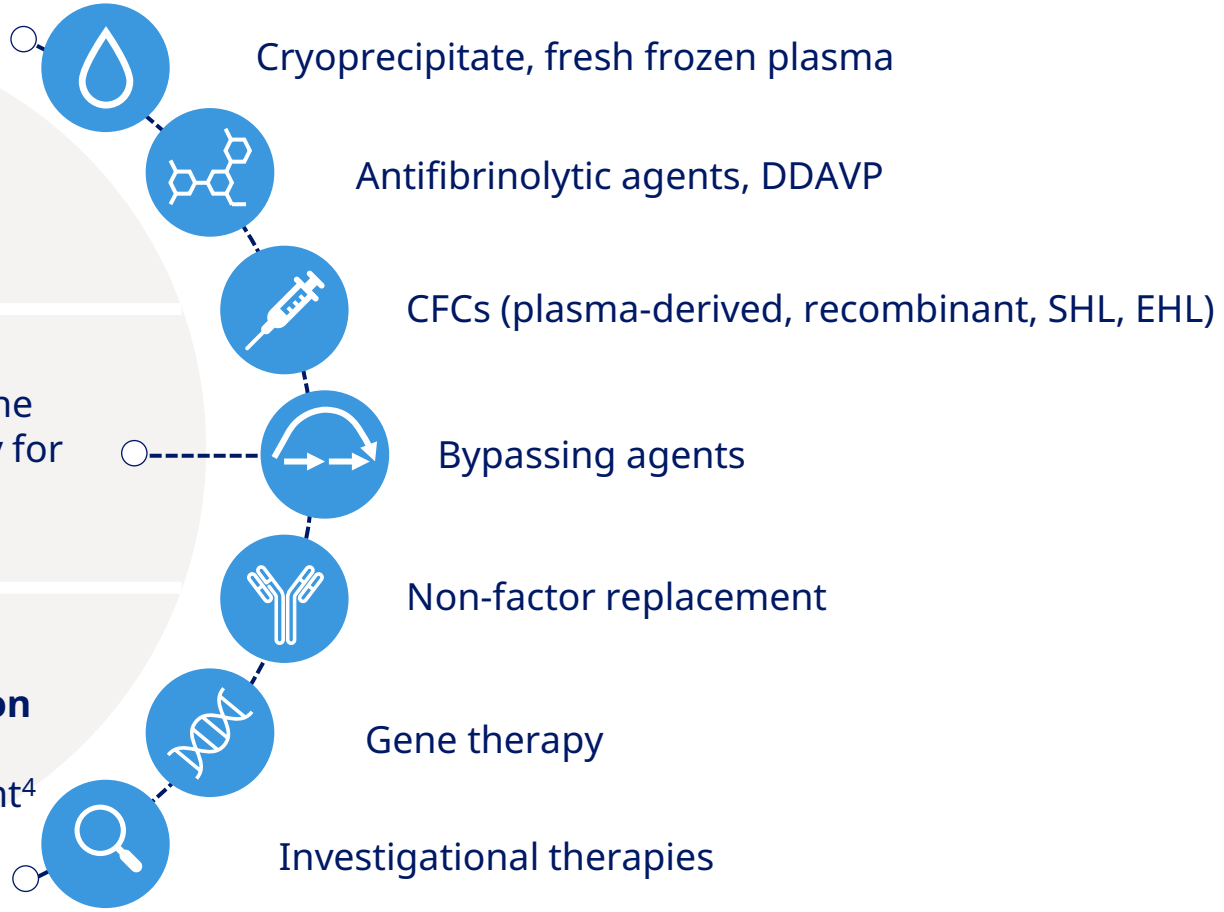
Individualization of hemophilia treatment

Hemophilia care should be individualized to choose the “optimal” treatment for PwH

Evolution of hemophilia care has resulted in efficacious treatments designed to reduce bleeding and improve functional status and QoL[1–3]

