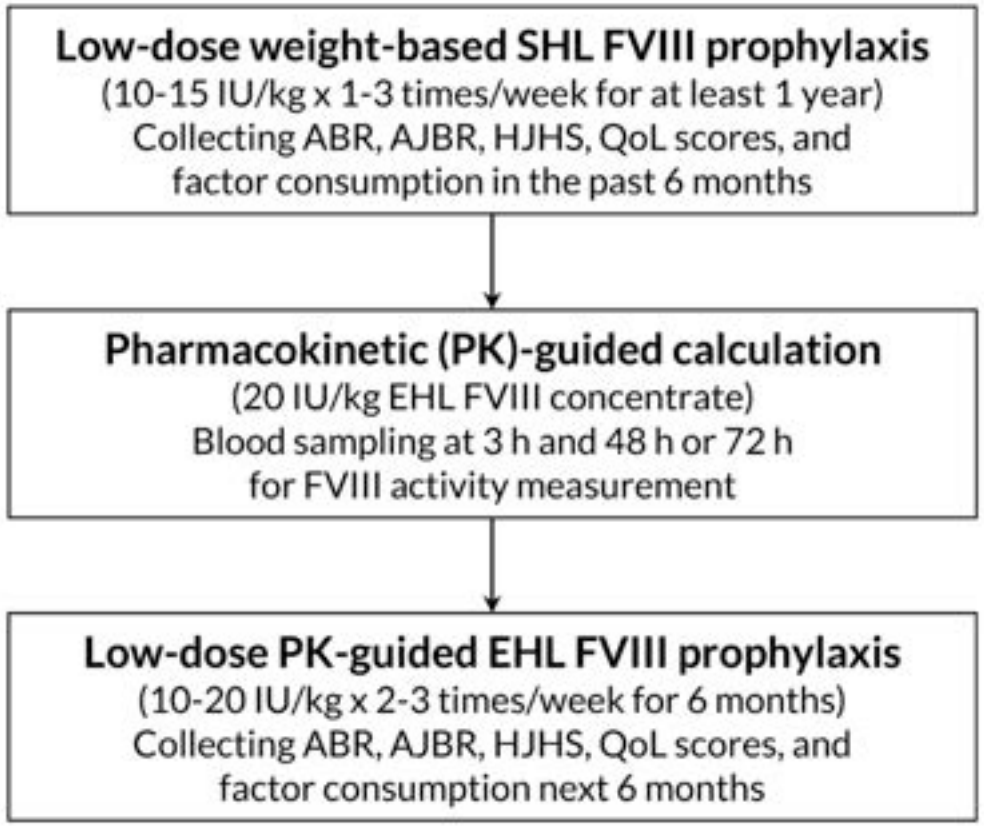
Interindividual variability



Carcao MD et al. Comparative pharmacokinetics of two extended half-life FVIII concentrates (Eloctate and Adynovate) in adolescents with hemophilia A: Is there a difference? J Thromb Haemost. 2019 Jul 2;17(7):1085–96.

Low-dose PK tailored proph



Rakmanotham, A., Moonla, C., & Sosothikul, D. (2023). Clinical outcomes of low-dose pharmacokinetic-guided extended half-life versus low-dose standard half-life factor VIII concentrate prophylaxis in haemophilia A patients. *Haemophilia*, *29*(1), 156–164. https://doi.org/10.1111/hae.14700x

Low-dose PK tailored proph

TABLE 5 The annualized factor consumption: Prophylaxis and breakthrough doses

Factor consumption (IU/kg/year)	Prophylaxis dosing			Breakthrough dosing		
	Low-dose weight-based SHL FVIII	Low-dose PK-guided EHL FVIII	*P*-value	Low-dose weight-based SHL FVIII	Low-dose PK-guided EHL FVIII	*P*-value
All patients (*N* = 15)						
Median (IQR)	1054.0 (533.0-1259.0)	1601.0 (1067.0-1826.0)	.005[a]	174.0 (92.0-409.0)	66.0 (9.0-140.0)	.005[a]
Mean (SD)	979.5 (450.7)	1496.5 (459.4)	.003[b]	254.2 (217.3)	97.6 (111.4)	.007[a]
Median (IQR) by age						
≤15 years (*N* = 5)	1155.0 (863.0-1418.0)	1744.0 (1727.0-2184.0)	.17[a]	133.0 (10.0-134.0)	9.0 (0-33.0)	.04[a]
>15 years (*N* = 10)	927.0 (533.0-1217.0)	1232.5 (1067.0-1638.0)	.01[a]	306.5 (113.0-436.0)	124.5 (40.0-170.0)	.04[a]
Median (IQR) by target joints						
Present (*N* = 11)	1054.0 (533.0-1259.0)	1215.0 (1054.0-1638.0)	.02[a]	311.0 (113.0-436.0)	123.0 (23.0-170.0)	.02[a]
Absent (*N* = 4)	1009.0 (620.5-1449.5)	1964.0 (1735.5-2247.5)	.09[a]	71.5 (9.0-133.5)	16.5 (0-49.5)	.08[a]
ABR (all patients)				22 (6-20)	10 (2-14)	.001

