Addressing unmet medical needs and health inequities in haemophilia A: expert consensus statements

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CONCLUSIONS

- The current study provides a structured framework to address health equity and achieve normalisation of haemostasis, once considered 'the unimaginable'
- This international consensus initiative on health equity aims to improve outcomes for people with haemophilia A (PwHA) by utilising current therapeutic options, and increasing collaboration and education
- Significant advances have been made in recent decades, but targeted actions need to be taken to achieve health equity for all PwHA, irrespective of financial resources, healthcare provision or geographical location
  - Aspire for high-sustained factor VIII (FVIII) trough levels or levels within the normal range for haemophilia A
  - Challenge the misconception that a small number of bleeds per year is acceptable, due to the long-term implications on joints, health-related quality of life, comorbidities, etc
  - Help to minimise or prevent chronic pain with the use of early, optimised prophylaxis and multidisciplinary team management including a pain specialist and a physiotherapist

INTRODUCTION

- With the introduction of emerging therapies in haemophilia A, including high-sustained (ultra-long half-life) FVIII replacement therapy, non-factor therapies and gene therapy, treatment goals are evolving and there is increased impetus to improve protection from bleeds and achieve 'health equity'
- In the context of haemophilia A, health equity refers to the aspiration to harness the improved pharmacological profiles of these emerging therapies to improve/preserve joint health, change the care paradigm, normalise haemostasis and enhance people's lifestyles, irrespective of sex, gender, age and disease severity[1–3]

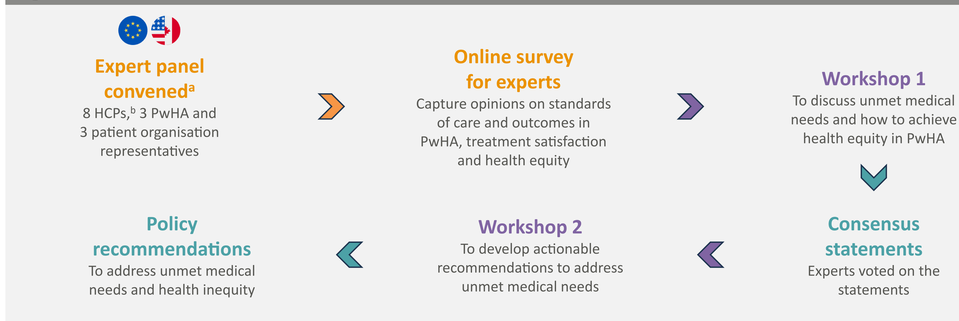
OBJECTIVES

- To address health inequities for PwHA by developing expert consensus statements and policy recommendations on closing the gap between the unmet needs and effective delivery of care

METHODS

- A structured, Delphi-based approach was used (**Figure**)

Figure: Overview of methods



[a]Expert panel members were selected based on their leadership roles in haemophilia A and involvement in health policy and advocacy work. [b]7 haematologists and 1 physiotherapist.
HCP, healthcare professional; PwHA, people with haemophilia A

RESULTS

Consensus statements on unmet needs

- Key unmet needs included that not all eligible PwHA receive optimised prophylaxis; microbleeds can occur despite prophylaxis, increasing the risk of long-term joint damage; chronic pain is highly prevalent and requires effective management; not all eligible PwHA receive comprehensive care via an multidisciplinary team, which is critical for optimising outcomes
- A series of 26 consensus statements was developed; consensus was reached for the majority of statements (25/26), including 13 with 100% agreement (**Table**)