Decision-making can be a complex process of selecting the most appropriate **treatment option** and dosing strategy for each patient[1]

As clinical characteristics (e.g., bleeding phenotype), lifestyle, and environment of PwH differ, **individualization of care is required** to ensure patient-centered care that targets optimal outcomes and preferences of each patient[4]



CFC, clotting factor concentrate; DDAVP, desmopressin; EHL, extended half-life; PwH, people with hemophilia; QoL, quality of life; SHL, standard half-life

1. Hermans C et al. Blood Rev 2022;52:100890; 2. Mannucci P. Haematologica 2020;105:545–53; 3. Konkle BA et al. Res Pract Thromb Haemost 2019;3:184−92; 4. Berntorp E et al. Blood Rev 2021;50:100852

Treatment individualization involves tailoring product type[1,2] and dosing regimen[1–4]

1. **Product type**—there are a variety of features to consider when selecting a hemophilia product:

Route of administration and MoA[4,5]

Product origin[6] (plasma-derived vs recombinant)

Dosing frequency[6]

Hemostatic efficacy/safety profile[4]

Convenience of administration[5,6]
- Vials per infusion
- Diluent volume,
- Reconstitution device

Storage temperature[6]

Access[7]

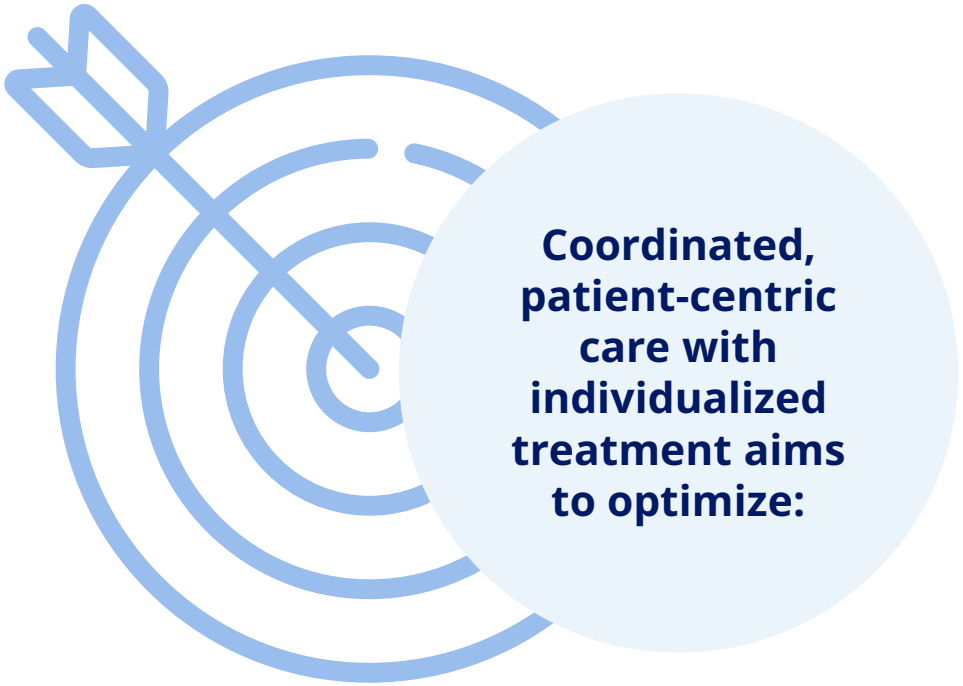
2. **Dosing regimen**—tailoring dose and frequency[4] as per indication to help prevent bleeds

MoA, mechanism of action

1. Mancuso ME et al. Haemophilia 2021;27:889–96; 2. Coppola A et al. J Clin Med 2022;11:801; 3. Collins PW et al. Haemophilia 2012;18(Suppl 4):131–5; 4. Srivastava A et al. Haemophilia 2020;26(Suppl 6):1–158; 5. Furlan R et al. Patient Prefer Adherence 2015;9:1687–94; 6. Tischer B et al. Patient Prefer Adherence 2018;12:431–41; 7. Okaygoun D et al. J Biomed Sci 2021;28:64

