On outcomes for hemophilia

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CHAPTER 3

Patient perspectives on novel treatments in hemophilia: a qualitative study

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Abstract

Introduction and aim

New treatments for hemophilia are under development or entering the market, including extended half-life products, designer drugs and gene therapy, thereby increasing treatment options for hemophilia. It is currently unknown how people with hemophilia decide whether or not to switch to such a new treatment. Therefore, we aimed to explore what factors may play a role when Dutch patients and parents of boys with moderate or severe hemophilia make decisions about whether or not to switch to a different treatment, and how disease and treatment characteristics may affect these decisions. This may aid clinical teams in tailored information provision and shared decision-making.

Methods

We conducted interviews among adults with moderately-severe or severe hemophilia and parents of young bots with severe hemophilia. We aimed to include participants from a variety of backgrounds in terms of involvement in the hemophilia community, age, treatment center and treatments. Participants were recruited through the Patients Society and a hemophilia treatment center. Semi-structured interviews were recorded and transcribed verbatim. Thematic content analysis was used to analyze the data.

Results

Twelve people with hemophilia and two mothers of boys with hemophilia were included. In general, participants reported to be satisfied with their current treatment. However, they considered ease of use of the medication (fewer injections, easier handling, alternative administration) an added value of new treatments. Participants were aware of the high cost of coagulation factor products and some expressed their concern about society's long-term willingness-to-pay for current and novel treatments, especially for increased usage due to high-risk activities. Participants also expressed their concerns about short-term and long-term safety of new treatments and believed the effects of gene therapy were not yet fully understood. Participants expected their treatment team to inform them when a particular new treatment would be suitable for them.

Conclusion

With the number of treatment options set to increase, it is important for health care providers to be aware of how patient experiences shape patients' decisions about new therapies.

Introduction

Hemophilia is a rare congenital coagulation disorder caused by a deficiency in either factor VIII (hemophilia A) or factor IX (hemophilia B), affecting 1 in 10,000 live births.[1] Hemophilia is classified into severe hemophilia (< 1 percent of normal), moderate hemophilia (1 to 5 percent of normal) and mild hemophilia (5 to and 40 percent of normal).[1, 2] The lack of coagulation factor VIII or IX causes spontaneous bleeds in patients with severe hemophilia, mainly into joints and muscles, causing debilitating and painful joint damage.[3] Treatment has evolved from whole blood transfusions prior to the 1960s to modern concentrated recombinant factor VIII and IX products. The deficient coagulation factor is administered two to three times a week by intravenous injection to prevent bleeds (prophylaxis). Unfortunately, many people with hemophilia were infected with hiv and / or hepatitis C (hcv) through whole blood products in the 1980s and early 1990s.[4] In the last few years, products with an extended half-life (requiring less frequent administration) have become available. The availability of treatment has improved life expectancy of people with hemophilia (PWH) [1, 5] and decreased bleeding rates and joint impairment.[6]

Despite these advancements,[6] a cure for hemophilia is not widely available yet and current treatment is still far from optimal. According to patients, products could be improved for frequency of administration,[7] efficacy of coagulation products (preventing bleeds),[8] mode of administration,[7] easier storage,[7, 8] fewer side effects (potential transmission of pathogens, antibodies against infused factor VIII or IX) and package (size, components of medication, logistics).[7, 8] Intravenous infusion of coagulation factor may pose a problem, especially for young children with delicate veins or for older people, for example due to increased difficulty in self-administration with increasing age.[9]

New treatments are under development or have recently been marketed that aim to address the disadvantages mentioned above, such as products with an extended half-life, gene therapy and products that affect the coagulation cascade through different mechanisms than replacing the absent coagulation factor. Some of these products may be administered subcutaneously and no longer require intravenous injections. However, new treatments may have drawbacks of their own, including known and unknown risks, as summarized in table 1.[10-14]

The Netherlands is a small country with high-quality health care and social security systems. The cost of coagulation factor is covered under public health insurance, with a deductible for specialist care. Several Factor VIII and Factor IX products are available to patients and providers. People with hemophilia receive care from one of six Dutch Hemophilia Treatment Centers and most people with severe hemophilia attend their clinic appointment annually.

