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APPG on Haemophilia and Contaminated Blood: Inquiry into Access to Treatment

Putting people with bleeding disorders at the heart of care

Contents

THE HAEMOPHILIA SOCIETY

This report was researched and written by The Haemophilia Society (Registered charity no. 288260 (Scotland SC039732) in their role as secretariat to the APPG with funding provided by Sobi. The views expressed are those of the APPG on Haemophilia and Contaminated Blood.

Foreword by Dame Diana Johnson and Sir Peter Bottomley

Despite big steps forward in the treatments available to people with bleeding disorders (PwBD), most are still seeing their lives held back by their condition. The APPG on Haemophilia and Contaminated Blood heard testimony and received submissions which showed disappointment among PwBD that they were not receiving better care and treatment. This report lays out the problems in detail and makes recommendations for the future.

This inquiry was launched in 2019 but was ultimately delayed in publishing its final report due to circumstances beyond our control. A general election followed by the COVID-19 pandemic led to a long delay from the initial call for evidence to publication. In that time some new treatments for bleeding disorders have been approved, a new tender has taken place and standards of care of treatment have moved forward. However, the recommendations in this report remain important and timely to help deliver the best outcomes for PwBD.

The NHS Five Year Forward View published in 2014 stated that 'there is broad consensus on what that future needs to be. It is a future that empowers patients to take much more control over their own care and treatment.' However, that future has not yet been achieved for most PwBD. There is a lack of understanding among PwBD of the treatment options available to them and most feel they are not very involved in decision making about their treatment.

While the APPG did see and hear examples of very good practice, it was deeply disappointing to see such significant variation across the UK. London and the South East in particular seemed to be better resourced, offering better multidisciplinary care and achieving better outcomes for patients. In other parts of the country, access to newer treatments and a full multidisciplinary team including physiotherapists and psychological support was much rarer. Inequities in access to diagnosis, care and treatment were particularly stark for women with bleeding disorders.

Many of the concerns raised in this report also featured in a peer review of all main centres across the UK which was published this year. It concluded that 'the under provision, or complete absence, of members of the core and extended multi-professional team was the most frequent and significant concern identified'. We agree with that conclusion.[1]

People with bleeding disorders want to live normal lives uninhibited by their condition, something that is within reach. However, without changes in approach this will only be available to the most vocal and engaged patients in certain parts of the country. We hope that clinicians, commissioners and the government read this report and consider its recommendations carefully in order to help this community truly realise their ambitions.

Dame Diana Johnson MP

Sir Peter Bottomley MP

Co-Chairs, APPG on Haemophilia and Contaminated Blood

Executive summary

1. Bleeding disorders are medical conditions which include haemophilia A and B, von Willebrand disease as well as other factor deficiencies and platelet disorders, in which the blood fails to clot properly. As rare conditions, prevalence within the general population is low, and throughout the UK only around 32,000 people are registered as having a bleeding disorder.[2]

2. People born with genetic bleeding disorders today receive care which builds on six decades of advances in treatment and clinical care. These advances have led, in the UK, to near universal access to safe and, to varying degrees, effective treatment. Life expectancy and quality of life for people with bleeding disorders now is radically different to care only decades ago. The widespread use of prophylaxis and access to multidisciplinary integrated care have turned many bleeding disorders from severely life-limiting disorders to manageable lifelong conditions with which people can expect to lead impeded but relatively normal lives to ages in line with average life expectancy.

3. Yet, despite these advances, living with a bleeding disorder in the UK still comes with a significant burden to ordinary life, including pain and joint damage, and there remains no cure or effective cure. The impact of living with a bleeding disorder remains significant and continues to result in health-related quality of life being lower than individuals without bleeding disorders. This is in contrast to some other high-income countries, where health-related quality of life for people with bleeding disorders (PwBD) can be on par with those without bleeding disorders.[3]

4. The results of this inquiry demonstrate that considerably more needs to be done to mitigate the burden to everyday life faced by PwBD. More significantly, a case exists not only to see a review, but a fundamental overhaul of the way bleeding disorders are managed and cared for in the UK. To achieve better outcomes for PwBD, reform to the current treatment paradigm, and the commissioning system behind it, is clearly needed.

5. Challenges, treatment gaps and unmet needs persist, and serious issues from lifelong disabilities, emotional distress and reduced health-related quality of life are still common for PwBD. But, promisingly, a bleeding disorder treatment revolution, nearly as dramatic as the introduction of factor concentrates (CFCs), looks set to take hold in the coming years. An opportunity now exists to push towards a system genuinely able to assist PwBD to transition into a bleed-free future. This is, however, only possible with reform.

6. This report sets out the current systems of care for genetic bleeding disorders, and how the commissioning and treatment systems work in theory and practice. The report's main purpose is to explore and provide a broad overview of the thoughts and views of people with bleeding disorders in the UK, in relation to their current standard of care and access to treatment.

7. Based on the evidence considered and the analysis below, the APPG believes that the following set of recommendations would begin to address both the issues raised and the unmet needs of PwBD the inquiry has identified and articulated throughout this report.

Recommendations

Recommendation 1 – Increased funding needs to be made available to ensure all PwBD who would benefit from multidisciplinary care are able to access it as needed, regardless of where they live in the UK. Specifically, all comprehensive care centres should have dedicated physiotherapy, occupational therapy, social work and psychology services.

Recommendation 2 – Care standards should be uniform across the UK. To ensure outcomes remain equitable, the APPG recommends the creation of a body capable of raising and addressing inequities which arise. Given the variation in staffing and resources levels between centres, and the implications this has on the level and basic provision of certain services that the APPG has been made aware of, it also recommends that a more detailed review is published.

Recommendation 3 – For the National Haemophilia Database to realise its full potential, and to ensure it is able to cope with the recommendations of this report, the APPG recommends that additional investment is made available both to it and to individual centres to improve and broaden data collection.

Recommendation 4 – To move towards achieving optimal outcomes the APPG recommends that the National Service Specification for Haemophilia needs to be updated, and the current treatment paradigm needs to reflect innovation in treatment regime in terms of products and treatment regimen and have far more ambitious expectations for PwBD.

Recommendation 5 – The level of influence commissioning decisions have over clinical freedom needs to be reduced. Clinician and patient preference must be a deciding factor in prescribing decisions. Commissioners must ensure that clinicians are able to offer their patients a choice over which treatment is right for them and must not be limited by restrictive tenders and commissioning guidance.

Recommendation 6 – Target trough levels should be raised to reflect the ambition to achieve zero bleeding episodes in people with haemophilia. Optimal trough levels should be decided by clinicians and their patients, reflecting a variety of lifestyle factors. Increasing dosing levels and intervals should not attract censure from commissioners. Personalised care should become a reality for all. Access to pharmacokinetic testing should be extended to all eligible PwBD and tailored dosing regimens for all PwBD requiring regular treatment. Personalisation and co-decision-making should become the norm.

Recommendation 7 – New treatments should routinely be made available immediately following licensing through a managed access programme with an agreement between the NHS and industry to manage costs.

Recommendation 8 – Further study is needed on the disparity between the severity of conditions, and whether those with moderate haemophilia are being undertreated due to misconceptions about their classification.

Recommendation 9 – Women, who make up the majority of diagnosed PwBD, should be offered equity of care from haemophilia centres and this should be reflected in the updated service specification.

Recommendation 10 – Strategies should be drawn up to develop links between haemophilia centres and services for older people. Education will be needed for healthcare workers caring for older people with bleeding disorders, whose needs will be unique.

Recommendation 11 – NHSE must ensure meaningful engagement with PwBD is effective, timely and accessible, and demonstrate the impact of stakeholder engagement, communicating it back to the bleeding disorder community. A regularly updated information website would address the lack of system transparency. Unless commercially sensitive, all meeting minutes in which decisions are made about the treatment and care of PwBD should be published.

Recommendation 12 – PwBD need to be informed to be empowered. NHSE should work collaboratively with The Haemophilia Society to create an online portal through which consultations could be launched, decisions communicated, and information published.

Recommendation 13 – A full review of the UK tender processes for bleeding disorder treatments should take place with the aim of creating a new system that incorporates a wider measure of value. This should include far greater consideration of patient-relevant outcomes and the impact on quality of life. The Commercial Medicines Unit should work collaboratively with patient groups including The Haemophilia Society, as well as a multidisciplinary expert working group, to plan how to incorporate a wider measure of value into the UK haemophilia tender exercises.

Recommendation 14 – A significant proportion of the savings made through the tender process should be reinvested in wider care and support for PwBD or used to fund new innovative treatments that address unmet needs.

Recommendation 15 – Commissioners should be required to consider a wider range of evidence of the value and impact of treatments so that their full benefit is weighed against the costs.

Recommendation 16 – Treatments should be considered by CPAG on their own merits and if clinically effective, demanded by patients and clinicians, and value for money, should be commissioned.

Recommendation 17 – The Government should ensure continuing shared working of the MHRA with the EMA and improve engagement with other leading licensing agencies including the FDA to accelerate marketing approvals for new treatments.

Recommendation 18 – A UK-wide steering committee should be set up on a statutory basis that brings together patient representatives, multidisciplinary healthcare professionals and commissioners to ensure a coordinated approach to treatment for PwBD.

Context and purpose of the inquiry

1. The adoption of factor replacement therapy and multidisciplinary comprehensive care in recent decades has seen life expectancy and quality of life dramatically increase, especially when contrasted with historic standards of treatment.

2. However, new treatments have been and are being developed which hold the potential to radically shift the treatment paradigm. These can deliver greater personalisation and better outcomes for people with bleeding disorders.

3. The changing nature of treatment and the diversification of the bleeding disorder population are presenting policymakers with a unique set of opportunities and challenges, which will dictate the 'direction of travel' for the next generation. Taking up the task of grasping these opportunites has the potential to deliver better outcomes for PwBD and ensure the UK regains its place at the forefront of care and treatment of PwBD.

4. This inquiry, and the recommendations this report puts forward, come at the time of an ongoing review of the role to be played by NICE going forward. This also chimes with the Government's prioritisation of life sciences and a debate about the sustainability of the NHS. This report seeks to maximise the opportunities this presents to improve the lives of PwBD. While reviews are currently being undertaken into the role of NICE, the future of commissioning for bleeding disorders is unclear. For now, however, most PwBD will continue to have their access to new treatments determined by NHS England from whom the rest of the UK takes its lead.

5. While this is an exciting time for the treatment of PwBD, with innovations in treatment the APPG wanted to ensure that the voices of PwBD were heard. The APPG undertook this inquiry, and the publication of this final report, to investigate the current systems, and to outline where they were working well and where reform was needed.

6. Throughout the inquiry this report has been shaped, through moving and emotive personal testimony, by hundreds of responses from PwBD and engagement with all relevant stakeholders including pharmaceutical companies, NHS representatives and multidisciplinary healthcare professionals. The result is a report that represents a synthesis of the expertise and experience submitted to the APPG with a bold and consistent set of reforms to be articulated to policymakers.

7. The APPG hopes this report will act as a useful resource for those looking to understand how 'access to treatment' impacts PwBD and how the systems of licensing, commissioning and procurement of treatments for PwBD work. In doing so, it aims to reassert the rights of PwBD to benefit from new innovative treatments, even if it reverses the cost-cutting trend of the last decade.

8. The APPG, through this and future projects, is working to ensure the current systems are fit for purpose, and that PwBD are able to live lives, in terms of health-related quality of life, on par with the general population.

9. This report is focused on access to treatment for PwBD now, and how best to improve and reform the system going forward, but the legacy of the contaminated blood scandal has cast a long shadow. While the processes for commissioning treatments must be equitable, robust and timely, decisions must also be made with this in mind. The issues and recommendations identified within this report are best understood within this context.

Who we are

1. The All-Party Parliamentary Group (APPG) on Haemophilia and Contaminated Blood is a cross-party group which has included over 100 MPs and members of the House of Lords who share an interest in bleeding disorders and the contaminated blood scandal.

2. The core purpose of the group is 'to promote awareness of, and campaign for, people with haemophilia and other bleeding disorders and people infected with blood-borne viruses due to contaminated blood and blood products used in their healthcare treatment'.

3. The group is led by Labour MP Dame Diana Johnson and Conservative MP Sir Peter Bottomley alongside vice-chairs including MPs from other parties represented in parliament.

4. The group meets regularly to get updates on developments in bleeding disorder care and treatment and on the inquiry into the historical use of contaminated blood and blood products. It seeks to represent the needs of these communities in parliament and in engagement with government, government bodies, the infected blood inquiry and the NHS.

5. The secretariat to the APPG is provided by The Haemophilia Society. In this role they maintain the membership information of the APPG and facilitate meetings of the APPG in conjunction with the chairs.

Acknowledgements

6. The APPG wishes to thank the bleeding disorder community who shared their hopes and fears about the future of their treatment and without whom this report would not have been possible.

7. They also wish to thank the healthcare professionals, NHS England and pharmaceutical company representatives who gave evidence to this inquiry. And particular thanks to Dr Dan Hart and all the staff of the Royal London Haemophilia Centre who hosted a visit by APPG members.

8. We would also like to thank APPG members Liz McInnes, Baroness Meacher and Jim Shannon who took oral evidence alongside the co-chairs of the APPG.

9. This report was written by The Haemophilia Society in their role as Secretariat to the APPG. The APPG thanks the members, staff and trustees of The Haemophilia Society for their continuing support of the work of the APPG.

10. Funding for this inquiry and the publication of this report was provided by an unrestricted grant to The Haemophilia Society from Swedish Orphan Biovitrium Ltd (Sobi Ltd). Editorial control lay solely with The Haemophilia Society and the APPG.

Method

1. It is important to recognise the role played by PwBD in the production of this report. The APPG is hugely grateful to the hundreds of people who took the time to respond, giving us their views of the current system, and articulating their understanding of how that system works, all in the hope of improving access to treatment, and the current standard of care, for other PwBD going forward.

2. Starting on the 1st April 2019 the APPG on Haemophilia and Contaminated Blood conducted an inquiry which aimed to document the current processes for licensing, procurement, commissioning and prescription of treatments, as well as the current standard of care and the outcomes for PwBD in the UK. When this report talks about bleeding disorders it means genetic bleeding disorders. Acquired bleeding disorders fall outside the scope of this report.

3. The evidence informing this inquiry comes from both primary and secondary sources. A systematic literature review was done to map available evidence on access to treatment and the current UK systems of licensing, commissioning and prescription of treatments for PwBD. It was based on an extensive review of grey literature, and peer reviewed work, with the aim of providing an accurate picture of the current landscape.

4. A quantitative analysis was done, using data on PwBD provided by the United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO). This data was thoroughly analysed with the aim of exploring the extent of the presently available treatment options and outcomes, available through the current system of licensing, procurement, commissioning and prescription.

