James Lind Alliance

Priority Setting Partnerships

The James Lind Alliance (JLA)
Setting priorities for bleeding disorders

Stop The Bleeding

Executive summary

The James Lind Alliance Bleeding Disorder Priority Setting Partnership came together following an initiative from the United Kingdom Haemophilia Doctors Organisation to set up a clinical studies group for all bleeding disorders, inherited and acquired. The aim of the PSP was to ask patients, carers and health professionals to identify and then prioritise the unanswered questions that concern them most about the diagnosis, treatment and care of people with bleeding disorders.

People with bleeding disorders, their families and health professionals have taken time to tell the PSP what questions they want to see answered by research. The more people who know about the Bleeding Disorder research priorities, the more likely organisations and individual researchers are to tackle the questions that patients, carers and health professionals have told us they want answered, so please help to spread the word about these priorities!

The top 10 research questions which have been identified are:

What is the role and cost effectiveness of blood clotting tests that give immediate results at the bedside (point of care) in managing medical, surgical or obstetric haemorrhage?
How can we balance the risk and benefit of antithrombotic (blood thinning) treatment for cardiovascular disease (including heart attacks and strokes) in patients with bleeding disorders?
What is the best haematological approach to management of severe haemorrhage after delivery?
How should heavy periods be managed in women with bleeding disorders?
What is the relationship between immune thrombocytopenic purpura (ITP) and fatigue?
What are the most effective treatments for acute and chronic pain in people with haemophilia?
What are the benefits of psychological and psychosocial strategies for support of individuals or families affected by bleeding disorders?
What are the genetic and environmental factors that predispose people to immune thrombocytopenic purpura (ITP)?
What is the best way to prevent or treat bleeds in people with bleeding disorders who have developed an inhibitor?
In people with haemophilia, what is the best way to tell the difference between pain from acute bleeds, non-bleeding muscle/ligament injury and long term joint damage?

Contents

Thank you

This Priority Setting Partnership would not have been possible without the patients, carers, healthcare professionals, organisations and patient groups who disseminated and participated in the survey, prioritisation and workshop. Thank you for your time and participation.

The study group would particularly like to thank their JLA Advisor Sheela Upadhyaya, JLA for independently facilitating the partnership and steering them so ably through the process and controlling their inclinations to stray from the task. Thanks also to the JLA Advisors, Toto Gronlund and Maryrose Tarpey who supported the final workshop and Marta Szczot for co-ordinating the project, all the organisation work and for keeping everyone in touch.

We have also been greatly helped by Bertie Bosredon who built the web pages and the surveys and Patrick Gallagher and the staff at CitySprint who designed and printed the flyers, posters and paper questionnaires.

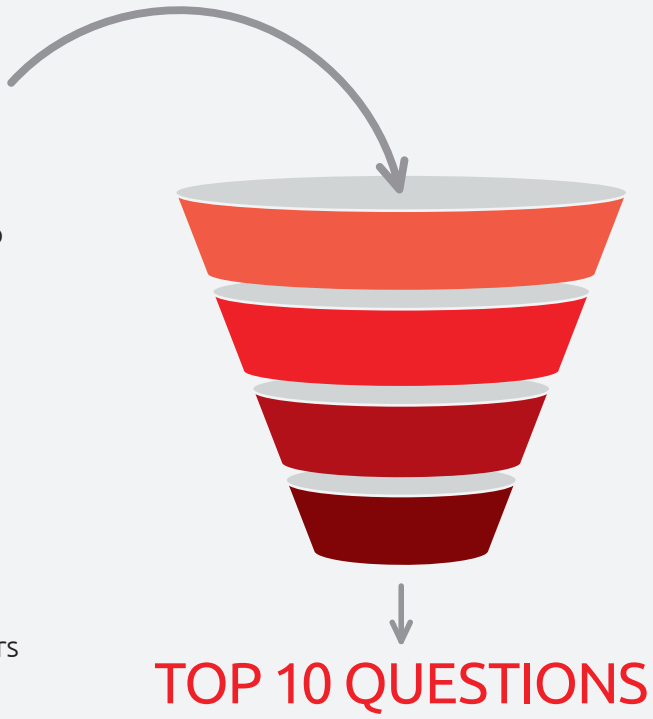
The bulk of the costs incurred in seeing this project through were met by the UKHCDO, but we are also grateful for unrestricted grants from Pfizer, Bayer AG, CSL-Behring and Novonordisk which enabled us to support attendance at the workshops.

Photographs from the workshop are reproduced with the kind permission of all participants.

The PSP study group

November 2018

1. 2 years in the making
2. A partnership program with the James Lind Alliance to setup a Priority Setting Committee coordinated by Sheela Upadhyaya
3. Following an initiative from the UK Haemophilia's doctors association led by Prof. Mike Laffan to setup a clinical study group about all bleeding disorders.
4. Adding in a group of patients, carers and health professionals to form a Steering Group
5. Producing a survey completed by a broad range of patients and healthcare professionals, generating more than 500 questions
6. Interim survey reducing the 500 questions to 66
7. Reviewing, discussing and then prioritising the top 10 unanswered questions to improve the diagnosis, treatment and care of people with bleeding disorders









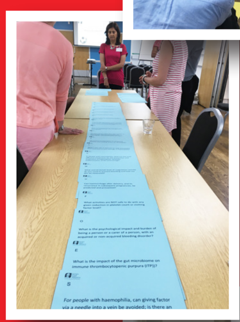

Workshop photos















Foreword

It has been an absolute pleasure bringing the patient and carer voice to the PSP bleeding disorders steering group. As the only UK wide charity for people with inherited bleeding disorders, we hear from many of our members about the significant challenges they face on a day-to-day basis, whether it is coming to terms with diagnosis or dealing with the physical and psychosocial impact of bleeding.

The patient and carer members brought a unique perspective to the group, both complementing the clinical expertise and ensuring the voice of those with lived-experience of an inherited bleeding disorder were integral to the process. Without their input, the result would not have been so comprehensive and meaningful.

One of the most interesting aspects of the PSP was learning about the difficulties other cohorts face from complications of bleeding, whether that be an acquired bleeding disorder or traumatic bleeding from childbirth or after surgery. It was fascinating to see that despite some differences, the patient and carer members aligned on many issues, and were open-minded about the range of conditions being represented to agree on the research priorities.

We are so pleased to have a top ten list of questions that as a group, we strongly believe and encourage should be answered by research, and hope this will lead to important advances for all our communities.

Liz Carroll
Chief Executive, The Haemophilia Society

I have very much appreciated being able to participate in the James Lind Priority Setting Partnership bleeding disorders steering group. My son suffers with severe haemophilia and so to be afforded a platform on-behalf of him and for the benefit of everyone affected by this condition was something that I and all the members of this group accepted with great care and responsibility.

The group has advocated a top ten list of questions to help further the care and treatment of blood disorders that affect our communities and I strongly support this research.

Over the last 2-years a great deal of time and dedication has been given to this cause and I would like to sincerely thank Professor Mike Laffan for leading this initiative along with all my fellow patient and carer colleagues.

Patrick Gallagher
CEO, CitySprint Group

"The PSP has been a wonderful opportunity to give patients a say in the direction of future research into bleeding disorders. As a sufferer of severe Haemophilia A, I have greatly appreciated having the chance to advocate for patient led research and I have felt heard throughout this process.

To all who completed our surveys, we are greatly indebted; it is the unknown multitude of completed surveys that made this project possible and have given our results clout. In addition, I would like to acknowledge the medical professionals in our group who have so enthusiastically invited patients into this process; in particular Professor Mike Laffan.

It is my hope that through dissemination of our findings, our research colleagues will be better able to ameliorate suffering and transform care of bleeding disorders in the 21st century."

William McKeown
Haemophilia NI Secretary

"Major blood loss in labour can have long term consequences for women's health and for some it can negatively affect their mental health. The project's involvement of user representatives and health professional stakeholders has helped to highlight the ongoing importance of studying causes and preventative measures of postpartum haemorrhage and bleeding disorders.

My personal experience of major blood loss after birth as a user representative and my experiences as a midwife were taken into account during the formation of the questions. The service user aspect of this project was well-balanced and inclusive. A very rewarding process."

Amanda Waterman

I was first diagnosed with ITP 25 years ago. When asked if I would join the PSP into bleeding disorders, I was more than delighted to accept this not to be missed opportunity to represent ITP patients.

As vice chair of the trustees of the ITP Support Association, I am extremely aware of the varying needs of patients and their concerns with regard to treatment, medications and above all their quality of life. Living with this rare bleeding disorder for many patients can be extremely difficult and cause anxiety and, in some cases, despair and depression.

The first meeting of the steering group emphasised the dedication of the medical professionals also invited to participate not to mention the breadth of their knowledge and experience. More importantly, they were eager to know the patients views and what was important to them.

Two years involvement was not only very interesting, informative and at times, intensive, but highlighted the common problems encountered by both ITP patients and haemophiliacs alike and probably many other bleeding disorders. This fact has been highlighted in the 10 questions eventually chosen at the final workshop. I feel sure I speak for all our patients saying we are hopeful the questions will be of sufficient interest to research organisations to commence research projects and find answers for this rare condition."