Rakmanotham, A., Moonla, C., & Sosothikul, D. (2023). Clinical outcomes of low-dose pharmacokinetic-guided extended half-life versus low-dose standard half-life factor VIII concentrate prophylaxis in haemophilia A patients. *Haemophilia*, *29*(1), 156–164. https://doi.org/10.1111/hae.14700x

ALTUVIIIO

- Approval status
  - FDA market approval, Feb 22nd, 2023
  - Taiwan Food and Drug Administration, Aug 31, 2023.
  - The Japanese Ministry of Health, Labor, and Welfare (MHLW), Sept 25, 2023.

- PRESS RELEASE
  - Swedish Orphan Biovitrum AB (Sobi®), Stockholm, Sweden, 19 May 2023
    - EMA accepted and validated marketing authorisation application for efanesoctocog alfa for treatment of haemophilia A.

ALTUVIIIO – WAPPS-Hemo data

		All (#22 patients)
Age (Years)	**Median** (IQR), **Min – Max** Mean +/- SD	**15.5** (11.75 – 26), **7 – 58** 20.9 +/- 13.8
BodyWeight (kg)	**Median** (IQR), **Min – Max** Mean +/- SD	**55.6** (47.2 -87.9), **23 – 118.3** 67.9 +/- 23.8
Height (cm)	**Median** (IQR), **Min – Max** Mean +/- SD	**173.0** (154.1 – 183.1), **115.9 – 190** 166.1 +/- 20.9
Dose (total U)	Median (IQR), Min – Max Mean +/- SD	2780.0 (2639 – 4286.5), 1171 – 5518 3331.8 +/- 1323.6
Dose (IU/kg)	**Median** (IQR), **Min – Max** Mean +/- SD	**51.6** (49.3 – 52), **32.4 – 57.4** 50 +/- 5.6

ALTUVIIIO – WAPPS-Hemo data

Parameter		All
	Pts #	22
Cmax (IU/mL)	Median (IQR)	1.0 (0.9 – 1.1)
AUC	Median (IQR)	69721 (58991 – 77565)
CL ml/mg*min	Median (IQR)	0.05 (0.04 – 0.06)
Vss (ml/kg)	Median (IQR)	52.3 (49.9 – 55.7)
Terminal Half Life (hr)	Median (IQR)	49.0 (45.1 – 52.0)
Time To 5% (days)	Median (IQR)	9.3 (8.2 – 10.3)
Time to 15% (days)	Median (IQR)	5.9 (5.1 – 6.9)

WAPPS-Hemo research database

ALTUVIIIO – WAPPS-Hemo data

Parameter		All	Blood Group O	Blood Group not O
	Pts #	22	3	3
Cmax (IU/mL)	Median (IQR)	1.0 (0.9 – 1.1)	1.11 (1.0 – 1.16)	0.98 (0.98 – 1.01)
AUC	Median (IQR)	69721 (58991 – 77565)	45877 45259 -56842)	79949 (70692 -83867)
CL ml/mg*min	Median (IQR)	0.05 (0.04 – 0.06)	0.05 (0.04 – 0.07)	0.04 (0.04 – 0.04)
Vss (ml/kg)	Median (IQR)	52.3 (49.9 – 55.7)	52.2 (50.5 – 56.1)	53.2 (50.9 – 55.4)
Terminal Half Life (hr)	Median (IQR)	49.0 (45.1 – 52.0)	36.5 (32.7 – 42.0)	55.0 (51.2 – 58.6)
Time To 5% (days)	Median (IQR)	9.3 (8.2 – 10.3)	6.5 (6.0 – 8.0)	10.3 (9.6 – 10.9)
Time to 15% (days)	Median (IQR)	5.9 (5.1 – 6.9)	4.1 (3.8 – 4.9)	6.9 (6.2 – 6.9)