Table: Consensus statements and levels of agreement

Statement	Agreement[a]
Prophylaxis	
Pr1. Spontaneous joint bleeds and subclinical bleeds (also referred to as microbleeds) can occur even with prophylaxis, which increases the risk of long-term joint damage in PwHA	100%
Pr2. The choice of prophylactic treatment will depend on the individual's clinical condition and preferences, the safety profile of each therapy, and its accessibility and affordability, but clinicians should strive to achieve optimal prophylaxis with the aim for each PwHA to achieve health equity and consequently attain a life undeterred by disease complications	100%
Pr3. High-sustained FVIII products used once weekly can achieve FVIII levels in the non-haemophilia range for prolonged periods, while extended half-life products will need to be used every 1 to 2 days (associated with increased burden and constitutes off-label use) to achieve the same level of protection. Barriers to routinely providing non-haemophilia range levels of protection may include costs and policy restrictions	90.0%[b]
Pr4. All PwHA should receive effective prophylaxis to achieve FVIII levels or equivalent haemostatic activity high enough to prevent, as a minimum, all spontaneous bleeds; on-demand treatment should not be used	81.8%
Pr5. Treatment options which can achieve FVIII levels in the non-haemophilia range for prolonged periods are expected to be available for PwHA in Europe in the near future	81.8%
Pr6. Heterogeneity in the availability of effective therapy between countries and even regions within the same country is one of several barriers to providing prophylaxis to all PwHA	72.8%
Outcome measures during prophylaxis	
O1. Haemophilia treatment goals need to be re-defined beyond annualised bleeding rates and should consider chronic pain, joint damage, functioning, social participation, quality of life and ultimately, health equity relative to the general population	100%
O2. There is an urgent need to establish consensus among medical professionals, patients, policy and decision makers on how to best assess the overall impact of care for PwHA, particularly with respect to PROMs and PREMs	90.9%
Pain	
Pa1. In some PwHA, pain is a consequence of irreversible arthropathy and can only be minimised by appropriate approaches such as high FVIII levels and MDT care. However, the perception that pain is an unavoidable consequence of the disorder should be challenged, as early optimised prophylaxis can prevent bleeds, thus preventing the development of arthropathy associated pain	100%[b]
Pa2. There is a need for more education and training on optimal pain management amongst haemophilia healthcare teams and greater involvement of pain specialists, ideally as part of the MDT responsible for managing PwHA	90.9%
Pa3. Chronic pain is highly prevalent in PwHA, and its effective management is a major unmet need	81.8%
Pa4. Pain is an indicator of poor joint health and plausibly an indicator of prior or current suboptimal haemostasis with insufficient FVIII levels	72.7%
Pa5. Some people with severe or non-severe haemophilia A may experience haemophilia-related pain. The use of painkillers in these patients adds to the burden of disease, and in serious cases may increase the risk of cardiovascular disease or dependence/addiction	60.0%[b]
Adherence	
A1. Non-adherence in PwHA may be attributed to the burden of treatment, venous access issues, a lack of knowledge amongst PwHA on the benefits of prophylaxis and accessibility issues to different treatment options and services	100%
A2. Advances in treatment options for PwHA are expected to alleviate the burden of treatment; these could benefit young adults and adolescents by providing greater convenience to fit with their lifestyle, as well as for older age groups by providing therapies that are simpler to administer and require less frequent injection	100%[b]
A3. There is a need to standardise the assessment of adherence, which may vary between countries and regions	81.8%
MDT management	
M1. Comprehensive care by an MDT of specialists is critical for optimising the management of PwHA and achieving health equity. However, there is a need to improve access to comprehensive care services as this is highly variable among different regions and/or countries	100%
M2. PwHA have an improved life expectancy but are more likely to experience comorbid conditions during their lifetime; this means that MDTs may have to be extended to include, for example, geriatricians and cardiologists who have an understanding of haemophilia A	100%
Knowledge sharing	
K1. There is a need for ongoing education for PwHA on the disease and its management to facilitate shared decision-making with HCPs; patient associations and haemophilia societies can play a key role in educating PwHA on general aspects of haemophilia A management	100%
K2. Caregivers of PwHA also require education to address potential uncertainties surrounding the condition and its treatment	100%
K3. PwHA, caregivers and all HCPs involved in managing PwHA need to be empowered to better understand the national healthcare structures and decisions that limit access to innovative therapies and care through sharing of knowledge	100%
K4. There is a need for greater awareness of and education around the healthcare needs for females with haemophilia A, including prolonged bleeding during menstruation or after an accident or surgery, and uncertainties relating to pregnancy and delivery	100%
K5. Achieving health equity could be facilitated by greater networking and knowledge-sharing between national health authorities, development of patient-centric guidelines, and better alignment between guidelines and policy implementation	80.0%[b]
Economic considerations	
E1. There is a need for ongoing dialogue with payers to drive policy change, which recognise the value of prophylactic treatments capable of achieving non-haemophilia FVIII target levels	100%
E2. Haemophilia A is a chronic condition that requires lifelong treatment. Approximately 90% of the costs of managing PwHA is attributed to the cost of therapies. However, there is a need to shift the focus of optimal prophylactic treatments from acquisition costs to the overall long-term economic value provided	90.9%
E3. Additional studies are required to better estimate the overall impact of prophylaxis for PwHA with respect to functional outcomes (e.g. ability to attend school and work), current and future healthcare usage/budgets, and quality of life	81.8%

The dark grey shaded cell represents the only statement for which consensus (agreement ≥70%) was not reached. [a]Proportion of participants scoring 4 or 5, where 4 = somewhat agree and 5 = strongly agree; [b]n=10 respondents (all other statements voted on by all 11 participants). FVIII, factor VIII; HCP, healthcare professional; MDT, multidisciplinary team; PREM, patient-reported experience measure; PROM, patient-reported outcome measure; PwHA, people with haemophilia A.

References

1. Skinner MW, et al. *Haemophilia*. 2020;26:17–24.
2. Hermans C, et al. *Haemophilia*. 2023;29:951–3.
3. Blatný J, et al. *Ther Adv Hematol*. 2024;15:20406207241285143.

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