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Quantifying the optimal factor VIII levels to achieve patient-centric and clinician-relevant outcomes among people with hemophilia A: a SHELF elicitation study

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ABSTRACT

Background: Hemophilia A is an inherited bleeding disorder caused by a deficiency of clotting factor VIII (FVIII), leading to joint bleeding and arthropathy. While prophylactic FVIII therapy reduces bleeding, evidence suggests maintaining higher FVIII levels (FL) may better protect joint health, particularly in physically active individuals and those with joint damage. However, data on optimal FLs required to prevent joint deterioration and complications remains limited.

Research design and methods: This study utilized the Sheffield Elicitation Framework (SHELF) methodology to elicit expert opinions on optimal FLs for patient-centric and clinical outcomes. Five European hemophilia experts participated in virtual workshops, providing probability-based estimates of FLs required to prevent bleed-related hospitalizations, orthopedic procedures, target joint incidence, and support physical activity without additional infusions or joint damage.

Results: Experts consistently recommended higher FLs for individuals with joint damage than for those without. Optimal average FLs ranged from 24% to 51%, exceeding traditionally recommended prophylactic trough levels (3–5%). Considerable uncertainty was noted around FLs for physical activity, reflecting the complexity of individualized care.

Conclusions: Standard prophylaxis regimens may not provide sufficient protection for all patients, particularly those with joint damage. A personalized treatment approach, targeting higher FLs when necessary, may be critical for optimizing outcomes.

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Hemophilia A; optimal factor VIII levels; expert elicitation; personalized prophylaxis; patient-centric outcomes

1. Introduction

Hemophilia A is a rare, inherited bleeding disorder characterized by a deficiency of clotting factor VIII (FVIII), resulting in recurrent bleeding episodes, predominantly affecting joints (hemarthrosis) [1,2]. Recurrent intra-articular bleeding leads to progressive hemophilia-related arthropathy, causing chronic pain, limited mobility, and persistent inflammation, substantially impacting physical function and quality of life [3,4]. Prophylactic treatment with FVIII replacement and non-factor therapies allows reduced bleeding episodes frequency and related complications, establishing prophylaxis as standard clinical practice for people with hemophilia A with a severe bleeding phenotype – showing marked benefits by comparison with episodic treatment [1,3,5,6].

Despite the widespread use of prophylaxis factor replacement therapy targeting FVIII trough levels between 3% and 5% [1], emerging evidence suggests higher FVIII levels (FL) provide superior protection against joint damage, particularly for individuals with an active lifestyle or existing joint morbidity [7]. Research in hemophilia A has shown that each 1% increase in factor level is associated with a 3.9% decrease in

the overall annual bleeding rate and an 18% reduction in the annual joint bleeding rate [8,9]. Recent UK expert consensus highlights maintaining an FL of ≥ 15 IU/dL as beneficial in protection against joint bleeding, with virtually no expectation of joint bleeding. However, achieving this in clinical practice may be challenging with currently available standard half-life (SHL) or extended half-life (EHL) FVIII concentrates due to treatment burden [3,8].

This may, however, be feasible with a recently approved ultra-long half-life (UHL) FVIII concentrate (efanesoctocog alfa), which provides a viable option for reaching and maintaining the non-hemophilia range ($>40\%$) without increasing treatment burden [10,11]. Additionally, experts agreed that treatments should be individualized and tailored to specific patient pharmacokinetic characteristics, as well as level of existing joint damage. In addition to the FL itself, more time spent above certain FL thresholds was also reported to reduce the risk of bleeding events [7,12].

Currently available evidence suggests that individual heterogeneity may render standardized prophylaxis regimens

inadequate to fully protect some individuals from joint bleeding and joint health deterioration. Clinician consensus indicates that a personalized treatment approach may be more likely to ensure adequate protection, particularly in the context of physical activity participation, and especially in patients with existing joint damage [7,13–15]. In this context, the treatment landscape for hemophilia A is currently expanding, and is set to provide the community with a new generation FVIIIa mimetics, which are currently being studied, or will become available in the near future. These, together with the recent approval of the first UHL FVIII concentrate, may substantially increase the feasibility of normalized hemostasis [10,11,16–18].