Comprehensive care and individualized prophylaxis target improved patient outcomes

Hemophilia guidelines recommend early initiation of regular, long-term prophylaxis and comprehensive care with input from an MDT of specialists[1]



Coordinated, patient-centric care with individualized treatment aims to optimize:

- **Protection** from bleeds[2,3]
- **Factor trough levels** and hemostatic efficacy[3,4]
- Patient **satisfaction** with treatment[3,5]
- **Adherence** to therapy[3]
- **Clinical outcomes**, including joint health[6] and pain[7]
- **Quality of life**,[2,5] including physical activity[4]

MDT, multidisciplinary team

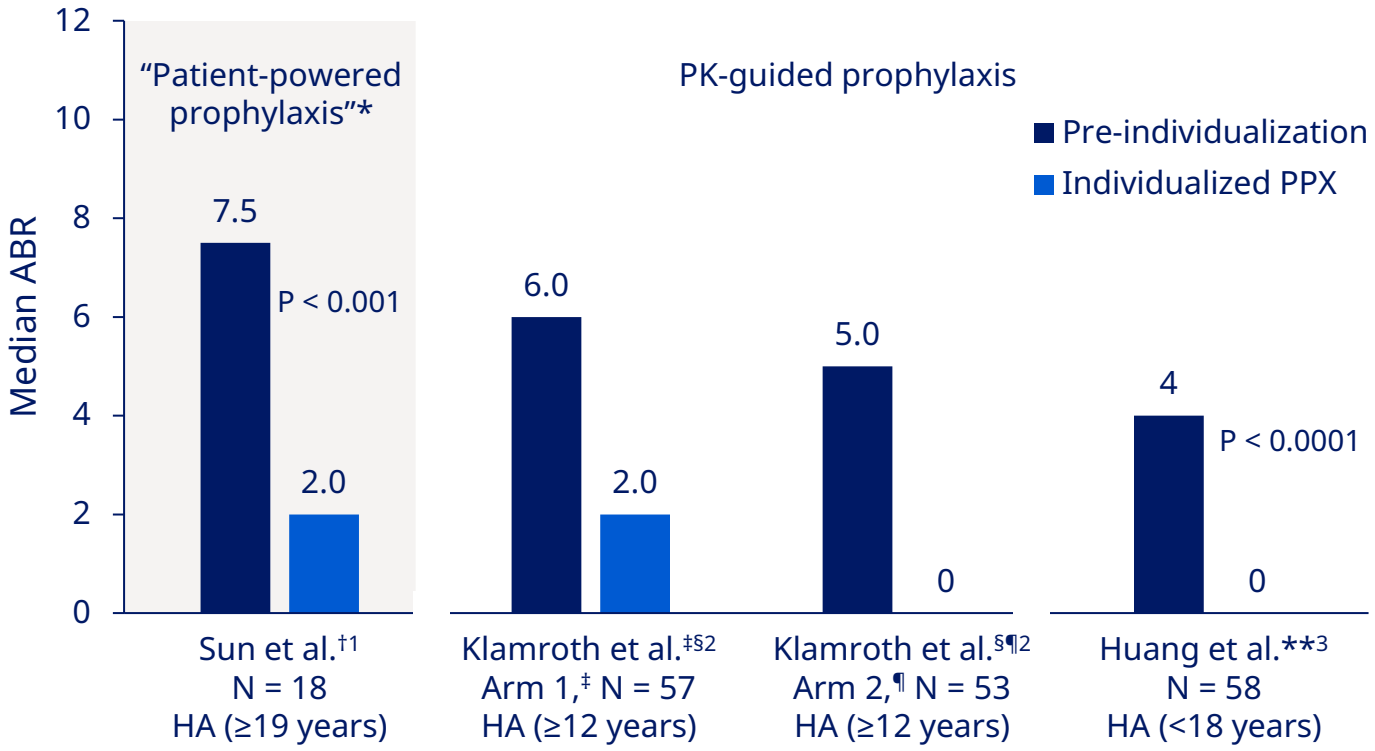
1. Mancuso ME et al. Haemophilia 2021;27:889–96; 2. Coppola A et al. J Clin Med. 2022;11:801; 3. Hermans C et al. Blood Rev 2022;52:100890; 4. Su J et al. Haemophilia 2020;26:e291–9; 5. Poon MC et al. Thromb J 2016;14(Suppl 1):32; 6. Pasi J et al. Ther Adv Hematol 2022;13:20406207221079482