Table 1: Overview of hemophilia A and B treatment products currently under development or marketed recently, with their benefits, potential disadvantages and mechanism of action.[10-14]

Type of product	Mechanism of action	Potential benefits	Potential disadvantages	On the market in the Netherlands
Extended half-life	Suppletion (Fc-protein or albumin fusion, PEGylation, albumin fusion decrease clearance)	Fewer infusions Higher trough levels	Fewer peaks for high-risk activities (e.g. sports) Unknown side effects of the accumulation of PEGs	Yes, since 2016
Non-factor coagulation replacement therapy	Bispecific antibody that links activated FIX and FX, mimicking the function of FVIII (emicizumab)	Option for persons with Hemophilia A (with or without inhibitors) No inhibitor development against FVIII Subcutaneous administrations Long half-life Excellent bleed control	Long-term risks still unknown Non-neutralizing antibodies against emicizumab Thrombotic complications (if combined with FEIBA) Cost	Yes (for patients with inhibitors only), since 2018
Products that rebalance the coagulation scale	Inhibition of TFPI (concuzimab), antithrombin (fitusiran) or activated protein C	No inhibitor development against FVIII or FIX Mode of administration Frequency of administration Long half-life	Thrombotic complications (fitusiran)	No, phase III trial
Gene therapy	(AAV) viral vector transfers FVIII or FIX DNA to liver, where it is expressed	Potential 'cure' for hemophilia, transforming severe into mild hemophilia or normality. No need for prophylaxis with factor concentrates.	Vector insertion into host genome Cancer (never observed in AAV-based gene therapy) Liver inflammation (transaminitis)	No, phase III trial (Hemophilia B) or phase I (Hemophilia A)

TFPI: tissue factor pathway inhibitor; AAV: adeno-associated virus

It is currently not sufficiently known which factors play a role in patients' decisions about whether or not to switch to a new therapy. Previous internet surveys conducted in Australia, Canada, the U.S. and Sweden reported that the frequency of clotting factor treatment administration,[15, 16] efficacy to prevent bleeds,[15, 16] manufacturer of the product,[15] and shared decision-making.[16] Finally, a study in Germany, Austria and Switzerland found that parents were more hesitant to switch to an extended half-life product than patients.[8] However, these questionnaires mostly presented a finite number of factors that may play a role in decision-making. Questionnaires also provide little information on how individuals' personal backgrounds (e.g. age) and their disease and treatment characteristics and experiences (e.g. bleeds history, experience with self-administration of coagulation factor, history of blood-borne infections) may affect decision-making. A better understanding of all factors that may play a role in decisions about treatment (both treatment and personal characteristics) will help hemophilia care providers provide tailored information when making shared decisions on the optimal management strategy of hemophilia,[17, 18] all of which are elements of patient-centered care.[19-21] Therefore, we aimed to explore what factors may play a role when Dutch patients and parents of boys with moderate or severe hemophilia make decisions about whether or not to switch to a different treatment, and how disease and treatment characteristics may affect these decisions.

Methods

Study design

We conducted a qualitative study among people with hemophilia A or B or parents of young boys with hemophilia A or B, using interview methods. We aimed to include participants with varying involvement in the hemophilia community, age, treatment center, and dosing, type and frequency of treatment (purposive sampling).[22] Prior to the interviews topic lists were prepared based on literature and clinical experience. These included questions about current and novel treatments, burden of hemophilia and its treatment and involvement in decision-making. Interview questions were revised iteratively after each interview so that new interesting issues that were raised could be explored in future interviews.[23] The topic list is included in the Electronic Supplemental Material.

Recruitment and data collection

Participants were approached through the Dutch Hemophilia Patient Society by an advertisement in a private Facebook group moderated by the Patient Society and the quarterly e-mail newsletter to members. Participants were also approached with an invitation letter of the hemophilia outpatient clinic of the Amsterdam University Medical

Centers, the Netherlands, or through word-of-mouth. After a positive response, interviewers introduced themselves over the phone and an appointment was established.