5. A patient survey run by The Haemophilia Society between 1 April 2019 and 12 July 2019 was used as evidence to inform the inquiry. The questionnaire included closed questions using scales, as well as free text questions that allowed respondents to provide more detail on their answers in their own words. Respondents were not required to answer the closed questions and were able to skip the free text questions if they did not wish to provide further detail. The surveys were completed online. The survey was intended to provide a level of baseline patient thought, serving to stimulate conversations between the APPG and commissioners and clinicians about institutional impediments and how relationships can develop further. In total, 254 PwBD and their family members contributed material, insights and information through the survey.

6. As with any patient survey, respondents were entirely self-selecting, and it cannot therefore be assumed representative, given the intrinsic bias any such survey of this size and scope inherently must be assumed to have. Not every respondent completed the entire survey, and this report does not give detailed response data for each question. The survey was sent out, via email, to all members of The Haemophilia Society opted into campaigning. It was also publicised and featured in various Haemophilia Society publications and on social media. The survey focused clearly on the views and opinions of PwBD, and their immediate caregivers (for children), on their current standard of care and systems by which their treatments are provided. This was an opt-in, non-randomised survey distributed among networks with the aim of supporting PwBD, so the findings must be interpreted in this context. The findings did, however, enable us to understand the experience of PwBD, and the needs of people affected by bleeding disorders.

7. To complement this submission by The Haemophilia Society, key expert stakeholders were engaged through a call for evidence. The APPG ran a call for evidence between 1 April 2019 and 12 July 2019.

PwBD, family members, carers, patient representatives, healthcare professionals, academics and industry representatives were invited to submit evidence online, which assisted in informing the report where information gaps were identified.

8. On three occasions, the APPG hosted oral evidence hearings in Portcullis House. To better understand the current landscape of standards of treatment and care for PwBD in the UK, the APPG sought out the opinions and experiences of PwBD, their families, healthcare professionals and representatives from the pharmaceutical industry, as well as representatives from NHS England. These events aimed to gather qualitative evidence and gave stakeholders the opportunity to provide oral submissions.

9. Overall assessment was based upon thematic analysis. This involved an initial review of all the evidence gathered through submissions and the identification of the key themes. Throughout the report, quotes are used that typify responses within their set category.

Note on devolution of health policy

10. Throughout this report access to treatment and standards of care are spoken about as if they were the same across the UK. In most cases this is true and currently there are no major differences in access in principle between different parts of the UK. However, health is a devolved policy area to Scotland, Wales and Northern Ireland and the NHSs in these countries are separate from NHS England (NHSE), which commissions treatment only for people living in England. It is possible that divergence in access to treatment could arise going forward. This aside, in practice there is substantial variation in quality of treatment and care and, as a result, outcomes across different parts of the UK, as there is a similar variation between the regions and centres in England.

11. When this report talks about the NHS it means the four health systems in each part of the UK. When this report says NHS England (NHSE) it specifically means the commissioning body for specialised healthcare in England.

Note on definition of commissioning and procurement

12. While procurement may be regarded as a policy neutral process, differentiated from commissioning and service provision, throughout the APPG inquiry the terms procurement and commissioning have been used interchangeably by almost every group of stakeholders engaged. The procurement of factor replacement products across the UK is directly linked to commissioning decisions and therefore a broader definition of both procurement and commissioning is used throughout this report.

1. An Introduction to bleeding disorders

1.1 Bleeding disorders

1.1.1 The term 'bleeding disorder' covers a set of rare genetic diseases which affect the body's ability to regulate blood clotting effectively. This is caused by a genetic defect which leads to a deficiency or dysfunction of certain cells or proteins in the blood.

1.1.2 Bleeding disorders include haemophilia A and B, von Willebrand disease (VWD), rarer factor deficiencies and platelet disorders. These genetic conditions are rare in the general population, with just over 32,000 people in the UK registered as having a bleeding disorder, of which less than a third require regular treatment.

1.1.3 Despite the relatively small number of patients, bleeding disorders treatment represents a significant cost to the NHS, and lifetime costs for people with severe bleeding disorders can easily run into millions of pounds.

1.1.4 As rare diseases, general healthcare professionals are often unaware of the implications that bleeding disorders can have, and even relatively minor injuries or treatments will require specialist attention if long-term damage is to be avoided.

1.1.5 If left untreated, or treated suboptimally, severe bleeding disorders can result in physical disability, and in extreme cases can be fatal. But if well managed, with treatment optimised, many negative impacts of bleeding disorders can be mitigated and PwBD can live well, although with slightly inhibited lives, into old age.

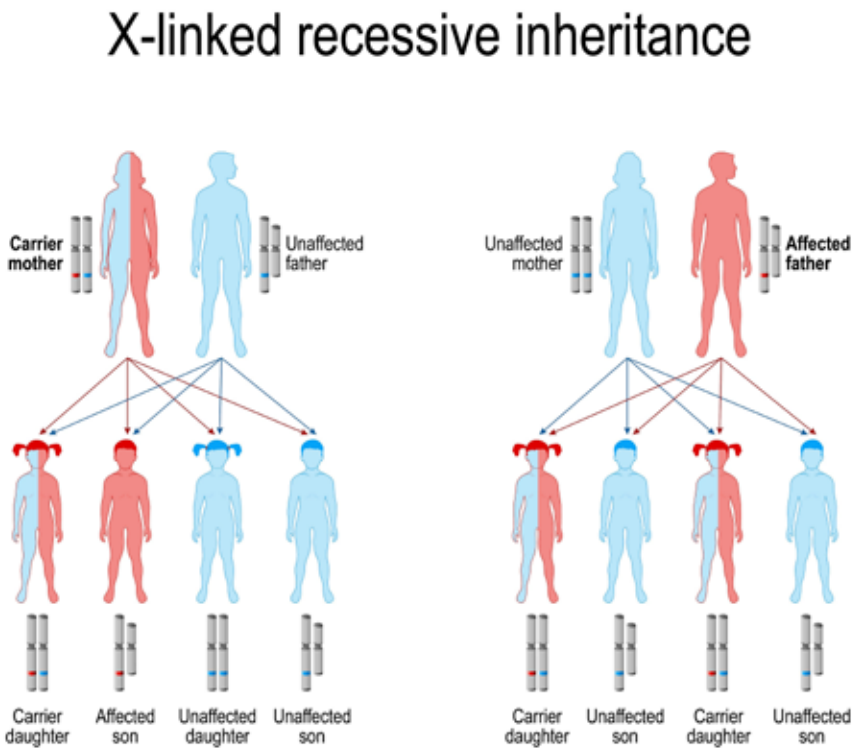
1.1.6 There are currently no cures for bleeding disorders, although treatment options continue to improve. New products including extended half-life treatments, purer or new recombinant CFCs and innovative non-replacement therapies are among a range of novel therapeutic approaches being demonstrated, with ongoing gene therapy trials leading the way towards a possible functional cure for some bleeding disorders.

1.1.7 Now and in the near future, treatments do hold the potential to revolutionise the current standards of care for bleeding disorders, if used optimally.

1.2 Haemophilia

1.2.1 Haemophilia, the most widely recognised bleeding disorder, is a rare genetic disorder caused by a deficiency in one of two specific clotting factors in the blood. A clotting factor is a protein that helps blood to clot.

1.2.2 Both haemophilia A and B are X-linked recessive conditions, meaning they are passed down on the X chromosome. Males with haemophilia will always pass the affected gene to their daughters, who may pass it onto their children, whereas their sons will not inherit the gene. All children of a female with the haemophilia gene have a 1 in 2 chance of inheriting the gene. Although a hereditary condition, approximately a third of all cases of haemophilia are caused by spontaneous genetic mutations.[4]



1.2.3 People with haemophilia do not bleed more than a person without it, but they tend to bleed for a much longer time. This is because after a blood vessel is injured in someone with haemophilia, the amount of fibrin that is formed is insufficient to maintain a robust clot.

1.2.4 Haemophilia varies in severity from severe to moderate to mild depending on the percentage of normal factor activity in the blood. In general, the lower this level the more bleeding problems the affected person will encounter. Severe and moderate haemophilia predominately affect males while females with the haemophilia gene often also have lower factor levels and many will be diagnosed with mild haemophilia.

Severity of haemophilia

Mild
In the general population people usually have clotting factor levels of between 50% and 150% of normal. People will be diagnosed with mild haemophilia if they have levels less than 40% of normal. People with mild haemophilia may not a have any symptoms on a day-to-day basis. The disorder may only become apparent after a significant injury or surgery, particularly if family history is unknown.

Moderate
People with factor levels above 1% and below 5% of normal are classed as having moderate haemophilia. People with moderate haemophilia deal with many of the same symptoms as those with severe bleeding disorders and some people with low levels of clotting factor have similar numbers of bleeds. Outcomes and symptoms vary depending on the exact factor level and bleeding tendency. Injury or trauma can lead to internal bleeding into joints or muscles**.**

Severe
For people with less than 1% of normal levels of factor VIII or factor IX bleeding can be more frequent and detrimental. Internal bleeding can occur spontaneously or following minor knocks. If poorly managed, outcomes can include permanent disability and reduced life expectancy. Common symptoms include a tendency to bruise easily, excessive bleeding from cuts that takes a long time to stop and a tendency to bleed into joints and muscles causing pain, swelling and limitation of movement.

1.2.5 As a genetic condition, known family histories allow for early diagnoses in most cases, with two-thirds of people born with haemophilia having a known family member with the condition. Even without this prior knowledge, most severe cases are diagnosed in infancy.

1.2.6 As a lifelong condition, treatment for haemophilia begins in infancy and is usually treated by replacing the missing clotting factor in the blood through an intravenous infusion of recombinant clotting factors VIII (haemophilia A) or IX (haemophilia B). These treatments are designed to replace the deficient clotting factor.

1.2.7 There are around 10,000 people with haemophilia in the UK. Of these, the majority have haemophilia A as it is approximately four times more common than haemophilia B.[5]

1.3 Von Willebrand disease

1.3.1 Von Willebrand disease (VWD), while less widely recognised than haemophilia, is the most common bleeding disorder. It is caused by a genetic defect that leads to defective or deficient von Willebrand factor (VWF), a clotting protein which binds factor VIII and platelets in blood vessel walls. VWD affects both men and women equally, though women may experience more symptoms linked to periods, pregnancy and childbirth.

1.3.2 Understood to affect as many as 1 in 1,000 people, VWD in its most common form is mild and frequently goes undiagnosed, with as many as 90 per cent of people with the disease unaware they have it. However, in its more severe forms, the symptoms are similar to those of haemophilia and require their own treatment regimes. Due to the function of VWF, mucosal bleeding (such nasal or oral bleeding) is more common in people with VWD.

1.3.3 VWD is split into three types with different inheritance patterns. Although VWD is found equally in men and women, women are more commonly diagnosed as they are often more greatly impacted.

- Type 1 is the most common and leads to lower VWF levels than normal. This can cause bleeding symptoms such as easy bruising, nosebleeds and heavy periods.
- Type 2 covers a range of genetic mutations that produce defects in VWF which impair its function. People with Type 2 VWD tend to have more severe bleeding symptoms than people with Type 1.
- Type 3 is the rarest form of VWD. It can lead to severe bleeding symptoms due to very low levels of VWF similar to severe haemophilia and often needs to be treated with infusions of replacement VWF.

1.4 Rarer bleeding disorders

1.4.1 Rarer bleeding disorders cover a range of other factor deficiencies and platelet conditions.

1.4.2 While these disorders vary in their severity, rarity and treatments, if unmanaged, or treated suboptimally, the symptoms of all bleeding disorders can be debilitating and even fatal. Appropriate treatment for these rarer bleeding disorders varies. Some can be treated with infusions of the missing clotting protein but for many of them this sort of treatment does not exist or does not work optimally.

1.4.3 The most common rarer bleeding disorders are deficiencies of factor VII or factor XI.

1.5 Symptoms

1.5.1 The symptoms of bleeding disorders will depend on type and severity of the condition, but the commonality is prolonged bleeding. Not all bleeds, however, are caused by a specific injury. Bleeds can occur spontaneously and could be joint bleeds (bleeding inside the joints) or muscle bleeds. If left untreated, or treated suboptimally, bleeds can have devastating long-term impacts. They can result in joint deformity or serious internal bleeding and in rare cases can be fatal (such as an intracranial haemorrhage). Bleeds cause irritation and pain in the affected area until treated.

1.5.2 Even with the good standards of current care, for many with a bleeding disorder the emotional impact too often goes unaddressed. The toll of a chronic (lifelong) condition is significant and can have a serious effect on the mental wellbeing of the individual, and their families and friends. Without access to the best treatments and appropriate care regimes, the consequences can be life altering, with the cost of not commissioning high in terms of the cost to human capital and symptomatic costs to other health budgets.[6]

1.6 Evolution of bleeding disorder treatment

1.6.1 As recently as the 1950s, treatment of bleeding disorders was limited to the transfusion of whole blood or plasma, which required hospitalisation, and was not very effective. For decades, fresh frozen plasma had been the primary treatment for haemophilia.

1.6.2 It was not until the 1960s that the first clotting factor concentrate was discovered, in the form of cryoprecipitate. In the late 1960s, plasma-derived clotting factors were isolated, which led to a paradigm shift in the management and treatment of haemophilia. This great advancement was made through a new method for preparing factor, allowing administration in a smaller volume, which could take place in an outpatient setting.[7,8]

1.6.3 By the late 1970s, freeze-dried factor VIII and IX concentrates (CFCs) had increased the average lifespan of people with haemophilia from 27 years in the 1940s to 60 years in 1980.[9] New treatments extended life expectancies dramatically. While this was a great advancement in treatment, there have been significant challenges with the use of human blood plasma.[10] By the 1980s, it was discovered that non-heat-treated human blood plasma transmitted potentially deadly blood-borne viruses, including HIV and viral hepatitis, and many people with haemophilia were infected before their use was discontinued in the mid-1980s.[11]

1.6.4 Safer, virally inactivated CFCs were used until the 1990s saw recombinant (genetically engineered) human factor products begin to be made available to people with haemophilia. Since then, dramatic increases in research have resulted in a new range of longer-lasting factor concentrates, novel non-replacement therapies and gene therapies.

1.6.5 For many other bleeding disorders, however, treatment still lags behind. A recombinant VWF treatment for people with VWD has only recently been licensed and is not yet widely used.
For some factor deficiencies there is a pure factor product available but for some there is not. Many rarer bleeding disorders have no specific treatment at all.

Two Children living with Haemophilia

Keith's story

Keith has lived with severe haemophilia all his life – yet thanks to his taking part in the factor VIII gene therapy trial he hasn't needed any treatment for two years.

Keith has been at the forefront of medical advances in haemophilia since the 1960s. His experience highlights the transformation of haemophilia treatment since his birth in 1952.

Under the care of the Royal Free Hospital in London, he was one of the first to have cryoprecipitate, then freeze dried products for home treatment and, in the 1990s, was put on the early trials of recombinant products.

Keith said: 'The world of haemophilia has advanced dramatically since I was a child. Thanks to gene therapy, I now have levels of 30 per cent – mild haemophilia, which has been liberating.'

