

Living with an inhibitor: Results from the Study of Haemophilia Experiences, Results and Opportunities in Children and young adults with long-standing inhibitors (the SO-HEROIC study)

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Long-standing inhibitors present many day-to-day difficulties for the affected individual; the unpredictability of bleeds, bleed management, pain and treatment efficacy all affect quality of life. This study explored these issues through focus groups of affected individuals aged 16–25 in the UK. The data from the focus groups was analysed for recurring themes, which were coded under three umbrella headings: 'daily impact', 'education and future' and 'resilience and support'. Participants felt isolated through geography and being extra 'rare' within the bleeding disorders community; used pain as a gauge of bleed resolution, often without use of analgesia; described transition to adult care as particularly worrying; and explained the potential impact of living with an inhibitor on future career options. Peer-to-peer networking could provide emotional support for these young adults, who could also be role models for the future. Despite the burden of living with an inhibitor and its treatment, participants described a good quality of life from their own



Image: Young men with inhibitors benefit from supportive relationships and can share experiences to benefit others in a similar position

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perspectives. With new therapeutic options for these individuals on the horizon, they look forward to a future with fewer bleeds and less pain.

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About 30% of people with haemophilia treated with factor replacement therapy develop inhibitors, of which one half to two thirds are classed as high titre inhibitors (≥ 5 Bethesda units) likely to cause significant impairment of prophylaxis.^[1,2] In the UK all children with inhibitors

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are treated with immune tolerance using recombinant factor VIII/IX in the first instance, with various success rates, followed by additional therapies such as plasma derived factor and immune suppression for those who are deemed resistant to first-line therapy. In those children for whom immune tolerance fails, bypassing agent therapy with rFVIIa (NovoSeven, Novo Nordisk A/S Bagsvaerd, Denmark) or Factor Eight Inhibitor Bypassing Agent (FEIBA) (Shire (formerly Baxalta), Deerfield, Illinois, USA) are used either following bleeding episodes or prophylactically to prevent bleeds.^[3] The presence of inhibitors impairs quality of life (QoL) in children with haemophilia and their caregivers^[4] and increases caregiver burden.^[5,6] Frequent bleeding episodes substantially impact family life, causing pain and worsening health and quality of life scores.^[7,8] Arthropathy and restriction of joint movement are worse than in people without inhibitors and, together with pain, occur at an earlier age. This is associated with greater impairment of mobility and absence from work and school.^[9]

Despite this quantitative evidence of the impact of having and living with an inhibitor, little is known about the impact on daily life of young people. A recent consensus report noted that the instruments used to measure QoL in people with haemophilia and inhibitors are complex, and not designed to deal with the day-to-day variability associated with erratic bleeding patterns and the differing concerns of children and adults.^[10] It is therefore possible that specialist haemophilia services do not fully recognise the needs of patients and families. It is believed that the number of children and young people with long-standing inhibitors reaching adulthood is increasing,^[3] and this has important implications for managing the transition to adult services.^[11]

This study aimed to better understand the impact and concerns of young people living with haemophilia and inhibitors across the UK, and the issues they face, through focus groups and interviews.

METHODS

Subject identification

We identified all young people aged 16–25 years with inhibitors via the National Haemophilia Database (NHD) by NHD number and centre attended. A questionnaire was sent to all identified young people via their haemophilia centres; the nurses at the centres identified the participants by the NHD number and forwarded the survey to them. The questionnaire was returned by freepost. Respondents were then invited to participate in focus groups.

Focus groups

We ran three focus groups. The first ran alongside a national inhibitor event; however, unfortunately, only one young person attended this meeting. Two others had indicated attendance but had bleeds on the day, which precluded them from travelling. The young man who was at the event suggested that a person with haemophilia facilitating the patient focus group would be more in-keeping with living with haemophilia, as they would have more of an understanding of the day-to-day issues this raises.

The second focus group was facilitated by a patient co-researcher. The focus group of young people from diverse socio-demographic and geographical backgrounds was audio recorded, transcribed verbatim, and coded by hand by the researchers. The third focus group was video recorded. This methodology has recently been used in a video diary research project about living with haemophilia to gain deeper insight into living with haemophilia and proved popular with participants.^[12] The participants in the video focus group were of similar socio-demographic backgrounds, and all were studying at, or had achieved degree-level education.

