Defects in haemostasis, specifically in the quantitative or qualitative properties of von Willebrand factor (VWF), result in the most commonly inherited bleeding disorder, von Willebrand disease (VWD). Of the three types of VWD, type 1 is the most common and has the mildest phenotype. Type 1 VWD has a symptomatic prevalence of approximately 1 in 1000, but a much smaller number of patients who are actually diagnosed. This discrepancy is a result of a lack of standardized diagnostic criteria. The objective of the Self-Administered Bleeding Assessment Tool (Self-BAT) Study is to develop and optimize, a standardized, self-administered BAT to quantify bleeding history, and to distinguish between normal and abnormal bleeding.

In Phase 1 of the study, the medical terminology in the expert-administered ISTH BAT was changed to a grade four reading level to produce the first version of the Self-BAT. Three subsequent versions of the Self-BAT were generated during optimization based on focus group feedback and statistical analysis. The Self-BAT was administered to a total of 38 control subjects and 20 subjects affected with type 1 VWD in Phase 1. Demographic information on all the subjects (gender, age) was collected and blood was drawn for determination of VWF antigen level, VWF ristocetin cofactor activity and factor VIII level. Bleeding scores calculated from the ISTH BAT and Self-BAT showed an excellent correlation of 0.869 in the final version.

In Phase 2 of the study, the Self-BAT was administered to 27 control subjects and 23 affected subjects with the objective to simplify the questionnaire by identifying questions which can discriminate between unaffected and affected subjects. It was determined through category-total, category-category and item-item correlations that there was not sufficient evidence to reduce the Self-BAT.
In conclusion, the Self-BAT functions as a simple and effective tool to distinguish between normal and abnormal bleeding and is suitable for adults to administer themselves. The Self-BAT has now moved on to prospective validation studies where it will be tested on subjects who have been referred to tertiary care, but not yet received a diagnosis, in order to test its ability to distinguish between normal individuals and those affected with type 1 VWD and, potentially, other mild bleeding disorders.
Co-Authorship

Angie Tuttle and Julie Grabell assisted in recruiting subjects and organizing visits to Kingston General Hospital in addition to carrying out Phase 3.

Lisa Thibeault collected all blood samples from control subjects.

Shirren Albert assisted in the DNA extractions and ABO blood group analyses.

Wilma Hopman assisted with statistical analyses and sample size calculations.

Dr. Paula James oversaw the study, wrote the grant and assisted in the design of the study, REB application and focus groups. In addition, Dr. James assisted in the writing and editing of progress reports and of this thesis.

All other work is my own.
Acknowledgements

I would like to take this opportunity to thank Dr. Paula James who gave me the opportunity to pursue my Masters degree and went above and beyond to ensure that I could work on a project that combined clinical and molecular-based research. It is with her guidance and support that I had the opportunity and the confidence to pursue my academic and personal goals over the last two years.

I’d like to thank Angie Tuttle and Julie Grabell for helping me out with the subject recruitment, running visits in the hospital and for remembering the things I forgot. I’d also like to thank Lisa Thibeault for collecting blood from every single one of our control subjects.

I want to thank Wilma Hopman for having the patience to teach me various methods of statistical analysis and for not ignoring my emails when she probably should have.

I would like to thank my thesis committee, Dr. Paula James, Dr. Michael Rauh and Wilma Hopman for supporting me throughout my degree and for eagerly participating in all their required duties. In addition, I want to thank to all members of the James and Lillicrap lab for teaching me endless skills and life lessons over the past four and a half years.

Finally, I would like to thank my parents and Andrew for their unwavering support and everyone else who has taken a chance on me in the past.
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<table>
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<th>Description</th>
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<tbody>
<tr>
<td>ADAMTS13</td>
<td>a disintegrin-like and metalloprotease with thrombospondin type 1 motif, 13th member</td>
</tr>
<tr>
<td>BAT</td>
<td>bleeding assessment tool</td>
</tr>
<tr>
<td>BS</td>
<td>bleeding scores</td>
</tr>
<tr>
<td>DDAVP</td>
<td>1-deamino-8-D-arginine vasopressin</td>
</tr>
<tr>
<td>FVIII</td>
<td>Factor VIII</td>
</tr>
<tr>
<td>FVIII:C</td>
<td>Factor VIII coagulant activity</td>
</tr>
<tr>
<td>GI</td>
<td>gastrointestinal</td>
</tr>
<tr>
<td>HMW</td>
<td>high molecular weight</td>
</tr>
<tr>
<td>ISTH</td>
<td>International Society on Thrombosis and Haemostasis</td>
</tr>
<tr>
<td>KGH</td>
<td>Kingston General Hospital</td>
</tr>
<tr>
<td>PBQ</td>
<td>Pediatric Bleeding Questionnaire</td>
</tr>
<tr>
<td>PFD</td>
<td>platelet function disorder</td>
</tr>
<tr>
<td>RCo:Ag</td>
<td>VWF ristocetin cofactor activity: VWF antigen ratio</td>
</tr>
<tr>
<td>SPSS</td>
<td>Statistical Product and Service Solutions</td>
</tr>
<tr>
<td>VWD</td>
<td>von Willebrand disease</td>
</tr>
<tr>
<td>VWF</td>
<td>von Willebrand factor</td>
</tr>
<tr>
<td>VWF:Ag</td>
<td>von Willebrand factor antigen</td>
</tr>
<tr>
<td>VWF:RCo</td>
<td>von Willebrand factor ristocetin cofactor activity</td>
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Chapter 1