Authors BB and MLW, undergraduate students in health sciences with some experience in interviewing, conducted semi-structured interviews between March and December 2017 at the participants' homes. The number of interviews was pre-determined to be 12 to 14. A sample size of 12 to 15 is considered sufficient to understand participants' experiences in thematic content analysis.[23] Interviews lasted between 37 and 82 minutes and were audio-recorded and transcribed verbatim.

Analysis

Thematic content analysis [23] was used to analyze the data. All interview transcripts were initially coded using open coding with the software program MAXQDA version 12 (http://www.maxqda.com). Three researchers (EvB, BB, MLW) discussed codes and agreed on a coding scheme, which was then applied to all transcripts. Codes were organized into main topics and reorganized into themes that were relevant to the research question, creating a thematic map. This map consisted of themes related to experiences with current and past treatment, reasons for whether or not to switch to new treatment options, and sources of information for these decisions. Within themes, we looked for differences and similarities between participants. Authors EvB, JvdB, SG and MJW discussed final codes and themes. Quotes were extracted to illustrate aspects of themes using participants' own words.

Ethics

Exemption from full dossier ethical approval was obtained from the research ethics board at the Amsterdam University Medical Centers. All participants provided written informed consent.

Results

Participants

Of 14 individuals who participated, 12 had moderate or severe hemophilia. Two were mothers of children with severe hemophilia (aged 7 and 10 years). The 14 participants reflected a variety of the Dutch population with moderate and severe hemophilia in terms of age, treatment center, needle fear, hiv and hcv infection status, perceived involvement in decision-making and membership of the Dutch Hemophilia Patients Society (table 2). Thirteen participants were on home-treatment (12 prophylaxis, one on-demand). One participant did not self-infuse but visited the hospital when he had a bleed. All used standard half-life recombinant coagulation factor products.

Table 2: Participant characteristics

Participant number	Age group[a]	Severity and type of hemophilia	Type of product (standard half-life recombinant coagulation factor concentrate)	Reported needle fear	Hiv or hcv infection	Perceived involvement in decision-making[b]	Member of Patients Society
P1	65-70	Severe HA	Prophylaxis, 500 IU daily	No	hcv (cleared)	Yes	Yes
P2	70-75	Severe HA	Prophylaxis, 1000 IU, 2 times per week	Yes	hcv	No	Yes
P3	25-30	Severe HB	Prophylaxis, 1000 IU, once every 4-5 days	No	hcv (cleared)	Yes	Yes
P4	Child <12	Severe HA	Prophylaxis, 750 IU, 3 times per week	Sometimes	None	No	Yes
P5	65-70	Moderate-severe HA	On-demand (mild phenotype)	No	None	Yes	Yes
P6	Child <12	Severe HA	Prophylaxis, 500 IU, 3 times per week	No	None	Yes	Yes
P7	40-45	Severe HA	Prophylaxis, 2000 IU, every other day	No	hcv (cleared)	Sometimes	Yes
P8	60-65	Severe HA	Prophylaxis, 1000 IU, 3 times per week	No	hcv (cleared)	No	Yes
P9	20-25	Severe HA	Prophylaxis, 1000 IU, 2-3 times per week (but irregular)	No	None	Yes	No
P10	60-65	Moderate-severe HA	On-demand (mild phenotype)	Unknown	hcv (cleared)	No	Yes
P11	55-60	Severe HA	On-demand (mild phenotype)	No	hcv (cleared), hiv	No	No
P12	35-40	Severe HB	On-demand (mild phenotype)	No	hcv	No	No
P13	25-30	Severe HA	Prophylaxis, 1500 IU, every other day (but irregular)	No	None	No	Yes
P14	55-60	Severe HA	Prophylaxis, 1000 IU daily	No	hcv (cleared)	No	No

HA: hemophilia A; HB: hemophilia B; IU: international units

[a]Participants' ages are presented in age groups to protect their privacy.