To that end, the Sheffield Elicitation Framework (SHELF) elicitation study by Martin et al. (2020) examined expert opinions on the optimal FVIII activity levels required for safe participation in physical activities among individuals with hemophilia [19]. Their findings highlighted that experts recommended higher FVIII levels with increased physical activity demands, recognizing greater uncertainty and variability associated with physical activity risk level and individual patient factors (such as joint health and pharmacokinetic characteristics) – in line with a previously published Delphi consensus statement [13].

There remains, however, a lack of published literature regarding the FVIII levels required not only to reduce or eliminate joint bleeding and enable safe participation in physical activity but also to prevent broader short- and long-term hemophilia-related outcomes, including hospitalizations, invasive orthopedic procedures, and the onset or progression of joint arthropathy. Identifying and characterizing these optimal FVIII thresholds could significantly inform clinical decision-making and management strategies, particularly where data supporting clinical recommendations are currently insufficient.

The aim of this elicitation study was to assess expert opinion on optimal FLs in hemophilia A to achieve core outcomes, and generate a probability distribution representing their knowledge and beliefs, while considering and quantifying uncertainty and variability.

2. Patients and methods

2.1. SHELF methodology

A number of methods to elicit expert opinions exist. However, when assessing uncertain parameters, systematically quantifying expert opinions and uncertainty, and considering elicited values across a plausible range are essential aspects. To that end, a structured elicitation methodology such as the SHELF provides a valid and intuitive approach that enables this [20].

The SHELF methodology systematically synthesizes expert opinions by eliciting probability distributions that represent expert knowledge and clinical experience and has been previously used for similar elicitation studies in hemophilia [19]. SHELF was selected not only because it allows the elicitation of specific parameters that are not currently available in the

evidence base, but also because of the ability to formally quantify uncertainty through structured probability distributions.

2.2. Elicitation procedures and definitions

Several outcomes were elicited through structured expert reflection during virtual elicitation workshops held between March 2021 and January 2023. The workshops were conducted by a lead facilitator with expertise in elicitation methodology, supported by two additional facilitators who guided the process but did not participate in providing estimations. Prior to the workshops, experts received detailed briefing materials outlining the methodology, relevant evidence, key definitions, and specific elicitation questions to be addressed.

During each workshop, participants initially engaged in practice exercises to ensure familiarity with the elicitation methodology. Experts then individually specified plausible ranges and assigned probability estimates to intervals within those ranges, constructing predictive probability distributions for each clinical parameter. Subsequently, they recommended optimal FVIII levels necessary to avoid specified clinical outcomes across different scenarios, both with and without the presence of joint damage.

In total, 12 distinct scenarios were evaluated, derived from six clinical outcomes assessed separately in contexts of both existing and no joint damage. Responses from all experts were aggregated, and probability distributions were fitted to the pooled data, to represent collective expert opinion comprehensively.

2.3. Definitions

Prior to the workshops, discussions were held on the definition of optimal FL, which was defined as the FL necessary to achieve the outcomes set out in each of the evaluated scenarios, in the expert's opinion.

Joint damage presence was defined as having one or more problem joints (a joint permanently damaged as a result of the patient's bleeding disorder, affected by having chronic pain and/or limited range of movement due to compromised joint integrity, with or without recurrent bleeding) [21].

2.4. Participants

SHELF methodological guidance generally recommends up to eight participants in an elicitation study [20]. A total of five leading European hemophilia experts were selected based on their knowledge of the condition and experience in the clinical care of people with hemophilia (PwH) or their position as a leading expert patient and experience in international advocacy. The group composition was chosen to represent holistic views and experience of hemophilia care, including hematologists ($n = 2$), a clinical physiotherapist operating in the bleeding disorders space ($n = 1$), a hemophilia nurse ($n = 1$), and an expert patient ($n = 1$). Two participants were from the United Kingdom, one from Ireland, one from Spain and one from Italy. Honoraria were provided for participation in the workshops, at fair market value.