Data from the focus groups were analysed for recurring themes by the study team, using modified grounded theory methodology.^[13]

Results

Twenty-eight young people with long-standing inhibitors were identified from the NHD data. They attended 16 haemophilia centres. The haemophilia nurses reported that six patients were ineligible for the study as they either no longer had an inhibitor (n=2) or they had other health issues (intracranial haemorrhage, autism, developmental delay) that precluded them from participation (n=4). A further four individuals with inhibitors were identified by nurses at the centres, who were also approached and agreed to participate.

Six young men with haemophilia A and a long-standing inhibitor responded to our initial survey. Immune tolerance therapy (ITT) had failed in four of the six; two of the six had not received ITT. All respondents described limitations on physical activity and noted that they had more bleeds that took longer to resolve because of their inhibitor. Four participants agreed to participate in a focus group. A further three participated in the video stories. Demographic data is shown in Table 1.

Data analysis

Data from the focus groups and the video interviews were analysed for recurring themes by the study team.

Table 1: Demographic data

PARTICIPANT	DIAGNOSIS	AGE	SEVERITY	ITT	CURRENT TREATMENT	CVAD
1	Factor VII deficiency	17	Severe	Yes	BPA prophylaxis	Yes
2	Haemophilia A	20	Mild	No	DDAVP or BPA on demand	No
3	Haemophilia A	18	Severe	Yes	BPA prophylaxis	Yes
4	Haemophilia A	22	Severe	Yes	BPA on demand	No
5	Haemophilia B	24	Severe	No	BPA prophylaxis	No
6	Haemophilia A	17	Severe	Yes	BPA prophylaxis	No

ITT – Immune tolerance therapy

BPA – Bypassing agent (NovoSeven or FEIBA)

DDAVP – Desmopressin

Table 2: Themes and sub-topics

DAILY IMPACT	EDUCATION AND FUTURE	RESILIENCE AND SUPPORT
Hospitals/transition/complexity of care	Issues at school	Importance of family
Self-management and treatment burden	Leaving home/going to university	Friends and relationships
Impact of bleeds	Careers and travel	Self-esteem
Pain	Future treatment(s)	Inhibitor community
Inhibitor knowledge and understanding		
Failed ITT		

Fourteen topics were identified, which are listed in Table 2. The themes were coded under three umbrella headings: 'daily impact', 'education and future' and 'resilience and support'. These are discussed further here with direct anonymous quotations to support the analysis and results.

DAILY IMPACT

Living with an inhibitor revealed daily issues mostly related to the unpredictability of bleeding, despite prophylaxis. This served as a daily reminder that haemophilia controlled the person rather than the person controlling haemophilia.

Hospitals/transition/complexity of care

There was a clear recognition that an inhibitor made routine treatment and assessment more complex. This included having to travel long distances to access specialist care, and a realisation that the level of care provided across regions of the UK was variable. This caused concerns that healthcare professional lacked knowledge and skills, and that young people had to be their own experts.

'Yes, it's unpredictability and stigmas around it. So, professionals hearing that you've got haemophilia and understanding what that means, but not really understanding how to deal with an inhibitor patient.'

Transition from paediatric to adult care raised concerns about loss of prior knowledge about the person with haemophilia, his inhibitor, his self-management skills and assessment of treatment outcomes, resulting in unnecessary hospital visits.

'Last year, I've just made the switch to the adult clinic. I don't know how it works. I was quite gutted to swap over, to be quite honest. The new consultant is great, but when you've worked with someone for all those years, you kind of ... they know you, so you don't really have to explain anything.'

Self-management and treatment burden

Treatment burden was described. The relentlessness of daily treatment, either for immune tolerance or when on bypassing agent prophylaxis, with little option for new therapies on the horizon, leads to a lack of control.

'It took me an hour and a half to inject that every morning, to mix it ... and I had to wait for it to mix, because Fanhdi and FEIBA don't mix very well ... So, it's taking half an hour to mix and then you've got to inject, but you can't inject that fast because that amount ... I can't remember how much it worked out at, but it's 100-odd ml – you can't just ram that into your veins without doing

some sort of damage. But you know, an hour to an hour and a half every morning...'

Ensuring adequate access to treatment when living away from home was complicated for some, who reported 'rules' at university halls of residence which impact on ability to store medication, in particular needles and syringes.