[b]Participants were asked whether they felt they were involved the decision-making about product and dose.

The results are described in three themes: 1) Current treatment, experiences and perspectives, 2) Factors related to deciding to switch to a new therapy, and 3) Sources of information regarding novel treatments.

Current treatment, experiences and perspectives

Experiences with current treatment were mostly positive, but self-administering treatment was sometimes described as a challenge.

In general, participants reported that current coagulation factor treatment was easy to administer, safe and effective in preventing bleeds. Younger participants reported it had always been part of their daily lives. On the other hand, older participants remembered that in the past treating themselves was more burdensome than nowadays because of the larger volume of past products, the need to carefully mix components of the medication and the longer time it required to infuse intravenously. They appreciated how much easier administration had become. Those on prophylaxis all reported that they adjusted their infusion schedules depending on their daily activities, but considered themselves adherent.

Three individuals in their 60s and 70s (P1, P2 and P8) said injecting at home had become more difficult in recent years due to scarring of the injection site or reduced eyesight. Participants 8 and 13 commented that self-infusing could be 'a hassle', and participant 8 found ordering, picking up and storing the treatment product quite an effort. Two participants sometimes experienced slipping of the needle from the injection site. One of the mothers said she sometimes felt pressure to perform the venipuncture when her son had an acute bleed.

All participants were aware that new treatments had recently become available or were under development. Despite the challenges they described with their current treatment, they said they did not need new products for themselves, but welcomed this development.

Many participants were aware of the high costs and tried to use their products responsibly. Eight participants (six on prophylaxis, two on-demand) spontaneously mentioned the current high costs of their coagulation factor products. The six participants who were asked about costs were aware that their treatment was expensive. Interestingly, six participants (three on on-demand treatment) reported that they avoided injections when possible in order to save costs for the health care system, against their physician's advice to take their coagulation factor when they needed it.

Participants reported to be grateful that the cost of their coagulation factor was covered by the health care system. Some were concerned about a perceived societal trend in which patients are increasingly responsible for their own health care costs. Participant 2, for example, remembered that sufficient amounts of coagulation factor were not always available in the past:

> *"It is a concern to me, because I can imagine [...] that treatment will become scarce again.* [The availability of] *treatment is not a given if costs get out of control. We are dependent on the solidarity of society"*

Furthermore, three of the older participants (P1, P2 and P8) expressed their concerns about younger patients engaging in physical activities such as skiing, soccer and mountain biking, because the costs of the increased prophylactic coagulation factor usage are for society. They thought the availability of hemophilia treatment may ultimately depend on society's willingness-to-pay for this increased usage. On the other hand, one of the mothers and four other younger participants said practicing sports should be possible for persons with hemophilia as long as they were careful and used prophylaxis. One young participant wondered about the costs of new extended half-life products:

> *"You would save a lot of injections* [with EHL products]*, and I don't know whether that would outweigh the higher costs of [this] new product. I don't mind the injections, I don't mind to infuse a bit more often, [...] I wouldn't necessarily want to do that* [higher cost] *to society".* (participant 3)

Factors related to deciding to switch to a new therapy

When asked, eight participants were open to trying new treatments (although some felt they did not urgently need them). Three younger participants (P9, P12, P13) with few bleeding problems (two on prophylaxis with irregular schedules, one on-demand) did not feel the need to switch because they were satisfied with their current treatment. The two mothers expressed a wait-and-see attitude for novel treatments because at the time of their interviews they thought new treatments would not be available soon, and they did not want to be the first to try a new therapy because of potential unknown risks. Decisions on whether or not to switch to a new therapy were multifactorial and not self-evident. Factors that may play a role in these decisions are summarized in table 3. Facilitating factors were improved ease of use of medication and better efficacy. Barriers were fear of unknown (short and long-term) safety and efficacy, and not wanting to be a research subject if there were risks involved. Below, we highlight some factors that shape participants' treatment decisions and describe them in more detail: ease of use of the medication and fear of the unknown.