2.5. Scenarios

Experts provided estimates regarding optimal FL required across six clinical scenarios based on specific outcomes: no bleed-related hospitalizations, no lifetime risk of invasive orthopedic procedures, no incidence and resolution of any existing target joints, ability to sustain minor trauma without bleeding, participating in physical activities without additional infusions, and participating in physical activity without acquiring chronic joint damage (see Table 1).

The scenarios were intentionally structured to maintain open discussion and to ensure that the factor level elicited was relevant enough for a wide variety of potential bleeding events, or physical activities, respectively.

2.6. Data analysis

Descriptive analysis was conducted to summarize the results. Probability distributions were fitted to expert responses, and the mean was estimated to describe the pooled elicited data for each parameter and scenario for experts' prediction of optimal factor level.

Per-respondent analysis was also undertaken, in order to represent the probability distribution of the individual expert

Table 1. Factor-level estimation scenarios.

| FLs required in each scenario (with and without joint damage) for: |
|--|
| 1 – Zero bleed-related hospitalizations |
| 2 – Zero lifetime risk of invasive orthopedic procedure due to hemophilia |
| 3 – Zero incidence of target joints and resolution of existing target joints |
| 4 – Ability to withstand minor trauma without a bleeding event (zero bleeds) |
| 5 – Ability to participate in physical activity without requiring additional prior infusions |
| 6 – Ability to participate in physical activity without acquiring chronic joint damage (problem joint) |

opinions and the distributions of the elicited parameters across scenarios (details provided in Appendix A). All analyses carried out as part of this study were conducted in Microsoft Excel.

3. Results

The elicitation study quantified expert perspectives on FL required to achieve clinical and patient-centric outcomes across multiple scenarios, and the findings highlighted differences based on the presence or absence of joint damage. Across scenarios, experts consistently recommended higher FLs required for people with existing joint damage, compared with those with no joint health issues. Figure 1 details the mean optimal FL for every scenario, with Table 2 providing further detail pertaining ranges and specific comments made during discussion, as to the sources of variability.

3.1. Bleed-related hospitalizations

When considering the optimal FL in order to avoid any occurrence of hospitalization due to bleeding events – experts, on average, recommended similar FLs with and without joint damage: 40% for people with existing joint damage and 37% for those without, ranging from 13% to 76% and 11% to 75%, respectively. The variability in expert opinions reflected differences in their clinical experiences and perspectives on bleed severity, with experts noting that this could include a spectrum of bleeding types and causes (e.g. traumatic/spontaneous, joint/muscle/soft-tissue, etc.). Despite similar pooled mean values, variability in expert opinion was characterized by a smaller degree of uncertainty for those with existing joint damage (Figure A1, ii).