WAPPS-Hemo research database

Talk objectives

1) General considerations and lesson learned from switching to EHL
   A) Impact of switching at the population level
   B) Impact of switching at the individual level
   C) Impact of tailoring prophylaxis with EHL

2) How to maximize the gain when switching to EHL?
   A) What is the guidance, if any?
   B) Switching support tool in WAPPS-Hemo

ISTH guidance on switching

- 1. PK-guided dosing of factor concentrates provides for more individualized prophylaxis and treatment in patients with hemophilia [17].
- 2. A sampling strategy for population PK analysis should include a minimum of two to four post-infusion time-points [17].
- 3. PopPK tools such as WAPPs-Hemo or OPTI-CLOT, which utilize a Bayesian approach to estimate individual PK profiles, provide a more practical approach to generating individual PK data, as compared with a classical PK approach [17].
- 4. Further studies are needed to assess the impact of integrating PK data into medical decision making on patient outcomes, factor utilization, bleeding events, quality of life and compliance [17].

- Ragni, M. v, Croteau, S. E., Morfini, M., Cnossen, M. H., & Iorio, A. (2018). Pharmacokinetics and the transition to extended half-life factor concentrates: communication from the SSC of the ISTH. *Journal of Thrombosis and Haemostasis*, *16*(7), 1437–1441. https://doi.org/10.1111/jth.14153
- Iorio A, Blanchette V, Blatny J, Collins P, Fischer K, Neufeld E. Estimating and interpreting the pharmacokinetic profiles of individual patients with hemophilia A or B using a population pharmacokinetic approach: communication from the SSC of the ISTH. J Thromb Haemost 2017; 15: 2461–5.

UKHCDO: Use of extended half-life products

- The choice of factor replacement product must involve shared decision-making with the person with haemophilia and/or their parent/legal guardian. Grade 1C
- Switching between factor replacement products may be performed in patients with more than 150 exposure days and no prior inhibitor. Grade 1C
- Recombinant FVIII and FIX EHL products should be used according to published UKHCDO guidance and used only when they provide clear clinical benefit over standard half-life products. Grade 1C

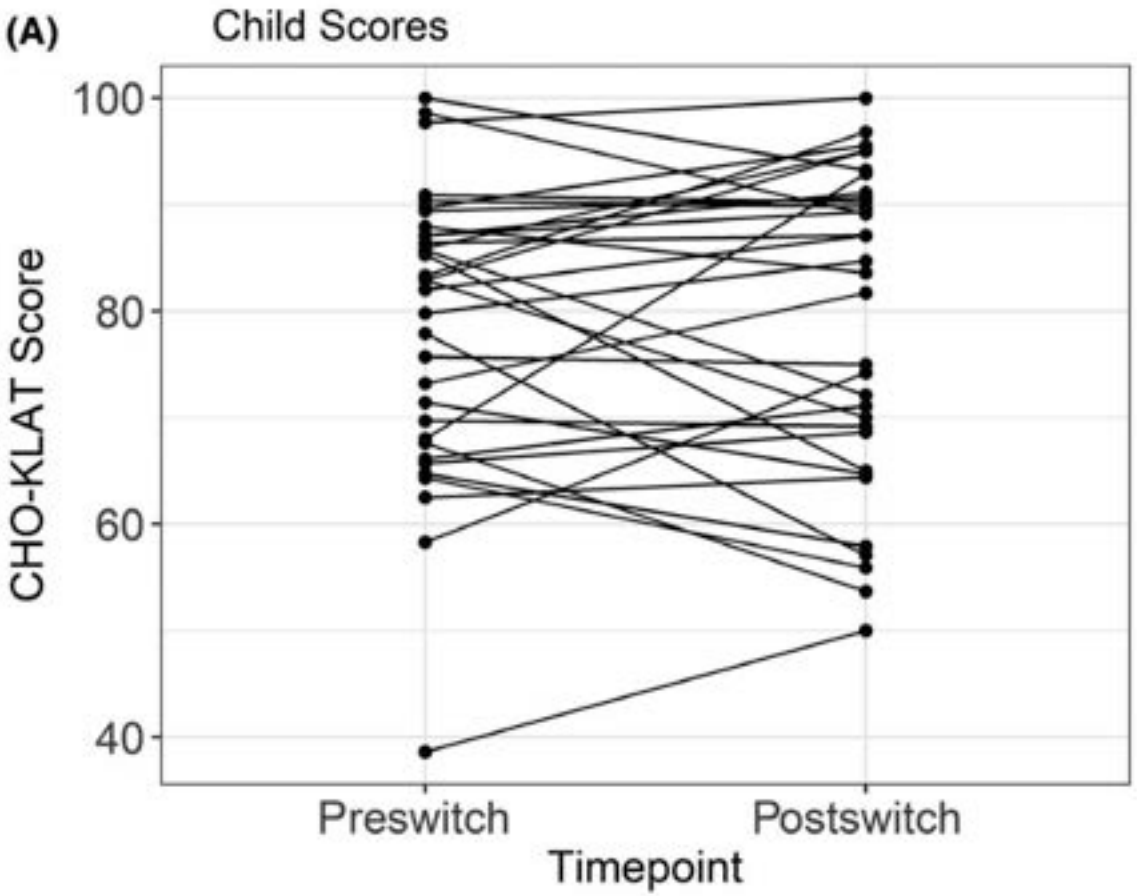
Rayment, R., Chalmers, E., Forsyth, K., Gooding, R., Kelly, A. M., Shapiro, S., Talks, K., Tunstall, O., & Biss, T. Guidelines on the use of prophylactic factor replacement for children and adults with Haemophilia A and B. *British Journal of Haematology*, 2020, *190*(5), 684–695. https://doi.org/10.1111/bjh.16704