Treatment individualization can result in improved protection from bleeds

- Reductions in ABR observed following transition to individualized prophylaxis[1–3]
- PK-guided prophylaxis targeting elevated trough levels can increase proportion of patients with zero bleeds[2,3]

- Individualized prophylaxis can improve health-related QoL,[1] physical functioning,[1] and reduce pain[4]

ABR outcomes with standard and individualized prophylaxis



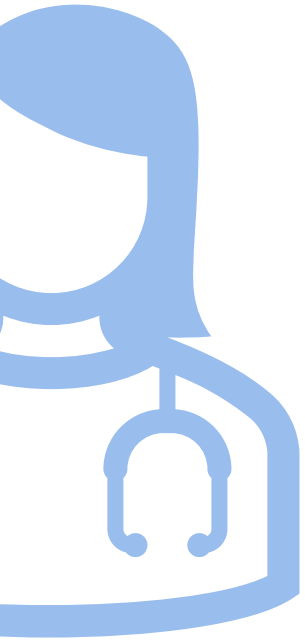
ABR, annualized bleeding rate; HA, hemophilia A; PK, pharmacokinetic; PPX, prophylaxis; QoL, quality of life

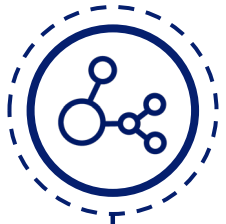
**Individualized prophylaxis established based on findings from motivational interviewing to discern patient values/experiences. †Comparison from the 12-month pre-study period to the 12-month study period. ‡PK-guided rurioctocog alfa pegol prophylaxis targeting 1–3% trough levels. §Comparison from 12-month pre-study period to second 6-month study period. ¶PK-guided rurioctocog alfa pegol prophylaxis targeting 8–12% trough levels. **PK-guided, trough-level escalating individualized prophylaxis; comparison from 6-month observation period (standard prophylaxis) to 24–30-month period on individualized prophylaxis*

1. Sun LH et al. Haemophilia 2017;23:877–83; 2. Klamroth R et al. Blood 2021;137:1818–27; 3. Huang K et al. Haemophilia 2022;28:e209–18; 4. Pasi J et al. Ther Adv Hematol 2022;13:20406207221079482.

Individualization of care is a dynamic process of shared decision-making between patients and their MDT

Shared decision-making: decisions around hemophilia treatment should be a collaborative process between the MDT and patient/caregiver[1,2]





- SDM should consider the **expertise and experience of PwH**, whose aspirations and concerns may differ to HCP's[1]
- SDM requires a **dynamic approach** that includes discussion of **goals**, **priorities** and **preferences** of PwH,[3] while also managing patient expectations
- SDM should consider **patient-centric treatment goals** (e.g., QoL, physical activity) in parallel with desired clinical outcomes[4]
- SDM **requires time investment**,[5] and is a **continual process** whereby decisions should be revisited[3] at least annually as therapies as the environment and **preferences of PwH change**
- SDM may help to **increase patient understanding, self-management,** and ability to **practice prophylaxis**[6]