Introduction
1. Introduction

1.1.1 Haemostasis and Coagulation

The vessel wall, platelets, coagulation factor cascade and fibrinolysis work together to prevent prolonged bleeding or thrombosis in normal conditions. When the vascular endothelium is disrupted through injury, clot formation is stimulated. Formation of a platelet thrombus at an injury site requires platelet adhesion and aggregation. Endothelial cells are the primary source of von Willebrand factor (VWF), which is essential for platelet adhesion. Platelets in circulation adhere to a damaged vessel via the exposed collagen and to VWF, which is also bound to collagen. Collagen guides platelet adhesion and activation while also anchoring platelets to the endothelium. Activation of the platelets by thrombin helps to recruit more platelets to the platelet plug. Once activated, the platelet surface facilitates thrombin generation, which recruits even more platelets and stimulates the conversion of fibrinogen to fibrin, stabilizing the clot. Thrombin also serves to cleave ADAMTS13 (a protease that cleaves VWF into smaller, less active subunits), which results in enhanced platelet binding and regulation of thrombus formation, decreasing the risk of thromboembolism. Deficiencies of any of these key factors can result in a bleeding disorder.

1.1.2 Von Willebrand Factor

The von Willebrand factor protein is encoded by the VWF gene, which at 180 kb is located on chromosome 12 (12p13.2) and contains 52 exons. The mature subunit consists of 2050 amino acids with 12 domains and is heavily glycosylated. VWF is synthesized in endothelial cells and megakaryocytes. Dimers are formed by the proVWF in the endoplasmic reticulum and are
then transported to the Golgi where additional disulfide bonds form multimers, some of which may exceed 20 million Daltons in size. The propeptide is cleaved in the Golgi by furin, glycosylation is completed and the VWF multimers are stored in Weibel-Palade bodies in endothelial cells or in α-granules in platelets. The VWF protein is required for platelets to bind to the damaged vessel wall in order to form a hemostatic plug or thrombus. Finally, the binding of VWF to FVIII results in the stabilization of FVIII and protection from degradation by proteases.

1.1.3 Von Willebrand Disease

Von Willebrand Disease is the most commonly inherited bleeding disorder in humans and is inherited in an autosomal fashion. A classic understanding of the disease is that it results from mutations in the VWF gene. Dr. Erik von Willebrand first described the disease as “pseudo-hemophilia”, a mucocutaneous bleeding disorder that seemed to affect females more than males.

1.1.4 Type 1 VWD

Type 1 VWD is the most common form of the disease, representing approximately 70% of all cases, and is characterized by a reduction in structurally normal plasma VWF levels. Type 1 VWD is inherited in an autosomal dominant pattern but may have variable expression within families due to incomplete penetrance. The most commonly reported symptoms in type 1 VWD include increased or excessive mucocutaneous bleeding manifesting as epistaxis, bruising, prolonged bleeding from trivial wounds, oral cavity bleeding, bleeding after surgery, dental extraction or childbirth and menorrhagia.
1.1.5 Diagnosis

In 2005, provisional diagnostic criteria for VWD were published, providing insight as to the criteria for family history, manifestation of bleeding symptoms and laboratory testing. A positive family history was defined as having one first-degree relative or two second-degree relatives having a positive history of abnormal mucocutaneous bleeding and lab results in accordance with type 1 VWD. Bleeding symptoms, to be deemed significant, required one symptom requiring a blood transfusion, two symptoms in the absence of transfusion or one symptom occurring on at least three separate occasions. Laboratory tests confirming type 1 VWD needed to show functional VWF at a decreased level in the plasma (less than 0.50 U/mL). The decrease could be in proportion with a decrease in VWF:RCo and FVIII, however the FVIII level can also be normal. The patient should have a normal multimer profile.