'I guess it's the main thing about moving away from home, and making sure that you order them at the right time; that you don't run out. I guess, for a large part, you're quite good at managing your own condition.'

Two participants had central venous access devices (CVADs) in situ to facilitate treatment. This would be unusual in adolescents of similar ages with haemophilia but without inhibitors, and added complexity and further burden to treatment, particularly with regard to time taken to care for the device.

'It would be much better [to not have a CVAD]. Because I'd just be able to get in the shower for five minutes and then go wherever I need to go, rather than the 50-minute rigmarole of changing dressings and doing the treatment and all that.'

Participants discussed deliberately skipping prophylaxis doses, and related this to treatment burden, particularly the amount of time needed and the impact this had on their lives. They discussed calculating risks of dose-skipping, recognising that bleeds may occur, but balancing this risk by altering daily activity to be in a state where bleeds were less likely.

'There were days I just wouldn't take it, because I'd have that moment where I'd be like, "Well, I've done this every day this week. I just want one day where I don't have to do it." And that didn't really create too much of an issue, to be honest, missing one day.'

Impact of bleeds

All participants described bleeds as being unpredictable, both in terms of occurrence and in response to treatment. Several had been hospitalised due to bleeding in the preceding year, which impacted significantly on their social lives, education and day-to-day activities.

'Its biggest impact, just the bleeds ... I spent more time in hospital that year. I was in quite a lot, just in and out with bleeds. The treatment wasn't working. They couldn't figure out what they were going to use to treat me, because NovoSeven wasn't working. FEIBA worked, I think, briefly, and then just kind of didn't work at all after that.'

Recognising bleeds early and treating them was seen as important; however, there was also a realisation that, despite good treatment, joint disease was already an issue. Some periods with few bleeds were reported, possibly related to age and activity.

'I think at the moment I have one [bleed] a month, like in my target joints and my elbows. But after I'd gotten through being a teenager, I definitely plateaued out, which I think is expected a bit.'

There were times when bleeds occurred spontaneously, leading to questioning treatment response and amending therapy for periods of time.

'I started to feel like I was bleeding more often than I should have, and it wasn't... it [bypassing therapy prophylaxis] just wasn't doing what it should have. So, I told the doctor, "I want off this".'

Deciding if joint stiffness was arthritis or bleeding was sometimes complex, with young people adopting a 'watch and wait' mechanism to see if the pain/stiffness worsened (indicating bleeding) or if it resolved spontaneously (arthritic stiffness).

Pain

Bleeding is painful for anyone with haemophilia. For those with inhibitors, where treatment response may be sub-optimal, pain can become a major issue. How pain can be quantified was discussed in the focus group. Most participants felt that their pain was managed poorly, with little insight from clinicians about how different individuals feel and report pain, and how long they have suffered pain before reporting to hospital for help.

'I don't really tend to use numbers to measure the pain, because I wouldn't know what a 10 is. I just tend to go with how much it bothers me. Like, if it's bothering me quite a bit, stopping me from doing what I want to do, I'll obviously

take painkillers. And then if that isn't working, I'll try something else or end up going to hospital, depending on how bad it is.'

'I normally don't take anything, unless I'm above a 7 [on a pain scale]. Most of the time I just grit my teeth and bear it, to be honest, because I don't like taking painkillers that much.'

Analgesia use was also discussed. Most participants were reluctant to take 'strong' analgesia; some stated that analgesic use affected bleed assessment and made them feel less in control of communicating about their bleed.

'I'd always tried not to take painkillers, because I didn't like not being able to feel how the bleed was improving. So, what would happen, I would take the painkillers and then I would go, "Oh, I can't feel this pain anymore. This is great," and I'd run about and make it worse. And I liked knowing my limits with it, I suppose.'

'All the time I was off my face on painkillers, so I didn't have the wherewithal to tell my parents what was happening.'

There appeared to be subliminal concerns about analgesia addiction, with participants revealing how they avoided analgesia until a point where they could no longer stand the pain or used analgesia to mask pain so that they could continue with essential daily activities such as work.

'I would say ... I take paracetamol when I've got achy, arthritic-y pain and for low-level stuff. And I have codeine at home that I take whenever the pain is just a bit too much. When you're crawling up the wall and you can't eat you can't do anything, you can't concentrate, all you can think about is the pain, then I would go to hospital and that's how I'd deal with it.'