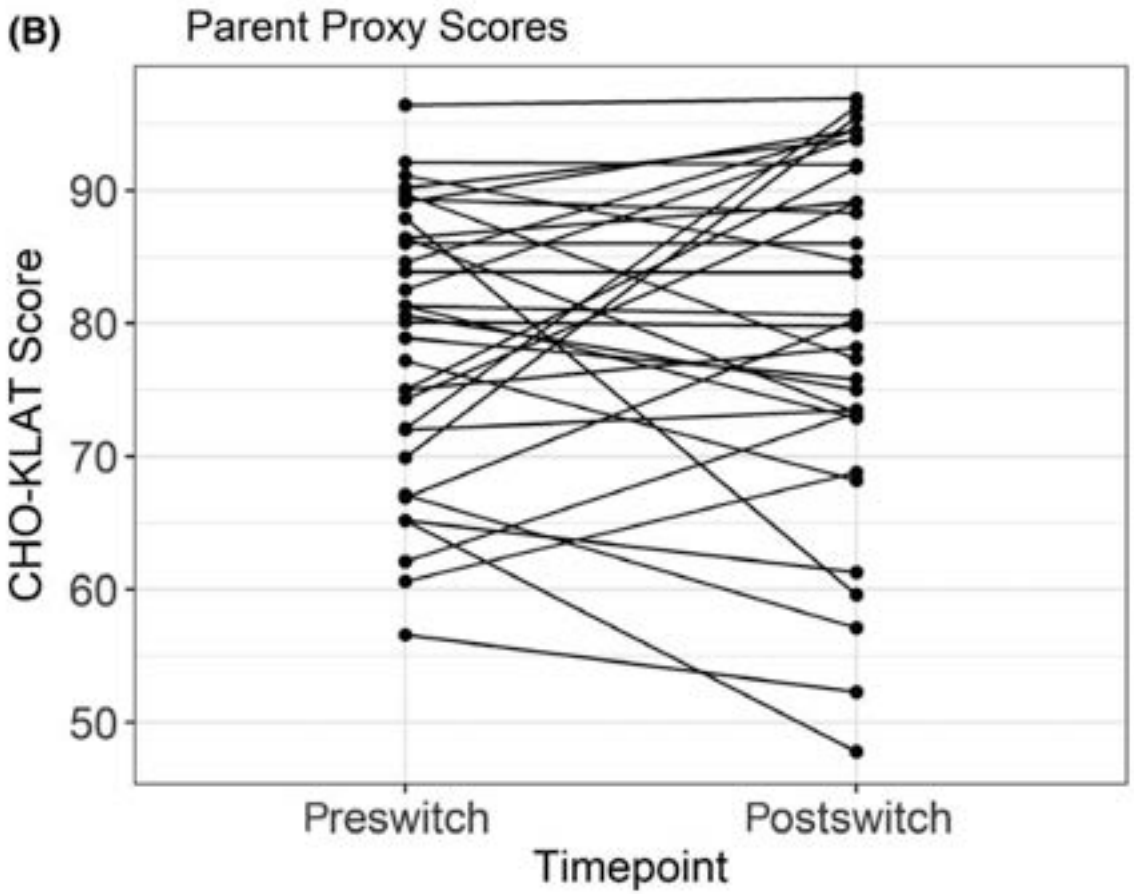
Practical guidance

- Fewer venipunctures
- Fewer bleeds/good control of bleeding episodes
- Greater protection against bleeds in different settings of daily living
- Possibility to increase physical activity and/or participation in activities
- Good safety profile
- Better quality of life