In the 1970s, Keith was involved in his local haemophilia group in Essex and in the following two decades became a trustee for The Haemophilia Society, while also pursuing his career in the Fire Service control room.

But joint damage due to his haemophilia resulted in Keith having his knee replaced, and an infection six years ago led to the amputation of his left leg. He has been fitted with a prosthetic limb but says he has not looked back.

Keith said: 'As a child I got used to the fact that I was going to have to live my life as carefully as I could. I've always tried to go out and do things, but you've got to know your limitations.'

'So having lived like that for most of my life, I am amazed to be in a position where I haven't needed treatment for two years. I don't have to worry about how much treatment I'm going to take and where my nearest centre will be if I'm going away. It's the most liberating treatment I've ever had.'

Keith now plans to make the most of his new freedom by doing more of his favourite hobbies, such as photography and flat-water kayaking. His experience makes him hopeful for improved quality of life for future generations of people born with haemophilia.

He said: 'For those that have haemophilia A and B and those with inhibitors, the future is so much brighter – they are almost going to live "normal" lives. If gene therapy is available to children, they will grow up not having any bleeds, not having damaged joints and not having to have joints replaced.'

2. Structure of care and treatment for people with bleeding disorders

'The aim of the service is to enable patients with haemophilia and other bleeding disorders to live as normal a life as possible, ensuring optimum treatment… to maintain a bleed-free existence where possible, whilst maintaining good joint health and general health.'
NHS England Standard Contract for Haemophilia

2.1 The network of specialist centres

2.1.1 Due to the relatively complex nature of the conditions, and the small population of people with bleeding disorders in the UK requiring treatment, care is provided through a network of specialist centres. As a lifelong condition with no cure, these specialist care facilities play a critical role in the wellbeing of PwBD. Excellent care for PwBD requires comprehensive multidisciplinary care and access to the best available treatments.

2.1.2 This network of specialist providers across the UK consists of 28 larger comprehensive care centres (CCCs), and around 40 smaller haemophilia treatment centres (HTCs). A haemophilia centre coordinates a PwBD's care, administers treatment and provides wider support. HTCs (which care for all bleeding disorders, not just haemophilia) will have at least one specialist haematologist while CCCs will provide multidisciplinary care from a range of professionals including specialist nurses, physiotherapists, psychologists, dentists, obstetricians, social workers, HIV and viral hepatitis consultants, laboratory scientists and orthopaedic surgeons. These care teams will often specialise in either adult or paediatric services, although some CCCs cover both children and adults. Specialists work in an integrated way to support an individual to optimise healthcare outcomes and ensure a minimal burden on everyday life.

2.1.3 PwBD in the UK are normally registered with their nearest centre and are then linked to a larger CCC for their wider care if required.

2.1.4 To achieve optimal outcomes, multidisciplinary care is essential. Access to comprehensive care remains a significant predeterminate for good patient outcomes, especially for those with severe forms, due to the complexity of managing bleeding disorders, which goes far beyond treating bleeding episodes.[12]

2.2 Managing and treating bleeding disorders

2.2.1 Before the advent of effective treatment in the 1960s, the life expectancy of someone with severe haemophilia in the UK was 11 years.[13] New treatments increased this dramatically, and by the 1980s life expectancy for those receiving appropriate treatment increased to 60 years. Today someone who receives optimal treatment can expect a life expectancy on par with the general population.[14]

2.2.2 Genetic bleeding disorders are present from birth, and without treatment those with severe conditions would be likely to experience significant disability within their first decades of life.

2.2.3 If left untreated bleeds can lead to severe pain, stiffness and swelling. Bleeding into joints can cause long-term damage and recurring bleeds can lead to chronic problems. The symptoms can be painful, socially destructive and can cause disability. For some, joint replacement surgery, or even amputation, can become necessary.

2.2.4 In addition to prophylaxis, additional or on-demand treatment needs to be prompt, and bleeding must be treated as soon as possible. Prompt treatment helps to relieve pain, shortens recovery times and reduces the chances of permanent damage. Optimising management reduces the risk of complications from joint bleeds, including impairment and deterioration in joint function, deformity, and loss of function, most commonly in knees, elbows and ankles.[15]

2.2.5 Current treatments for bleeding disorders act to replace or replicate the deficient or faulty clotting factor or help clotting through assisting or bypassing certain functions. Treatments must be tailored to replace the specific deficient or missing clotting factor.

2.2.6 Treatment is not only used to stop bleeding episodes as they occur, but its key aim is to prevent the bleeding episodes from occurring in the first place and prevent potential long-term damage.

2.2.7 The treatment options available differ depending on the type and severity of the bleeding disorder. Treatments are not yet able to cure bleeding disorders: however, with optimal treatment they significantly reduce the chance and impact of a bleed. PwBD, depending on the severity of their condition, will be treated for bleeding either prophylactically or on demand.

- On demand is where the relevant factor or other product is used to treat an episode of prolonged bleeding in response to a bleed occurring. When bleeding episodes occur, immediate factor replacement treatment is often required to stop the bleeding and should be administered as quickly as possible after the bleeding has started to prevent long-term damage. On-demand treatment is rarely preferred for severe patients as it cannot prevent long-term damage as effectively.
- Prophylaxis is the name given to regular (usually 2-3 times a week, although for some people it is more or less often) treatment to prevent bleeds, usually in the form of intravenous infusions (injections) of the required factor. It is designed to increase the concentration of coagulation factor in the blood. Most people with severe haemophilia and many with moderate will be on this type of treatment.

2.2.8 To be most effective, the level needs to be high enough to protect from spontaneous bleeding episodes as well as bleeding in response to minor injury. As the baseline levels of clotting factor rise, spontaneous bleeding episodes become less likely.[16] The lower the natural levels of clotting factor, the greater the need for preventative treatment (prophylaxis).

2.2.9 Prophylaxis is credited with revolutionising treatment, especially for those with severe haemophilia. Optimal prophylaxis, for example, affords children the best chance of reaching adulthood without major joint or muscle damage. Quality of life, life expectancy and long-term outcomes have improved immensely, and many people now live a full and productive life. However, patients' adherence to their prophylactic treatment, as well as the dosage level of the regimen, determines its efficacy.

2.2.10 Prophylaxis is widely accepted as the best treatment for people with severe conditions. While many people with moderate forms and some mild forms may benefit, often they do not have access. This can lead to worse outcomes, which is discussed later in this report.

2.2.11 Prophylaxis is effective in reducing bleeding events, yet it is demanding and expensive. Over the last decade, costs can be over £100,000 per patient per year in the UK and far more in countries such as the USA and in mainland Europe. Despite this, at current dosing levels it has not managed to prevent arthropathy (a condition caused by a breakdown in the joint lining) and is prone to poor adherence, which can further reduce its effectiveness. Administering treatment can be time-consuming, as it involves several steps and places a substantial burden on PwBD and their parents or carers.

2.2.12 While the treatment for people with bleeding disorders has improved considerably over the past several decades, challenges, treatment gaps and unmet needs persist.

2.3 Half-life: implications

2.3.1 Clotting factor must be infused regularly, as it is used up by the body. The rate at which it is used up is measured by its half-life. The half-life, for example, of FVIII is on average between 8 and 12 hours, although half-life will vary for each individual. The most common treatments used are standard half-life (SHL) products, while extended half-life treatments (EHLs) (which can increase the time between infusions) are a relatively recent innovation. EHLs can offer the potential to reduce bleeding episodes and the burden of treatment. Innovative non-replacement therapies are also now available that need to be administered even less frequently and often do not require venous access.

2.4 Trough levels

2.4.1 A trough level is the lowest concentration of factor reached before the next dose is administered. This may be at or above the patient's endogenous factor level. Historically, prophylaxis has treated to a trough level of only 1 per cent, which has for most people been unsuccessful at fully preventing bleeding episodes. While some clinicians now treat to a higher level, many still do not. Currently, some PwBD are unable to access improved treatment regimens, with higher trough levels, and the improvements in the protection against bleeding that affords.

2.4.2 This is the result of the current treatment paradigm. Currently, factor levels just above 1 per cent are widely considered acceptable in the UK, despite clear evidence demonstrating that this is an outdated misconception, and that these levels are associated with an increased risk of bleeds.[17]

2.4.3 It is now understood that trough levels of 1 per cent are inadequate to prevent all bleeding, and data exists to show what might be a more appropriate level.[18] The current treatment paradigm is discussed at length later in this report. However, the APPG is aware that treatment standards including trough levels were under review as this report was researched and new guidelines have now been published.[19]

3. Current outcomes and quality of life of people with bleeding disorders

3.1 The impact of bleeds

3.1.1 Every bleeding episode can have significant, debilitating and detrimental impacts. Aside from the severe pain and restrictions of the bleeding episodes themselves, and the potential to cause long-term and life-changing disabilities, bleeds can be deeply emotionally distressing and have been shown to significantly affect quality of life.

3.1.2 As well as joint stiffness and a reduced range of motion, PwBD can experience significant acute pain during bleeding episodes and chronic pain due to arthropathy, leading to disability and impaired quality of life.[20]

3.1.3 Presently, despite this being the stated aim of treatment, bleed-free lives remain unattainable for the majority of people with severe bleeding disorders. Worryingly, even a relatively small number of joint bleeds can have permanent repercussions.

3.1.4 For those living with bleeding disorders, it is not just about the bleeding episodes themselves, but the impact they have. Bleeding disorders affect joints, muscles and mobility; they require PwBD to carefully plan social activities and impact career choices, lifestyle and relationships. The submissions to the APPG have shown how bleeding disorders have the potential to impact on all aspects of daily life, and that a relatively small number of bleeding episodes can have significant detrimental impacts that continue across people's lives.

3.2 International comparisons

3.2.1 Recent research has shown that when asked to report on mobility, self-care, usual activities, pain, discomfort, anxiety and depression on a scale where 1 represents the best imaginable health state, and 0 the worst, UK people with haemophilia reported an average health state of 0.59. To put this in context, this is significantly lower than the country's national population average of 0.85.[21] UK-based people with haemophilia experience a health-related quality of life that is substantially lower than the general population.[22]

3.2.2 In contrast to the UK, people with haemophilia in France, Germany, Italy and Spain have reported higher average health scores – with people with haemophilia in Germany reporting the highest health-related quality of life at 0.9. This score places people with haemophilia, in terms of health-related quality of life, on par with the country's national population average. This demonstrates that it is possible for PwBD to have health-related quality of life at parity with the general population. It is worth noting that Germany spends over twice as much per capita on bleeding disorder care and treatment than the UK.[23]

'The United Kingdom reported the lowest HRQoL scores in the study'
Analysis of CHESS study data*

3.2.3 The average health states of haemophilia patients in Italy, France and Spain are lower than those in Germany, at 0.84, 0.73 and 0.63 respectively. Except for Spain, these averages are closer to their respective national population averages, which currently stand at 0.89, 0.87 and 0.91 respectively.

[a] *An Assessment of Annualized Bleeding Rates and Quality of Life Among Severe Haemophilia A and B Individuals in Europe - available from https://www.postersessiononline.eu/173580348_eu/congresos/WFH2016/aula/-PP-T_56_WFH2016.pdf*

3.2.4 These reports from haemophilia communities across the EU5 (France, Germany, Italy, Spain and UK) demonstrate that people with haemophilia in the UK are less well managed than those in comparator countries in Europe. Haemophilia patients in the UK experience the lowest health-related quality of life in the EU5. They have a lower health-related quality of life than the average population in the UK and a significantly lower health-related quality of life than their peers in France, Germany and Italy.[24]

3.3 Burden of treatment

3.3.1 Current treatments are effective in reducing bleed rates. However, the burdens and complications arising from living with a bleeding disorder remain significant.

3.3.2 Anyone born today with a bleeding disorder is likely to have significantly better long-term outcomes than those born 50 years ago or even only 20 years ago. However, even now, primary school-aged children are missing time at school and their parents are giving up work to care them. People in their 20s are being forced to change careers, and older people are concerned about their long-term care needs.

3.3.3 The burden of having a bleeding disorder remains significant, with 75 per cent of patients having physical problems, and 43 per cent of adults and 54 per cent of caregivers having anxiety issues.[25]

3.3.4 In addition to the demanding treatment regimen and general practicalities of managing a chronic health condition, this inquiry has identified specific issues for PwBD.

3.3.5 At the time of this report, most people with haemophilia were on factor replacement therapy. For people with severe haemophilia treated with SHL treatments, intravenous injections for their routine prophylaxis are normally required 2–3 times a week, but for some as often as once a day. This is a serious burden of the current treatment paradigm, as it takes significant time and poses problems, particularly for people with venous access issues.

3.3.6 The burden of intravenous injections needs to be recognised, and products used to treat bleeding disorders should be as easy to use as possible.

3.4 Bleeds and joint damage

3.4.1 For many PwBD, bleeding episodes remain a significant feature of living with a bleeding disorder. This can result in chronic pain, significantly impaired mobility and haemophilic arthropathy. The higher the number of annual bleeds, the more likely PwBD are to see lowered health-related quality of life.

3.4.2 For people with severe or moderate haemophilia as few as two bleeds into the same joint during a short period of time can cause permanent and irreversible damage that reduces quality of life. The bleeding damages the synovium (the lining of the joint) as well as the cartilage and surrounding tendons and tissues. This leads to pain and can lead to loss of movement and strength in the joint.

3.4.3 It is clear that the number of bleeding episodes PwBD have is linked to their health-related quality of life outcomes and potential disabilities that arise. In severe cases, patients can lose their ability to walk and may require wheelchair assistance or orthopaedic surgery to repair or replace damaged joints.[26] Orthopaedic surgery, including joint replacement, is an option when a joint is badly damaged, but can lead to further costs to the health system in the longer term.

3.4.4 The number of joint bleeding episodes it takes to cause permanent damage varies. However, the goal of zero bleeding episodes (consistent with NHSE's stated ambition for people with bleeding disorders to be bleed free) is critical to improving health-related quality of life and joint health. Evidence suggests that even a small number of bleeding episodes into joints can cause long-term damage.[27]

3.4.5 Due to the advances made in treatment over the decades, joint damage is found more commonly in older PwBD, who did not have access to the same level of care presently possible. New treatments can reduce the likelihood that it will occur further still. However, for now joint damage is still common in children with severe and moderate haemophilia.

3.5 Mental health

3.5.1 While the physical implications of having a bleeding disorder can be highly detrimental, PwBD can also be negatively affected by the psychological impacts of the condition. Recent research has found that as many as 42 per cent of patients with severe haemophilia experience mental health issues.[28] This supports findings from the existing literature that mental health issues are more common within bleeding disorder communities than they are in the general population.

3.5.2 While the lack of specialised services, including mental health support, is detailed in this report, it is important to note that those with unaddressed mental health needs are less likely to be in employment than those with physical illness alone. The lack of universal mental health support for PwBD now, while saving money in the short term within certain healthcare budgets, may be increasing costs in the long term to the wider welfare system.