This reveals how people with chronic pain and intermittent acute pain are able to override their pain thresholds, with or without analgesia, to participate in day-to-day activities. While this indicates great strength of character, it also highlights the potential 'risks' that people with inhibitors are prepared to take – or have to take – to maintain a career and income to achieve financial stability.

Inhibitor knowledge and understanding

Most participants had developed inhibitors within a few exposure days as very young children. All had gone through several attempts at immune tolerance, had extended periods of bypassing agent prophylaxis, and exhibited many signs of living with a long-term inhibitor. They had 'learned' their inhibitor knowledge in many differing ways, all coming to an understanding of complex medical knowledge and utilising this to come to terms with their current condition, seemingly without anger or frustration.

'It turns out that my appointment previously to that – I had the inhibitor – they said that I'd picked up a very low-level inhibitor, but apparently they don't really do anything with that because it can just go away itself at that sort of stage. So, they left it until... they were going to leave it until I went back to the next appointment, assuming it was going to be okay. But obviously it wasn't; the inhibitor had gotten worse and it started to have an impact.'

Failed immune tolerance therapy (ITT)

Most participants had undergone lengthy periods of ITT. As immune tolerance had failed, they were left with the option of bypassing agent therapy either on-demand or as prophylaxis, with limited success.

'The inhibitor is the unpredictable bit. I don't have any experience of normal haemophilia, but I imagine that you know your limits of what you can and can't do. With an inhibitor, I just don't. I've got no idea what's going to set off a bleed.'

EDUCATION AND FUTURE

Issues at school

Unlike boys with haemophilia who are usually able to participate fully in all school activities, the participants in this study described how living with an inhibitor had had a negative impact on their schooling, with many reporting missing time from school because of bleeds.

'I missed loads and loads of school. And when you used to go back, the teachers would be a bit... like, "Why have you been off for so long?" and I'd be like, "Oh, I had a bleed," and they're like, "A bleed?" Part of me thinks that they must have thought I was skiing or something. There were times where I'd be off for six or seven weeks.'

This impacted on educational achievement, with several participants reporting struggling academically at school because of the time they missed, and being unable to 'catch up' with basic education that was necessary for later study:

'I didn't really get a chance to get to grips with things that are taught all the way through school. That was tricky later on, especially in secondary school, where I was less absent but just never properly learnt the skills to deal with the classes that you'd need to be good at.'

Participants recounted attending school in wheelchairs and having extra tuition to try to keep up academically with peers, either during hospitalisation or at school. Those who had received extra tuition saw it in a positive light, recognising their need for it at the time. They also reported that it helped with academic credibility, enabling them to access further education and the possibility to have careers in their chosen fields.

Leaving home/going to university

Four participants had left home to go to university. They described this as a key stage in their lives in growing their independence. There was recognition of their reliance on parental support, particularly in the early days at university, to negotiate the logistical hurdles of having haemophilia, including keeping supplies in halls of residence, establishing new haemophilia support links (new hospitals/nurses) and attending lectures.

'You have to make those connections in new places, and you need to go and get to know them. And it's one of those things that people who don't have haemophilia, don't have any condition, just don't think about.'

'Moving into university for the first time was really stressful and being worried about treatment supplies. Supplies is something I didn't want to be having to panic about.'

Careers

Inhibitors have impacted on career choice in both positive and negative ways. One participant described how they had changed their career choices. Having an inhibitor precluded them from their first career option, but with perseverance they had found a career that was similar but 'less risky'.

'I wanted to be a sniffer dog handler in the police force, but I can't do that with my bleeding disorder. So I'm having to look at another way around it, by looking at security.'

Another changed his career options to a less physically demanding area. He was still able to work within the field he wanted, but in a different role.

'I still know exactly what I want to do and I'm going to aim for it. It's just I've had to tailor that over the years, rather than aim for it all my life. I aim to be a teacher because I know that I could manage that alongside being a haemophiliac. And the unpredictability that comes with an inhibitor doesn't really matter as much when you've got a job that isn't incredibly physically strenuous.'

One participant realised that living with haemophilia and an inhibitor had opened up career pathways that he would never have chosen without his regular contact with healthcare professionals.

'After all that had happened, I then decided to go on and study physio ... I got really interested in haemophilia, it probably motivated me. It's a strange thing to say, but I actually think haemophilia has done me more good than it has harm. And I realise that's the strangest thing in the world to hear someone say, but ... it really has, career-wise and stuff. I would never have thought of being a physio otherwise.'