Derek Elston

Helping to organise and run the Bleeding disorders has been a great experience and a privilege. The successful conclusion endorses our decision to choose this as the first project for the clinical studies group originally set up by the UKHCDO.

I am certain that it has broadened the outlook of all the members and generated a genuinely useful set of questions that will help achieve our goal of promoting useful research in this area. I'd like to thank all the members of the group for the help and support and personally thank our coordinator Sheela Upadhyaya without whom we would not have been able to do this.

Prof Mike Laffan

The intention of the UKHCDO when it decided to set up a Clinical Studies group was that it should be a forum promoting and facilitating research into bleeding disorders. It was also intended that the group should include all bleeding disorders in its remit and not restrict itself to hereditary forms.

At that time, we were not aware of the JLA and its role in promoting research. However, I am delighted that the CSG have discovered the JLA and collaborated with it in carrying out this priority setting partnership which fits very well with all our original goals. I look forward to helping the CSG pursue the answers to the very important questions they have identified and cooperating further with the other participating groups to improve care for all those with bleeding disorders.

Dr Ri Liesner
Chair UKHCDO

Introduction and background

The James Lind Alliance (JLA) is a non-profit making initiative, established in 2004. It brings patients, carers and clinicians together in Priority Setting Partnerships (PSPs). These partnerships identify and prioritise uncertainties, or 'unanswered questions', about the effects of treatments that they agree are the most important. The aim of this is to help ensure that those who fund health research are aware of what really matters to both patients and clinicians. The National Institute for Health Research (NIHR – www.nihr.ac.uk) hosts the JLA to oversee the processes for priority setting partnerships, based at the NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC), University of Southampton.

The Bleeding Disorders Priority Setting Partnership (PSP) came together following an initiative from the United Kingdom Haemophilia Doctors Organisation (UKHCDO) to set up a clinical studies group for bleeding disorders. The aim of the group was to promote research into bleeding disorders in general and not restrict itself to haemophilia and related inherited bleeding disorders. When it first met, the clinical studies group recognised that an important first step would be the formation of a PSP with the James Lind Alliance.

The aim of the PSP was to ask patients, carers and health professionals to identify and then prioritise the unanswered questions that concern them most about the diagnosis, treatment and care of people with bleeding disorders.

The Steering Group

Steering Group members were identified to oversee the PSP's process while representing the perspectives and interests of patients with bleeding disorders, carers and healthcare professionals. They approved the aims and objectives of the process, tested and ensured written materials were accessible to a range of audiences. They provided expert opinions on data analysis and evidence checking.

The Steering Group members were:

Charlotte Camp, HCD Economics

Liz Carroll, Chief Executive of the Haemophilia Society

Professor Peter Collins, Consultant Haematologist, University Hospital of South Wales

Derek Elston, Patient representative, ITP Support Association

Patrick Gallagher, Patient representative

Dr Kate Khair, Clinical Academic, Centre for Outcomes and Experience Research in Children's Health, Illness and Disability (ORCHID), Great Ormond Street Hospital and Chair of UK Haemophilia Nurses Association

Professor Mike Laffan, Consultant Haematologist, Imperial College London

Dr William McKeown, Patient representative

Jamie O'Hara, HCD Economics/ University of Chester

Dr Susie Shapiro, Consultant Haematologist, Oxford University Hospitals NHS Foundation Trust

Dr Simon Stanworth, Consultant Haematologist for NHS Blood Transfusion Service, Oxford University Hospitals NHS Foundation Trust

Dr David Stephensen, Physiotherapist, Kent Haemophilia Centre, East Kent Hospital University NHS Trust, Haemophilia Centre, Royal London Hospital, Bart's Health NHS Trust

Sheela Upadhyaya, JLA Adviser

Amanda Waterman, Patient representative

Laurence Woollard, Patient representative- On The Pulse Consultancy

The group was chaired by Sheela Upadhyaya from the JLA and with medical leadership from Professor Mike Laffan.

More information about members of the Steering Group, and the PSP protocol, can be found at **www.jla.nihr.ac.uk**

The process

Getting started

After Prof Mike Laffan was asked by the UKHCDO to set up a Clinical Studies Group (CSG) a group of doctors, health care professionals and patients and carers was assembled. The aim of the CSG was to promote and facilitate research into bleeding disorders and in particular to draw the attention of the NIHR to this area. The CSG met twice in 2015 during which time Tom Kenny from NIHR introduced the group to the James Lind Alliance (JLA). After some discussion the CSG agreed that forming a Priority Setting Partnership with the help of the JLA would be an excellent way begin setting out to achieve its aims.

A proposal to the JLA was drawn up and submitted. The JLA responded by putting the group in touch with one of its facilitators, Sheela Upadhyaya who agreed to take on this project. With her advice, a smaller group, a subset of the CSG, was brought together to form the PSP study group and begin the process of identifying the top 10 questions for research into bleeding disorders.

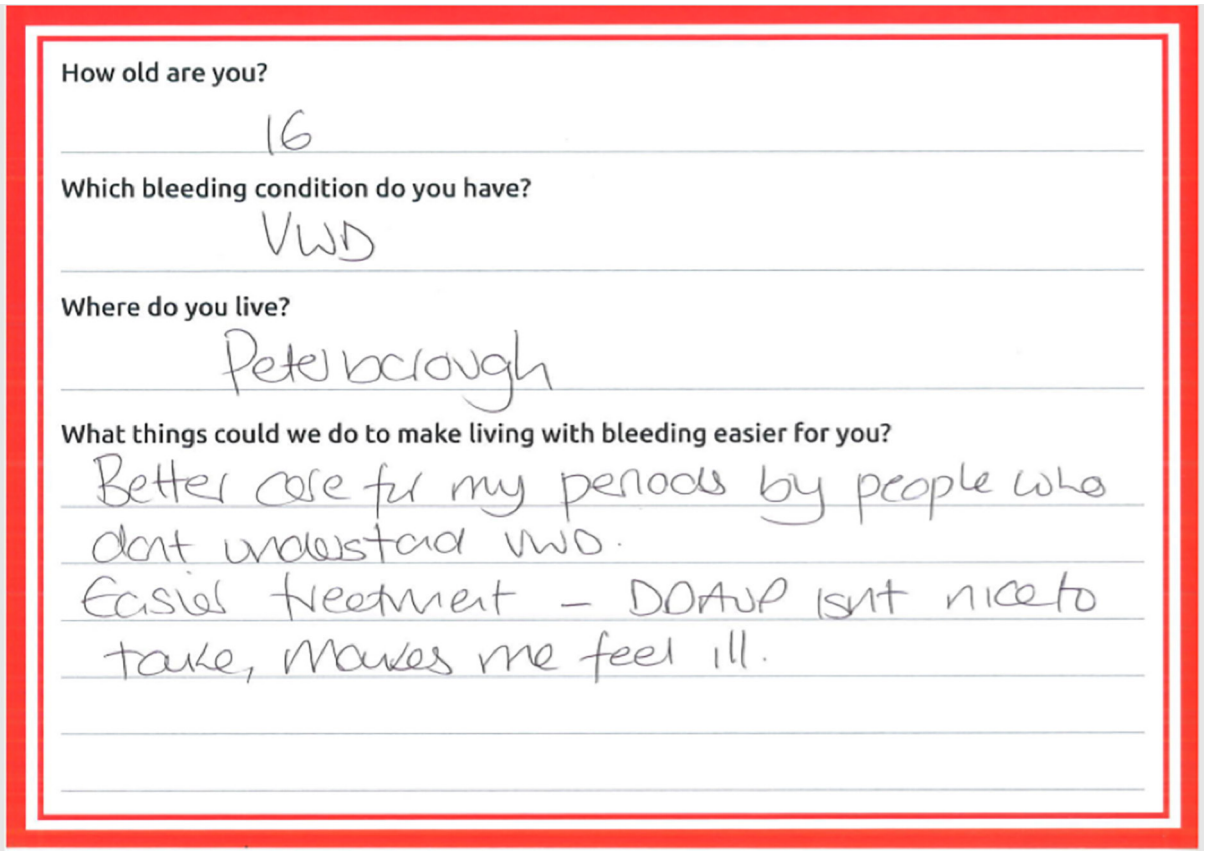
Setting up and the first survey

One of the key principles of the PSP process is that the questions should come from a broad range of patients and health care professionals. The PSP already represented this principle but to generate the questions it was necessary to engage with a much larger number of people. A professional web designer, Bertie Bosredon, was commissioned to produce a website incorporating the information surrounding the PSP, the composition of the steering group, and giving access to the online surveys. The PSP then designed the questionnaires which were used to gather opinions and questions from the community. Reviewing the results of other PSPs and their literature was very helpful in designing the website and survey specific to people with inherited and acquired bleeding disorders. The questionnaire was then trialled amongst colleagues before going live.