Patients with plasma VWF levels at the lower end of the normal range are often difficult to distinguish from those with normal levels. However, even in milder cases, a strong inverse relationship has been shown between bleeding score and VWF levels in the literature. Further complicating the diagnostic process is the nature of the type 1 VWD mutations, many of which have incomplete penetrance. VWF levels can also vary as a result of many different genetic and environmental factors. One such example is the effect of blood group on plasma VWF levels. Individuals with group O blood tend to have a 25-30% decrease in VWF, regardless of disease status.

Another possible standardized method of diagnosis for Type 1 VWD is mutation analysis. However, because the VWF gene is large (180 kb) and complex, this is not always a feasible option. Additionally, multiple studies have shown that ~35% of type 1 VWD cases do not have identifiable mutations within the VWF gene. Previous literature has shown that a more reliable diagnostic method is a quantitative analysis of bleeding symptoms using a standardized
bleeding questionnaire. The consequences of over-diagnosing type 1 VWD include the risk of unnecessarily administrating plasma derived products or bleeding complications\(^8\). The risks of under-diagnosing type 1 VWD include bleeding after surgery, childbirth or trauma and are discussed in 1.1.9.

1.1.6 Type 2 VWD

Type 2 VWD, a more rare form of the disease (20-30% of cases) results from a qualitative defect in the VWF protein and is divided into multiple subtypes. Defective VWF-dependent platelet function defines type 2A, 2B and 2M and defective FVIII function and decreased FVIII levels is characteristic of type 2N\(^10\). The multimer profile may show a lack of HMW multimers (2A and 2B), a normal profile (2M and 2N) or it may show supranormal multimers in the Vicenza type (a rare and distinct variant of VWD with low plasma VWF levels and unusually large VWF multimers)\(^11\). It is possible to identify the subtype of type 2 VWD by identifying the VWF domain in which the mutation is contained and thus predicting the results of the defect.

Generally characterized by mild-moderate bleeding, type 2 variants often present with similar bleeding symptoms as patients with type 1. Type 2 is mainly inherited in an autosomal dominant manner, except 2N, which is recessive, and has a more complete penetrance than VWD. Easier than type 1 VWD to diagnose, most patients with type 2 VWD will have a characteristically low VWF:RCo level compared to the VWF:Ag level\(^12\). Individual responses to DDAVP in type 2 vary and require a trial to establish benefit. If the response is poor, treatment with human-derived may be required\(^1\).
1.1.7 Type 3 VWD

Type 3 is the most rare (approximate prevalence is 1 in 1 million in Western countries) and most severe form of VWD, inherited in an autosomal recessive fashion. Characterized by extremely low and often immeasurable levels of plasma VWF (< 0.05 U/mL), patients with type 3 may require lifelong replacement therapy to avoid life-threatening internal and external hemorrhaging. Factor VIII (FVIII) levels are usually low but measurable. Symptoms of type 3 VWD include all symptoms of type 1 and 2 VWD but also include musculoskeletal bleeding (similar to hemophilia A) and the presentation is often more severe 13.

1.1.8 Treatment

Desmopressin (DDAVP), a derivative of anti-diuretic hormone was first used to treat hemophilia A and VWD and is the recommended course of treatment for type 1 VWD in the event of minor trauma or in preparation for minor surgery. DDAVP, administered intravenously or intranasally, raises the levels of VWF and FVIII in the plasma, without the need for blood-derived products and at a reduced cost, by promoting their release from storage sites. However, patients must first have measurable levels of protein to release in order for DDAVP to be effective. If used repeatedly, there is evidence that efficacy may be decreased as protein stores are exhausted 14. Alternative treatment consists of replacement therapy using human-derived products. Antifibrinolytic amino acids (such as tranexamic acid) may also be used to treat less severe mucosal bleeding15.
1.1.9 The Undiagnosed, Affected

Mild bleeding disorders, such as type 1 VWD, are often overlooked because of the overlap of bleeding symptoms with unaffected individuals and a general lack of awareness. VWD has a symptomatic prevalence of approximately 1 in 1000 Canadians\(^6\). However, far fewer are actually diagnosed because of the lack of objective diagnostic criteria. Bleeding specific to women poses a particularly difficult issue. Bleeding from the reproductive tract during menses and childbirth is normal in women and often not discussed with others, even primary care physicians. Often, the only frame of reference a woman has for determining “normal” bleeding is by comparing her bleeding to that of her mother or other female family member. However, because VWD is hereditary, if the entire frame of reference is skewed, a woman may never know her bleeding is abnormal without objective criteria. Therefore, mild bleeding disorders are especially under-diagnosed in women with menorrhagia\(^{16}\). Another issue with the undiagnosed, affected is that many times a mild bleeding disorder will not present until after a hemostatic challenge such as a trauma or surgery. If undiagnosed, the issue can quickly become severe and put the patient at risk if proper treatment is not administered.