3.6 The socio-economic impact of bleeding episodes

3.6.1 Further to physical and mental health complications arising from having a bleeding disorder, PwBD are also disadvantaged by the indirect costs of their condition. The impact of bleeding episodes, and the physical outcomes and mental health problems which can result from this, have often overlooked indirect costs. Due to the current standards of treatment, many PwBD continue to miss days from school or work, which results in productivity losses and reduced academic achievement.

3.6.2 PwBD often even have restrictions in terms of which careers are available to them, and the APPG has received several personal testimonies reflecting the negative impact of bleeding disorders in terms of careers. For some, performing their chosen career ceased to be possible due to the consequences of their condition and PwBD are more likely to be unemployed than the general population.[29] This is also indicated by studies suggesting that people with severe haemophilia participate less in full-time work.[30]

3.6.3 For children, research has shown that those who have a lower number of bleeding episodes per year are also associated with higher academic achievement. Children who have a higher number of bleeds are more likely to be absent from school and achieve less academically. These findings have been reported even after controlling for variables such as IQ and parent education.[31]

Key facts from the Probe study (probestudy.org/)

- Early retirement due to health was reported in 48.1% of early retirees with haemophilia vs 3.6% of early retirees without bleeding disorders
- Part-time working due to health was reported in 31.4% of part-time workers with haemophilia vs 3.8% of part-time workers without bleeding disorders

3.7 Travel

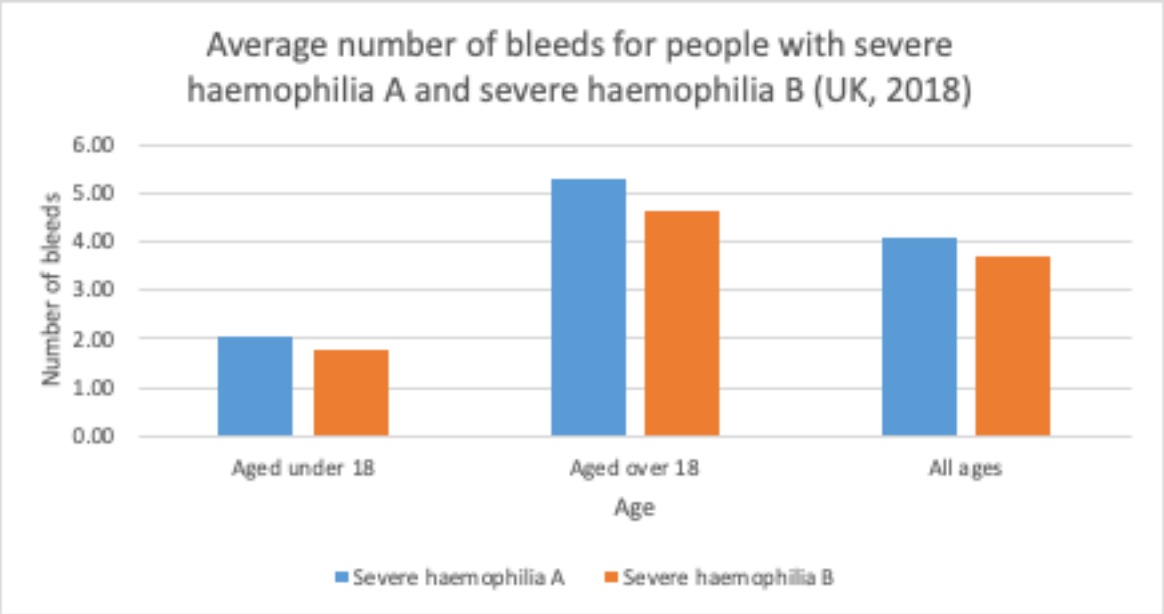
3.7.1 As covered already, PwBD are treated through a series of specialist centres, and require continual management and support from a multidisciplinary team of healthcare professionals. As not all people have access to a multidisciplinary centre close to them, many have to travel considerable distances to access centres that can provide them with specialist care.

'No local treatment is available so I have to travel an hour's journey!'
Person living with a bleeding disorder

3.7.2 This alone can have a negative impact on quality of life, as it adds worry about the distance to travel, a financial burden that comes with travelling long distances, and the additional costs of having to take time off work/school to attend.

3.8 Current outcomes

3.8.1 Current outcomes for PwBD can optimistically be described as suboptimal. A significant proportion of people with haemophilia bleed multiple times a year. Over a third (35 per cent) of adults with severe haemophilia A and B bled more than four times last year. The average number of bleeds for people are shown below.[a]



[a] *Parliamentary Question 240996 – Parliamentary Under-Secretary (Department of Health and Social Care) published the number of patients with severe haemophilia A and haemophilia B for 2018 by the number of bleeds they had. (Answered 09/04/19)*

3.9 Economies of bleeds

3.9.1 Beyond the implications that bleeding disorders have on individuals, economically bleeding episodes have a direct cost to the NHS and wider welfare system. Few holistic studies have been undertaken to investigate this, but while optimal outcomes would increase the doses or intervals of dosing, increasing the amount of factor needed, this cost could be partially offset by the societal value of better outcomes, as well as the reduced downstream costs incurred by the health and welfare services.

3.9.2 The costs of joint surgery, medical staff time at A&E, and eventually care of the disabilities arising are significant, and the societal and welfare implications of poor outcomes are not insignificant.

3.9.3 Overall, the physical and psychological impacts of living with a bleeding disorder affect PwBD in their academic and professional lives, which in turn contributes to lower levels of health-related quality of life.

3.10 A bleed-free future?

3.10.1 For people with bleeding disorders, every avoidable bleed matters. By working to stop every bleed, the most harmful consequences of bleeding disorders can be significantly reduced, if not entirely mitigated. Through a new generation of treatments people with bleeding disorders can begin to aspire to a bleed-free future.

3.10.2 The submissions to the APPG, and the available literature, confirm that UK PwBD have substantial unmet needs. Health-related quality of life for UK-based PwBD falls far behind their peers in France, Germany and Italy and indicates that PwBD in the UK have worse outcomes including higher annual bleed rates, a greater degree of joint deterioration, greater levels of mental health problems and a greater loss of work productivity and school achievement.

3.10.3 Under the current treatment paradigm, even when fully compliant with treatment, this has not been sufficient to achieve life free from bleeds for the majority of PwBD and does not remove the negative impacts of living with a bleeding disorder.

3.10.4 PwBD in the UK have reported relatively low health-related quality of life scores, but this has yet to have spurred reform. The ongoing work of the APPG is looking to reflect on the current system and will set out a series of recommendations for reform, aimed at addressing the evident unmet needs of all PwBD whether they have VWD, haemophilia, another factor deficiency or a platelet disorder.

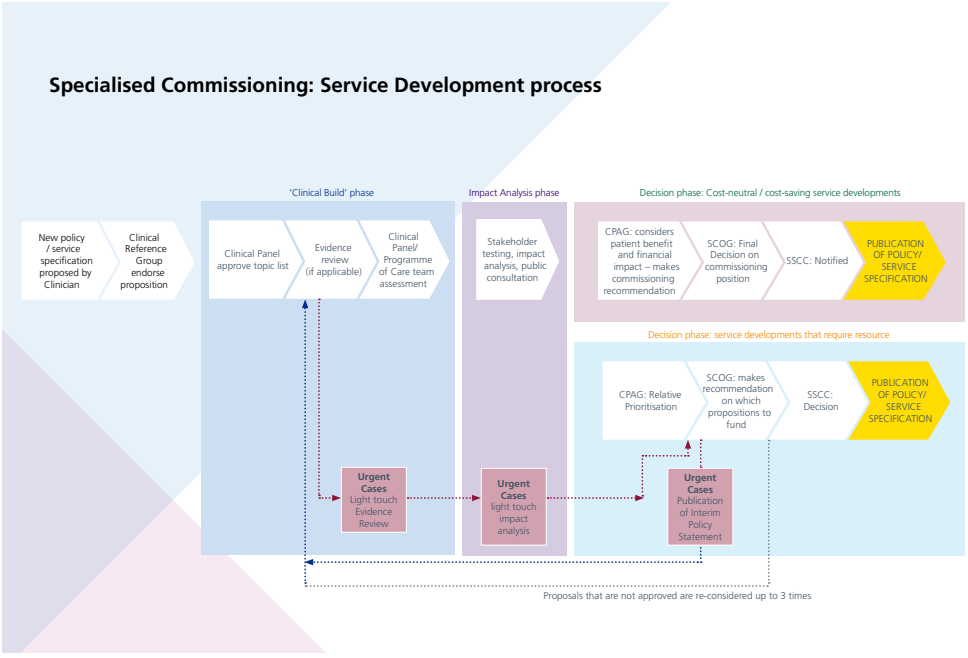
4. The current procurement and commissioning regime

4.1.1 While it is important for PwBD to have access to innovative treatments, currently the greatest determinate of outcomes is whether PwBD have access to comprehensive care, and whether that care is personalised. The commissioning systems need to facilitate this personalisation of care and must be flexible enough to support clinical freedom and patient choice.

'There should be "personalised and coordinated health services", and services need to change to support 'patients' own life goals.'
NHS Five Year Forward View

4.1.2 Most rare disease areas, including bleeding disorders, are commissioned directly by NHSE to ensure access to treatments that are both effective and a good use of NHS resources. Scotland, Wales and Northern Ireland make their own commissioning decisions but have generally made decisions similar to NHSE. Clinical policies (the commissioning position on a particular treatment and in what circumstances people will receive the treatment) are used to determine commissioning positions, which are developed via the work of the Clinical Reference Group (CRG) following a standard process that has three phases.[32]

4.1 Specialised commissioning and CPAG



4.1.1 The clinical build is the first of three phases to form a national clinical commissioning policy. The second phase is the 'impact analysis' which is considered at the National Programme of Care Board. The third and final stage is the 'decision' through the Clinical Priorities Advisory Group (CPAG) and Specialised Commissioning Committee.

4.1.2 NHS England explains that: 'The impact analysis is the second of three phases to form a national clinical policy. It is coordinated and managed by the National Programme of Care (NPOC) team and concludes through a Gateway managed by the relevant Programme of Care Board. During this

[b] *From https://www.england.nhs.uk/publication/infographic-specialised-commissioning-service-development-process/ NB: SCOG no longer exists as a separate committee stage*

phase, the draft proposition is subject to informal stakeholder testing, impact assessment, formal public consultation and an equality assessment. A Commissioning Implementation Plan Is developed to consider in advance the timing and method of implementation if the proposition is then approved during Phase C (Decision).'

4.1.3 'The decision is the final stage of three phases to form a national clinical commissioning policy. It is coordinated and managed by the Clinical Effectiveness Team (CET) and concludes with the publication of the policy. There are two Gateways within this phase: Clinical Priorities Advisory Group (CPAG) [and the] Specialised Commissioning Committee (SCC).'[33]

4.1.4 NHS England relies on CPAG to review all new treatments coming for each of the therapeutic service areas, and to make recommendations back to the NHS board on which of those to fund. After a commissioning policy has been developed by the CRG and a draft produced, it enters CPAG's evaluation process. The evaluation is to determine whether the commissioning policy should be prioritised for funding. For new treatments requiring additional investment, the prioritisation process is carried out twice a year to determine what will be routinely commissioned.

4.1.5 The CPAG rates each policy submitted to them on a scale of 1–3 for effectiveness and a scale of 1–3 for cost using a Boston Matrix. This enables them to rank all the policies they have considered into five levels of priority. Through this method, they can compare treatments for bleeding disorders against other new advances in other conditions. When treatments for bleeding disorders are reviewed through the CPAG, they are competing with other disease areas (other medicines, medical devices and new services, in unrelated therapeutic areas), and are assessed with a pricing model which looks at costs per patient of the treatment, rather than costs to the health system overall.

4.1.6 The CPAG then makes its recommendations to NHS England, which determine which levels will be funded, with those in unfunded levels able to return for further review in a later round. They can be reconsidered on a maximum of three occasions.

4.1.7 This process is highly competitive, and has a constrained budget, which is used for all the treatments going through it. All the treatments which go through this process at the same time are compared against one another and funded from the same budget. Innovations are not, therefore, assessed solely on their own merits, but are also assessed against the needs of other groups of patients (in other disease areas) and the need to focus investment where there is greatest patient need.

4.1.8 Despite plans to increase transparency, the deliberations of CPAG are not held in public, so the public are unable to gain much insight into how decisions are made during the prioritisation process. While patient groups are invited to the first day of meetings they are not able to see how the new treatments are evaluated and ranked.[34] The presentation of evidence to be used in the decision has recently been opened to public viewing, however minutes of the meetings are published months later and do not provide detail on the ratings provided. Recent trials to allow patient groups to provide information on patient experience have been suspended and concerns remain that there is too little focus on patient-relevant outcomes.

4.2 Tenders

4.2.1 While decisions on whether a new treatment is funded are made at an NHS level through NHS England's CPAG and similar processes in Scotland, Wales and Northern Ireland, a UK-wide tender process sets the price that hospitals pay.

4.2.2 Due to the rarity of bleeding disorders, and the comparatively high cost of treatment, tendering is undertaken on a UK-wide basis. Most treatments are procured through a series of tender exercises carried out by the Commercial Medicines Unit on behalf of the NHS. In these tender exercises, suppliers submit information about their product alongside a price. This allows the creation of frameworks which set out which products can be purchased by haemophilia centres and an agreed UK price. The frameworks and supplier contracts specify that only registered haemophilia centres can purchase products on the frameworks. Where more than one product is available in a given category of treatment, the lowest cost supplier may be awarded the largest volume contract or selected as the preferred supplier.

4.2.3 Decisions on what products can be prescribed and at which doses is planned on a countrywide level by commissioners in NHS England, NHS Scotland, NHS Wales and Health and Social Care in Northern Ireland, taking into account the framework prices. Some products have had their use restricted with reference to these framework prices.

4.2.4 The current tender process works on the basis that treatments are merely commodities and has one primary objective – cost minimisation. Currently, PwBD are assumed to be homogenous and current outcomes are set as the standard to be achieved, which facilitates the continuation of this commissioning system.

4.2.5 Stakeholders, including representatives from patient groups, are part of the process to agree the tender framework but have been unable to change a system that weighs cost as the vast majority of the decision.

4.2.6 In addition to cost, which is usually 75 per cent or more of the decision basis, the tenders consider security of supply and ease of use. In the ease of use category patients' and healthcare professionals' opinions are considered. However, the tender does not consider the effectiveness of a product, patient preference beyond ease of use, outcomes or safety.

4.2.7 The tender exercises have been successful in achieving the cost minimisation objective as the UK pays among the lowest prices in the world for recombinant factor VIII compared to other well-developed health systems and has been reducing costs while factor use has risen in the UK.

4.2.8 From 2005 onwards, this new tendering approach was taken to support the commissioning of treatments in a cost-effective manner, at a price acceptable to the NHS. While the tender system achieved substantial savings, its success was only predicated on the types of treatment available at the time.