A logo was chosen and 'Stop The Bleeding UK' was adopted as the name for the website and twitter handle (@StopbleedingUK). The survey was advertised as widely as possible using all available routes. This included patient group and professional group mailing lists as well as personal contacts. Laurence Woollard took the lead in promoting this project through social media. It was recognised not all would have access to the internet and paper questionnaires were prepared and available from support associations and in clinics.

The PSP defined the scope of the survey which would include questions relevant to patients with inherited or acquired bleeding disorders within the UK. The PSP scope included children from 8 years and above and so the PSP steering group discussed how to engage this group. With the benefit of having a paediatric nurse specialist nurse on the group it was agreed to develop printed postcards. These postcards (for children less than 16 years old) were distributed to clinics which treated children with inherited bleeding disorders and/or ITP. The postcards were also used at summer camps seeking children's and young people's views of areas that they thought were important for future care and research.

The initial survey was open between April and September 2017. This survey simply asked people to submit the questions that they would like answered by research.



How old are you?

16

Which bleeding condition do you have?

VWD

Where do you live?

Peterborough

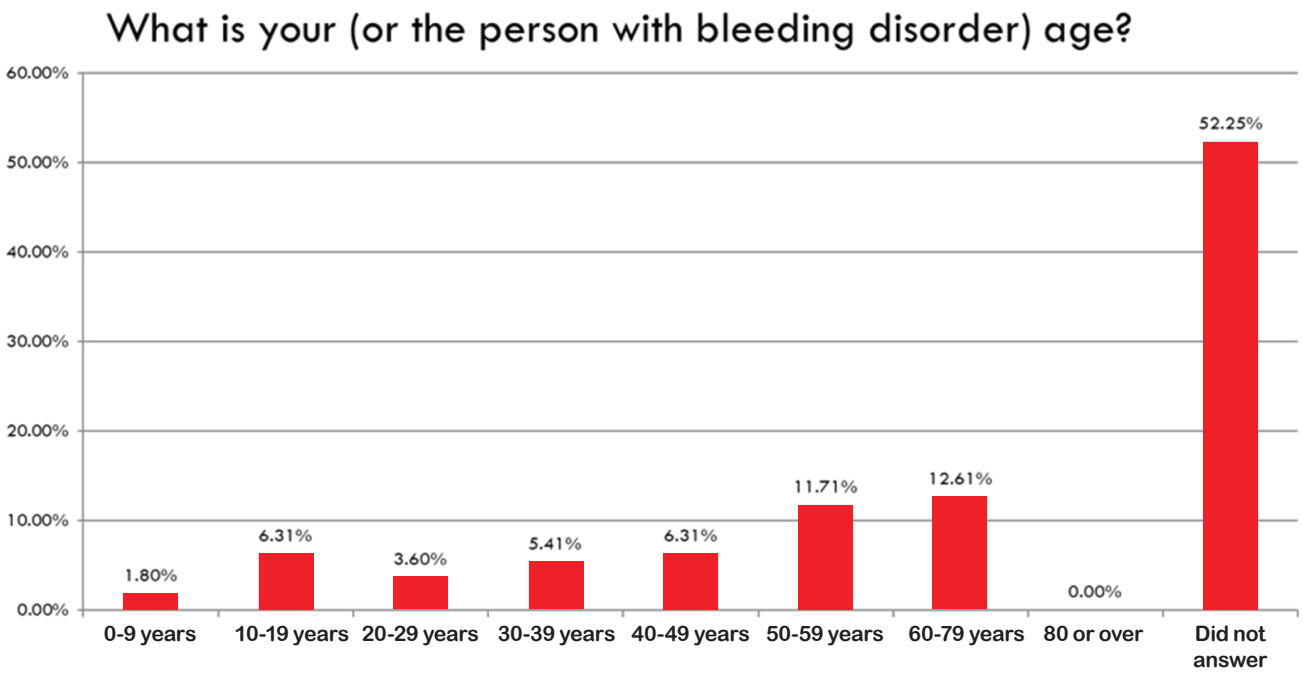
What things could we do to make living with bleeding easier for you?

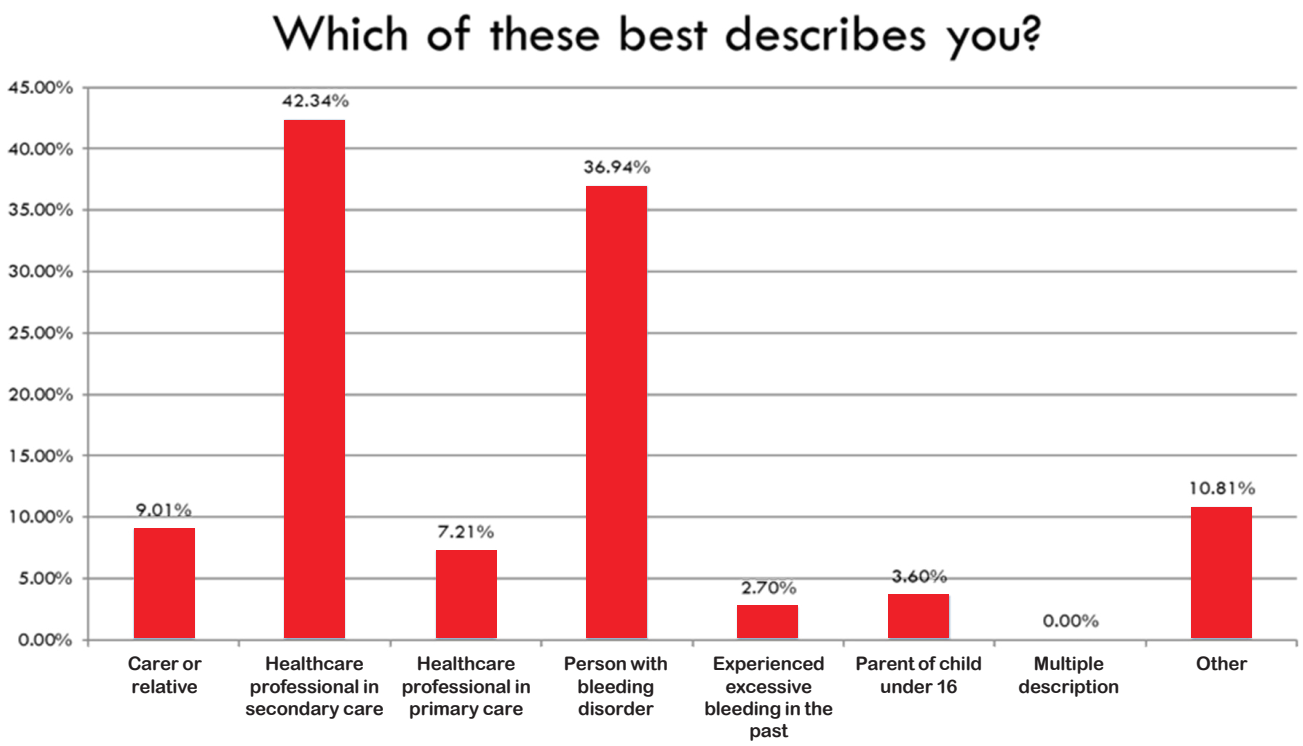
Better care for my periods by people who dont understand VWD.
Easier treatment - DDAVP isn't nice to take, makes me feel ill.