1.1.10 Bleeding Questionnaires and Bleeding Scores

In order to diagnose a patient who has reported problems with bleeding the physician must obtain a detailed and objective bleeding history. While some bleeding disorders present with severe or very characteristic bleeding symptoms, those with milder symptoms pose a distinct challenge. The main challenge is that the mild bleeding symptoms that are often associated with the more mild bleeding disorders, such as type 1 VWD, also occur in the normal population. One study showed that, conservatively, 25% of normal males and 43% of normal females reported at least one bleeding symptom\(^{17}\). In these cases, it is therefore difficult for patients and physicians to
identify a bleeding history as significant or not. In addition, bleeding history retold by a patient 
can be skewed or influenced by a number of factors (i.e. education, experience or personality) and 
is subject to a lack of objectivity. These challenges may result in bleeding being over or 
underreported, creating a need for an objective diagnostic criteria\textsuperscript{18}. The estimated prevalence of 
false-positives is 0.4\%, defined as having low VWF levels, bleeding and a family history of 
bleeding all by chance\textsuperscript{19}.

1.1.11 The Vicenza Bleeding Questionnaire

In 2005 Rodegheiro \textit{et al.} published a physician-administered standardized bleeding 
questionnaire and bleeding score. Patients were asked about their bleeding history including all 
the commonly reported bleeding symptoms afflicting those with VWD. Each symptom was 
graded on a scale of 0 to 3. A score of 0 would indicate the absence of a symptom. A score of 1 
would indicate the presence of a symptom, a score of 2 would indicate the patient was referred to 
a specialist or offered detailed laboratory investigation for the symptom and a score 3 would 
indicate evaluation and intervention (i.e. treatment). The final or cumulative bleeding score was 
determined by summing up all bleeding symptoms reported. A cumulative score of 3 or greater 
for males and 5 or greater for females was determined to be abnormal. The questionnaire was 
validated using controls and type 1 VWD obligatory carriers, who were defined by the presence 
of an offspring and another first-degree relative with a confirmed diagnosis. The questionnaire 
produced by this group was found to be quite specific (98.6\%) but less sensitive (69.1\%) for 
identifying those with VWD\textsuperscript{18,17}. 

1.1.12 The MCMDDM-1 VWD Questionnaire

In order to improve the sensitivity of the Vicenza questionnaire, the MCMDDM-1 questionnaire was developed with an additional severity category for each bleeding symptom (score of 4) for the most severe presentation (i.e. requiring a blood transfusion for treatment). In addition, a negative score (-1) was introduced to account for situations with an increased bleeding risk in which bleeding did not occur (i.e. surgery). The cumulative bleeding score was calculated in the same way.\(^7\)

1.1.13 The Condensed MCMDDM-1VWD Questionnaire

Both the Vicenza and MCMDDM-1 questionnaires required an administration time of approximately 40 minutes. In order to reduce the administration time the questionnaire was condensed by retaining only the details that directly affected the bleeding score. Administration time was reduced to a total of 5-10 minutes. Cumulative bleeding scores of 4 or greater were deemed abnormal. The sensitivity of the condensed MCMDDM-1 questionnaire was 100% with a specificity of 87% when validated prospectively on individuals being investigated for the first time with bleeding and/or bruising, with a negative predictive value of 1. The condensed questionnaire showed an excellent correlation to the full-length version and is considered an efficient and effective tool in the evaluation of patients for VWD.\(^6\)

1.1.14 The Pediatric Bleeding Questionnaire

A criticism of the bleeding questionnaires published before 2009 was that they were specifically created to evaluate adults. Children present with some of the bleeding symptoms reported by adults but they may not have had the opportunity to undergo certain hemostatic challenges (i.e. surgery, menses) because of their age. Therefore, the MCMDDM-1 questionnaire
was modified to include pediatric-specific symptoms such as umbilical stump bleeding, cephalohematoma, post-circumcision bleeding, post-venipuncture bleeding and macroscopic hematuria. The scoring system was not changed. The mean BS was determined (0.5) and using 2 standard deviations a normal range was determined (-1.5 – 2.5). Because bleeding scores cannot be given in half increments, the abnormal bleeding score was defined as ≥2. The PBQ was found to have a sensitivity of 83%, a specificity of 79%, a high negative predictive value (0.99) meaning it rarely misclassifies those who are affected as unaffected, and is capable of distinguishing between normal and children affected with VWD\textsuperscript{20}.