Table 3: Factors that may play a role in making decisions about switching to new therapies

Reason	Barrier/facilitator	Key points
Ease of use of the medication	Facilitator	The ease of use of the medication could be improved by: easier to carry, store and mix. less frequent injections, or a (perceived) lack of need for injections altogether with a cure. alternatives for intravenous injections: other locations for injecting (subcutaneous) or alternative administration routes (tablet or nasal spray).
Equally good or better bleed prevention	Facilitator	A new therapy should: provide protection against bleeds that is at least as good or even better than their current therapy. have sufficiently high peak and trough levels.
Fear of the unknown	Barrier	Participants were concerned about still undiscovered transmittable pathogens and antibody development. For gene therapy, they were concerned about long-term safety of the therapy and thought these effects were not yet fully understood.
Do not want to be a guinea pig / research subject	Barrier	Participants felt uncomfortable to participate in a trial because of unknown risks or to be the first to try a new therapy.

Facilitator: Ease of use of the medication

A majority of eight participants (of whom seven had been co-infected) mentioned that they preferred to inject less frequently. Three young adults (participants P3, P9 and P13) who reported no problems with their current injection schedules viewed fewer injections as an added value to new therapies that they were looking forward to, but they did not consider fewer injections to be absolutely necessary for them. They each mentioned an example of others for whom extended half-life products with lower injection frequency would be especially valuable: for children, for a brother who was not as adherent, or for others who had more bleeds. Participant 1 reported to look forward to being able to inject every three days instead of daily, which he expected to be a reality in five years. For another older participant (P2) with a hepatitis C infection in the past, each injection meant a presumed infection risk and for this reason he was looking forward to any reduction in injection frequency.

Participants 3 and 12 would prefer a cure for hemophilia instead of fewer injections, although they said they had few bleeding problems. Furthermore, participant 8, who was reluctant to switch because of his experiences with hepatitis C treatment in the past, commented that he would only switch if the frequency of injections of extended half-life products was considerably lower:

> *"If I had to switch to a different medication, I would switch to one with a longer half-life. That would be a bit better for me so I have to inject less often. But the savings* [in half-life] *are not that big [...], from 14 to 17 hours. I didn't think that was very impressive. For that reason I have not switched this time."*

Other reasons participants wanted to inject less frequently were the effort it required to plan injections and carry and store their coagulation factor products. For example, participant 12 travelled frequently for work and thought the packaging should be easier to carry with him. Participant 13 proposed alternative locations for his intravenous injections, such as a finger or a thigh. When asked about their recommendations for drug development companies, several participants also suggested different administration routes such as a tablet, a nasal spray, an ingestible nanotube with coagulation factor or a subcutaneous device as alternatives.

Barrier: Fear of the unknown

A few participants were concerned about potential risks of new coagulation factor products, such as inhibitor development and potential undiscovered transmittable pathogens. For extended half-life products, participants 8 and 3 expressed their concerns about having a low trough level for a longer time than with standard half-life products, making them more vulnerable to bleeds. A young participant (P3) was not convinced safety was properly studied. On the other hand, he and one of the mothers were willing

to try an extended half-life product because they thought they could always return to the standard half-life product.

Many participants thought gene therapy was promising, but they were also concerned about its long-term safety and the risks of adverse effects.

> *"It's a virus that you inject in your body, which may cause a liver infection, which would have to be inhibited with corticosteroids.[...] On the other hand, it's such a temporary side effect, and if you benefit from that the rest of your life..."* (participant 3)

An older participant (P2) said he was hesitant to switch to a new treatment, because he currently used a product that was effective in controlling bleeds, and he did not want to risk replacing his current treatment for one with uncertain effects. He considered the experience of two others with hemophilia who had undergone gene therapy as part of a trial in his decision:

> *"I know two guys that participated in a gene therapy trial. One was out of luck, he didn't achieve higher factor levels. The other one did. Yes, fantastic if it works. [But] they don't know it yet. [...] So you have to ask yourself... [...] it would be a pure gain if it works. On the other hand, if you have good treatment, why would you change it?"* (Participant 2)

When asked, participants often mentioned they wanted to be well informed about possible risks and side effects when making decisions about new treatments.