Escobar, M., Santagostino, E., Mancuso, M. E., Coppens, M., Balasa, V., Taylor, J. A., Iorio, A., & Negrier, C. Switching patients in the age of long-acting recombinant products? *Expert Review of Hematology*, 2019, *12*(sup1), 1–13. https://doi.org/10.1080/17474086.2018.1564032

QoL





Carcao, M., Zunino, L., Young, N. L., Dover, S., Bouskill, V., Hilliard, P., Price, V. E., & Blanchette, V. S. (2020). Measuring the impact of changing from standard half-life (SHL) to extended half-life (EHL) FVIII prophylaxis on health-related quality of life (HRQoL) in boys with moderate/severe haemophilia A: Lessons learned with the CHO-KLAT tool. *Haemophilia*, *26*(1), 73–78. https://doi.org/10.1111/hae.13905

Álvarez-Román, M.-T., Shapiro, A. D., Ragni, M. v., Palmborg, H., Bystrická, L., Szamosi, J., Casiano, S., & Chambost, H. (2023). Long-term outcomes of prophylaxis with a recombinant factor VIII Fc or recombinant factor IX Fc in patients with hemophilia previously treated on demand. *Research and Practice in Thrombosis and Haemostasis*, *7*(6), 102163. https://doi.org/10.1016/j.rpth.2023.102163

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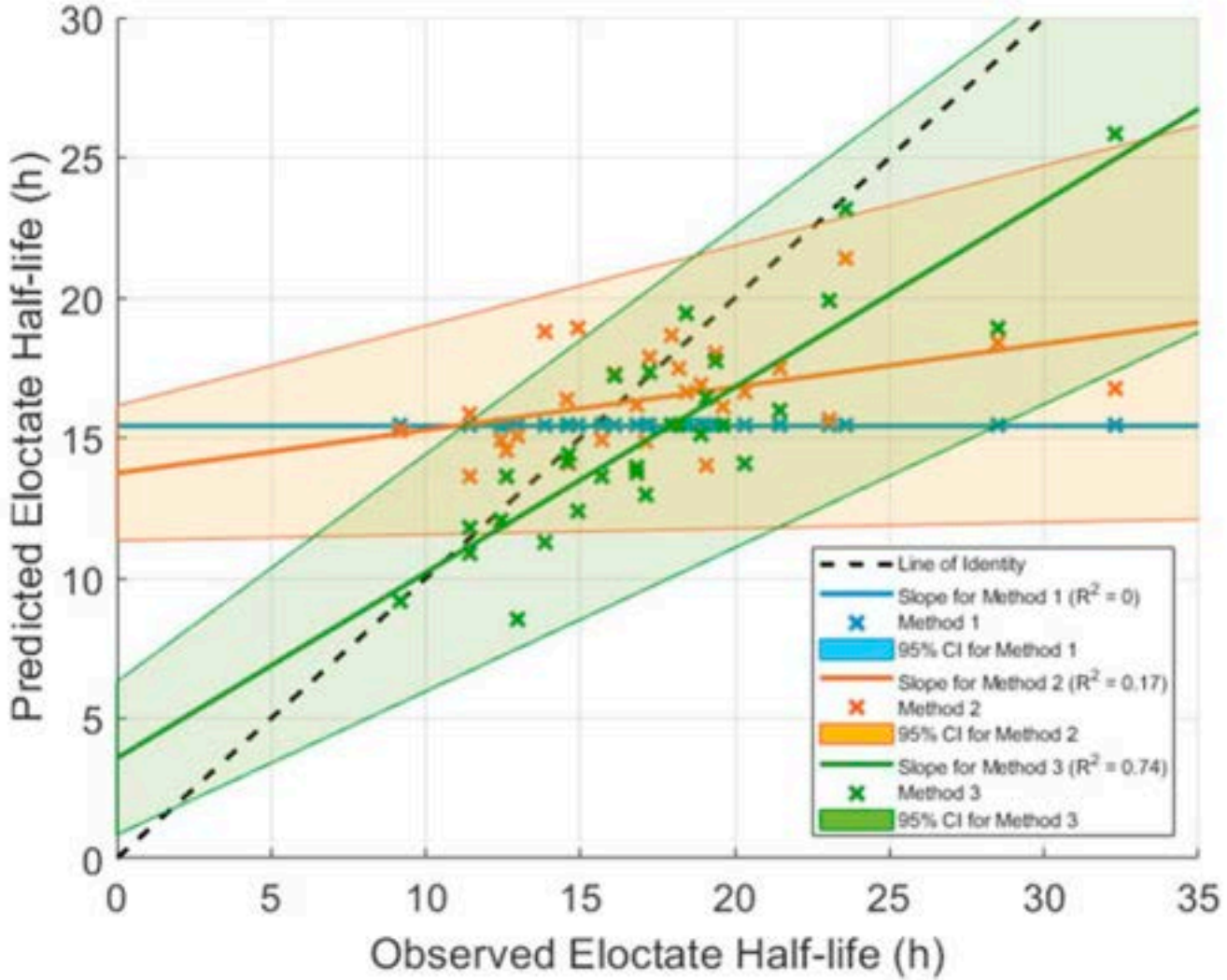
PK profiling across switching