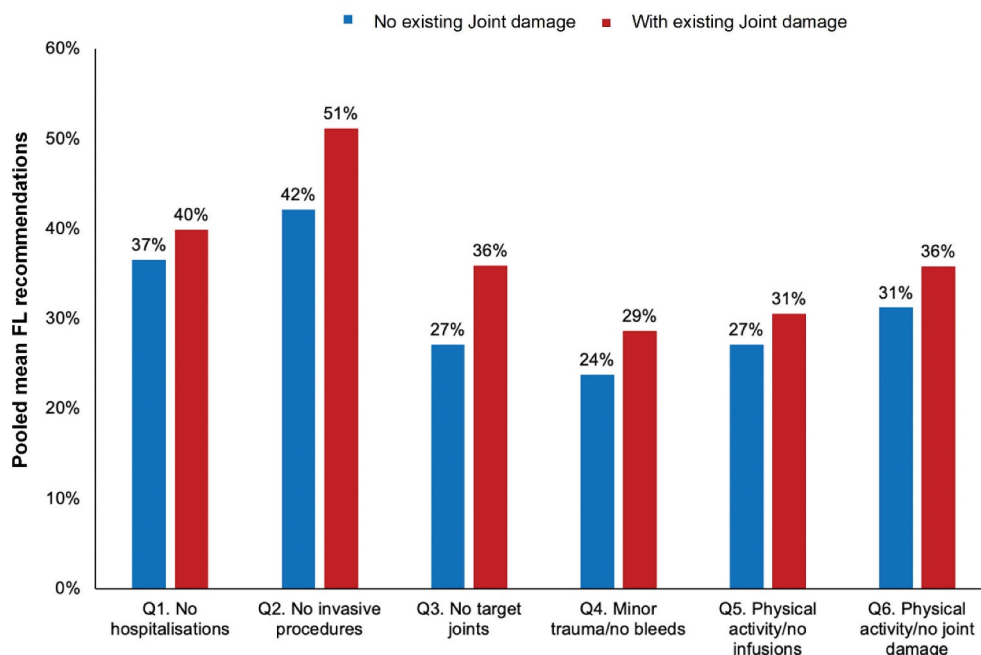


Figure 1. Pooled mean FL recommendations for both joint damage scenarios.

Table 2. Mean FLs, elicitation ranges, and expert observations across scenarios and joint health levels.

| Scenario | Joint health | Mean FL (%) | Range (%) | Uncertainty/Expert Variability Notes |
|---|----------------------|-------------|-----------|--|
| 1. Avoid bleed-related hospitalizations | No joint damage | 37% | 13–76% | Moderate variability; narrower uncertainty intervals compared to joint damage group |
| | With joint damage | 40% | 11–75% | Comparable range; reduced uncertainty indicative of stronger consensus among experts |
| 2. Prevent lifetime invasive orthopedic procedures | Without joint damage | 42% | 10–83% | Generally low uncertainty; with one expert suggesting adequacy at lower thresholds |
| | With joint damage | 51% | 31–90% | Substantial inter-expert variability; one expert proposed levels as high as 80% for sufficient protection |
| 3. Avoid & resolve target joints | Without joint damage | 27% | 7–61% | Reasonable inter-expert concordance with a relatively narrow elicited range |
| | With joint damage | 36% | 10–61% | Increased uncertainty, reflecting the complexity of managing preexisting joint damage |
| 4. Withstand minor trauma without bleeding | Without joint damage | 24% | 4–58% | Marked variability; divergence in views on whether trauma-related bleeding is joint-dependent |
| | With joint damage | 29% | 10–58% | Slightly elevated recommendations with persistent variability across expert judgments |
| 5. Participate in physical activity without additional prior infusions | Without joint damage | 27% | 6–63% | Considerable variability, largely influenced by anticipated physical activity intensity |
| | With joint damage | 31% | 8–70% | Increased factor level proposed for joint damage scenarios; some experts advised levels exceeding 60% |
| 6. Participate in physical activity without acquiring chronic joint damage (problem joints) | Without joint damage | 31% | 17–62% | Moderate variability; emphasis placed on activity nature and joint-specific risk profiles |
| | With joint damage | 36% | 24–73% | Marginally elevated factor level compared to prior scenario; general consensus but residual spread remains |

Abbreviations: FL: Factor level.

3.2. Prevention of orthopedic procedures

Similarly to bleed-related hospitalizations, experts recommended an optimal FL of 42% PwH without existing joint damage to prevent invasive orthopedic procedures, with median estimations ranging 10–83%. In contrast, experts suggested substantially higher FLs – around 51% – for PwH with existing joint damage, with mean FLs ranging 31–90%. The wide variability in these recommendations highlights differing perspectives on optimal FL requirements. For individuals without joint damage, experts generally demonstrated low uncertainty around FL values near 40%, although one expert suggested that an FL as low as 10% might adequately prevent the need of joint procedures (Figure A2, i). Conversely, for PwH with existing joint damage, experts consistently indicated that substantially higher FLs around 50% would be optimal, with one expert advocating that FLs could need to be as high as 80% to fully mitigate the risk of joint deterioration and subsequent surgical interventions (Figure A2, ii).