Revealing haemophilia and inhibitors in the career market was discussed: who to tell, when to tell, and what to tell. One young man described how he felt potential employers would see him as a liability, even before they met him.

'It's not impacted yet, but it definitely will impact on my employability. Because employers are going to see an unpredictable, serious medical condition, and they're just going to throw my application in the bin, I imagine.'

Another described how revealing his haemophilia had lost him a job, and how he now keeps his medical condition 'secret' until at least the interview.

Future treatment(s)

This group of young people revealed that they were knowledgeable about their own lives, their treatment and care. When asked about their futures, what treatment might be like, and their dreams and wishes for the future, there were mixed responses, with some optimism about treatments on the horizon.

'For me it [trial] seemed like the only kind of option to have a permanent kind of solution to it [inhibitor]. It's [subcutaneous injection] a bit uncomfortable. It can be quite tender to touch afterwards, but it's not really an issue. Maybe a month will go and I'll have not had a bleed, or I'll have one very small bleed that required one dose of treatment.'

Others were more reticent about future therapeutic options, believing that either there was no new treatment that would benefit them, that the time was not right for them to do trials now, or that their haemophilia centres were unclear about availability and potential benefits of trials for them as individuals.

'To be honest, I don't think anything is going to benefit me that greatly, but just because I've got the condition I'm quite interested in what's happening and what's new, and different opportunities to make it easier for the youngsters that are getting diagnosed moving forward.'

There was discussion about variation in treatment, dependent on the geographical area where participants lived, or which centre they attended. There was agreement that the number of people with inhibitors in each haemophilia centre was small, with larger centres having more patients and thus, they thought, better access to new therapies and overall better care. It was felt that this inequity was unfair and should be remedied.

'I just hope, at some point in the future, all the centres are the same. Because I feel like sometimes maybe the people in [named city] maybe get better treatment than, say, people that are living in [named town].'

RESILIENCE AND SUPPORT

The interviews and focus groups reveal a community of resilient young adults, who are striving to live as near

normal lives as possible. They have described their daily lives, and how they cope with bleeds, immobility and pain. They are determined young adults who have reached their current life status due to support from friends and family, who they describe as being key players in their lives.

Importance of family

Family are clearly the most important support mechanism in younger children's lives. In this study, family remained important supporters, even when young adults had left home and moved considerable distances to attend university or work in other cities. There was, however, recognition not only of how important that family support was, but how the inhibitor had affected the whole family and not just the individual with it.

'I suppose we're that sort of family that just try and get on with things and don't really let it get in our way, if possible. You know, we deal with it when we have to, but if we can avoid having it get in the way too much, we'll do our best to do that, obviously not let it get on top of us.'

Friends and relationships

Following on from school, friendship is a key area that is valued by the individual.

'My close mates, they're aware of it [haemophilia] but even still, they don't really understand it. We don't talk about it. It's just a case of it's there and if something was to happen they'd know what to do.'

Some reflected on amusing and positive aspects of being a friend of someone with an inhibitor.

'My friends are all pretty good; looking after me, making sure I was alright – they were all just thrilled to have a friend in a wheelchair, pretty much.'

One young man reflected on not being the only person with health challenges at university, and how sharing health experiences with people with other long-term conditions could also be positive in gaining friendship and support.

'There was one person who lived in my halls; he had a condition... I can't even remember what it was. It was kind of nice that we both...

I suppose we probably bonded over the fact that we were both kind of the weird ones with medical conditions.'

Self-esteem

There was discussion of haemophilia making people the people that they are today, with participants expressing that they would not know how to live with a different, 'normal' lifestyle. Despite all the negative things that each person had gone through, there was positivity about how they presented themselves, spoke about their lives and saw their futures. All the participants were vocal, engaged, interesting and self-aware; they portrayed great self-worth, resilience and self-esteem.

'I worry more that other people think ... It doesn't bother me, but they're like, "Oh, he's in a wheelchair," you know, like judging what they think it will be like, stuff like that. That can be a bit annoying.'

Inhibitor community

How to seek and obtain support was discussed during the focus groups. For most, support came directly from family and friends. The focus group itself was seen as supportive and was, for some, the first time they had spoken to someone else living with an inhibitor. There was a recognition that they could be role models themselves – showing that life with an inhibitor can be good.