4.2.9 Over the last decade innovation in available treatments has been dramatic but has not been mirrored by a reformed commissioning system. The current tender systems view treatments of the same type merely as commodities, assuming them to be 'therapeutically equivalent'. In practice, most new treatments for PwBD have only been introduced if they can be shown to be cost saving or cost neutral to the NHS.

4.2.10 This drive to reduce costs is limiting access to innovative treatments – directly impacting patient outcomes and clinician choice. Recent changes to the tender system have allowed newer, innovative treatments to be part of the tender and make it on to the frameworks. However, the tenders make no attempt to compare across different types of treatments for efficacy or cost- effectiveness.

5. FX case study

5.1.1 The issues faced by many PwBD are often exacerbated for those with the rarer bleeding disorders, as the rarest conditions are inherently faced with additional challenges. While this report has illustrated many of these challenges, too often for rarer conditions there is a total absence of effective treatment. This means that people with the rarest conditions are often not seeing the benefit of advances in treatment.[35]

5.1.2 While all bleeding disorders are rare, some conditions are even rarer. Factor X (FX) deficiency is an example of this, and is an ultra-rare bleeding disorder, with a prevalence of 1:1,000,000 with fewer than 40 people in the UK who require routine treatment.

5.1.3 The current standard of treatment in the UK for FX deficiency was prothrombin complex concentrate (PCC). This is a mix of clotting factors that includes FX, but also contains other, unneeded, clotting factors.

5.1.4 A few years ago, a new treatment, Coagadex, which is a pure FX concentrate, was licensed for treating FX deficiency. At this time of this inquiry Coagadex, however, was still not routinely available in the UK. While new treatments continue to be discovered for many PwBD, those with FX deficiency for example were not seeing these advances, and patients with FX deficiency were unable to access this innovative treatment.

5.1.5 While Coagadex had been licensed since March 2016, as of the end of 2019 it had failed to receive funding on either of the occasions it has attempted to go through the CPAG process. This is despite it clearly meeting an unmet clinical need.

5.1.6 Unfortunately, and despite Coagadex being the only licensed factor X treatment, patients requiring it in the UK were being denied access, even in the face of strong evidence of need from leading clinicians.

'I took part in the Coagadex trial and was then allowed to stay on the product until October 2016. I had hoped taking part in the trial would see the first factor X product to be licensed and that others could benefit as well. Understandably, at the time I was extremely upset that I had been told that I could no longer take Coagadex.'
Person with FX deficiency

5.1.7 The APPG also learned that those patients previously enrolled in UK-based clinical trials had their treatment changed to be taken off Coagadex and put back on to their previous treatment. This is an example of NHS actions in practice preventing the adoption of new tailored treatments that have been shown to improve the lives of PwBD. Regrettably, Coagadex (whose development was funded by the UK government and is manufactured in the UK) was being used by patients in other European countries, but not the UK.[c]

5.1.8 If funding was so difficult to secure for the step from PCC to a pure factor product, the APPG has concerns over access to future innovations for rarer bleeding disorders as they are licensed. Currently, a new recombinant treatment for FXIII deficiency remains unavailable on the NHS.

[c] *Just prior to completion of this report Coagadex was approved by the CPAG and has been routinely funded since April 2020, four years after the licensing of this UK-developed product.*

6. Gene therapy

6.1 The future of treatment

6.1.1 The introduction of clotting factor concentrates in the 1970s, and the opportunity it afforded to infuse at home, revolutionised the care and lives of many PwBD. Over the course of the last 30 years, the development of recombinant factors devoid of human proteins, with ever increasing half-lives, has again changed the treatment paradigm, to a point where it is now possible for some PwBD to lead lives with virtually no bleeding episodes and their associated consequences. This can happen if treatment is personalised, with clinicians free to prescribe dose and interval levels of products, in consultation with the patient, that are most clinically effective.

6.1.2 The current standard of care for PwBD whose condition is severe is to use factor replacement to limit spontaneous bleeding and to attempt to curtail the long-term detrimental consequences of multiple bleeding episodes. However, current treatments often have a significant burden attached to them. Barriers to optimal outcomes when using SHL products appear high, and while EHL products mitigate some of these barriers, a potentially curative treatment is gene therapy.

6.1.3 In parallel to the rapid development of EHL treatments, a revolution has been underway with novel products and gene therapy, which are now reaching maturity. The potential to overcome the bulk of the burden of treatment and the implications of suboptimal outcomes is now in sight. Gene therapies for haemophilia A and B are in late stage trials and have the potential to transform the way patients are treated.

6.1.4 While delving into detail on the specifics of the breakthrough in modern era gene therapy is beyond the scope of this report, it is important to note that haemophilia specifically is an optimal target for gene therapy as it is a monogenic disorder, and several products are now in late phase clinical trials. A form of gene therapy is likely to be licensed in the near future and holds the potential to provide long-term treatment to prevent bleeding or even effectively cure haemophilia.

6.1.5 However, the eventual introduction of gene therapy, while a promising (and potentially curative) treatment, has an issue, which is its cost. A key challenge facing the health service, not just for bleeding disorders, is how to bridge the widening gap between innovative treatments and the realities of the fiscal constraints facing the NHS. For PwBD, and the systems designed to support them, a key challenge will be trying to move forward with market access for gene therapy once it has been licensed. It is the APPG's view that the current commissioning systems are not set up to support the procurement of such high cost curative therapies, and to the APPG's knowledge, work is not currently sufficiently advanced in how to address this.

6.1.6 The limited timeframes in which NHS commissioners currently operate dramatically reduce the ability of this system to procure these treatments, regardless of these treatments arguably being more predictable in their long-term costs, which would be offset over the lifetime of patients.

6.2 Payment approach? Commissioning gene therapy

6.2.1 For haemophilia, the current commissioning and tendering processes work well for SHL coagulation factor products. However, they are not suitable for treatments such as gene therapies and do not have a mechanism to compare different types of treatment such as new EHL and non-replacement therapies.

6.2.2 The APPG do not expect this situation to change as the 2020 tender exercise for the next 2–4 years haemophilia A framework is not expected to compare different types of treatments and will instead have preferred products within a series of lots.

6.2.3 This imminent arrival of a potential cure raises unique challenges in terms of evaluation and the payment models that would allow the treatments to be commissioned.

6.2.4 There is a range of potential payment models that could be used to the benefit of PwBD and the NHS. While this report will not go into detail on those models, an ideal approach would meet the needs of key stakeholders by:

- enabling broad patient access
- achieving affordability within the longer-term financial planning and budgetary requirements of the NHS
- providing appropriate returns on investment to support future pharmaceutical innovation
- being able to offset costs over the life of PwBD
- demonstrating long-term clinical effectiveness, based on outcomes valued by patients.

6.2.5 While not an exhaustive list, payment models to be reviewed should include risk-sharing agreements (which could include money-back guarantees if outcomes are lower than expected), outcomes-based payment and payment instalments spread over a period of time, as opposed to just upfront payment.

'Tendering is not a suitable way of procuring gene therapies, and new approaches to paying for such treatments are likely to be needed. Discussions should start now and options should be prepared.'
uniQure

6.2.6 The current issue is that, as far as the APPG has been made aware, NHSE is not currently undertaking high-level discussions on gene therapy payment models. A situation may therefore arise in which new therapies become licensed, and a time lag limits patients' quick access to new treatments. While the APPG does not favour any particular payment model, it recommends NHSE and commissioners in Scotland, Wales and Northern Ireland begin reviewing models which could offer PwBD better access to innovations such as gene therapy.

6.2.7 To ensure access to upcoming innovative treatments, greater flexibility is needed in terms of financial planning. Short-term 'siloed' planning, often looking for in-year savings, fails to take account of holistic cost. Multi-annual budgets and pricing models would reflect the changing nature of the pharmaceutical landscape for bleeding disorder treatment. This would help deliver the introduction of revolutionary innovative treatment.

7. An appraisal of the issues

In light of the current situation and state of treatment and care for PwBD, below is an appraisal in detail of the issues they face alongside recommendations to improve satisfaction and outcomes.

7.1 Disparities in treatment provision across the country

7.1.1 For PwBD, optimal care requires far more than just access to the most clinically appropriate drugs. While it is critical for PwBD that their clinical teams can prescribe the treatments deemed most appropriate for any specific individual, good outcomes can only be assured through access to multidisciplinary care in parallel to this.

7.1.2 As detailed previously in this report, the best care for people with bleeding disorders is provided through access to a multidisciplinary team of specialists, including clinicians, physiotherapists, specialist nurses, lab managers, psychosocial support and other staff.[36]

7.1.3 Given it is accepted that the extensive needs of people with bleeding disorders are best met through the coordinated delivery of comprehensive care provided by a multidisciplinary team of healthcare professionals,[37] it is deeply concerning that the nature of the treatment delivered varies wildly between centres.

'It came as a bit of a shock to discover that other centres are offering different options especially as some seem to be more efficacious [than] the only option made available to me.'
Person living with a bleeding disorder

7.1.4 Standards differ from centre to centre, not only in regard to the level of service provided, but also whether certain services are provided at all. In many parts of the country PwBD have no routine access to vital services, and these unacceptable variations of care provided have devastating effects on individuals and their families. PwBD and clinicians have also reported differences in the dosages of factor replacement therapies they receive and different target trough levels.

7.1.5 In terms of evidence submitted, the APPG has identified disparities in provision of a range of services. While some people have been able to access a high standard of all the multidisciplinary services they require, others have been unable to access more than basic clinical care. While national standards of care already exist, and are scrutinised at peer review by the UKHCDO, at present the APPG is not aware of any national systems being in place to ensure their implementation.

7.1.6 The current service specification recognises the need for physiotherapy to both aid recovery in the case of bleeding events and to monitor treatment outcomes through joint assessments. Yet, there is huge disparity in funded hours for physiotherapy.

7.1.7 PwBD, their carers and families have highly complicated and quite unique psychological needs that need dedicated, specialist support. Studies have suggested that people living with chronic conditions, such as bleeding disorders, are up to three times more likely to experience emotional difficulties compared to those without a chronic condition.[38,39] Anxiety and depression occur in up to a third of people with haemophilia.[40,41,42] While there is a general disparity between centres in services provided, inequality in access to physiotherapy and mental health support is wide. Access to psychological support is even more limited than physiotherapy, with many centres providing limited or no access at all.

7.1.8 The severely limited nature of contracted hours for physiotherapists, psychologists and social workers negates the benefits of a truly multidisciplinary care system and significantly impacts the ability to provide holistic, specialised care. Quality of life and outcomes are reduced as a result.

'There is huge disparity in funded hours for physiotherapy in haemophilia services across the UK which leads to inequality for patients.'
Haemophilia Chartered Physiotherapists Association

7.1.9 The APPG is aware that the UK Haemophilia Centre Doctors' Organisation has recently completed a comprehensive process of peer review and audit, using the expertise of the Quality Review Service (QRS). This report details which centres are achieving service standards and will provide data to review the true level of variation in access to care. The APPG has been made aware that some centres have seen considerable growth in their number of patients but have not received additional funding to support appropriate access to services for this increase, which the APPG hopes will be raised by the ongoing UKHCDO audit process.

7.1.10 While this audit is incredibly useful in terms of determining disparities, highlighting where provision is inadequate and identifying in which service areas and localities it is most dramatic, it is only a first step. Only a UK-wide multidisciplinary oversight body would be able to use this to lead on to a more standardised provision of care.

7.1.11 For PwBD to achieve better outcomes, the overall aims of treatment for bleeding disorders must become more ambitious. Constant access to comprehensive care is vital to achieve this, and at present an obvious disparity exists in the standards of care. The care and treatment of PwBD is currently determined by a 'postcode lottery'.

7.1.12 Submissions to the APPG, albeit anecdotal, have further acknowledged that provision was geared towards those with severe haemophilia to the detriment of many people with mild or moderate haemophilia and other bleeding disorders.

Recommendation 1 – Increased funding needs to be made available to ensure all PwBD who would benefit from multidisciplinary care are able to access it as needed, regardless of where they live in the UK. Specifically, all comprehensive care centres should have dedicated physiotherapy, occupational therapy, social work and psychology services.

Recommendation 2 – Care standards should be uniform across the UK. To ensure outcomes remain equitable, the APPG recommends the creation of a body capable of raising and addressing inequities which arise. Given the variation in staffing and resources levels between centres, and the implications this has on the level and basic provision of certain services that the APPG has been made aware of, it also recommends that a more detailed review is published.

7.2 Data

7.2.1. The UK National Haemophilia Database is globally recognised as being at the forefront of data collection in the management of bleeding disorders. The National Haemophilia Database, if adequately funded, could be reprioritised to include improving patient outcomes, as opposed to its current focus on monitoring the volume allocations of the national contract and evaluating its fiscal implications.

7.2.2 Currently, outcomes outside of clinical care indicators such as bleed rates are not well measured. Clinical outcomes do not account for value in terms of the burden of treatment, or other outcomes perceived as important by PwBD. Haemophilia centres also face a burden of fully compliant data collection and should be assisted in this important task.

7.2.3 Practically, even the outcome data currently collected is not made publicly available in full. Without access to this data, it is not possible to engage in further work to determine, for example, the extent to which standards of care vary. The lack of data hampers transparency and makes it exceedingly difficult to fully understand the causes of the poor outcomes outlined throughout this report.

7.2.4 The National Haemophilia Database, if appropriately funded, could work with PwBD and The Haemophilia Society to design methods of capturing and recording the outcomes that are most important to PwBD. Data on more complex outcomes would help facilitate a more holistic assessment of the value of treatments and could assist in developing an understanding of the benefits that changes in care delivery can generate. Data on the burden of treatment should become more prominent within the commissioning processes, as it would enable additional weighting of treatments when they are commissioned.

7.2.5 Without improved data collection of patient-centric outcomes and quality of life measures it would be difficult to improve clinical strategies in the appropriate ways on a national scale. As additional outcomes measures are recorded, PwBD would be able to examine their outcomes (and those of their centre) in relation to their peers. Data on outcomes produced by individual centres would inform and empower PwBD.

7.2.6 To ensure that the collection of data is improved across the entire network of centres, those centres with a history of the highest adherence rates of data collection could be encouraged to share their good practice with centres with the lowest adherence rates.

Recommendation 3 – For the National Haemophilia Database to realise its full potential, and to ensure it is able to cope with the recommendations of this report, the APPG recommends that additional investment is made available both to it and to individual centres to improve and broaden data collection.

7.3 Aiming higher for PwBD

7.3.1 The stated outcome of bleeding disorder care in the UK is to enable people with bleeding disorders to lead as normal a life as possible, which can realistically only be achieved through targeting treatment at achieving zero bleeding episodes. However, as the APPG learned, clinical practice in the UK focuses too often on minimum treatment standards, meaning that PwBD are often forced to treat to the lowest 'safe' factor level. While many clinicians do engage with their patients, and where possible within the current system, make joint decisions, patient-centric outcomes may not always be central to the decision-making process. For many PwBD, their lifestyle still does not factor into treatment decisions.