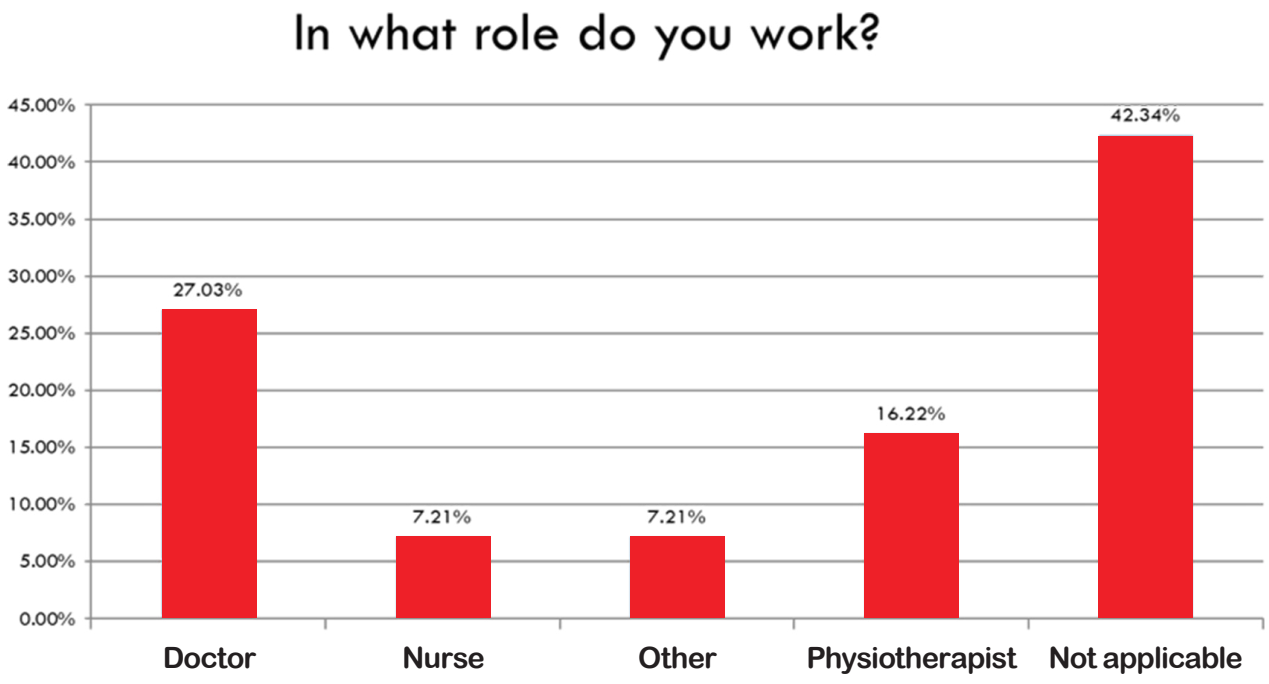
Figure 1.Example of children's survey

A total of 213 initial surveys were returned comprising nearly 500 questions. Approximately one-third of respondents (n=68; 32%) identified themselves as a healthcare professional; the same number (n=68; 32%) described themselves as someone who had experienced excessive bleeding in the past, or who was currently diagnosed with a bleeding disorder. The remaining respondents (n=77; 36%) were relatives or carers of someone with a bleeding disorder, representatives of organisations supporting patients with bleeding disorders, or a combination of the above.

During the course of this survey the characteristics of the respondents was regularly monitored to ensure that it was representative of all the relevant groups and a wide age and geographic range. Some of these characteristics are shown in the Tables below. They are unfortunately not complete because many people chose not to report their personal details.


What is your (or the person with bleeding disorder) age?
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
1.80%
6.31%
3.60%
5.41%
6.31%
11.71%
12.61%
0.00%
52.25%
0-9 years
10-19 years
20-29 years
30-39 years
40-49 years
50-59 years
60-79 years
80 or over
Did not answer


Which of these best describes you?
45.00%
40.00%
35.00%
30.00%
25.00%
20.00%
15.00%
10.00%
5.00%
0.00%
9.01%
42.34%
7.21%
36.94%
2.70%
3.60%
0.00%
10.81%
Carer or relative
Healthcare professional in secondary care
Healthcare professional in primary care
Person with bleeding disorder
Experienced excessive bleeding in the past
Parent of child under 16
Multiple description
Other


In what role do you work?
45.00%
40.00%
35.00%
30.00%
25.00%
20.00%
15.00%
10.00%
5.00%
0.00%
27.03%
7.21%
7.21%
16.22%
42.34%
Doctor
Nurse
Other
Physiotherapist
Not applicable


Where do you live?
70.00%
60.00%
50.00%
40.00%
30.00%
20.00%
10.00%
0.00%
27.03%
0.00%
0.90%
0.00%
7.21%
64.86%
England
Northern Ireland
Scotland
Wales
Outside UK
Did not answer

Defining the questions

After the closure of the first survey, all the questions returned by contributors were sorted and categorised. Out of scope questions such as those asking for information were removed. A total of 478 questions remained. Some of these questions were asked repeatedly by many people, but in slightly different ways. Similar questions were grouped together and an overarching question was written which summarised all the questions in that group. A small number of questions were only asked once. These were added to a long list with all the summary questions. We then checked the published evidence from research that has been carried out in the past, and removed the questions that previous research had already answered. At the end of this stage, we had 66 unanswered questions (see Appendix B). These questions then went forward to the second, prioritisation, survey.

The second survey

For the prioritisation survey the 66 questions were placed on the website and an invitation distributed to all those who had participated in the first survey and those who had expressed a wish to be involved in the second as well as via the same networks. In this survey, participants were asked to list in order, their choice of the 10 most important questions. The PSP considered whether the ranking scores should be separated in some way, such as into acquired and inherited disorders in order that they could be weighted according to the number of participants. However it was decided that this was not possible because in each case some people would want to vote in more than one division. The second survey was therefore left open for everyone to choose from all 66 questions and all votes were treated equally.

Between May and June 2018, 111 people took part in the prioritisation survey. Approximately half of respondents (n=55; 49%) identified themselves as a healthcare professional; slightly less (n=44; 40%) described themselves as someone who had experienced excessive bleeding in the past, or who was currently diagnosed with a bleeding disorder. The remaining respondents (n=12; 10%) were relatives or carers of someone with a bleeding disorder, representatives of organisations supporting patients with bleeding disorders, or a combination of the above.

The score for this survey were calculated as follows.

- **Points for the healthcare professionals and the patient/carer responses were counted separately to take account of different numbers in the two groups and to identify areas of agreement.**
- **Each question was then given a score according to their ranking by each participant. Each ranking of 1 scored 10 points, 2 scored 9 points and so on down 1 for each time a question was ranked 10.**
- **The total score for each question was calculated and the questions ranked in each group from 1-66**
- **The agreed target for the final workshop was approximately 25 questions and so the top 12 were taken from each group.**
- **We then identified two questions which scored moderately highly in both groups and whose combined score merited inclusion in the final workshop. These two similar questions were merged making a total of 25 questions.**
- **The final list was agreed at a meeting of the PSP.**

The ranking and raw scores were presented to the steering group. The steering group then agreed to take the top 25 questions to the final workshop. They were assured that all types of bleeding disorders were represented in the 25 questions and therefore the top 25 were appropriate.

25 Questions for the final workshop

The top 25 research questions which have been identified are:

A	In people with haemophilia, what is the best way to tell the difference between pain from acute bleeds, non-bleeding muscle/ligament injury and long term joint damage?
B	Can a home testing device to record low platelets and clotting factors be developed?
C	What is the relationship between immune thrombocytopenic purpura (ITP) and fatigue?
D	What is the role of exercise for both prevention and treatment of joint damage in haemophilia?
E	What is the impact of the gut microbiome on immune thrombocytopenic purpura (ITP)?
F	What activities are NOT safe to do with any given reduction in platelet count or clotting factor level?
G	How can we balance the risk and benefit of antithrombotic (blood thinning) treatment for cardiovascular disease (including heart attacks and strokes) in patients with bleeding disorders?
H	In people with haemophilia, what are the most effective treatments for the prevention and treatment of haemophilic synovitis (inflammation of the joint lining)?
I	What causes the onset of immune thrombocytopenic purpura (ITP)?
J	Is there an effective substitute for steroids in the treatment of immune thrombocytopenic purpura (ITP)?
K	When is treatment for immune thrombocytopenic purpura (ITP) required?
L	What are the benefits of psychological and psychosocial strategies for support of individuals or families affected by bleeding disorders?
M	What is the best haematological approach to management of severe haemorrhage after delivery?
N	What causes exacerbations of immune thrombocytopenic purpura (ITP)?
O	What is the psychological impact and burden of being a person or a carer of a person, with an acquired or non-acquired bleeding disorder?
P	What are the genetic and environmental factors that predispose people to immune thrombocytopenic purpura (ITP)?
Q	What is the best way to prevent or treat bleeds in people with bleeding disorders who have developed an inhibitor?
R	How can immediate (at the bedside/in the clinic) ultrasound help with management of haemophilia?

S	For people with haemophilia, can giving factor via a needle into a vein be avoided; is there an alternative to intravenous administration of factors?
T	Are there factors other than "the number of joint bleeds" that are associated with haemophilic arthropathy (joint damage)?
U	Can haemorrhage after delivery, and its recurrence in subsequent pregnancies, be predicted and prevented?
V	What are the most effective treatments for acute and chronic pain in people with haemophilia?
W	What overall (total) level of coagulation activity do you need to prevent bleeding and how can this be measured?
X	How should heavy periods be managed in women with bleeding disorders?
Y	What is the role and cost effectiveness of blood clotting tests that give immediate results at the bedside (point of care) in managing medical, surgical or obstetric haemorrhage?

The priority setting workshop

The final stage of the PSP was held in London on Saturday 7th July 2018. The aim of the final workshop was to choose the top 10 priorities from the shortlist of 25 questions. The majority of the 29 people attending this final workshop had not been members of the PSP and so gave an independent view of the questions. They comprised those with different bleeding disorders, carers and health professionals (surgeons; anaesthetists; nurses; carers and academics) and some who had taken part in both the surveys. They were recruited through the Steering Group members' networks, via patient and clinician groups and through social media.

The workshop was facilitated by Sheela Upadhyaya from the JLA assisted by two further JLA facilitators, Toto Gronlund and Maryrose Tarpey and coordinated by Marta Szczot. The participants were divided into three groups and asked to consider the order in which the 25 questions should be prioritised within a given time limit. This allowed the groups to discuss and debate the merits of one question over another along with sharing personal experiences and perspectives. The outcome of the morning sessions were then captured and an aggregate ranking presented to the group after lunch.