'Within the haemophilia community, we need to kind of raise the awareness of inhibitors, because people don't know what they are. Before I got diagnosed, I didn't know it was a thing.'

Given the small number of children and young people with long-standing inhibitors, a support community could be established in the UK or EU. One study participant recently attended the European Haemophilia Consortium Inhibitor Summit. He reported the positive impact of the summit for him personally and stated that it had made him want to continue sharing experience and expertise with others in the UK.

Discussion

This is the first study we know of to engage young adults with long-standing inhibitors in qualitative research that examines, from their perspective, life with an inhibitor. We used mixed methods – interviews, focus groups and videography – to play to

the participants' strengths. This has revealed a small community of resilient young adults who are keen to share personal experiences individually and in a group, to support others in similar situations.

We have described how having a long-term inhibitor impacts on daily life, resulting in unpredictability. Bleeds have a significant impact on planning, leading to restrictions in activity and increased reliance on parents and family, compared with young people of similar ages with haemophilia only. Despite being predominantly treated with bypassing agent prophylaxis, most participants described bleeding episodes that were unpredictable and treatment of bleeds as burdensome. Morfini et al^[14] described how prophylaxis with bypassing agents improved quality of life for people with inhibitors. Bleed reduction is only possible with repeated injections and full treatment compliance. In an observational study of FEIBA use, only 24.5% of participants on prophylaxis were bleed-free for a year, with a mean of five bleeds per year being experienced^[15]. Prophylaxis with NovoSeven reveals only a 45-59% reduction in bleed rate, resulting in repeated bleeds^[16].

Despite a clear understanding of the need for prophylaxis, several participants discussed deliberately skipping doses. They related this to treatment burden, particularly the amount of time needed and the impact this had on their lives. It is well known that adolescents with haemophilia struggle with adherence to prescribed therapy^[17,18]. This is in part because of time constraints, which are made worse by the need for ongoing CVAD use, as this demands more care and attention to limit infection risk^[19]. Dose-skipping can lead to further bleeds, impacting on mobility and the ability to go to school or work, and causes considerable pain.

We have discovered that pain is a significant issue for this group of young people. They describe putting up with pain ('I just grit my teeth and bear it') because they dislike the side-effects of analgesia, and of opioids in particular. Pain has recently been described in a cohort of younger children with haemophilia in the UK treated with prophylaxis and is poorly understood by haemophilia healthcare professionals^[20]. Further work is needed to understand this reluctance to improve pain assessment and to inform the use of non-pharmacological alternatives (e.g. physiotherapy, complementary therapies, exercise) that might improve pain management.

With regard to the future, in terms of education and careers, we found that schools had been less than helpful at coping with reduced mobility, and

that managing self-treatment at university presented organisational challenges. More positively, peer relationships were good. Despite the practical challenges, study participants strive to live as normal a lifestyle as possible, adapting and adjusting in 'ad-hoc' ways to fulfil their dreams. Young describes how difficulties with high school education have an impact on higher education and career choice for those with inhibitors, given their limited mobility due to haemophilic arthropathy^[19]. In our study, all participants were studying (or hoping to study) at higher education facilities, and were choosing careers that were feasible, given their physical abilities. Career choices had been made and changed based on perceived limitations (moving from the police force to security, for example), but also as a result of personal experience. One participant had chosen physiotherapy as a career because of his personal involvement with healthcare provision. Achieving a 'position in society' through higher education is recognised as an important step to adulthood for young men with haemophilia^[21].

Growing up 'feeling different', even within one's own family, is another aspect of living with an inhibitor. Palareti et al describe how haemophilia 'plays a role in the individual's growth within the family' and how this impacts on all aspects of daily life^[22]. Participants in this study have told us that living with an inhibitor is misunderstood even by their relatives with haemophilia and can lead to isolation. Family support is crucial for children growing up with haemophilia^[23]. During adolescence the child develops self-management skills and takes on self-responsibility from his parents^[24]. The loss of this support as adolescents move into higher education or away from home is challenging for some^[25], with many having to fully manage care ('self-infusion, ordering supplies, maintaining adherence and navigating the healthcare system') for the first time^[26]. Participants in this study described this as a major challenge, particularly for management of 'stock levels' due to the unpredictability of bleeds.