7.3.2 With optimal treatment, using recent innovations, the potential exists to bring the burden of living with a bleeding disorder into parity with that of other chronic diseases, such as diabetes. Through personalisation of care, the concept of treating the specific individual would be a suitable way of bringing bleeding disorders into a comparable state to other chronic disease areas.[43]

7.3.3 The APPG has been made aware of a growing concern that current treatment standards, in terms of the doses and intervals of infusions, remain trapped in an outdated treatment paradigm. Discussions and research are now underway on whether people with bleeding disorders in the UK are receiving the most suitable dose or frequency of treatment to optimise outcomes.

7.3.4 Prophylaxis has greatly improved outcomes when compared to episodic treatment and has resulted in substantially better outcomes for PwBD. Yet for many, prophylactic treatment models are still based on the 1970s/80s concept of prophylaxis, which only aimed to maintain trough levels above 1 per cent at all times. As detailed earlier, many PwBD continue to report health-related quality of life far below those without the condition, in contrast to some other European countries which have now achieved parity with the general population without the condition.

7.3.5 With the significant innovation in treatment of the last 3 years, and the introduction of new treatment options, it is worth noting that the NHS England Standard Contract for Haemophilia (All Ages) (which covers all bleeding disorders) has not been updated since 2013 and remains in draft form.

7.3.6 Even taking the expectations of the service specification as it currently stands, the outcomes for PwBD remain far from the stated aim. Significant numbers of PwBD are not bleed free, and over a third of adults with severe haemophilia had in excess of four bleeding episodes in 2018.[44]

7.3.7 While the outcomes for PwBD have been detailed previously in this report, it highlights that even if current minimum standards of care are being met they are inadequate to ensure optimal outcomes.

Recommendation 4 – To move towards achieving optimal outcomes the APPG recommends that the National Service Specification for Haemophilia needs to be updated, and the current treatment paradigm needs to reflect innovation in treatment in terms of products and treatment regime and have far more ambitious expectations for PwBD.

7.3.8 The possibilities these changes present afford the opportunity to improve the lives of PwBD. Failing to update the service specification has led to a situation in which the majority of UK PwBD are unlikely to see the full benefit of new treatments that have entered the market in recent years. The current service specification fails to account for the full range of benefits of more recent treatments and therefore creates barriers to access as it has become outdated, failing to adapt to the increased diversity of treatment options available.

7.3.9 Looking at an example of haemophilia care, clotting factor levels at or just above 1 per cent are widely considered acceptable in the UK. It is, however, generally understood that higher average trough factor levels enable PwBD more freedom to participate in an increased range of 'normal' activities, and to live freer lives. Higher factor levels can allow greater levels of physical activity and social activities with peace of mind and have been shown to reduce the number of bleeding episodes. The current treatment paradigm, of treatment regimens treating to 1 per cent, has failed to stop bleeds, but more PwBD could be bleed free under higher intensity treatment.[45,46,47]

7.3.10 Given the changing nature of treatment in the last few decades, and the extensive literature which has been produced on treatment (doses/intervals), the clinical direction of travel now appears to favour treating to a higher trough level than 1 per cent, a level which has proved inadequate to prevent all bleeding.

7.3.11 In many cases, higher trough levels have demonstrated far more clinical effectiveness. For example:

- at a trough of 5 per cent, 76 per cent of patients remain bleed free
- at a trough level of 15 per cent, 94 per cent remain bleed free
- at a trough level of 30 per cent, 100 per cent remain bleed free.[48]

7.3.12 However, outcomes are highly individualised: even at the same trough level different bleeding tendencies exist and people with haemophilia will have differing pharmacokinetic (PK) responses to CFCs. A far more personalised approach is needed, where the treatment regimen is tailored to each individual based on trough levels, lifestyle and bleed-free activity.

7.3.13 As the APPG is aware of the suboptimal outcomes of significant numbers of PwBD, we must conclude that clinicians are either not enabled to treat to a higher level, or the current set level is too low.

7.3.14 The UKHCDO report highlights the different levels of factor usage for treatment across the UK. This resource documents significant differences in factor usage across different centres, and while there are clinical reasons for different usages (such as body weight) the disparity is greater than what would be expected.[49]

7.3.15 Worryingly, even though raising factor levels could reduce the chances of experiencing a bleeding episode and improve outcomes, the APPG has been made aware that clinicians in certain parts of the country have been cautioned against increasing factor levels by commissioners, due to the potential cost implications. Currently, even though some clinicians support aiming for higher trough levels, fear of censure from commissioners is preventing them from implementing them.

7.3.16 This pressure to ensure costs are constrained is increasingly influencing clinical behaviour and is now preventing PwBD from accessing higher factor levels. Tender outcomes and commissioning decisions are dictating both the treatment product and treatment regimen of that product, in some cases. This is creating a perception among some PwBD that cost containment is taking precedence over clinical opinion.

7.3.17 Incredibly, several APPG submissions have detailed that on occasion directives have been issued by NHS England stating that certain products should not be prescribed, and that PwBD should be switched to cheaper alternatives even if someone is stable on their treatment.

'We have to take whatever treatment our centre lobs at us.'
Person living with a bleeding disorder

7.3.18 Another consequence of the system is that PwBD have been switched from products they are comfortable with in order to meet contractual obligations set by the tender or to move to a lower cost product. Individual prescribing decisions are being driven by the prices set in the tender rather than patient and clinician preference.

Recommendation 5 – The level of influence commissioning decisions have over clinical freedom needs to be reduced. Clinician and patient preference must be a deciding factor in prescribing decisions. Commissioners must ensure that clinicians are able to offer their patients a choice over which treatment is right for them and must not be limited by restrictive tenders and commissioning guidance.

7.3.19 PwBD, in collaboration with their clinical team, should be empowered to access the full range of safe and efficient treatments. While new treatments may not be clinically appropriate for all, in cases where the benefit does exist, either clinically or in terms of the burden of treatment, PwBD need to be free to switch to the most appropriate treatment.

7.3.20 Competition-inspired cost minimisation can be considered an appropriate model for standard half-life products (such as recombinant FVIII), where therapeutic equivalence can be argued. However, in other cases different treatments do not produce equivalent outcomes and cannot be adequately compared by a commissioning system that remains situated within an outdated treatment paradigm. The tender system should ensure that all licensed treatments, which are by definition safe and effective, are available to haemophilia centres to prescribe the most appropriate treatment to each patient. The role of commissioners is to create a framework that enables this.

7.4 Responding to patient heterogeneity

7.4.1 Across disease areas, the NHS has been committed to delivering a radically different experience for patients. Personalisation of care, and improving patient choice, has become central to the aims of the NHS.[50]

7.4.2 A stated goal of the Department of Health and Social Care, as set out in April 2016, is 'significantly improving patient choice by 2020 and in doing so, empowering patients to shape and manage their own health and care'.[51]

7.4.3 For PwBD however, patient choice is heavily restricted by the current tender and commissioning process, which is primarily focused on cost control and has limited the scope of clinicians to provide individual packages of care tailored to individual needs.

'We have never had a choice of treatment.'
Person living with a bleeding disorder

7.4.4 The NHS has now instigated national policy initiatives aimed at personalising treatment. However, at present, clinical practice focuses on minimum treatment standards and for many, patient-focused outcomes are not always central to the decision-making process. Personalised care is far from universal, and treatment for people living with bleeding disorders has not evolved in a way that is aligned with the broader shifts in NHS policy. Again, this is reflected in the NHS haemophilia service specification not having been updated since 2013, pre-dating these major policy shifts.

7.4.5 The NHS Long Term Plan, published in January 2019, states that personalised care will become 'business as usual' across the health and care system. However, the view of the APPG is that the current systems of commissioning do not allow for the necessary level of clinical decision-making, or patient choice, to enable effective personalisation of care.

7.4.6 Given that impacts vary from person to person, personalisation of care is vital, as it focuses on the individual tendency to bleed (phenotype) rather than a one-size-fits-all approach designed to treat all patients with a certain factor level in the same way. The level of personalisation varies wildly, centre to centre, and needs to become standard.

7.4.7 To reach an appropriate decision in terms of treatment, it is critical to consider what outcomes matter most to the patient, as the APPG has been made very aware that this may differ greatly to what clinical outcomes are typically considered by commissioners.

7.4.8 While many clinicians already have a relationship with their patients which allows detailed discussions that can identify what patients want from their treatments, some do not. This could be down to a lack of resources and clinician time. In general, increases are needed to core funding for care services for bleeding disorders to ensure clinical teams have the time required to personalise care in this way. The most appropriate person in a centre to personalise treatment may be a nurse, a doctor or a physiotherapist. An effective system also relies on there being clinical freedom to access different treatments, giving clinicians and PwBD choice.

7.4.9 Currently, the opportunity exists to personalise care further, which given the nature of patient heterogeneity would improve outcomes. Treatment can be tailored to suit lifestyle, physical activity and PK response. Patients have individual PK responses to factor concentrates and need individualised treatment plans. Dosing and dosing frequency can be tailored to improve outcomes for patients. PK profiling should become routine for all eligible patients.

7.4.10 However, any attempts to further personalise care currently will be hampered by the lack of treatment choice available. Anecdotally, the APPG is aware of several people with severe haemophilia who have been unable to access EHL products, instead being required to remain on SHL products.

Recommendation 6 – Target trough levels should be raised to reflect the ambition to achieve zero bleeding episodes in people with haemophilia. Optimal trough levels should be decided by clinicians and their patients, reflecting a variety of lifestyle factors. Increasing dosing levels and intervals should not attract censure from commissioners. Personalised care should become a reality for all. Access to pharmacokinetic testing should be extended to all eligible PwBD and tailored dosing regimens for all PwBD requiring regular treatment. Personalisation and co-decision-making should become the norm.

Scott's story

Scott Mclean, aged 28, has, until recently, struggled to get the right treatment for his severe haemophilia A which has impacted his work prospects and his leisure activities.

Damage to Scott's veins over 20 years of self-injecting has made administering his treatment increasingly difficult. He was getting to work late and sometimes having to inject in his workplace. Employers started asking about his haemophilia, making Scott self-conscious and wary of talking about his condition.

Added to this, his factor levels were dropping to low levels after only four hours, necessitating further treatment if Scott intended to exercise after work.

He felt better treatment options must be available, but with no suggestions from his centre he had to do the research himself, using the internet and information from The Haemophilia Society.

Yet when he attempted to discuss the problem with his centre, he was told that his factor levels were 'good enough', and his requests for a higher dose or an extended half-life product were turned down.

He was also discouraged by his consultant from running – a pursuit he particularly enjoys.

Scott said: 'All my life, when I've gone for an appointment I've been asked how my haemophilia is, how many bleeds I've had and what exercise I'm doing. No one asks how I'm coping with my haemophilia and how it impacts on my lifestyle. It should be more than treating the haemophilia, it's treating the person and understanding what they want to get out of their life.'

After pressure from Scott, he was put on a newly approved novel treatment in January 2020, but it was not until he changed centres recently that he felt he has received sufficient support in adapting to the new drug. He is now on fortnightly treatment with a back-up plan if this does not suit him. His last consultation lasted three and a half hours – appointments at his previous centre lasted for 20 minutes.

Scott believes the key to effective haemophilia treatment lies in listening to the needs of the patient and being on top of the ever-changing treatments in this field.

He said: 'We're now talking about how people with haemophilia can do so much more, but it's only because their treatment allows it. If you're not getting the right treatment then those opportunities aren't there.'

7.5 Rarer bleeding disorders

7.5.1 As in other rare disease areas, in general PwBD suffer adversely from the relatively small patient populations they belong to.

7.5.2 While many of the issues presented in this report apply to PwBD regardless of the specific type they have, people with the rarest bleeding disorders inherently suffer from the implications of even smaller patient populations (as shown in the case study on Coagadex above). People with the rarest bleeding disorders often have reduced options in terms of access to drugs. If treatments are available at all they were expensive to develop, which in small patient populations means higher prices.

'This makes me feel that by having factor X deficiency I am at a disadvantage from having a different inherited bleeding condition.'
Person living with a bleeding disorder

7.5.3 For haemophilia A and B, the current processes have worked fairly well for some coagulation factor products, however for other bleeding disorders the system is less successful. FX deficiency is not the only rare bleeding disorder that is failing to see the benefits in advances in treatment. A new recombinant product (NovoThirteen) currently exists to treat factor XIII deficiency, but while licensed for routine prophylaxis it is not being commissioned for use in the UK.

7.5.4 PwBD acknowledge that the health service has finite resources, and that no realistic system in the current fiscal climate would offer patients unfettered access to every treatment. However, the systems of commissioning for all bleeding disorders need to address the current imbalance in selecting treatments, away from cost and towards the stated NHS aim of increasing patient choice, particularly for rarer bleeding disorders that still lack adequate treatment.

7.5.5 The disparity between bleeding disorders is stark, and the evidence presented to this inquiry suggests that a systemic prejudice exists against rarer bleeding disorders. For many, the challenges of managing their condition are exacerbated by the absence of an effective treatment. The treatment for rarer diseases should, where possible, be on parity with that for less rare conditions.

7.5.6 Currently, the funding route for new products, especially for ultra-rare diseases, is too complex, convoluted and unpredictable, and in practice the system works against ultra-orphan treatments, in favour of more common conditions. The specialised commissioning system, as is, has been shown to be unsuitable for ultra-rare diseases.[52]

'Other factor deficiencies have moved on from plasma-derived to recombinant factors. Whereas, … personally I feel that I am going backwards with my treatment.'
Person living with a bleeding disorder

7.5.7 A result of these current systems is that inequitable access exists among and within bleeding disorders. For certain disorders, life-changing medicines are not being made available to those who need them, with only highly suboptimal treatments commissioned in their place. The implications of fewer effective medicines being funded is not only significantly limiting the quality of life of those directly impacted, but sets a future precedent for rare diseases more generally: that provided a treatment is keeping you from hospitalisation, it is perfectly acceptable.

7.5.8 Due to cost-focused restrictions and lack of sufficient evidence, PwBD do not have access to optimal treatment or optimal standards of care and are potentially being treated to a lower standard than patients in other disease areas. Instead, a system can be created that ensures access as soon as market authorisation is granted with further evidence of the value of the product then able to be collected through NHS use of the product.[53]

Recommendation 7 – New treatments should routinely be made available immediately following licensing through a managed access programme with an agreement between the NHS and industry to manage costs.

7.6 Moderate haemophilia

7.6.1 The report has discussed how gaps exist in the provision of services such as physiotherapy or mental health support. While a disparity exists between parts of the country, for people with non-severe bleeding disorders the disparity can be even wider. For many people living with non-severe bleeding disorders, access to multidisciplinary care is further rationed in a way it is not for those with more severe conditions.