In order to share opinions across the group as a whole the composition of the three groups was then rearranged and the new groups provided with the aggregate ranked questions to debate. This allowed the groups to explore where there were differences and synergies across all three groups. The three groups discussed the ranked questions and made some alterations to the ranked questions These ranked scores were then added together and presented back to the whole group to agree the final ranking. The top 6 questions from each working group were found to be the same. The whole group then discussed which questions should be in the remaining four places until there was consensus.

Whilst individual's initial priorities were obviously informed by their own experience, by coming to the workshop and taking part in a number of small group discussions, everyone got to hear other people's views on which questions were most and least important to them. This helped the group understand what motivations each person had, which supported the group as a whole to reach an agreement on the questions that should be a priority. This was in line with the broader aims of the JLA: namely, to build consensus and shared understanding between lots of very different groups with a shared interest in research.

The final agreed list of top 10 questions is given below.

The Top 10 Questions

	Top 10 questions	Why is it important to answer this question
1	**What is the role and cost effectiveness of blood clotting tests that give immediate results at the bedside (point of care) in managing medical, surgical or obstetric haemorrhage?**	If a patient is bleeding then blood clotting tests are used to help manage patients and guide transfusion of blood products. Standardly blood samples are taken and tested in a laboratory. It can take 1-2 hours for the results of these tests to be available to the doctors. Different tests are now available which allow blood to be tested by clinicians next to the patient, allowing a result in about 40 minutes. The tests are different, and the role and effectiveness of the bedside tests compared to traditional tests in managing these patients is not known.
2	**How can we balance the risk and benefit of antithrombotic (blood thinning) treatment for cardiovascular disease (including heart attacks and strokes) in patients with bleeding disorders?**	Patients with bleeding orders are not protected from development of arterial disease and atrial fibrillation which usually require anticoagulation or antiplatelet therapy. These therapies incur an increased risk of bleeding which will be more marked in patients with bleeding disorders. It is therefore very important to find the right balance between protecting patients from heart attacks and stroke and inducing a risk of bleeding which might also be fatal.
3	**What is the best haematological approach to management of severe haemorrhage after delivery?**	Postpartum haemorrhage (PPH) or major obstetric haemorrhage (MOH) is bleeding that occurs either immediately after birth or within 6 weeks. There are a number of causes of bleeding that health professionals need to be aware of including atony (uterine tone), tears in the perineum, clotting issues and tissue ie placenta. With an occurrence of 0.78/100,000 postpartum haemorrhage is the 2nd leading cause of death in maternity and has remained at this rate for previous years and this is why it is vital more research and resources are invested in identifying and treating haemorrhages sooner. The MBBRACE (Mother and babies: Reducing risks through Audits and Confidential enquiries across UK) 'Saving Lives, Improving Mothers' Care' report with data from 2014-2016 showed that for 28% of the women who died, an improvement in care may have changed the outcomes. Working with the Team in the PSP project allowed the questions that affect people with both acute and chronic bleeding disorders to be considered and recognised. Hopefully more research will be funded to understand the causes and better treatments of PPH and prevent further maternal losses.
4	**How should heavy periods be managed in women with bleeding disorders?**	As well as causing significant blood loss, sufficient to cause anaemia, heavy menstrual bleeding can be a significant barrier to normal activity and have a negative impact of quality of life for women. The problem is not always explained entirely by the bleeding disorder and therefore requires close collaboration with a gynaecologist to find the most effective and satisfactory approach for individual women. This may well be a combination of haemostatic and hormonal or even surgical methods.

	Top 10 questions	Why is it important to answer this question
5	What is the relationship between immune thrombocytopenic purpura (ITP) and fatigue?	Fatigue is a most common complaint made by patients with ITP. The degree of fatigue varies from patient to patient and in severe cases can be extremely debilitating and can lead to the patients being unable to hold down employment. There have been many investigations to determine if fatigue is a side effect of ITP, all of which have proved positive. However, there has been no research into what causes fatigue in patients with ITP and the relationship to a reduction of platelets in the blood either due to low platelet production; platelet destruction or the effect of other organs within the body.
6	What are the most effective treatments for acute and chronic pain in people with haemophilia?	People with haemophilia experience pain on many occasions in their life. This can be from injecting their treatment, having a joint bleed or when a joint has had many bleeds, and a painful arthritis develops. The pain from this arthritis is there every day and can stay for many years – this is called chronic pain. Due to lack of treatment in their youth, many adults with severe haemophilia have chronically painful, multi-joint pain in the elbows, knees and ankles. Often people find it painful to do even day to day things like walk or go to work. In studies where people with haemophilia have been asked if they have chronic pain, 50% say that they do. Between 35-50% report that current treatments they have tried for chronic musculoskeletal pain are not very effective and this has significant debilitating personal and healthcare resource impacts.
7	What are the benefits of psychological and psychosocial strategies for support of individuals or families affected by bleeding disorders?	Although therapeutic strategies for bleeding disorders can be very effective they are not available for all patients. Moreover, even effective strategies can be difficult to accommodate and require limitations of activity and lifestyle. These factors can impact the life of the individual and their family, as can knowledge that the disorder is inherited. It is important to know whether psychological and psychosocial therapy can ameliorate these effects.
8	What are the genetic and environmental factors that predispose people to immune thrombocytopenic purpura (ITP)?	The advances in genetic medicine in recent years has led to questions being asked in respect of most conditions. ITP is no different and the question has often been asked "is ITP caused by a genetic defect which is hereditary or due to a genetic defect at birth. Similarly, are there external environmental factors which may have an adverse effect on the body's genetics or organs ? " There has been very little research undertaken into ITP being connected with either a genetic defect or external factors other than viral infections as being the possible cause of ITP. It is thought more consideration should be given into research into defective genetic structures within ITP patients and the effects of external factors such as pollution and viral transmission within the environment.
9	What is the best way to prevent or treat bleeds in people with bleeding disorders who have developed an inhibitor?	At present we have a small number of agents available to treat bleeding episodes in patients with inhibitors. However none of them is reliably effective and excessive use runs the risk of inducing thrombosis. New approaches to haemophilia treatment may be able to reduce bleeding in these patients but again are not completely effective, are designed for prophylaxis rather than acute bleeding and may interact dangerously with existing bypass therapies. All of which makes it important to determine the optimum doses and combinations to maximise benefit and minimise risk.
10	In people with haemophilia, what is the best way to tell the difference between pain from acute bleeds, non-bleeding muscle/ligament injury and long term joint damage?	Joint bleeding is the main characteristic of haemophilia. When a joint bleeds it is very painful as well as becoming swollen and difficult to move. When a joint has had many bleeds, arthritis develops and this can cause disabling joint pain, stiffness and reduced mobility. Overuse of an arthritic joint or injury may cause inflammation of the joint, together with pain and limited movement; symptoms that are similar to that of a joint bleed. To offer appropriate treatment and, in turn, regain optimal functional ability, accurate diagnosis of bleeding and non-bleeding episodes is essential. Currently, the diagnosis of joint bleeding and non-bleeding episodes is made empirically by patients who treat themselves at home. However, the overlap in clinical symptoms between acute bleeds, non-bleeding muscle/ligament injury and long term joint damage joint arthritis make it challenging to differentiate between the conditions.

The 15 questions (from the original 25 discussed at the workshop) that did not make the final Top 10 are listed in Appendix A.

Out of scope questions

The remit of JLA was to identify and prioritise unanswered questions about the effects of treatments and interventions (including for diagnosis and care) which is how the scope and aim of the Bleeding Disorders PSP was defined. From the survey, however, a number of questions arose which were outside the scope this PSP, but which were never the less of clear importance to people with bleeding disorders, their families and healthcare professionals. These questions were recorded during the data analysis and are listed at Appendix B. There is commitment from the organisations represented on the Bleeding Disorder PSP Steering Group to review and consider how to make use of these questions. Other organisations and groups working with people with bleeding disorders are encouraged to take note of the out-of-scope questions and consider their relevance for bleeding disorders campaigning and awareness-raising activities.

Next steps

The Top 10 unanswered questions identified by this PSP were presented to the UKHCDO on 14th November 2018. This report and the Bleeding disorders top 10 questions will be placed on the JLA website. The JLA will work with Steering Group members and the NIHR to promote the questions to researchers and research funders. The Steering Group members will continue to promote the top 10 questions to researchers and research funders. The UKHDCO will work with the NIHR and other relevant funders to assess their suitability for its research programs.

What can you do to help?

People with bleeding disorders, their families and health professionals have taken time to tell the PSP what questions they want to see answered by research. The more people who know about the Bleeding Disorder research priorities, the more likely organisations and individual researchers are to tackle the questions that patients, carers and health professionals have told us they want answered. Please help to spread the word about what needs to happen.