Belonging to this small sub-section of people with haemophilia can be isolating. Those in this study lived in geographically disparate areas of the UK, and for some this was the first time they had met another person with an inhibitor. Peer-to-peer networking for this group could provide emotional support. Due to the logistical difficulties of meeting face-to-face, this could be through online networks for those with haemophilia and/or inhibitors^[27,28].

Conclusion

The number of young adults living with an inhibitor continues to grow as more people live longer with haemophilia in the post-HIV era. We have shown that good QoL can be achieved from the patients' own viewpoint, but requires intensive treatment, good adherence, and regular healthcare provider intervention and attention. Treatment is burdensome, and patients benefit from supportive relationships with family and peers, as well as healthcare providers. These relationships can be 'virtual' as well as face-to-face, sharing experiences to benefit others in a similar position. With good treatment, overall outcomes are promising, with participants attending higher education and planning future careers that will enable them to be a valuable part of society.

New therapeutic options (new factor therapies with extended half-lives and non-factor therapies) offer opportunities for this group of individuals. For the first time, they can look forward to a life with less or no bleeds, less treatment (particularly intra-venous) and a lower disease/treatment burden. Access to the new treatments is currently limited. These therapies are still undergoing clinical trials and participation is determined by the motivation of haemophilia centre staff to become involved and by geographical constraints. The participants in this study were acutely aware of these constraints and hoped, very vocally, for a health service that could provide the same standard of care for all people with haemophilia and inhibitors across the UK. This is something we, as healthcare providers, should also strive for.

Limitations

This is an observational study of a small number of young adults from similar socio-demographic backgrounds, with long-standing inhibitors in the UK, describing their personal experiences. The results reported in this study therefore may not be generalisable and may not reflect the views of young people from more financially or socially disadvantaged backgrounds, who did not participate in the focus groups. This requires further study. However, trustworthiness in qualitative research supports the argument that findings are 'worth paying attention to'^[29]. We believe that the results in this study add valuable insights for haemophilia healthcare providers.