	PopPK model of first product	PopPK model of second product
Method 1	–	$\begin{cases} CL = CL_{pop} \\ V1 = V1_{pop} \\ Q = Q_{pop} \\ V2 = V2_{pop} \end{cases}$
Method 2	–	$\begin{cases} CL = CL_{pop} \times f_{CL}(FFM, AGE) \\ V1 = V1_{pop} \times f_{V1}(FFM) \\ Q = Q_{pop} \\ V2 = V2_{pop} \times f_{V2}(FFM) \end{cases}$
Method 3	η_{CL} and η_{V1} calculated from first product	$\begin{cases} CL = CL_{pop} \times f_{CL}(FFM, AGE) \times e^{\eta CL} \\ V1 = V1_{pop} \times f_{V1}(FFM) \times e^{\eta V1} \\ Q = Q_{pop} \\ V2 = V2_{pop} \times f_{V2}(FFM) \end{cases}$

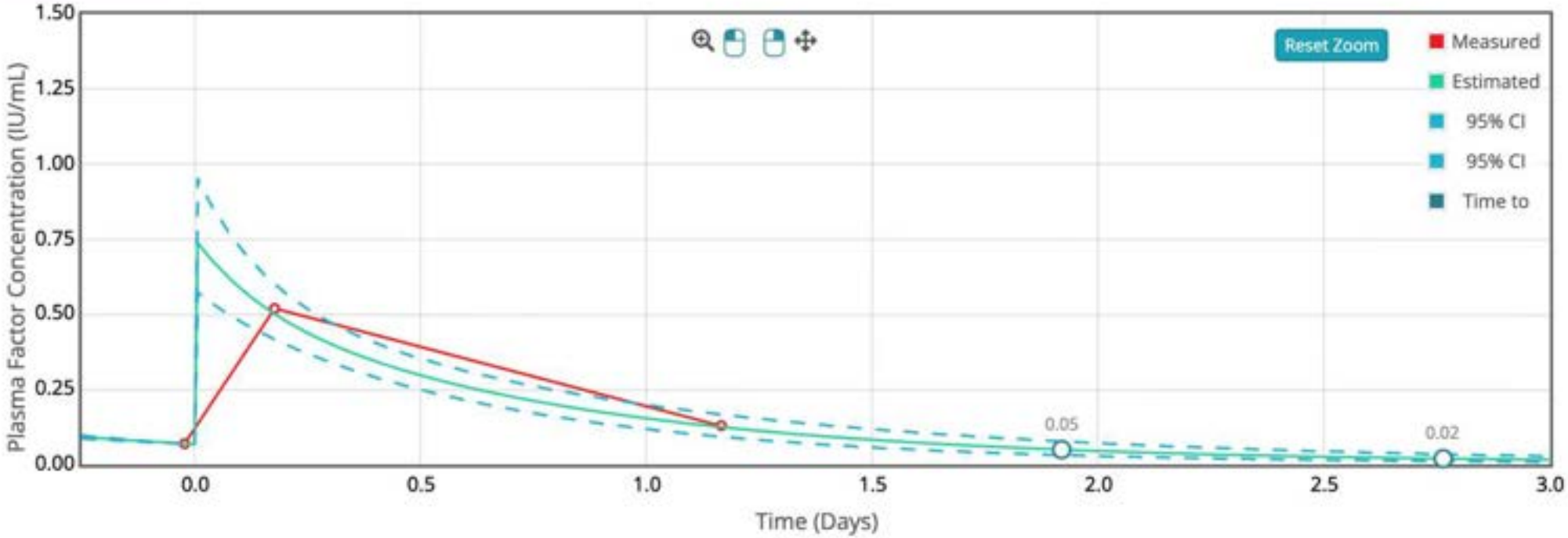
Yu, J. K., Iorio, A., Chelle, P., & Edginton, A. N. (2019). A comparison of methods for prediction of pharmacokinetics across factor concentrate switching in hemophilia patients. *Thrombosis Research*, *184*(August), 31–37. https://doi.org/10.1016/j.thromres.2019.10.023