1.1.15 The ISTH Bleeding Assessment Tool

In 2010 the International Society on Thrombosis and Haemostasis established a Working Party to publish and endorse a single BAT to standardize reporting of bleeding symptoms for use in adult and pediatric populations. The Working Party combined the previously validated work from the questionnaires in circulation and the scoring systems to create the ISTH BAT and ISTH scoring system of 0-4 for each bleeding symptom reported. Validation studies are ongoing\textsuperscript{21}.

1.1.16 Limitations of BATs

Though some BATs have a high degree of clinical utility, bleeding assessment tools in circulation have limitations as well, mostly associated with the scoring system. In each scoring system whether it be 0 to 3, 0 to 4 or -1 to 4, the severity of the bleeding symptom takes priority over the frequency, which could potentially be important. For example, should a subject have one instance of a nosebleed requiring a blood transfusion or 5 nosebleeds requiring blood transfusions, the subject would receive the same score for the nosebleed category. In this way, the
questionnaires can become saturated – especially when evaluating more severe bleeding disorders. However, when the goal is to discriminate between individuals affected with mild bleeding disorders and unaffected individuals, score saturation is less of a limitation\textsuperscript{21}. Furthermore, and most relevant to this project, all bleeding assessment tools that are currently in circulation are expert-administered requiring trained research associates, nurses or physicians to administer the questionnaire. This can be problematic from a resource perspective, especially in a busy clinical setting. Additionally, the requirement for expert-administration is a barrier to more widespread use of such tools.

1.1.17 Quality criteria for evaluating health status questionnaires

When comparing measurement properties of health status questionnaires, such as bleeding assessment tools, there are certain criteria that should be evaluated. Content validity, or the extent to which concepts of interest are represented by the questionnaire, can be evaluated by identifying the target population, the interpretability or readability and by justification of any item selection or reduction. Internal consistency, the extent to which questionnaire items are measuring the same concept, should be analyzed using correlations to ensure there is no redundancy. Reproducibility, the degree to which stable subjects provide similar answers during repeated measurements or “test re-test reliability” should be performed within a reasonable and justified timeline. Agreement can be represented by the standard error of measurement or the limits of agreement, represented by a Bland-Altman plot. Finally, reliability, calculated with the Intraclass Correlation Coefficient, should be at least 0.70 in a sample size of 50 subjects\textsuperscript{22}. 

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1.1.18 Objectives

The Self BAT study was separated into 2 distinct phases. Phase 1: Generation and Optimization and Phase 2: Item Reduction.

**Phase 1 Objective:** To generate a self-administered version of the ISTH BAT and optimize the questionnaire to have a high level of agreement with the original ISTH BAT.

**Hypothesis:** The Self BAT will show a high level of agreement to the ISTH BAT and the scores obtained from each will be highly correlated.

**Phase 2 Objective:** To reduce the Self BAT to be as efficient as possible by identifying the questions capable of discriminating between unaffected and affected individuals.

**Hypothesis:** The symptoms most prevalent in type 1 VWD will be the most valuable when discriminating between unaffected and affected individuals.
Chapter 2

Methods
2.1 Phase 1

2.1.1 Generation of the Self-Administered Bleeding Assessment Tool (Self-BAT)

The first version of the Self-BAT was created by changing the language of the ISTH BAT\textsuperscript{21} to a grade four reading level which was deemed appropriate for all participating adults based on other health-related quality of life questionnaires in circulation\textsuperscript{23}.

2.1.2 Control subject recruitment

In order to recruit the first group of control subjects, an advertisement was placed in the Kingston Whig Standard, the main local newspaper. Subjects were asked to phone the recruiting line and were screened over the phone according to the eligibility criteria. Healthy adults (18 years of age or older) who were not pregnant and not on prescription medication were eligible to participate.

2.1.3 Affected subject recruitment

Affected subjects were recruited from the bleeding disorders clinic at Kingston General Hospital and were required to have a confirmed diagnosis of type 1 VWD and could not be pregnant at the time of the study. A type 1 VWD diagnosis would consist of VWF antigen and/or ristocetin cofactor of between 0.05 – 0.50 IU/mL, a RCo:Ag ratio > 0.6 and a normal VWF multimer profile.
2.1.4 Data collection

Control and affected subjects were separately brought into Kingston General Hospital two times, in groups of 5 to 7 individuals, and administered the ISTH BAT by an expert in one visit and to complete the Self-BAT in the other. The order in which the questionnaires were administered was randomized using a computer-based random number generator. On the second visit to the hospital four tubes of blood were collected from each subject by our study nurse. Both questionnaires were scored according to the ISTH 0 to 4 scoring key. Scores and demographic information were entered into an encrypted and password-protected computer database. The questionnaires were kept in a locked filing cabinet in the laboratory space with restricted access. The blood samples were stored in the -80 freezers as plasma and in the -20 freezers as whole blood for DNA extraction with subject consent. Ten affected subjects who completed the final version of the Self-BAT volunteered to retake the questionnaire 5-8 months after the first administration time, allowing for calculation of test re-test reliability.