3.3. Target joint incidence and resolution

When discussing protection against the development of target joints and resolution of existing ones, experts recommended an optimal FL of 27% (range: 7–61%) for PwH without chronic joint damage. For PwH with existing joint damage, experts indicated a higher mean optimal FL of 36% (range: 10–61%), reflecting greater variability and highlighting substantial uncertainty and differing expert opinions regarding effective FL requirements in scenarios involving existing joint morbidity (Figure A3, ii).

3.4. Minor trauma without bleeding events

The average FL indicated to provide protection against bleeding from minor trauma was an average FL of 24% (range: 4–58%) for

individuals without joint damage and 29% (range: 10–58%) for those with existing joint damage. Experts differed notably in their assessments, with some indicating that bleeding due to minor trauma is not necessarily linked to joint damage and therefore the recommended levels should be equivalent (Figure A4, i and ii). Another expert pointed out, however, that if the minor trauma were to impact an already damaged joint, the optimal protective FL may need to be higher.

3.5. Physical activity without need for additional prior infusions

Experts recommended an average FL of approximately 27% (range: 6–63%) for individuals without joint damage to be able to engage in physical activities, without the need for additional prior infusions. Slightly higher recommendations, averaging 31% (range: 8–70%), were provided for individuals with existing joint damage. Substantial variability was noted among expert opinions for both scenarios. One expert advocated for higher optimal FLs (60–70%), highlighting that variations in joint damage severity and physical activity intensity might require substantially elevated FLs to ensure protection across all situations. Conversely, another expert confidently suggested lower FLs of around 5–10%, sufficient for most cases. All experts acknowledged the substantial uncertainty in these estimations, emphasizing the necessity of individualizing FL recommendations based on specific activity intensity and joint damage status (Figure A5, i and ii).

3.6. Physical activity without inducing chronic joint damage

In the context of the above estimation, experts provided similar recommendations. However, a slightly higher FL was estimated to ensure the avoidance of new joint damage acquisition. Experts recommended a mean FL of 31% (range:

17–62%) for those without joint damage and 36% (range: 24–73%) for those with existing joint damage (Figure A6, ii). While the estimation was less uncertain than that described in 3.5, experts noted that the intensity and nature of physical activity, as well as location and degree of joint damage, were sources of uncertainty. This further underscored the complexity of balancing FLs with maintaining physical activity, its intensity, and the level of existing joint damage.

4. Discussion

This article presents the findings of an expert elicitation study carried out with a group of hemophilia experts to collect optimal FLs to achieve specific patient-centric and clinician-relevant outcomes, currently unavailable in the literature, in the context of the presence or absence of chronic joint damage. In the absence of readily available clinical data, the SHELF methodology was leveraged, in order to provide relevant estimates, while describing and accounting for uncertainty [20].

The multidisciplinary expert group consistently proposed factor levels far exceeding traditionally recommended trough levels in published clinical management guidelines (3–5%) [1], particularly in individuals with existing joint damage. The overall consensus in most scenarios highlighted that PwH with existing joint damage should be better protected with higher FLs than those with no joint damage. This highlights the clinical perception of a need for higher prophylactic thresholds to achieve optimal patient outcomes and reduce joint morbidity, suggesting that a standard prophylaxis regimen may not always provide optimal protection against bleeding events and joint damage.

The experts emphasized that the interpretation of FLs related to physical activity should be considered in the context of the nature and risk profile of each activity, as clinicians are encouraged to continue tailoring treatment decisions to individual needs, with differential considerations needed for PwH engaging in regular physical activity versus those engaging in it more sporadically. Similarly, another SHELF elicitation study by Martin et al. reported hemophilia expert recommendations that FLs should increase as physical activity intensity and risk profile increase [19]. In both our study and the aforementioned, experts expressed greater uncertainty in their FL recommendations related to outcomes where individual patient characteristics made clinical management particularly complex, further emphasizing the importance of a management approach tailored to clinical characteristics and lifestyle [19].