7.6.2 Moderate patients, even those who have a severe bleeding phenotype, are disadvantaged by their treatment 'classification'. The APPG understands that the annual bleed rate of people with severe haemophilia is lower than people with severe phenotype moderate haemophilia.

Recommendation 8 – Further study is needed on the disparity between the severity of conditions, and whether those with moderate haemophilia are being undertreated, due to misconceptions about their classification.

7.6.3 Currently, new innovative treatments are often limited to those with severe haemophilia, and the introduction of gene therapy could widen this disparity between patient classifications. If only people with severe haemophilia can access these new treatments, it means that those differences in outcomes for people with moderate haemophilia will become worse.

7.7 Women and bleeding disorders

7.7.1 Severe haemophilia occurs predominately in males and historically women were only considered carriers, however this does not reflect the reality for women with haemophilia. This inquiry has highlighted the challenges of bleeding associated with menstruation, pregnancy and childbirth. In broader terms, across bleeding disorders, women are disproportionately affected by conditions such as VWD, other factor deficiencies and platelet disorders such as Glanzmann's thrombasthenia.

7.7.2 For many women, getting an accurate diagnosis is a slow process, and many have to face unacceptable delays before receiving a formal diagnosis. Even, simple diagnostic tests for factor levels appear to be difficult for women to obtain. Post-diagnosis, treatment options remain limited, because the focus of care remains on those with severe haemophilia, often to the detriment of other groups.

7.7.3 The APPG has been made aware that under-diagnosis is widespread among women with bleeding disorders. For example, the prevalence of VWD is estimated at 1 in 1,000.[54] However, while this level of prevalence would indicate close to 70,000 people in the UK having von Willebrand disease, the National Haemophilia Database includes just over 10,000. This would suggest that large numbers of women are not being treated by haemophilia centres but are navigating primary care or living with undiagnosed symptoms.

'Adult care for females with bleeding disorders [is] very poor.'
Person living with a bleeding disorder

7.7.4 Without specialist care, those woman living with a bleeding disorder may be receiving inappropriate care, including being at risk of unnecessary hysterectomy, with studies confirming that women with VWD are more likely to undergo a hysterectomy, and at a younger age. [55,56]

Recommendation 9 – Women, who make up the majority of diagnosed PwBD, should be offered equity of care from haemophilia centres and this should be reflected in the updated service specification.

7.8 Ageing with a bleeding disorder

7.8.1 Due to the contaminated blood scandal of the 1970s and 80s, currently being investigated by The Infected Blood Inquiry[57] , a generation of PwBD was infected with viruses. Many died as a result and those left are living with co-morbidities from their infections as well as the legacy of historical treatments. However, for the first time there is a generation of older people with bleeding disorders who need special care to ensure their condition is well managed as they age.

Recommendation 10 – Strategies should be drawn up to develop links between haemophilia centres and services for older people. Education will be needed for healthcare workers caring for older people with bleeding disorders, whose needs will be unique.

7.9 Empowering PwBD through transparency

7.9.1 During this inquiry, disparities have been documented throughout the bleeding disorder healthcare systems. From access to multidisciplinary care to treatment regimens, the experiences of PwBD can vary to a staggering degree.

'I wish I could be given more knowledge and understand treatments better. At present I do not know much and I wish more could be done to help my baby's bleeding disorder.'
Person living with a bleeding disorder

7.9.2 From the evidence presented to the APPG, often those with the best outcomes have been those most able to navigate the care systems successfully. Access to reliable information has been key to them becoming more empowered patients, able to take control of their treatment and its outcomes. Yet, easily accessible and detailed information aimed at PwBD is scarce.

7.9.3 PwBD need information about products and treatment regimens to be able to most effectively engage in joint decision-making. If NHSE's stated aim of developing personalised care is to be implemented, while the clinical and commissioning side requires reform so too does patient access

to relevant information, which would enable them to effectively engage in co-decision-making about their treatment.

7.9.4 NHSE needs to provide information about available treatments and its decisions on access. In doing its work it should actively seek out the views of PwBD or provide funding to enable The Haemophilia Society to provide this service.

7.9.5 This information, to be seen as impartial by PwBD, should be produced in collaboration with PwBD themselves, and delivered through patient groups such as The Haemophilia Society. This work, while crucial, would require funding, which it may not be appropriate for the pharmaceutical industry to provide. Nor should PwBD be expected to pay for it directly, meaning statutory funding should be considered.

7.9.6 Bleeding disorder communities are clear in their desire to understand how decisions that determine their access to treatments are made. They want to see a set of systems which work collaboratively and effectively together, while ensuring their own views and opinions are taken into account.

7.9.7 The NHS commissioning process is complex and convoluted, and too often PwBD feel unable to influence or understand its deliberations and decisions. Even now, meetings held by groups such as the CRG are largely closed to the public, without the publication of useful minutes. This needs to be reformed, with not only decisions but also the process and deliberations behind the decisions being made available to patients. The current systems are not transparent, which must change if the NHS aims to see empowered patients, in line with the NHS mantra nationally across disease areas.

7.9.8 While PwBD recognise the need for a fair and appropriate use of the NHS's finite resources, they need to see how those decisions are made, and rightly want to have a role in the processes which determine their quality of life.

7.9.9 For policymakers, it must be remembered that PwBD are the key stakeholders. Frameworks, guidelines and commissioning decisions need to reflect this reality, and PwBD need to be 'in the room' when any decisions are made and be part of making those decisions.

7.9.10 Currently, there is insufficient access to information around decision-making procedures and the outcomes of commissioning decisions. Minutes of meetings of the CRG, except for occasional commercially sensitive information, should be published in full.

7.9.11 This inquiry has shown the degree to which many PwBD are entirely unaware of what treatments and types of care they should be able to access. NHSE should be working to encourage and facilitate dialogue between clinicians and patients about how they can manage their conditions better, and what they can expect in terms of that management.

'I want to have more information from my consultant about new treatments and be offered new treatments to help me in living my life. My consultant does not give me information about new treatments.'
Person living with a bleeding disorder

7.9.12 NHSE needs to recognise the experiences and voices of PwBD, and ensure they are valued and supported as an essential partner. Promoting the involvement of PwBD in all decisions relevant to the management or treatment of their condition is key to achieving this.

Recommendation 11 – NHSE must ensure meaningful engagement with PwBD is effective, timely and accessible, and demonstrate the impact of stakeholder engagement, communicating it back to the bleeding disorder community. A regularly updated information website would address the lack of system transparency. Unless commercially sensitive, all meeting minutes in which decisions are made about the treatment and care of people with bleeding disorders should be published.

Recommendation 12 – PwBD need to be informed to be empowered. NHSE should work collaboratively with The Haemophilia Society to create an online portal through which consultations could be launched, decisions communicated, and information published.

7.9.13 A recurring issue found across most areas of bleeding disorders services was the level of transparency. While the APPG found it difficult, in certain areas, to access what it considered relevant information, for those less familiar with the system, or with less time to attempt to navigate it, these systems would be impenetrable.

7.9.14 This lack of transparency goes beyond the commissioning systems to a lack of public information on treatment types and little information on why some treatments were approved for routine commissioning and some were not. Information on the performance of different centres was not easily available and there was little information on what recourse PwBD had when they did not receive the expected level of service.

7.9.15 This issue, not unique to bleeding disorders – as evidenced in one of the Public Accounts Committee's main criticisms of NHS specialised services generally being a lack of transparency[58] – should be addressed.

7.10 Procurement and commissioning

7.10.1 Despite major changes to the standards of care in bleeding disorders, most notably haemophilia, in the past decade this has not been reflected in major changes to the ways treatments are commissioned.

7.10.2 New haemophilia treatments give the opportunity to significantly increase trough levels and levels of bleed protection, while also reducing the burden of treatment. However, access to these treatments varies as the tender system constrains patients and clinicians in terms of available treatments.

7.10.3 For example, most patients on SHL products would benefit from EHL treatments but commissioning restrictions allow clinicians to only prescribe them to specific patients. More recently licensed, Emicizumab for haemophilia A is another treatment that provides improved bleed prevention but remains restricted in who it can be prescribed for.

7.10.4 Since the introduction of recombinant treatments in the 1990s, decades passed without major innovations in treatment. Costs for treatment were high, and the burden of treatment significant. In 2005, the UK began to use a national tender exercise to procure treatment. Since then, the UK has seen considerable savings in the cost of treatment.

7.10.5 The competition introduced by the national tender is often credited with creating major savings, for example with driving the unit price of factor VIII products down by 80 per cent since 2005. Prior to the licensing of newer products, the tender system worked well in driving down the cost of SHL treatments.

7.10.6 The tender exercise for haemophilia A treatments works by assuming therapeutic equivalence of the available SHL products and then comparing them against each other, predominately on price, which makes up 75 per cent of the ranking criteria. EHLs, plasma-derived FVIII and Emicizumab are included as separate lots. In each lot all available products are compared and ranked on cost with some consideration of security of supply and ease of use.

7.10.7 For any given type of treatment it is expected that the lowest cost product will be the one prescribed. Patient and clinician preference are of limited importance in what product is prescribed.

7.10.8 The tender system makes no attempt to compare different types of haemophilia A treatment and so takes no account of differing outcomes or safety profiles, either within or between lots. It is feared that the continuing use of a cost-minimisation process is now coming at the cost of innovation.

'For a country that is world leading in haemophilia, the industry is expressing concerns about launching new products into this country first as it appears to be based on cost alone without taking any account of associated improvements in clinical outcome.'
UKHCDO

7.10.9 Concerns exist that the current tender system could lead to the UK being deprioritised by companies launching newer innovative treatments. The APPG has also identified a range of other issues the system has created.

7.10.10 A tender process also assumes that a number of equivalent products exist, which while true for haemophilia A is not the case for ultra-rare bleeding disorders such as factor X and XIII deficiency. In the EU there are licensed factor X and factor XIII products, but at the time of the inquiry neither was currently commissioned by NHSE or any other parts of the NHS.

7.10.11. This means that for many PwBD, it is commissioners not clinicians who are determining their treatment product, and that commissioning decisions dictate how a whole group of PwBD are managed, as opposed to the aim of optimising patient outcomes.

7.10.12 Choice for PwBD and clinicians is therefore limited, to achieve low price, and clinicians are prevented from prescribing the patient-preferred treatment. Clinicians are forced to prioritise their patients and treat accordingly. For example, even if clinically appropriate for more of their patients, a clinician would be unable to switch all their patients onto an EHL product.

Only half of PwBD felt able to influence decisions about which treatments are prescribed to them.
Conclusion of 2019 Patient Survey

7.10.13 EHL products for haemophilia have been available to patients in England since 2016. While multiple variables were at play, as the APPG was made aware of at the parliamentary evidence session, clinicians lacked the ability to switch all of their patients, and many were forced to prioritise patients.

'Manufacturers, including Sobi, may struggle to launch new treatments if there is a requirement to participate in a tender process which remains geared towards encouraging uptake of the cheapest treatments, rather than giving patients the choice of a range of innovative treatments or focusing on the patient outcomes with different treatment options.'
Sobi

7.10.14 Pharmaceutical companies also expressed fears that the nature of the tender exercises is disincentivising further research and innovation.

Recommendation 13 – A full review of the UK tender processes for bleeding disorder treatments should take place with the aim of creating a new system that incorporates a wider measure of value. This should include far greater consideration of patient-relevant outcomes and the impact on quality of life. The Commercial Medicines Unit should work collaboratively with patient groups including The Haemophilia Society, as well as a multidisciplinary expert working group, to plan how to incorporate a wider measure of value into the UK haemophilia tender exercises.

7.11 Cost minimisation

7.11.1 While across most disease areas general rises in health spending are expected, bleeding disorders have been perceived as an area in which savings can be made. The trend of reducing costs of the last decade has entrenched a myth that the cost of treatments for bleeding disorders will continue to decline, giving wildly unrealistic long-term fiscal expectations.

7.11.2 The APPG has heard reports that that this unrealistic expectation is now limiting access to innovation in treatments, as it has been reported that commissioners have censured clinicians who have been too willing to switch their patients to EHL products.

'The current approach of prioritising cost over meeting any other needs requires review, to prevent further problems in the future.'
Haemophilia Nurses Association

7.11.3 For a country that has been world leading in bleeding disorder care, the APPG is concerned to see that commissioning appears to be based in practice solely on cost, without reviewing the associated improvements in outcomes for PwBD.

Recommendation 14 – A significant proportion of the savings made through the tender process should be reinvested in wider care and support for PwBD or used to fund new innovative treatments that address unmet needs.

7.12 Patient understanding of commissioning

7.12.1 Commissioning plays a critical role in eventual patient outcomes, but it is not delivering for PwBD. Patient perception is that the commissioning system is designed to save money, not to ensure optimal patient outcomes. PwBD deserve commissioning to consider the outcomes they value to a far greater degree. This requires the system to recognise that not all treatments are generic and do not produce the same outcomes.

Fewer than one in five PwBD were aware of the processes by which NHS treatments are selected and funded
Conclusion of 2019 Patient Survey

7.13 Measuring the outcomes that matter to patients

7.13.1 The commissioning systems are further hampered by a lack of relevant outcome measures valued by PwBD. New measures of value are needed to reform the commissioning system. Outcomes, outside of clinical care indicators such as bleed rates, are not presently well measured or valued. Clinical outcomes do not account for the burden of treatment, or other outcomes perceived as important by PwBD. PwBD should be involved in developing outcome measures which are most relevant to their lives. This is needed to ensure future treatments, and treatment paradigms, are designed with the outcomes that PwBD value as important at their heart.

7.13.2 If wider patient-centric outcomes measurements were collected, a more systematic way of looking at the impact a particular treatment could be developed. A widely recognised and respected set of outcomes measures is that proposed by the coreHEM project.[60] Through this process, the frequency of bleeds, factor activity level, duration of expression, chronic pain, healthcare resource use and mental health were identified as the core outcomes to be measured in addition to regulatory mandated adverse effects.

7.13.3 This APPG report recognises that choices made in the healthcare system – the allocation of resources – must address the fundamental reality that resources are not unlimited, that for each decision an opportunity cost exists, and that dilemmas over how to pay for additional services proliferate throughout the NHS.

7.13.4 In Managing Public Money the Treasury set out principles for good procurement across government. Obtaining value for money 'means securing the best mix of quality and effectiveness for the least outlay over the period of use of the goods or services bought. It is not about minimising up front prices.' It goes on to say 'whole life cost' rather than lowest purchase price is a key factor in determining value.[61]

7.13.5 Achieving value would therefore require a reorientation towards patient outcomes, away from cost. Modern commissioning processes should be focused on enhancing individual care standards, while in parallel ensuring value for money for the NHS. By refusing to evaluate in a holistic manner, the wider societal value of the treatment, such as enabling a child to have better school attendance or adults to have more productive working lives, is being ignored. Also ignored are the longer-term cost implications of poor outcomes on the wider NHS budget, as well as on the welfare system.