Sources of information regarding novel treatments

Participants reported that their most important source of information was their physician or nurse. Six of them (all age groups, members and non-members, different perceptions of involvement in decision-making) said they discussed the development of new therapies with their treatment team during their clinic appointment and trusted that their physician would inform them at the time a particular new treatment was suitable for them.

> *"The doctors are specialists [...] and at some point they'll say: 'hey, we have this new treatment for you', so I'll say: 'sure, bring it on!'" (participant 11)*

Those who were members of the Dutch Hemophilia Patients Society also expected the society to provide information about the types of treatment that are under development. Participants regularly received information from this source, for example from annual general meetings, the society's website, Facebook page, annual camping weekend and their biannual magazine. Some participants were active in the Facebook group and used it to exchange experiences with peers. Participant 11, on the other hand, was not particularly interested in the information provided by the patients' society.

A few people also searched for information on the internet. However, participant 14 said it was difficult to know what terms to search for and participant 8 said information from other countries, with their different care settings, was difficult to apply to his own situation.

Discussion

In our interview study we found that people with moderate or severe hemophilia and parents of young boys with hemophilia were generally satisfied with their current treatments. They considered different aspects of novel treatments important in their treatment decisions, including ease of use of the medication, better bleed control and safety. However, some participants shared concerns about unknown risks of new therapies. As an additional finding, the financial burden of current treatment on the health care system appeared to be a concern for a few participants, because they felt societal willingness to pay might not be a given in the future. Participants wished to receive information about new treatments, including their risks and benefits from the Patients Society as well as their hemophilia treatment team.

Previous studies have identified similar considerations of persons with hemophilia as important features of extended half-life products.[8, 16] For example, in assessing a series of hypothetical treatment scenarios with three treatment attributes each (injection interval, participation in physical activity, annual risk of bleed), patients and parents of boys with hemophilia ranked bleed control as the most important.[16] Another questionnaire study about expectations and concerns of extended half-life products reported injection frequency to be the most important feature of these products.[8] Our study enriched this knowledge by describing the reasons for the desire for a lower injection frequency: a presumed infection risk, planning injections and not having to carry and store treatment products. Interestingly, many participants considered themselves adherent even though they skipped infusions, and found treatment products with lower injection frequency especially suitable for 'others'.

An interesting finding is that the societal financial burden of current hemophilia treatment is a concern for some participants. Costs of current treatment have been identified as an important feature of hemophilia treatment in previous discrete choice experiments that aimed to elicit patient preferences.[24, 25] Several participants in our study tried to save costs for the health care system. Older participants appeared to be more conservative in allowing people with hemophilia to engage in high-risk activities than younger participants. Unlike older generations, younger participants grew up with treatment available and may therefore consider it a given. One participant spontaneously mentioned his concern for the cost of new therapies specifically. Given that the costs of current treatment were important to most participants, it is probable that costs also play a role in decisions about novel therapies. In the Netherlands, the cost

of coagulation factor is covered by the health care system, but all participants in our sample were aware of the high costs and some even tried to save costs by avoiding self-infusion, even when they had a bleed. Possibly, recent media attention surrounding health technology assessments, pricing and reimbursement decisions for expensive drugs in rare diseases may have shaped participants' opinions.[26] Costs of future novel treatment options, for example of gene therapy, are still unknown, making this difficult to address in patient-clinician interactions. However, it may be of value to patients if care providers are able to share what they do and do not know about costs of current and future treatments.

Knowledge about which features of novel treatments are important, including real and perceived risks such as pathogen transmission, may help the hemophilia treatment team tailor information provision and patient education efforts. In order to structure this information in these interactions a shared decision-making tool may be used. An interactive digital platform may further personalize information provision. Our findings may serve as a starting point for the contents of a shared decision-making tool. We suggest to explore this further in focus groups of patients and caregivers of patients.