2.1.5 Laboratory analysis

We collected 4 tubes of whole blood from each subject, separating half the tubes into platelet-poor plasma. With the plasma, we looked at the VWF antigen, FVIII levels, and ristocetin cofactor activity of each subject to confirm their control or affected status, according to our standard definition of type 1 VWD. From the whole blood, DNA was extracted to determine ABO blood group and was kept in the freezer for future related studies with subject consent.
2.1.6 Separation of platelet-poor plasma

Whole blood was spun in the centrifuge (Beckman) for 10 minutes at 2200g in order to separate the plasma from the red blood cells. The plasma was then pipetted into 500µl aliquots into 1.5mL tubes and frozen at -80°C.

2.1.7 VWF antigen ELISA

VWF antigen levels were measured by coating an Immulon 4 HBX plate (Dynex) with 100µl of Rabbit Anti-Human VWF (DAKO), diluted to 10µg/ml. The plate was incubated at 4°C overnight. Plasma samples were diluted with binding buffer (10 mM sodium phosphate, 145 mM NaCl, pH 7.2) using titer tubes (Biorad). A standard curve was prepared using reference plasma with dilutions beginning at 1:20. The plate was washed with 200µl wash buffer (PBS, 10 mM sodium phosphate, 500 mM NaCl, and 1% Tween 20, pH 7.2) 3 times using the plate washer before 100µl of sample was added to each well. The plate was incubated at room temperature for 2 hours and then washed as above. Detecting antibody (Rabbit Anti-Human VWF HRP, DAKO) was added to the plate at a concentration of 1.1µg/µl before a 1-hour incubation. The plate was washed as above and then the colour reagent (7.5 mL 0.1M Citric Acid-Phosphate Buffer, 5 mg of dissolved o-phenylenediamine (OPD) and 3.1 µl of 30% peroxide) was added to the plate until the standard curve was apparent. The reaction was stopped with 1M H2SO4 and the results were read at 492 nm on the plate reader (VERSAmax).
2.1.8 VWF ristocetin cofactor assay

The ristocetin cofactor assay is used to measure the ability of VWF to induce platelet aggregation. The aggregometer (Chrono-log) was first calibrated with standard curves using both normal and abnormal (quick-thawed, Precision Biologic). Lyophilized platelets (Helena Laboratories) were reconstituted with TRIS-buffered saline and was added to cuvettes with a stir bar, placed into the aggregometer and allowed to incubate for 4 minutes. Once the incubation was over, ristocetin (American Biochemical and Pharmaceutical Corporation) was added to each cuvette for two minutes before the thawed plasma sample was added. After the addition of the plasma, the aggregometer measures the ability of the subject VWF to induce platelet aggregation using measurements of light transmission.

2.1.9 FVIII analysis

Normal and abnormal control FVIII were used to create a standard curve (Precision Biologic) along with the STAGO reagents. Thawed subject plasma samples were loaded in the STAGO Compact machine to obtain a FVIII level by measuring the ability of subject FVIII to correct the PTT of FVIII-deficient plasma.

2.1.10 DNA extraction

To isolate the patient DNA from whole blood the salt extraction method was used as referenced by Nurnberger and Lahiri\textsuperscript{24}. Whole blood (5 ml) was transferred into a 15 mL centrifuge tube and 5 ml of low salt buffer was added (10mM Tris-HCl pH 7.6, 10 mM KCl, 10 mM MgCl\textsubscript{2} and 2 mM EDTA). Nonidet P-40 (Sigma, 125 μl) was added to the tube to lyse the
cells. The tube was centrifuged at 2200 RPM for 10 minutes at 21°C (Beckman). The supernatant was removed and the nuclear pellet (DNA) was washed with the low salt buffer. This was repeated 3 times until the pellet was white in colour and there were no remaining red blood cells. The pellet was then re-suspended in a high salt buffer (10mM Tris-HCl pH 7.6, 10 mM KCl, 10 mM MgCl$_2$, 0.4M NaCl, and 2 mM EDTA). 50 μl of 10% SDS was added to the suspension and mixed gently before being incubated at 55°C for 30 minutes. 0.30 ml of NaCl (6M) was added to the tube and mixed before centrifuging again at 12000 RPM for 5 minutes. The supernatant was saved and the pellet discarded. 100% ethanol (room temperature) was added to the tube to precipitate the DNA. The precipitated strands were removed from the tube and added to a microcentrifuge tube containing NaCl (6M) and stored at 4°C.
2.1.11 ABO blood group analysis