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Reference

- Collins PW, Palmer BP, Chalmers EA, et al; UK Haemophilia Centre Doctors' Organisation. Factor VIII brand and the incidence of factor VIII inhibitors in previously untreated UK children with severe hemophilia A, 2000-2011. *Blood* 2014; 124: 3389-97.
- Peyvandi F, Mannucci PM, Garagiola I, et al. A randomized trial of factor VIII and neutralizing antibodies in hemophilia A. *N Engl J Med* 2016; 374: 2054-64.
- Collins P, Chalmers E, Alamelu J, et al. First-line immune tolerance induction for children with severe haemophilia A: a protocol from the UK Haemophilia Centre Doctors' Organisation Inhibitor and Paediatric Working Parties. *Haemophilia*. 2017 Sep;23(5):654-9. doi: 10.1111/hae.13264.
- Dekoven M, Wisniewski T, Petrilla A, et al. Health-related quality of life in haemophilia patients with inhibitors and their caregivers. *Haemophilia* 2013; 19: 287-93.
- DeKoven M, Karkare S, Lee WC, et al. Impact of haemophilia with inhibitors on caregiver burden in the United States. *Haemophilia* 2014; 20: 822-30.
- Lindvall K, von Mackensen S, Elmståhl S, et al. Increased burden on caregivers of having a child with haemophilia complicated by inhibitors. *Pediatr Blood Cancer*. 2014 Apr;61(4):706-11. doi: 10.1002/pbc.24856.
- Neufeld EJ, Recht M, Sabio H. Effect of acute bleeding on daily quality of life assessments in patients with congenital hemophilia with inhibitors and their families: observations from the dosing observational study in hemophilia. *Value Health* 2012; 15: 916-25.
- Recht M, Neufeld EJ, Sharma VR, et al. Impact of acute bleeding on daily activities of patients with congenital hemophilia with inhibitors and their caregivers and families: observations from the Dosing Observational Study in Hemophilia (DOSE). *Value Health* 2014; 17: 744-8.
- duTrel S. Physical and psychosocial challenges in adult hemophilia patients with inhibitors. *J Blood Med* 2014; 5: 115-22.
- Hermans C, Auerswald G, Benson G. Outcome measures for adult and pediatric hemophilia patients with inhibitors. *Eur J Haematol* 2017; 99: 103-11.
- Young G. Transitioning issues in adolescent to young adult hemophilia patients with inhibitors: an approach for a growing population. *Blood Coagul Fibrinolysis* 2010; 21 Suppl 1: S7-10.
- Phillott A, Khair K, Loran C, et al. HaemophiliaLIVE: an ethnographic study on the impact of haemophilia on daily life. *J Haem Pract* 2014; 1(3): 14-20. doi: 10.17225/jhp00030.
- Charmaz K. 'Discovering' chronic illness: using grounded theory. *Soc Sci Med* 1990; 30 (11): 1161-72.
- Morfini M, Auerswald G, Kobelt RA, et al. Prophylactic treatment of haemophilia patients with inhibitors: clinical experience with recombinant factor VIIIa in European Haemophilia Centres. *Haemophilia* 2007 Sep; 13(5): 502-7.
- Negrier C, Voisin S, Baghaei F, et al; FEIBA PASS Study Group. Global Post-Authorization Safety Surveillance Study: real-world data on prophylaxis and on-demand treatment using FEIBA (an activated prothrombin complex concentrate). *Blood Coagul Fibrinolysis* 2016 Jul; 27(5): 551-6.
- Young G, Escobar MA, Pipe SW, Cooper DL. Safety and efficacy of recombinant activated coagulation factor VII in congenital hemophilia with inhibitors in the home treatment setting: a review of clinical studies and registries. *Am J Hematol* 2017 Sep;92 (9): 940-5.
- Duncan N, Kronenberger W, Roberson C, Shapiro A. VERITAS-Pro: a new measure of adherence to prophylactic regimens in haemophilia. *Haemophilia* 2010; 20(1): 39-43.
- Van Os SB, Troop NA, Sullivan KR, Hart DP. Adherence to prophylaxis in adolescents and young adults with severe haemophilia: a quantitative study with patients. *PLoS One* 2017 Jan 19; 12(1): e0169880. doi: 10.1371/journal.pone.0169880.
- Young G. Transitioning issues in adolescent to young adult hemophilia patients with inhibitors: an approach for a growing population. *Blood Coag and Fibrinolysis* 2010; 21 (Suppl 1): S7-10.
- Khair K, Holland M, Bladen M, et al; SO-FIT Study Group. Study of physical function in adolescents with haemophilia: the SO-FIT study. *Haemophilia*. 2017 Nov; 23(6): 918-25. doi: 10.1111/hae.13323.
- Poti S, Palareti L, Emiliani F, Roderigo G, Valdre L. The subjective experience of living with haemophilia in the transition from early adolescence to young adulthood: the effect of age and the therapeutic regimen. *International Journal of Adolescence and Youth* 2017. doi: 10.1080/02673843.2017.1299017.
- Palareti L, Poti S, Cassis F, Emiliani F, Mayino D, Iorio A. Shared topics on the experience of people with haemophilia living in the UK and the USA and the influence of individual and contextual variables: results from the HERO qualitative study. *Int J Qual Stud Health Well-being* 2015; 10:28915. doi: 10.3402/qhw.v10.28915.
- Khair K, Gibson F, Meerabeau L. 'I can always rely on them': the importance of social support for boys with haemophilia. *J Haem Pract* 2014; 1(1): 10-16. doi: 10.17225/jhp00005.
- Limperg P, Peters M, Gibbons E, et al. Themes in daily life of adolescents and young adults with congenital bleeding disorders: a qualitative study. *Haemophilia* 2016; 22(4): e330-3. doi: 10.1111/hae.12961.
- Garrino LE, Picco I, Friguerra D, Rossi P, Roccatello D. Living with and treating rare diseases: experience of patients and professional health care providers. *Qual Health Res* 2015; 25(5): 636-51. doi: 10.1177/1049732315570116.
- Brand B, Dunn S, Kulkarni R. Challenges in the management of haemophilia on transition from adolescence to adulthood. *Eur J Haematol* 2015 Dec;95 Suppl 81: 30-5. doi: 10.1111/ejh.12582.
- Khair K, Holland M, Carrington S. Social networking for adolescents with severe haemophilia. *Haemophilia* 2012 May; 18(3): e290-6. doi: 10.1111/j.1365-2516.2011.02689.x.
- European Haemophilia Consortium. The European Inhibitor Network. Available from <https://inhibitor.ehc.eu> (accessed 28 January 2018).
- Lincoln YS, Guba EG. *Naturalistic Inquiry*. Newbury Park, Ca: SAGE; 1985.



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