Notably, the elicitation did not stratify physical activity by impact or intensity level. Experts highlighted this as a major source of variability in FVIII requirements, noting that low- versus high-impact activities likely necessitate different protective thresholds. In addition, the group further reflected on the correlation and causation between joint damage and the levels of activity that PwH undertake. Given the suggested factor levels required in the presented scenarios, this could mean that with the current standard of care additional factor is required to support safe participation in physical activity [22].

In addition, in the case of some scenarios (especially related to FL to achieve zero bleed-related hospitalizations,

as well as FL for zero incidence of target joints and resolution of existing target joints), the expert group highlighted reduced alignment in elicited values. They indicated that it may be difficult to elicit ideal values in these scenarios as FLs providing optimal protection in the specific situation may also depend on other circumstances, such as traumatic and/or non-joint bleeding events. It was also suggested, however, that the reduced alignment may be due to the ambition of some experts to aim to provide levels that are in the ‘normal’ range to people with hemophilia A. Significantly, reaching and sustaining these factor levels in the ‘normal’ range, is now feasible with the introduction in clinical practice of a novel UHL concentrate, efanesoctocog alfa, without increasing injection frequency and treatment burden [10]. Moreover, the wide ranges may also highlight the need for an individualized treatment approach, based on the specific clinical situation of each individual.

Furthermore, when considering the avoidance of surgical intervention in those with established joint damage, experts recommended that the estimations should be interpreted with caution. This is due to the fact that, in cases where pain is related exclusively to the chronic status of already deteriorated joints, FLs may have limited effect on avoiding surgical intervention.

The group also considered the difference between load-bearing joints as compared to other joints, in the context of an optimal FL to avoid joint damage progression. They noted that, while the elicited FLs were an average recommendation across both joint categories, differences in protective FLs are likely to exist in practice. They further noted, however, that the FL to provide protection against joint damage progression in load bearing joints should take precedence as these are the ones that are more likely to be affected and therefore those that are likely to require higher FLs for effective protection.

The results of these study may find applicability in the design and/or evaluation of future evidence, providing a blueprint for future studies exploring PK-Tailored treatment regimens, in the context of the level of joint health, as well as the patient’s lifestyle and physical activity levels, to further inform shared decision-making processes. The application of the SHELF methodology in this study may also further inform the design of future clinical studies evaluating the impact of higher trough levels on hemophilia-related outcomes, especially in the context of prior joint damage.

The results of this study should be considered in the context of the methodology used. The aims were to collect unavailable and unknown data and therefore comparative evidence in the published literature may be extremely limited or completely lacking. SHELF is a structured approach aimed at capturing estimates of unavailable data via expert knowledge [20].

To evaluate the internal and external validity of the elicited data, the evaluation of similar scenarios with different elicitation methodologies and comparison of obtained results may be beneficial [23].

The validity of the elicited results is also necessarily related to the selection of experts, parameter selection as well as the assumptions tied to the elicited parameters. In this context, a limitation of our study was that all the experts involved were

from Europe. Future elicitation may apply a similar approach involving experts from other geographic areas, allowing comparison of estimated parameters. Secondly, the number of evaluable parameters and scenarios is necessarily limited, and therefore we could not evaluate these in the context of differing levels of joint damage, different types of joint (load-bearing/non-load bearing) and/or different intensities, frequencies, and risk profiles of physical activities. The variability in expert opinions emphasizes the complexity of managing hemophilia A and underscores the importance of personalized therapeutic approaches. These results align with previous research emphasizing the benefits of tailored prophylactic regimens based on patient-specific factors, including joint health and activity levels [13,19,24].

The results should also be considered in the context of elicitation time frame. When the elicitation were carried out, treatments that would allow a high-sustained FL were not available. This highlights the ambition of treaters to ensure adequate, sustained, and appropriate protection from hemophilia A sequelae, which is now feasible thanks to innovative treatments.

In conclusion, individualized therapy, aiming for higher baseline factor levels, especially in those with existing joint damage, may be critical to optimizing clinical outcomes in hemophilia A.