PK profiling across switching



Yu, J. K., Iorio, A., Chelle, P., & Edginton, A. N. (2019). A comparison of methods for prediction of pharmacokinetics across factor concentrate switching in hemophilia patients. *Thrombosis Research*, *184*(August), 31–37. https://doi.org/10.1016/j.thromres.2019.10.023

PK Estimate | Validation Point | Updated PK Estimate



PK Study Data

ID	Factor Concentrate	Tot IU	IU/kg	End of infusion
	Kovaltry	2000	31.7	2022-01-01 08:00

Time Elapsed (hh:mm)	Pre-dose	Plasma Factor Concentration	Notes
-00:35	✓	0.070 IU/mL (7.0%)	
+04:12		0.520 IU/mL (52.0%)	
+27:56		0.130 IU/mL (13.0%)	

The WAPPS-Hemo calculator switching support function: first scenario – keep the same treatment plan

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Treatment Plan	Kovaltry			Jivi		
	Mo	We	Fr	Mo	We	Fr
Dose, IU	2000	2000	2000	2000	2000	2000
Infusion Interval, Days	2.0	2.0	3.0	2.0	2.0	3.0
Peak, IU/mL (95% CI)	0.7 (0.565-0.908)	0.73 (0.609-0.918)	0.73 (0.617-0.918)	0.92 (0.787-1.164)	0.98 (0.868-1.192)	0.99 (0.890-1.193)
Trough, IU/mL (95% CI)	0.043 (0.012-0.095)	0.045 (0.013-0.103)	0.016 (0.002-0.051)	0.106 (0.034-0.211)	0.114 (0.035-0.233)	0.043 (0.007-0.129)
Weekly Dosage, IU	6000			6000		
Time above 0.01 IU/mL	100%			100%		
Time above 0.03 IU/mL	90%			100%		
Time above 0.15 IU/mL	43%			72%		
	Save			Save		

For dosage and administration of Damoctocog alfa pegol, please refer to the package insert.

The WAPPS-Hemo calculator switching support function: second scenario – less frequent infusions

McMaster University
HEALTH RESEARCH METHODS, EVIDENCE, AND IMPACT

Treatment Plan	Kovaltry		Jivi	
	Mo	Th	Mo	Th
Dose, IU	2000	2000	2000	2000
Infusion Interval, Days	3.0	4.0	3.0	4.0
Peak, IU/mL (95% CI)	0.69 (0.540-0.906)	0.7 (0.559-0.908)	0.89 (0.720-1.159)	0.91 (0.762-1.164)
Trough, IU/mL (95% CI)	0.015 (0.002-0.045)	**< 0.01** (0.001-0.026)	0.039 (0.006-0.105)	0.017 (0.001-0.063)
Weekly Dosage, IU	4000		4000	
Time above 0.01 IU/mL	94%		100%	
Time above 0.03 IU/mL	65%		89%	
Time above 0.15 IU/mL	27%		47%	
	Save		Save	

The WAPPS-Hemo calculator switching support function: third scenario – dose calculation to achieve target trough