Appendix A

Other questions discussed at the final workshop

Can a home testing device to record low platelets and clotting factors be developed?
What is the role of exercise for both prevention and treatment of joint damage in haemophilia?
What is the impact of the gut microbiome on immune thrombocytopenic purpura (ITP))?
What activities are NOT safe to do with any given reduction in platelet count or clotting factor level?
In people with haemophilia, what are the most effective treatments for the prevention and treatment of haemophilic synovitis (inflammation of the joint lining)?
What causes the onset of immune thrombocytopenic purpura (ITP))?
Is there an effective substitute for steroids in the treatment of immune thrombocytopenic purpura (ITP)?
When is treatment for immune thrombocytopenic purpura (ITP) required?
What causes exacerbations of immune thrombocytopenic purpura (ITP)?
What is the psychological impact and burden of being a person or a carer of a person, with an acquired or non-acquired bleeding disorder?
How can immediate (at the bedside/in the clinic) ultrasound help with management of haemophilia?
For people with haemophilia, can giving factor via a needle into a vein be avoided; is there an alternative to intravenous administration of factors?
Are there factors other than “the number of joint bleeds” that are associated with haemophilic arthropathy (joint damage)?
Can haemorrhage after delivery, and its recurrence in subsequent pregnancies, be predicted and prevented?
What overall (total) level of coagulation activity do you need to prevent bleeding and how can this be measured?

Appendix B

Similar questions grouped by topic

Table A
Can intravenous administration of factor be avoided Is there an alternative to the intravenous route for administration of factors?
What devices or training could be given to help locate veins in people with bleeding disorder to make blood tests and factor administration easier; without the need for Ports or indwelling access devices?
Table B
What activities are safe to do with any given reduction in platelet count?
What is the role of exercise for both prevention and treatment of joint damage? Some evidence?
What is the role of point- of- care ultrasound in the management of haemophilia?
In people with haemophilia, what are the most effective ways to differentiate between pain from acute bleeds, non-bleeding musculoskeletal injury and chronic arthropathy?
What is the 'optimal' prophylactic replacement regimen or the optimal trough level for people with haemophilia or severe VWD?
Table C
What factors are responsible for inhibitor development and how can inhibitors be prevented?
What is the best treatment to eradicate an inhibitor?
What is the best way to treat bleeds in people with inhibitors?
Table D
What is the relationship between dietary supplements, vitamins, minerals and bleeding?
What is the impact of the gut microbiome on ITP?
Table E
What is the relationship between ITP and fatigue?
Table F
What is the psychological impact and burden of being a person or a carer of a person, with an acquired or non-acquired bleeding disorder?
What are the benefits of psychological and psychosocial strategies for support of individuals or families affected by bleeding disorders?

Table G
Is there an effective substitute for steroids in the treatment of ITP?
What factors determine the need for treatment in ITP?
When should splenectomy be performed for ITP?
Table H
What factors can guide thromboprophylaxis post-partum in patients with bleeding disorders?
Can PPH, and its recurrence in subsequent pregnancies, be predicted and prevented?
What is the best approach to management of severe PPH?
Does PPH have an impact on post-natal depression, bonding with a baby, breastfeeding and post-traumatic stress, and if so what is the best intervention to mitigate this?
What is the best treatment for acquired haemophilia A and how likely is it to recur in subsequent pregnancies?
How we can improve early recognition of PPH?
Table I
What causes initial presentation of ITP (What causes the onset of ITP?)
What causes exacerbations of ITP?
What are the genetic and environmental factors that predispose people to ITP?
Table J
Can a home testing device to record low platelets and coagulation factors be developed?
What is the best diagnostic test to predict bleeding in an individual with an inherited bleeding disorder?
What is the best diagnostic test to monitor therapy in an individual with an inherited bleeding disorder?
What is the best diagnostic test to predict bleeding in an individual with an acquired bleeding disorder?
What is the best diagnostic test to monitor therapy in an individual with an acquired bleeding disorder?
What is the correlation between coagulation factor levels and bleeding ?
What level of coagulation do you need to prevent bleeding and how can this be measured?
Why do some patients with similar clotting factor levels have different bleeding severities – both within the same family and between families?

Table L
What is the role and cost effectiveness of point of care tests of coagulation in medical or surgical haemorrhage?
What is the role and cost effectiveness of point of care tests of coagulation in obstetric haemorrhage?
What is the role of point of care tests of coagulation in diagnosing and monitoring inherited bleeding disorders?
Table M
In people with haemophilia, what are the most effective interventions for the prevention and treatment of haemophilic synovitis?
What are the most effective interventions to treat acute and chronic pain in people with haemophilia?
Are there factors other than "the number of joint bleeds" that are associated with haemophilic arthropathy?
In people with bleeding disorders, what is the impact of bruising and how should it be treated?
Table O
How should heavy periods be managed in women with bleeding disorders?
How should gum bleeding be managed in people with bleeding disorders?
Table Q
What is the optimal management and the role of different products (eg FFP, PCC, Fg concentrate, cryoprecipitate) in major haemorrhage, including cardiac surgery, and is this different in children compared to adults?
What treatments are most effective for mucosal bleeding (eg; nose bleeds, mouth bleeds, heavy periods.)?
Does physical activity have an effect on mucosal bleeding?
How should standard half-life and extended half-life products be used for maximum efficacy – can they be used interchangeably?
How should new non-replacement agents to treat haemophilia and gene therapy be used?
What are the roles of tranexamic acid and desmopressin (DDAVP) in bleeding disorders?
Table S
How can we balance the risk and benefits of antithrombotic therapy for cardiovascular disease in patients with inherited and chronic bleeding disorders?
Table T
What is the correlation between factor levels and bleeding in carriers of bleeding disorders?

Table U
Can haemophilia be treated with gene therapy?
What are the genetic causes of inherited bleeding disorders?
What genetic factors contribute to acquired bleeding disorders?
Table K
How should haematuria in patients with severe haemophilia be managed?
Are NSAIDs taken with PPI safe to take if I'm on prophylaxis?
What are the platelet and clotting abnormalities in myeloproliferative neoplasms that underlie bleeding complications in MPN.
In light of the above question is there any difference in boys who are spontaneous mutations and therefore may have had interventions when they were born. I.e. all the interventions we try to avoid such as ventouse forceps etc.
In patients with angiodysplasia and VWD what is the role of antiangiogenic drugs?
Is there a higher incidence of co-morbities in haemophilia sufferers i.e. Rheumatoid arthritis and stress related issues and what effect might these have on the presentation /prognosis
If a women normalises her levels during pregnancy should she be allowed an epidural for labour/delivery?
Is there a link with intracranial haemorrhage and neurological problems such as epilepsy and other conditions such as autism.

Appendix C

The list of out-of-scope questions

NON RESEARCH AND OUT OF SCOPE QUESTIONS TABLE ZK		
Submission ID	**What question(s) about the treatments for bleeding and bleeding disorders would you like to see answered by research?**	
1	ZK	Factor x deficiency awareness and treatment
17	ZK	Has the interferon and ribravarin treatment for contaminated blood related hepatitis c caused neurological deficits?
20	ZK	With regard to support for people with bleeding disorders, is there any research to measure outcomes with regard to distance travelled to A&E in the event of trauma or bleeding episodes?
21	ZK	Is there an optimum time by which an injured individual with a bleeding disorder should be transported to A&E?
40	ZK	I was originally misdiagnosed. It took over 2 weeks for the correct diagnosis. In which time I had 8 days of blood thinners. Which made my bleeding/haematomas worse. How can I help improve the awareness and diagnosis for future cases? Especially as I was told at a later date by a GP that you don't Acquired Haemophilia- thankfully I had a letter headed up with from the hospital on me at the time. Otherwise she wouldn't have believed me (as she was condescending when she informed me you don't acquire it)
42	ZK	I found there was little support for my condition. The brochure I revived in hospital on my condition was useful but all photos were of retired people. I feel I do not fit most bleeding groups - Haemophilia society and women bleeders are for permanent bleeders, rather than temporary bit severe ones. In time a few of us have found each other internationally to support each other and newly diagnosed. The Haemophilia Society have newly diagnosed weekends, but these are aimed at babies/ children and their families. When asked about other conferences e.g. Inhibitors they have told me if is not appropriate for me. When I thought it could be - as all cases require immunosuppressant treatment. Most I had contact with have had a different chemo option to the one I had
45	ZK	Research and trials going forward
324	ZK	Raising awareness of the need for good oral health and prevention of dental disease to avoid invasive treatment.
46	ZK	When will my child aged 3 be eligible for more advanced treatment
50	ZK	What treatments are available to bleeders?
51	ZK	What are the potential side effects, long term and immediate
58	ZK	How children transition to puberty and adulthood
61	ZK	Would like to know why it all happens
63	ZK	Are there anymore treatments that might be about to be available, for e.g. My ITP is Steroid reactive. So the most responsive way is what they call a short sharp shock over a few weeks with prednisone. Due to the side effects with this it would be great to know if there is about to be an effective alternative
70	ZK	I want more awareness for people to acknowledge ITP as a disorder that you cant always see on the surface