5. Conclusions

This expert elicitation analysis found that factor VIII levels required to achieve various clinical and humanistic outcomes ranged between 24% and 51%, on average, and provided much-needed insight into clinical considerations regarding the hemophilia treatment. Considerations of PwH's individual characteristics and goals in daily life may be essential to an effectively tailored treatment regimen that should consider time spent at an adequate factor VIII level.

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Declaration of interest

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Reviewer disclosures

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Author contributions

All authors were involved in the interpretation of the data; the drafting of the paper and revising it critically for intellectual content; and the final approval of the version to be published. In addition, C Mighiu, T Blenkiron, and T Burke contributed to the conception and study design, and analysis of study data. All authors agree to be accountable for all aspects of the work.

Ethical approval

Given the elicitation methodology and the procedures followed as part of this study, no ethics approvals were required.

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References

1. Srivastava A, Santagostino E, Dougall A, et al. Wfth guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020;26 (Suppl 6):1–158. doi: [10.1111/hae.14046](https://doi.org/10.1111/hae.14046)
2. Escobar M, Sallah S. Hemophilia A and hemophilia B: focus on arthropathy and variables affecting bleeding severity and prophylaxis. *J Thromb Haemost*. 2013;11(8):1449–1453. doi: [10.1111/jth.12317](https://doi.org/10.1111/jth.12317)
3. Laffan M, McLaughlin P, Motwani J, et al. Expert United Kingdom consensus on the preservation of joint health in people with moderate and severe haemophilia A: a modified Delphi panel. *Haemophilia*. 2024;30(2):306–319. doi: [10.1111/hae.14934](https://doi.org/10.1111/hae.14934)
4. O'Hara J, Walsh S, Camp C, et al. The impact of severe haemophilia and the presence of target joints on health-related quality-of-life. *Health Qual Life Outcomes*. 2018;16(1):84. doi: [10.1186/s12955-018-0908-9](https://doi.org/10.1186/s12955-018-0908-9)
5. Manco-Johnson MJ, Kempton CL, Reding MT, et al. Randomized, controlled, parallel-group trial of routine prophylaxis vs. on-demand treatment with sucrose-formulated recombinant factor VIII in adults with severe hemophilia A (SPINART). *J Thromb Haemost*. 2013;11(6):1119–1127. doi: [10.1111/jth.12202](https://doi.org/10.1111/jth.12202)
6. O'Hara J, Sima CS, Frimpter J, et al. Long-term outcomes from prophylactic or episodic treatment of haemophilia A: a systematic review. *Haemophilia*. 2018;24(5):e301–11. doi: [10.1111/hae.13546](https://doi.org/10.1111/hae.13546)
7. Valentino LA, Pipe SW, Collins PW, et al. Association of peak factor VIII levels and area under the curve with bleeding in patients with haemophilia A on every third day pharmacokinetic-guided prophylaxis. *Haemophilia*. 2016;22(4):514–520. doi: [10.1111/hae.12905](https://doi.org/10.1111/hae.12905)
8. den Uijl IEM, Fischer K, Van Der Bom JG, et al. Analysis of low frequency bleeding data: the association of joint bleeds according to baseline FVIII activity levels. *Haemophilia*. 2011;17(1):41–44. doi: [10.1111/j.1365-2516.2010.02383.x](https://doi.org/10.1111/j.1365-2516.2010.02383.x)
9. Jones C, Wu Y, Kragh N, et al. The association of factor VIII activity levels with bleeding and quality of life in haemophilia A: findings from the European CHES II study. *Orphanet J Rare Dis*. 2025; Accepted: in print.20(1). doi: [10.1186/s13023-025-03699-z](https://doi.org/10.1186/s13023-025-03699-z)
10. von Drygalski A, Chowdary P, Kulkarni R, et al. Efanesoctocog alfa prophylaxis for patients with severe hemophilia A. *N Engl J Med*. 2023;388(4):310–318. doi: [10.1056/NEJMoa2209226](https://doi.org/10.1056/NEJMoa2209226)
11. Lissitchkov T, Willemze A, Jan C, et al. Pharmacokinetics of recombinant factor VIII in adults with severe hemophilia A: fixed-sequence