HCP, healthcare professional; MDT, multidisciplinary team; PwH, people with hemophilia; QoL, quality of life; SDM, shared decision-making

1. Hermans C et al. Blood Rev 2022;52:100890; 2. Berntorp E et al. Blood Rev 2021;50:100852; 3. Valentino LA et al. J Haem Pract 2021;8:69–79; 4. Skinner MW et al. Haemophilia 2020;26:17–24; 5. Ankolekar A et al. PLoS One 2021;16:e0259844; 6. van Balen EC et al. Haemophilia 2019;25:938–45

Shared decision-making for treatment individualization requires education and patient empowerment

Patient education and engagement is essential to inform treatment choice;[1] PwH should be empowered to understand their role in SDM

Patient education may help to improve adherence and compliance to prescribed treatments[1]

PwH should be educated on features of treatment e.g., how they work, effects/limitations, expected outcomes, administering/monitoring[1,2]

HCPs require education and use of skilled communication for effective SDM in an evolving and complex treatment landscape[2]

Patient education can occur via dialogue and use of visual aids/interactive tools to simplify concepts and considerations around treatment[2]

HCP, healthcare professional; MDT, multidisciplinary team; PwH, people with hemophilia; SDM, shared decision-making

1. Berntorp E et al. Blood Rev 2021;50:100852; 2. Valentino LA et al. J Haem Pract 2021;8:69–79

There are multiple variables to consider for treatment individualization (1/2)

Clinical characteristics

- Venous access[1]
- Joint damage and MSK health[2,3]
- ABO Blood group[4]
- Pain[1]
- Inhibitors[1]
- Comorbidities[1] (e.g., CV disease, thrombotic risk)
- Current/past/ concomitant treatment[1]
- Age[1]

Bleeding phenotype[1,2]

- Treatment and dose may be reviewed and adjusted by HCPs according to bleeding pattern:
  - Bleed history
  - Severity of bleeds
  - Frequency of bleeds
  - Location of bleeds
  - Timing with respect to last infusion

Pharmacokinetics[1]

- Where able, treatment and dose may be reviewed and adjusted by HCPs to target high trough levels for effective prophylaxis[2,5]
  - Half-life, AUC, incremental recovery and peak factor levels may also be important for determining optimal coverage[5]
- Tools available for Bayesian PK-guided dosing (e.g., WAPPS, MyPKFiT)[5,6]
- Challenges for routine PK assessment: burden of classical PK sampling,[5] access to monitoring tools,[7] monitoring novel therapies[8]

AUC, area under the curve; CV, cardiovascular; HCP, healthcare professional; MSK, musculoskeletal; PK, pharmacokinetic; WAPPS, Web-based Application for the Population Pharmacokinetic Service.

1. Hermans C et al. Blood Rev 2022;52:100890; 2. Srivastava A et al. Haemophilia 2020;26(Suppl 6):1–158; 3. Seuser A et al. Blood Coagul Fibrinolysis 2018;29:509–20; 4. Singkham N et al. Haemophilia 2022;28:230–8; 5. Hermans C et al. Ther Adv Hematol 2020;11:2040620720966888; 6. Mingot-Castellano ME et al. Haemophilia 2018;24:e338–43; 7. Delavenne X and Dargaud Y. Thromb Res 2020;192:52–60; 8. Lenting PJ. Blood Adv 2020;4:2111–8

There are multiple variables to consider for treatment individualization (2/2)

Patient preferences and lifestyle

- Physical activity[1]
- Preferences[2]
- Perceptions of treatment[1]
- Lifestyle[1]
- Quality of life[1]
- Adherence[1]
- Psychological ecosystem: motivation, understanding, ambitions[1]

Local healthcare environment

- Healthcare resources[1,2]
- Family support[1]
- Environment for switching[1]
- Access/coverage[1]

1. Hermans C et al. Blood Rev 2022;52:100890; 2. Berntorp E et al. Blood Rev 2021;50:100852