7.13.6 The principles of effective commissioning are:

- patient engagement – engaging patients at all stages of the commissioning cycle
- clinician-led – enabling clinicians to play a pivotal role at the heart of designing and delivering research and evidence-based treatment options
- comprehensiveness – meeting all healthcare needs, in terms of the population at large as well as on an individual level.

7.13.7 Health-related costs may be incurred in a range of social spheres, making it important to include all costs for a relevant time period, even if they fall under different budgets. For instance, a new treatment may increase the pharmaceutical budget, but over time produce savings in other parts of the system to partly or fully offset this increase, such as lower hospitalisation costs or fewer monitoring requirements. Savings may also occur in other sectors of the economy, for example, when sickness absences, early retirement due to disease, or premature death are avoided. For efficient resource allocation, decisions should consider the full impact of therapies, regardless of where effects occur. Economic evaluations, then, must be wide-ranging to capture all potential benefits. Using this more holistic approach would help decision-makers avoid an overly narrow budget-specific perspective, which would miss the important benefits accrued in other areas and produce suboptimal results for the allocation of resources.

'The current climate in the UK is not encouraging for companies bringing innovative products to patients for haemophilia, primarily due to the review process which is driven by price rather than value.'
Spark Therapeutics

7.13.8 There is a need for commissioning and tender systems for bleeding disorders to appraise their effectiveness and relevance. The APPG would like to see a more holistic approach, with the input of PwBD key to its redesign. To create clinical freedom, and to facilitate patient choice, treatments should be evaluated against outcomes that matter most to patients, not cost concerns. In the UK there is a need to develop an alternative system that would enable value-led decisions to be made in a more equitable and transparent way. This may also include modifying the governance structure to improve specific aspects of the evaluation process.

7.13.9 Treatment and commissioning methods must adapt as new therapeutic technologies and strategies offer superior outcome potential. This will require a move towards patient-centric commissioning with downstream cost consideration, with evaluations needing to be multi-criterial with appropriate weighting.

Recommendation 15 – Commissioners should be required to consider a wider range of evidence of the value and impact of treatments so that their full benefit is weighed against the costs.

'More consultation with people affected by haemophilia is needed. People affected by haemophilia should be actively involved in decision-making processes.'
Person living with a bleeding disorder

7.14 The NHS England prioritisation process

7.14.1 The current NHS England prioritisation process, in which funding is allocated across all specialised disease areas, does not ensure PwBD are able to access the best treatment for them. Funding is dependent on what other demands there are on the wider NHSE specialised commissioning budget at that time and leads to different conditions competing for funding.

Recommendation 16 – Treatments should be considered by CPAG on their own merits and if clinically effective, demanded by patients and clinicians, and value for money, should be commissioned.

7.14.2 With an increase in licensing of new rare disease treatments expected which will bring advances in care as well as treatments for conditions where no previous treatments existed, the Government should consider how it will make these new treatments available to patients. The Cancer Drugs Fund has improved access to new treatments for people with cancer and a similar model could be effective in improving access to treatment in rare diseases.

7.15 Licensing

7.15.1 The goal of licensing is to ensure patients have access to safe, efficacious and optimal treatments. Before a drug can come to market, it is legally required to gain a marketing authorisation (product licence) by a regulator. In the UK, the regulatory body is the Medicines and Healthcare Products Regulatory Agency (MHRA), although presently in most cases treatments for bleeding disorders are licensed through the European Medicines Agency (EMA) which grants marketing authorisations for all member countries.

7.15.2 With the UK leaving the European Union this may change, and it remains unclear how the MHRA will undertake the assessment of new marketing authorisation applications or whether they will continue to work with the EMA. The current processes are rigorous and ensure patient safety, although the APPG has been made aware that with most treatments there is a time lag in licensing between the FDA in the USA and the EMA, to the detriment of European patients.

7.15.3 This potential change presents opportunities and challenges and could dramatically impact how long it takes for patients to be able to access innovative treatments. However, with appropriate resources, the MHRA could take a more flexible approach to meet the unmet medical needs in the UK. In addition, closer collaboration between the MHRA and commissioning bodies at earlier stages could be key to ensuring drugs are not only licensed but are able to reach patients quicker than is currently possible.

7.15.4 To ensure PwBD have access to innovative treatment, in a timely manner, reforms are needed to ensure the UK remains an attractive destination to launch products.

7.15.5 Led by a combination of the UK's departure from the EU, the lack of clarity over the future role of the MHRA, and commissioning issues, the APPG is aware that for many pharmaceutical companies launching new products is becoming increasingly less attractive. In practice, few firms will ever not launch new products in the UK, but with the NHS paying some of the lowest prices in the world for bleeding disorder treatments, it is possible many will deprioritise the UK for launching products. UK patients may then face delays in access to innovative treatments.

7.15.6 Another concern is that the development and launch of innovative new treatments that could address unmet need will be hampered if the UK loses its status as an attractive location for pharmaceutical investment. Some firms have suggested that that they will undertake clinical trials elsewhere if there is a risk the UK system will not commission those treatments. This would represent a great loss to patients and could have a detrimental impact on the UKs reputation within life sciences.

'We are hopeful that more can be done to expand the scope and effectiveness of EAMS so that people with bleeding disorders have quicker access to promising innovative treatments.'
Roche and Chugai

7.15.7 The current system is acting as a discouragement to developing and licensing new products for rare disease in the UK. This could be a major detriment to patients, and the UK economy as a whole, as other markets become more attractive and investment and clinical trials drift elsewhere.

Recommendation 17 – The government should ensure continuing shared working of the MHRA with the EMA and improve engagement with other leading licensing agencies including the FDA to accelerate marketing approvals for new treatments.

7.16 A single lead body for bleeding disorders

7.16.1 Presently, in the UK there is no single body or organisation that oversees bleeding disorders from commissioning to standards of care. Oversight is distributed among different bodies, with various levels of intra-body engagement.

7.16.2 Within NHS England, the Blood and Infection National Programme of Care provides leadership and oversight of the development and delivery of a comprehensive work programme to achieve demonstrable improvements in the quality, equity, value and outcomes of commissioned specialised services.

7.16.3 For clinical advice and leadership, the NHS relies on the Clinical Reference Group (CRG), which uses its specific knowledge and expertise to advise NHS England on the provision of services for bleeding disorders. Observers from Scotland, Wales and Northern Ireland attend CRG meetings and report back to their parallel commissioning systems.

7.16.4 However, commissioned by the UKHCDO the Quality Review Service has recently undertaken a peer review/audit of haemophilia centres across the UK to review standards of care. Management of the National Haemophilia Database is also overseen by the UKHCDO.

7.16.5 These organisations, while having slightly differing remits, have significant overlap in terms of their work, aims and objectives. This approach fractures what could be a coordinated UK-wide system, and contrasts with other systems used in countries that achieve better outcomes for PwBD.

7.16.6 In Ireland, for example, the National Haemophilia Council has sole oversight of bleeding disorder care and treatment and plays a statutory role.[63]

7.16.7 The National Haemophilia Council's role covers both high-level planning and the day to day of living with a bleeding disorder. The body makes recommendations to the Minister for Health, independently. It has secure government funding, providing the resources required to fulfil its role, and is heavily focused on patients, as they make up a significant part of its decision-making board.

7.16.8 It has the responsibility of overseeing the quality and standards of care and produces an annual report on the state of care in Ireland, which it then provides to the minister. As well as auditing the standards of treatment, its remit covers funding for multidisciplinary care with the aim of ensuring sufficient provision.

7.16.9 Currently, for PwBD in England (and across the UK) neither the advisory role of the CRG or UKHCDO equates to the independent, patient-led, appropriately funded and integrated approach of the National Haemophilia Council.

7.16.10 A body should be established by statute not only to inform but also to influence government decision-making on the management of bleeding disorders.

7.16.11 Its terms of reference should be set in such a way as to ensure overarching responsibility for all decisions relating to the treatment and management of bleeding disorders, from addressing standards of care to the selection of the most appropriate treatments for PwBD. All changes of policy relating to bleeding disorders should be reviewed by this body. Its aim would be to raise the standard of care, in areas that PwBD identify, and to ensure the experiences of PwBD fully inform desired standards going forward.

7.16.12 While this body would function as a multidisciplinary partnership between those involved in the care of people with bleeding disorders, and PwBD themselves, PwBD should remain at its heart.

7.16.13 This would put PwBD at the heart of the design and delivery of services for bleeding disorders. Going forward, we would want to see recommendations, such as those made by this report, being discussed and acted upon by a body such as this.

Recommendation 18 – A UK-wide steering committee should be set up on a statutory basis that brings together patient representatives, multidisciplinary healthcare professionals and commissioners to ensure a coordinated approach to treatment for PwBD.

8. Conclusion

8.1 While a range of new treatments for bleeding disorders is expected to be licensed over the coming years, concerns persist over the ability of the current system to adapt as these new treatments become available.

8.2 At present, and if left unreformed, the current system of commissioning is unlikely to make these new treatments available to all clinically appropriate patients, instead restricting access to new developments. In some cases new treatments may not be commissioned at all, and if commissioned, will be rationed to a restricted group of patients or limited to lower than optimal doses.

8.3 The tender system now means the UK pays some of the lowest prices for CFCs among high-income nations, which is generally seen as a positive outcome for the NHS. However, seeking the lowest possible costs without regard for total value is a problem, both for PwBD now and in the future. For patients now it fails to optimise outcomes, and in the years to come there are very real dangers that the situation could deteriorate. Good commissioning should go beyond seeking to minimise the unit cost, and financial savings should not be obtained at the cost of undermining appropriate forms of clinical freedom and patient choice. The drive to pay increasingly low prices could drive out competition and could lead to companies leaving the UK market or deprioritising the UK, increasing the time it takes for PwBD to access innovative treatment by years.

8.4 While controlling costs is important, its focus needs to be proportionate. Companies cannot produce innovative treatments and continue to invest in further research if they are not profitable.

8.5 The NHS has made substantial savings through the bleeding disorder tender exercises since 2005, with estimates suggesting over £500 million to have been saved. However, the APPG has been made aware that these savings have not been reinvested into the care and management of PwBD. In practice, as described throughout this report, the desire to continue to save money within bleeding disorder treatment is now coming at the cost of innovation and better outcomes for PwBD. While the APPG accepts the need to be financially prudent, this cost concern should not be dramatically impacting on the quality of care and choice of treatment options available to patients.

8.6 A modern commissioning system for bleeding disorders must balance affordability concerns against the outcomes for PwBD. Cost constraints with too little regard for outcomes are dangerous and self-defeating and will in the long term lead to false ‘savings’ by limiting clinical outcomes.

8.7 If left unreformed, the system could continue to evolve in ways contrary to the needs of PwBD, and against the spirit of personalisation presently underpinning the health service. Further focusing on exclusively minimising costs will come at the expense of quality of treatment and care and ongoing innovation.

8.8 This report has clearly highlighted potential hazards, and without the government and NHS commissioners taking action to avoid them the outcomes for PwBD could be further reduced relative to other comparable high-income countries. With the range of treatments likely to be available to treat PwBD widening and the need to reduce inequities in service provision now as pivotal as it has even been, now is the time for NHSE to review its commissioning priorities.

8.9 Current procurement and prescribing processes for bleeding disorder treatments fail to account for the full range of benefits of more recent treatments and therefore create barriers to access. We believe that NHSE's procurement, licensing and commissioning processes have become outdated, failing to adapt to the increased diversity of treatment options available to patients. It has failed to adapt to the increased availability of new treatments because of its focus on unit price and not outcomes for patients. This has had the unintended effect of restricting access to these treatments based on cost, thus creating barriers to access for clinicians and patients.

8.10 The development of new treatment options set to enter the market in the coming years has demonstrated the obsolete nature of the current system, which is already struggling to cope with innovation. The longer reform is delayed, the longer patients will be forced to wait for access to better treatments.

Appendix A: Data and survey results

Patient number tables

Bleeding disorder (Registered on the National Haemophilia Database, April 2017 to March 2018)	Male	Female	Total number	Number requiring treatment
Haemophilia A	6,121	2,038	8,159	3,409
Haemophilia B	1,233	562	1,795	702
Von Willebrand disease	3,923	6,875	10,798	1,062
Rarer bleeding disorders	4,286	6,803	11,089	693

Key results of the survey

To what extent is your lifestyle impacted by the treatments made available to you?

Total Answered	222	
Negatively impacted	32	14.41%
Neither positively or negatively impacted	95	42.79%
Positively impacted	86	38.74%
Don’t know	9	4.05%

To what extent do you feel you are able to influence the decisions that are made about which treatments can be prescribed for you?

Total Answered	222	
Not at all	40	18.02%
Only a little	65	29.28%
To some extent	54	24.32%
Quite a lot	38	17.12%
Very much	14	6.31%
Don't know	11	4.95%

How aware are you of the processes by which NHS treatments are selected and funded?

Total Answered	222	
Not at all aware	117	52.70%
Only a little aware	61	27.48%
Aware to some extent	34	15.32%
Quite aware	9	4.05%
Very aware	1	0.45%

Appendix B: Contributors

Oral evidence sessions

The APPG had three oral evidence sessions in parliament in Summer 2019 and heard evidence from the following three groups. The APPG also visited the Royal London Hospital in July 2019.

12 June 2019 – People with bleeding disorders

- Keith Colthorpe
- Scott Mclean
- Paul Sartain
- Vicky Jones (unable to attend in person, but submitted a letter)

26 June 2019 – Pharmaceutical companies

- Richard Eaton, Integrated Franchise Lead – Rare Conditions, Roche
- Sam James, Director of External Affairs, Takeda
- Alan Walshe, Franchise Head, Haematology, Takeda
- Neil Dugdale, Vice President and General Manager, UK and Republic of Ireland, Nordics-Baltics, Sobi
- Steve Bojakowski, Patient Access Director, UK and Republic of Ireland, Sobi

10 July – NHS and clinicians

- Dr Pratima Chowdary, Consultant Haematologist, Royal Free Hospital, representing the UKHCDO
- Cathy Edwards, Clinical Programmes Director, Specialised Commissioning, NHS England
- Claire Foreman, Head of Acute Programmes, Specialised Commissioning, NHS England
- Dr Edward Tuddenham, Emeritus Professor of Haemophilia, UCL

Other evidence

In addition to the patient survey responses evidence submissions were received from:

- BioMarin
- BioProduct Laboratory (BPL)
- CSL Behring
- European Haemophilia Consortium
- Freeline Therapeutics
- Haem-Psych Association
- Haemnet
- Haemophilia Chartered Physiotherapists Association (HCPA)
- Haemophilia NI
- Haemophilia Nurses Association (HNA)
- Haemophilia Scotland
- The Irish Haemophilia Society
- NHS England
- Novo Nordisk
- Roche and Chugai
- Sobi
- Spark Therapeutics
- Takeda
- UKHCDO
- uniQure
- World Federation of Hemophilia (WFH)
- And a number of individuals with bleeding disorders

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