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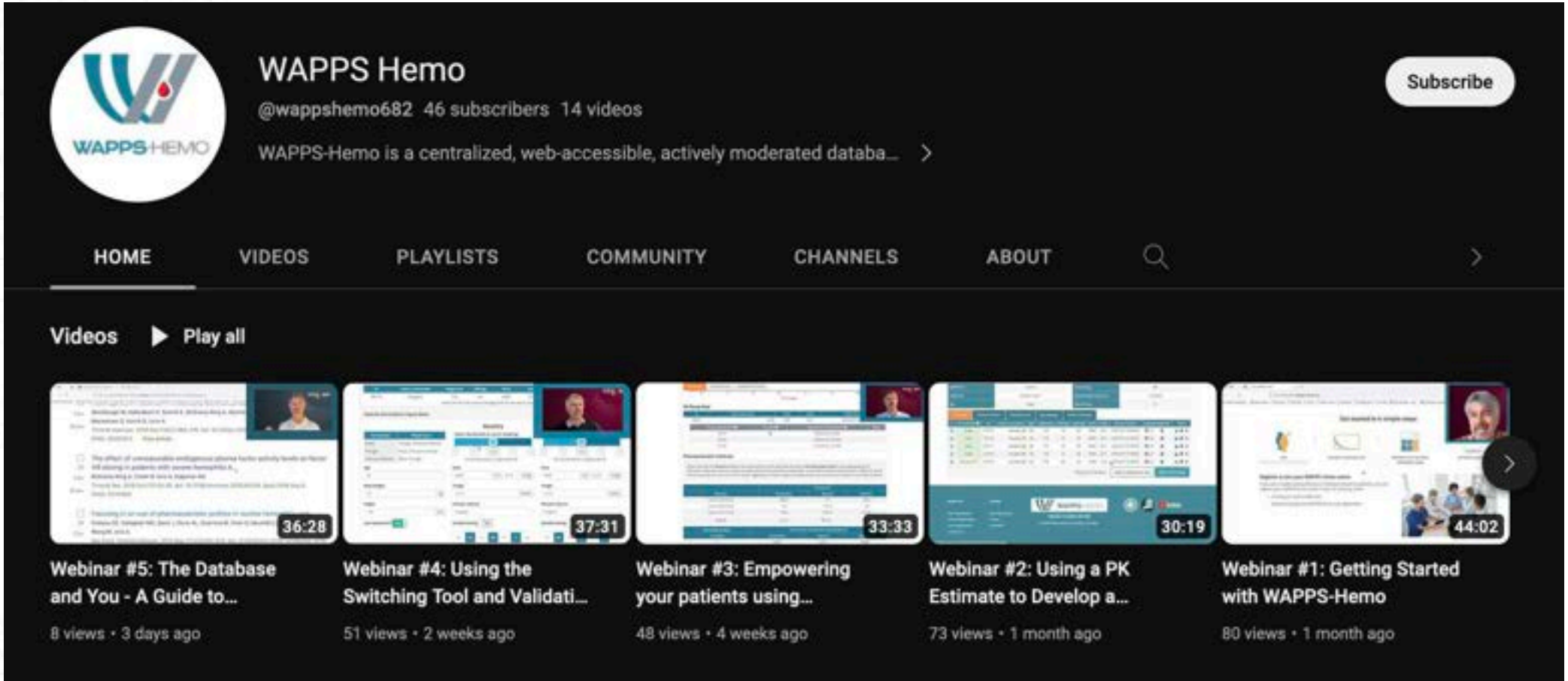
HEALTH RESEARCH METHODS, EVIDENCE, AND IMPACT

Switch simulation input data

Treatment Plan	Kovaltry	Jivi
Dose, IU (95% CI)	4724 (1108-32065)	1431 (396-9660)
Infusion Interval, Days	3.0	3.0
Peak, IU/mL (95% CI)	1.64 (0.315-14.546)	0.65 (0.160-5.622)
Trough, IU/mL	0.03	0.03
Weekly Dosage, IU	11023	3339
Time above 0.01 IU/mL	100%	100%
Time above 0.03 IU/mL	100%	100%
Time above 0.15 IU/mL	55%	45%
	Save	Save

Educational webinar series

- WAPPS-Hemo YouTube channel: https://www.youtube.com/@wappshemo682/featured



TAKE HOME MESSAGES

A) At the population level, switching to EHL **im** **linical outcomes** and **may reduce** usage and cost; it **may imp** e and QoL

B) At the individual level, patients wit PK do generally gain more, including BG type O. **Diff** **ave differently** on products with different HL r gy

C) Current guidelines rec **er EHL for all patients**, tailor their prescription w **ing them in patients who will benefit**

D) WAPPS-Hemo has roduced a switching tool supporting **"educated guessing** ticipated performance on a target EHL to attempt reducing the urden and risk of the **trial&error alternative** approach.

Thank you!