Strengths and limitations

A strength of our study is that it included a variety of perspectives on new treatments, illustrated by quotes. We purposively included people of different ages, including parents of young boys, and with varying involvement in the hemophilia community (active or no membership of the Dutch Hemophilia Patients Society). This was done because we presumed differences in knowledge of new treatments. We also considered it important to include parents of young boys with hemophilia to explore how they viewed treatment decisions for their sons. Although the disease context of mothers is different from that of patients, we included them because they are responsible for making treatment decisions on behalf of their sons. In line with previous research,[8] the mothers in our sample were somewhat more hesitant than patients to switch to a new treatment. Our study adds that this was because they preferred to wait for more information to become available on effectiveness of these treatments.

A potential limitation may be that the first six participants responded to an advertisement through the Patients Society and therefore may have been better informed and more interested than average to discuss their views on treatment. Therefore, in order to obtain perspectives of representatives of the complete hemophilia community, the next eight participants were approached through the outpatient clinic at the Amsterdam University Medical Center. In both groups, participants knew about gene therapy and extended half-life products, but other options, such as by-passing agents or other non-factor replacement treatments, were not mentioned.

A second limitation may be that participants could have expressed a more positive satisfaction with their current treatment than their true experience. Participants were

interviewed at their homes by two investigators relatively new to the field of hemophilia, and the experiences participants shared about their current treatment may have been more positive than what they would have shared with their own care provider. However, our aim was not to elicit all possible problems participants may experience with their current treatment, but to explore the factors that may play a role in patients' and parents' decisions about current and new treatment options.

Lastly, extended half-life products and non-factor replacement products have become available in the past two years. It is possible that participants are now better informed about these novel therapies than they were at the time of their interviews. Participants' perceptions may have changed as a result of this: acceptability of newer products may have increased. However, we believe that many of the concerns expressed may be applicable to decisions on any type of treatment product switch, regardless of whether the switch is made to a novel therapy or an existing one.

Conclusion

New treatments for hemophilia are becoming available in the next few years, increasing the number of options patients and providers can choose from. Patients have a voice in these decisions. We confirmed previously identified barriers and facilitators that play a role in making these decisions, and added that costs of treatment may play a role. It is important for hemophilia treatment teams to be aware of these factors in providing information to facilitate shared decision-making.

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Supplement

Topic list for interviews[1]

Questions that were added after the initial interviews are underlined

Opening questions:

1) Please tell me a bit about yourself
2) Type of haemophilia

Questions below were phrased as 'In the past.... How is that going now?' and 'Some people say they need a change, others are satisfied with the way things are. How is that for you?'

Past

- History of disease
  - Co-infections, inhibitors
  - Can you feel the start of a bleed?
- History of treatment
  - Treatment schedule
- What went well / bad?
- Do you still notice the consequences?
  - Impact on daily life
  - View on treatment

Today

- How do you experience your current treatment?
  - Impact on daily life
  - Treatment of the consequences of haemophilia (e.g. physiotherapy)
  - Costs
- What goes well / bad?
  - Needle fear
  - Adherence
  - Specific situations
  - Advice on lifestyle (agreement?)
  - Logbook
  - Social life
- Freedom of choice in treatment
  - Who decides?
  - Relationship treating physician (has it changed?)
  - Does care provider share knowledge / provide information?
- Which aspect of treatment would you change?
  - With whom to share this?
  - In contact with other patients?

Future

- Opinion new therapies
  - What do you need? (mechanism, mental health, clinic review)
  - Reasons whether or not to switch
  - Other needs?
- Knowledge of new treatments
  - Source of information
  - Information needs
  - Influence of treating physician
- Willingness to participate in research
- Ageing independently
  - What do you need for that?

Ending questions:
Looking at the past, the present and future, what advice would you give to drug development companies?
Information about respondent (age, education, which treatment centre, member of Patients Society)

[1]Because of the exploratory nature of this study, the topic list contains more questions than can be addressed in the paper. In the results section, we focus on the topics most relevant to the research question.