71	ZK	I want professionals who listen to their patients and don't simply go by a text book!
72	ZK	Why is there not enough information around about these disorders. Even when you have appointments at the hospital. They need more promotion even on tv.
73	ZK	What causes the disorder
74	ZK	Why are the treatments aimed at treating only symptoms?
75	ZK	Why should standard practice set a precedent for handling cases without due diligence in finding out the true cause?
76	ZK	Why are all immune disorders treated with chemicals and sometimes surgery when nutrition, nervous system and body systems are largely ignored
78	ZK	Fatigue
79	ZK	What medicine has worked best for you?
98	ZK	I know that GPs don't know much about ITP, but surely they should know there are specialist centres.
107	ZK	Why isn't there enough awareness about ITP
109	ZK	What treatments for PPH can be administered outside of a hospital environment?
115	ZK	Why is there hardly any awareness about ITP
116	ZK	How and who can help me raise awareness about ITP
117	ZK	Who would help me set up a fundraiser (all money going towards ITP)
125	ZK	See below
126	ZK	Improving the evidence on transfusion management of acquired bleeding disorders in a non-trauma setting such as cardiac, obstetric, gastro-intestinal bleeding, oral anticoagulant-associated bleeding etc.
135	ZK	Could there be a cure?
138	ZK	Diagnosis
150	ZK	Diagnosis
151	ZK	Causes?
154	ZK	Better awareness amongst GPs and blood clinic professionals of the risks of ITP sufferers and what to do about it. Better awareness of patient concerns (drug side effects) and lifestyle balance (perhaps low platelet count is acceptable to avoid drug side effects). More 'partnership' approach from day one - it's potentially serious, but it didn't have to be made so frightening! After initial diagnosis, we were left fearing that my Mum could die from internal bleeding within minutes and without warning. It was not clear that this risk was tiny and could be minimised with sensible precautions.
158	ZK	How they occur
159	ZK	Whether they are curable
160	ZK	Types of treatments available and side effects associated with said treatments
190	ZK	Why it happens
191	ZK	Why more information isn't available
193	ZK	Diagnosis, treatment of & communication about PPH

197	ZK	According to the site [http://patient.info/doctor/immune-thrombocytopenia-pro] "prognosis is generally benign, even in refractory cases." Patients need clarification and understanding of when ITP is likely to be benign and when it is not, particularly if pt subjectively experiences no observable symptoms such as frequent nose bleeds.
217	ZK	Basics revisited showing the coagulation pathway and sign posting where the pathologies occur and how the solution resolves it
220	ZK	An answer to why it has happened.
221	ZK	How long are the treatments effective for and possible side effects
237	ZK	General long term safety
241	ZK	Why is there not more being done to find a genetic solution to eliminate haemophilia once and for all. It would save the NHS millions each year.
243	ZK	Is there a potential treatment using gene therapy
244	ZK	Period management
245	ZK	What are the side effects of Rituximab, if any, 6 months or longer after treatment.
247	ZK	Can the short term use of Steroids , once stopped, cause light headedness, tiredness,
249	ZK	How do you explain it to younger family members?
250	ZK	Where can I access easy information to inform my work colleagues?
251	ZK	Does treat effect daily life?
252	ZK	ITP
254	ZK	How to diagnose bleeding disorders in women who are carriers of Haemophilia
255	ZK	Options for available emotional support
256	ZK	Effects of treatment long term
270	ZK	I've had very little support for two sons, as to when it's best to take medications, they are both mild and didn't find out they had it until 12 and 7 years. How do I get more support? How do I know if they have a muscle bleed? I don't know the signs? Since diagnosis we haven't had any appointments or information.. How can I teach my sons what to look for and to look after themselves if I don't know how best to help them?
271	ZK	My eldest son (12)on diagnosis was told to stop all sports apart from swimming, he played rugby and football..
272	ZK	My eldest (12) has really struggled with his diagnosis but he's received no support, we've had the initial hospital appointment 2 years ago then nothing, our GP has no experience of haemophilia so has said he can offer no guidance or support. How can I support him when I know so little about it myself and really struggle to find info when slot of it is very conflicting!
273	ZK	School... they totally freak out when anything happens.. How do I get more information into schools so they can understand?
276	ZK	Inhibitors
278	ZK	ITP
279	ZK	More awareness of young women and bleeding
280	ZK	Improve awareness by testing at birth and at medicals.
302	ZK	Support for people with severe joint damage caused by bleeding. Pain relief, and mental support for those with daily pain and coming to terms with disability

303	ZK	NA
305	ZK	Knowledge awareness and Practice of health professionals to stop bleeding
306	ZK	Awareness of the bleeding
307	ZK	Effective Diagnosis
308	ZK	And Effective treatment
310	ZK	Prevention
312	ZK	What are the ideal characteristics for patients for a treatment recording system ?
326	ZK	More understanding for children and more information on Itp in children
331	ZK	Do platelets play any other roles in our bodies other than clot the blood?
333	ZK	Would a register of all ITP patients, including all known (or remembered) previous infections, help research into finding causes and triggers for ITP?
387	ZK	Modelling mild bleeding as a complex genetic trait
398	ZK	Better understanding platelets function disorders
411	ZK	Can Haemophilia be cured?
435	ZK	Support and awareness for patients who have minor blood disorders and how it can potentially be over looked
456	ZK	Would a better understanding of the cause of ITP produce more effective treatments?
459	ZK	The intake of alcohol
460	ZK	What is the best medicine
469	ZK	Being able to do more sport
470	ZK	Better care for my periods by people who don't understand VWD
472	ZK	Less visits to hospital in London, better to go at hospital at home, less bruises I don't like looking at them
475	ZK	Fun things like football, rugby, basketball, boxing
476	ZK	Meeting other people, giving blood, going to more labs
477	ZK	Come here again
2	ZK	Support for factor x deficiency
13	ZK	Being a carrier of haemophilia - reproductive choices now and in the future
23	ZK	Diagnosis
24	ZK	Support
25	ZK	Information
26	ZK	Treatment
31	ZK	Tips for coping with daily prophylaxis / immune tolerance that is ongoing
32	ZK	Better help with using vein. Training and days off

35	ZK	Is Stem Cell Research being trialled to cure Severe Haemophilia A.
123	ZK	Is there a simple means of identifying the cause of a bleeding disorder without the need to access specialist facilities?
143	ZK	Is low dose penicillin still recommended following a splenectomy as a result of ITP?
144	ZK	Is it ok to be taking long term penicillin 36 years after a splenectomy ?
146	ZK	If the NHS were to become privatised, would the cost of treatment be passed on to the patient?
169	ZK	I am teaching my haematologist about ITP, why are regional clinicians not keeping up with current research and data ? **He knew nothing about the ITP association !**
174	ZK	Should the risk of haemorrhage or thrombosis be considered when assessing if pregnant women are allowed to try to progress naturally in labour or should it be discussed regarding risk in the antenatal period?
175	ZK	Does skin to skin contact between mothers and babies immediately after birth reduce the occurrence and severity of post partum haemorrhage?
177	ZK	Is there a root cause for these disorders and could they be spotted and controlled from birth or sooner.
180	ZK	Primary identification of a haemophilia
185	ZK	How can its effects on life be minimised safely.
186	ZK	Why is there not regular screening?
187	ZK	Prevention of bleeding following childbirth
188	ZK	Awareness
195	ZK	What is the impact of severe postpartum haemorrhage on the ability of mothers to successfully breastfeed?
196	ZK	How can women with a severe postpartum haemorrhage be supported to effectively breastfeed their new-born?
198	ZK	Consider various forms of patient education and anticipate questions that educated patients (albeit those without medical training) want to know. For example: **How can patients diagnosed with ITP be proactive about their own health (particularly if they already follow a Mediterranean diet and drink little or no alcohol)?**
211	ZK	Time to obtain cross matched blood from declaration of a massive pph throughout the uk.
212	ZK	What would be the fastest way to improve long term health of people with haemophilia?
216	ZK	Awareness of issue
223	ZK	How can fatigue be best avoided?
228	ZK	How are children with a bleeding disorder supported in schools?
233	ZK	What is the best way to manage episodes of bleeding both in prevention and treatment
257	ZK	Support in injecting at home
258	ZK	Information and sources on available treatment when travelling
287	ZK	Are guidelines about menorrhagia inclusive of testing for a bleeding disorder!
289	ZK	Now clear of HCV is there any boundaries I should be aware of ? Work, family, infection.
290	ZK	Why did family member die of cancer unable to get diagnosis due to fear of any treatment, due to no understanding of vWD and having to wait several months to see haematology specialist.