ABO blood groups were determined using the mutagenically separated polymerase chain reaction. Two sets of PCR reactions were performed, each amplifying nucleotides at position 261 and 703 from cDNA at the ABO locus (chromosome 9). Two forward primers and one reverse primer of different lengths were designed specifically for each reaction, producing a 216 bp, 195 bp, 126 bp, and 106 bp fragment. PCR products were obtained using 10 ng of DNA in a 50 μl reaction mixture and electrophoresed on a 3% agarose gel. ABO genotypes were determined by the intersection of the predicted alleles from the two PCR reactions. A picture of predicted outcomes from Lee et al is shown below (Figure 1). 25

![Figure 1](image_url)

**Fig. 1.** MS-PCR patterns of the six known ABO genotypes. Lane M is the pGEM marker. Lanes 1–6 are samples with genotypes AA, AO, BB, BO, AB and OO, respectively. (A) Shows the products from MS-PCR I. Ten μl of PCR products were electrophoresed in 4% Nusieve 3:1 agarose gel for 40 min in 100 V. (B) Shows the products from MS-PCR II. PCR products were run using the same conditions as for (A), but only for 25 min.
2.1.12 Focus groups

At the end of the second visit, each group of 5 to 7 individuals were invited to participate in a focus group where they could share their opinion of the questionnaire and their experience answering it. In addition to the subjects, myself, Angie Tuttle and Julie Grabell (clinical research associates) and Dr. Paula James (P.I.) were also present in each group session. Focus groups have been identified in clinical research as being the quickest and most cost-effective method of obtaining subject opinions and capable of accruing detailed information on a wide range of issues surrounding a specific topic\(^2\). Our focus groups were used to promote discussion of the questionnaire and of the study in general with each session being tape-recorded (Appendix E). The focus groups followed a semi-structured interview format.

Collectively we found that in each focus group we were alerted to any mistakes in the questionnaire, any questions or vocabulary that were unclear and in general got a sense of how efficiently the questionnaire would function as an assessment tool. This ultimately became our greatest resource throughout the optimization process.

2.1.13 Optimization

The first version of the questionnaire (Appendix C) was administered to 23 control subjects with minor vocabulary changes and grammatical errors fixed along the way, based on focus group feedback. Version 2 (Appendix D) was created by modifying each question stem to remove the word “problem”. We found unanimously across subjects that there was a strong opposition to being asked “Have you ever had a problem with ____________” which was contained in each question stem originally. We decided to remove with the word “problem” and evaluate whether the subject had a problem with a certain bleeding symptom by evaluating the
answers to the questions that followed the stem. This version was much more accepted among focus groups.

Version 2 was administered to 15 control subjects before being optimized again, based on focus group feedback. We found that with this version, there was some medical terminology that was unfamiliar to many subjects (i.e. subdural) therefore words were replaced and version 3 was created.

Version 3 (Appendix E) was the first version to be administered to the affected group. It was administered to 10 affected subjects before the final revision was made. The final revision consisted of splitting the questionnaire into an “undiagnosed” and “previously diagnosed” version. The main reason for doing so was to collect more information from the affected group. After the questionnaire was split, the “previously diagnosed” version was split into a “before” and “after” diagnosis category for each question stem. This allowed us to gain more information about when the symptoms occurred, and whether the subject had received prophylactic treatment before any hemostatic challenge. By doing so, we had the ability to score the questionnaires using the 0 to 4 scoring system or the -1 to 4 scoring system. However, if the subject had received prophylactic treatment prior to the aforementioned surgery this score would be incorrect and the appropriate score would be 0.

The final version, version 4 (Appendix F and G), was then administered to a final 10, affected subjects with little to no negative feedback or suggestions from the focus group (Appendix H). Therefore, it was decided that this version would proceed into phase 2, the item-reduction phase.
2.1.14 Statistical analyses

Throughout the optimization process, the cumulative scores from each questionnaire were recorded into our database. We compared the score that each subject received on the ISTH BAT to the score they got on Self-BAT with an intraclass correlation coefficient calculation (ICC) using SPSS. The goal was to have an ICC of greater than 0.80\(^2\), which would represent a high correlation between the two questionnaires and indicate that there was a high level of correlation between the scores obtained using the expert-administered ISTH BAT and the Self-BAT. In order to evaluate the agreement between the ISTH BAT and the Self BAT, a Bland-Altman plot was constructed. We optimized the Self-BAT until we reach our goal ICC value and until focus group feedback was quiet and then moved on to Phase 2.