- single-dose study of octocog alfa, ruriocogog alfa pegol, and efanesocogog alfa. *Res Pract Thromb Haemost.* 2023;7(4):100176. doi: [10.1016/j.rpth.2023.100176](https://doi.org/10.1016/j.rpth.2023.100176)
12. Soucie JM, Monahan PE, Kulkarni R, et al. The frequency of joint hemorrhages and procedures in nonsevere hemophilia A vs B. *Blood Adv.* 2018;2(16):2136–2144. doi: [10.1182/bloodadvances.2018020552](https://doi.org/10.1182/bloodadvances.2018020552)
 13. Iorio A, Iserman E, Blanchette V, et al. Target plasma factor levels for personalized treatment in haemophilia: a Delphi consensus statement. *Haemophilia.* 2017;23(3):e170–79. doi: [10.1111/hae.13215](https://doi.org/10.1111/hae.13215)
 14. Zhou JY, Barnes RFW, Foster G, et al. Joint bleeding tendencies in adult patients with hemophilia: it's not all pharmacokinetics. *Clin Appl Thromb Hemost.* 2019;25:1076029619862052. doi: [10.1177/1076029619862052](https://doi.org/10.1177/1076029619862052)
 15. Castaman G, Jimenez-Yuste V, Gouw S, et al. Outcomes and outcome measures. *Haemophilia.* 2024;30(S3):112–119. doi: [10.1111/hae.14990](https://doi.org/10.1111/hae.14990)
 16. Teranishi-Ikawa Y, Soeda T, Koga H, et al. A bispecific antibody NXT007 exerts a hemostatic activity in hemophilia A monkeys enough to keep a nonhemophilic state. *J Thromb Haemost.* 2024;22(2):430–440. doi: [10.1016/j.jth.2023.09.034](https://doi.org/10.1016/j.jth.2023.09.034)
 17. Bowyer AE, Hickey K, Kitchen S, et al. A next generation FVIII mimetic bispecific antibody, Mim8, the impact on non-factor VIII related haemostasis assays. *Haemophilia.* 2023;29(6):1633–1637. doi: [10.1111/hae.14884](https://doi.org/10.1111/hae.14884)
 18. Holme PA, Blatný J, Chowdary P, et al. Moving towards normalization of haemostasis and health equity: evolving treatment goals for haemophilia A. *Haemophilia.* 2024;30(5):1109–1114. doi: [10.1111/hae.15031](https://doi.org/10.1111/hae.15031)
 19. Martin AP, Burke T, Asghar S, et al. Understanding minimum and ideal factor levels for participation in physical activities by people with haemophilia: an expert elicitation exercise. *Haemophilia.* 2020;26(4):711–717. doi: [10.1111/hae.13985](https://doi.org/10.1111/hae.13985)
 20. Oakley J, O'Hagan A. Shelf: the Sheffield Elicitation Framework (Version 3.0). Sheffield (UK): School of Mathematics and Statistics, University of Sheffield; 2018.
 21. Burke T, Rodriguez-Santana I, Chowdary P, et al. Humanistic burden of problem joints for children and adults with haemophilia. *Haemophilia.* 2023;29(2):608–618. doi: [10.1111/hae.14731](https://doi.org/10.1111/hae.14731)
 22. Mahlangu J, Iorio A, Kenet G. Efficacy of emicizumab state-of-the-art update. *Haemophilia.* 2022;28 Suppl 4(Suppl 4):103–110.
 23. Fischer K, Lewandowski D, Janssen MP. Estimating unknown parameters in haemophilia using expert judgement elicitation. *Haemophilia.* 2013;19(5):e282–288. doi: [10.1111/hae.12166](https://doi.org/10.1111/hae.12166)
 24. Ferri Grazi E, Sun SX, Burke T, et al. The impact of pharmacokinetic-guided prophylaxis on clinical outcomes and healthcare resource utilization in hemophilia A patients: real-world evidence from the CHESS II study. *J Blood Med.* 2022;13:505–516. doi: [10.2147/JBM.S363028](https://doi.org/10.2147/JBM.S363028)