291	ZK	Why do I always struggle to get any treatment from GP/dentist, and children's vaccines due to the fear of vWD(the Unknown)
292	ZK	Why do diabetics get free prescriptions, but haemophiliacs/von willibrands sufferers don't?
293	ZK	Why so many medical professionals are still unaware that women bleed too?
294	ZK	Why do universities only offer support for bleeders that declare themselves disabled, yet most bleeders cant get disability benefits?
304	ZK	Why is the treatment of inhibitors so limited?
311	ZK	What are the expectations and views of patients with severe bleeding disorders about clinic review appointments ??
313	ZK	What are the levels of knowledge and understanding of GPs and tertiary care professionals about bleeding disorders ?
316	ZK	What is ideal dose and how many doses
318	ZK	Awareness and relationship with dentistry
319	ZK	Patients need to be area that dental treatment is more complex when they have a bleeding disorder - patients, parents and carers need to be area of the benefits of preventing dental disease
320	ZK	Is it possible to try and get more hospitals that are listed as ITP centres of excellence.
322	ZK	Will there ever be a successful treatment for ITP that doesn't cause bad side effects?
325	ZK	Education of medical staff so that any unexplained bruising or joint swelling provokes a blood test to eliminate the haemophilia.
337	ZK	What is the role for allied health in the future of haemophilia care delivery - more community outreach/care?
338	ZK	What is the impact on quality of life of things that we do with/to people
339	ZK	How do we educate local hospitals to not mis-diagnose
347	ZK	Collaborative research between centres i.e. working as a group in the South West looking at e.g. dental work and then producing guidelines that are available to all, to ensure equity for patients.
348	ZK	Looking at how nurses role improves patients experience of care, reduces hospital stay etc.
350	ZK	Community , GP , and emergency portal awareness
351	ZK	What new treatment options are there for patients with inhibitors?
353	ZK	What research is there into platelet disorders and how to diagnose and treat?
356	ZK	How can we involve the patients more in treatment decisions?
362	ZK	Should I be concerned about the size of the clots during my period?
364	ZK	What support (e.g. financial, emotional, occupational) needed? What impact of bleeding disorders on these areas in Scotland?
367	ZK	Prevention of bleeding
368	ZK	The devising of Care Quality Commission (minimum) requirements of senior citizens (e.g. 65+) residential/nursing home residents for bleed support/prevention.
377	ZK	What percentage of original publications in haemophilia have no conflicted authors at all?
380	ZK	Who is best/most effective in carrying out outpatient clinics for patients with bleeding disorders, doctors or nurses?

382	ZK	How can we increase awareness of the significance of bleeding disorders in the A and E department
383	ZK	Diagnosis and treatment
394	ZK	What is the Best way to transfuse blood components in acute bleeding outside the setting of haemorrhage?
396	ZK	All the above questions in children and adults.
408	ZK	Treatment when angiogram needed ?
413	ZK	Can treatment have an extended effect?
427	ZK	How can we improve access to dental care
428	ZK	Is gene transplant a viable treatment
433	ZK	Do haemophiliacs benefit from having a service animal?
464	ZK	I've had I for several years ,my lowest count was 54 but suddenly it has dropped to 19 with no apparent symptoms and I've been put onto steroids while awaiting an appointment with haematology is there an alternative medication as I'm not happy to be on steroids or perhaps this is a temporary arrangement ?
465	ZK	Stop harassing me to transition, put Kale in charge, get delivery details sorted =right amounts sent all staff be more approachable and friendly
466	ZK	To create a new medicine, rise a donation
467	ZK	Better treatment to stop, heal bleeds, physio gym closer to home, better pain medicines (non sleepy)

Appendix D
Glossary

Arthritis	Inflammation and damage in the joints, which are therefore often painful.
Acquired bleeding disorder	A bleeding disorder that develops during life. In distinction from inherited bleeding disorders
Anaemia	A reduced level of haemoglobin in the blood causing a reduced ability to carry oxygen.
Angiodysplasia	Abnormal blood vessels which have an increased tendency to bleed
Angiogram	A special X-Ray carried out to look particularly at blood vessels
Antithrombic	A treatment to reduce the ability of the blood to form clots. Consequently also increases the risk of bleeding.
Arterial disease	Disease of the arteries: high pressure blood vessels carrying blood with oxygen from the heart to the rest of the body.
Atony (uterine tone	Lack of muscle activity in the uterus. This allows bleeding to be prolonged.
Cardiovascular disease	Disease of the heart and the blood vessels, usually resulting in blood clots.
Care Quality Commission	A body set up by the government to inspect and ensure the quality of care provided by hospitals

Clotting factors	Protein molecules in the blood that play a role in blood clotting.
Coagulation	The formation of blood clots - usually in response to bleeding.
Co-morbities	Disorders that exist alongside another disorder and may make its treatment more complicated or difficult.
Contaminated blood	In this context refers to blood that contained diseases (such as hepatitis and HIV) that were then transmitted to the person receiving the blood or products made from the blood.
Desmopressin (DDAVP)	A drug, modelled on a natural hormone, that releases stores of Factor VIII and von Willebrand factor from the linings of blood vessels.
Epidural	An injection in to the space around the spine producing loss of sensation in the legs and any point below the injection.
Epilepsy	A disorder in which there is abnormal brain activity resulting in uncontrolled, often violent, movements with temporary loss of consciousness
Extended half-life and half-lfe products	Treatments for haemophilia (factor concentrates) that stay longer in the blood. This may allow injections to be less frequent.
Factor	This refers to one of the blood clotting proteins. It is often used to refer to the concentrates of these proteins.
Gene therapy	An alternative way of treating inherited disorders caused by a defective gene. The patient receives an injection containing a working copy of the gene responsible which therefore corrects the disorder.
Gut microbiome	The bacteria living in the gut
Haematomas	A large bruise, large enough to form a lump or mass.
Haematuria	Blood in the urine
Haemophilia	An inherited disorder of blood clotting which results in abnormal bleeding which is often spontaneous and into joints and muscles. The disorder is due to lack of coagulation factor 8 or 9
Haemophilic arthropathy	Damage to the joints caused by the bleeding in haemophilia
Haemophilic synovitis	Inflammation and swellling of the lining of the joint caused by bleeding into the joint in haemophilia
Haemorrhage	Bleeding
Haemostatic	Tending to help blood clot formation and reduce or terminate bleeding
HCV	Hepatitis C virus. An infection of the liver caused by a virus that can be transmitted by blood transfusion or infected blood products such as factor concentrates made from blood.
Hepatitis c	see above
Immune disorders	Disorders of the immune system. Often disorders in which the immune system attacks a normal part of the body. But also disorders in which the immune system cannot adequately defend you against infections.
Immune thrombocytopenic purpura (ITP)	A disorder in which the immune system attacks platelets and platelet production. This causes a deficiency of platelets (thrombocytopenia) and consequently an increased risk of bleeding
Indwelling access devices	Devices to help make intravenous injections easier. They are usually tubes, one end of which lies in the vein and the other protrudes through the skin so that it can be used for the injection.
Inherited/non-acquired bleeding disorder	An increased tendency to bleeding caused by an inherited defect in a gene. It can therefore pass from parents to children.
Inhibitor	Something that prevents one of the coagulation proteins from working properly. In haemophilia this is often an antibody produced by the body, but it might also refer to drugs used in patients with thrombosis

Interferon	A chemical the body produces in response to infection. High doses can be used to treat hepatitis.
Intravenous	Something delivered into a vein
Joint bleed	Bleeding into a joint. This is typical of the bleeding seen in haemophilia
Menorrhagia	Heavy periods. Now often call 'heavy menstrual bleeding' (HMB)
MPN	Myeloproliferative neoplasms (see below)
Mucosal bleeding	Bleeding from surfaces such as the mouth and throat where there is no covering of thickened skin.
Myeloproliferative neoplasms	A group of bone marrow disorders resulting in increased production of blood cells and an increased risk of thrombosis.
NSAIDs	Non steroidal anti-inflammatory drugs. These are similar to aspirin and impair platelet function resulting in an increased tendency to bleeding.
Obstetric	Relating to pregnancy
Perineum	The floor of the pelvis. In women this includes the vagina and birth canal and so is a potential site of bleeding after child birth
Platelets	Small fragments of cells that circulate in the blood. They are essential for normal blood clotting.
Ports	Refers here to artificial devices implanted under the skin to facilitate intravenous injections
Postpartum	After childbirth
PPI	Proton pump inhibitor. These drugs reduce the ability of the stomach to produce acid
Prednisone or prednisolone	This is a drug based on a normal hormone. It is used to reduce inflammation and problems caused by the immune system.
Prophylaxis	The administration of treatment pre-emptively to prevent problems (e.g. bleeding) occuring (rather than treating them after they have occurred)
Ribavirin treatment	Ribavirin is an antiviral treatment - previously used to treat hepatitis C
Rituximab	Rituximab is an antibody directed against the immune system. It can be used to reduce immune system activity.
Synovitis	Inflammation of the lining of the joints. For example after bleeding into the joint.
Thromboprophylaxis	Treatment given to prevent thrombosis.
Thrombosis	A blood clot which forms inside an intact blood vessel (i.e. not produced as a consequence of bleeding)
Tranexamic acid	Tranexamic acid is a drug that helps stabilise blood clots and helps reduce bleeding.
Ventouse forceps	Ventouse and forceps are sometimes used to assist delivery of a baby. However they can produce bleeding.
VWD von willebrands	von Willebrand disease is a bleeding disorder due to deficiency of a blood protein called von Willebrand factor.

Stop The **Bleeding**

www.jla.nihr.ac.uk