2.1.15 Sample size

* A priori sample size calculations were not completed prior to the start of the Phase 1, as this Phase did not involve a specific intervention or effect size. Instead, a convenience sample consisting of all volunteers over an 8-month period was utilized, after which the measure was revised and retested over several iterations. A sample size of 50 has been shown to be adequate for testing associations or drawing inferences was used as a general guideline, and where appropriate, the more conservative non-parametric tests were used instead of parametric tests to test inferences. Our sample size was deemed large enough when the ICC value was appropriate (greater than 0.80) and when there was no more negative feedback emerging from the focus groups\(^2\).
2.2 Phase 2

2.2.1 Objectives

The objective of Phase 2 was to reduce the number of items on the Self-BAT by identifying the most discriminatory questions using statistical analyses. By reducing the questionnaire to only the discriminatory questions, the goal was to shorten completion time and maximize efficiency.

2.2.2 Methods

New control and affected subjects who were not involved in Phase 1 were recruited for Phase 2, using the same procedure and the same eligibility requirements as in Phase 1. Instead of filling out both the Self-BAT and the ISTH BAT, subjects in each group only filled out the Self-BAT (based on the correlation found in Phase 1) and required only one visit to Kingston General Hospital. Blood was collected in the same manner for each subject, and the same laboratory values were analyzed. In total, 27 controls and 23 affected subjects completed Phase 2 of the study.

2.2.3 Statistical Analysis

The demographic information for each subject was collected from the subject data form. Differences between the gender (Mann-Whitney) and age distribution (chi-square analysis) were examined for each group using SPSS. Mean VWF antigen, ristocetin cofactor activity and FVIII levels in addition to the range and standard deviation were compared between the control and
affected group (Mann-Whitney). The distribution of ABO blood groups was also compared across both control and affected groups (chi-square). Finally, the mean bleeding score and range were analyzed for both groups (Mann-Whitney). The Mann-Whitney test was used for ordinal data sets and chi-square analyses for categorical data.

Ten of the affected subjects who completed Version 4 of the Self-BAT volunteered to re-do the questionnaire anywhere from 5-8 months after the first administration. This enabled us to compare both scores and evaluated test re-test reliability using ICC (SPSS).

In order to identify the most discriminatory questions, or the questions that are best at distinguishing between unaffected and affected, several statistical analyses were completed. Category-total correlation (ICC, SPSS) was calculated for each of the 13 categories of the Self-BAT to determine the contribution from each category to the overall score. A high category-total correlation (greater than 0.9) would indicate a category that largely contributed to the overall score while a low total would indicate a smaller contribution. If the contribution from one category is small enough (correlation of less than 0.3), consideration can be given to removing that category.

Category-category correlations (Pearson, SPSS) were performed for each of the 13 categories of the Self-BAT. High correlations (greater than 0.9) indicate categories that are measuring the same thing and therefore may be eliminated due to redundancy. Low correlations (less than 0.3) indicate that the two categories being compared are measuring different things.

Finally, chi-square tests were completed for each of the 67 items on the questionnaire to determine any significant differences between the responses of the control and affected group. Any significant differences indicate that the item being measured is discriminatory, and therefore can distinguish between the control and affected group.
2.2.4 Sample size

Again, *a priori* sample size calculations were not completed prior to the start of the Phase 2, as this Phase did not involve a specific intervention or effect size. Instead, a convenience sample consisting of all volunteers over a 9-month period was utilized. Additionally, considerations were the same as for Phase 1, although the planned statistical analysis for this Phase was different as described above.\(^\text{27}\)
Chapter 3

Results
3.1 Phase 1

3.1.1 Demographic information, ABO blood group and bleeding scores

Demographic information from the subject data form (Appendix C and D) was compiled into an SPSS database. Differences in age and gender distribution were compared between control and affected groups. Mean VWF antigen levels, FVIII levels and VWF ristocetin cofactor activity determined for the control and affected group. ABO blood group was also determined for each group in addition to the mean bleeding scores and ranges. In the control group for Phase 1, 2 of the samples were excluded due to an accidental sample thaw.

Table 1. Demographic information, laboratory values and bleeding scores (Phase 1)

<table>
<thead>
<tr>
<th></th>
<th>Control (n=38)</th>
<th>Affected (n=20)</th>
<th>p-value</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>18/20</td>
<td>2/18</td>
<td>0.006</td>
<td>Chi-square</td>
</tr>
<tr>
<td>Mean age (range)</td>
<td>39 (18 to 72)</td>
<td>36 (18 to 59)</td>
<td>0.294</td>
<td>Mann-Whitney</td>
</tr>
</tbody>
</table>

**Laboratory Values**

<table>
<thead>
<tr>
<th></th>
<th>Control (n=38)</th>
<th>Affected (n=20)</th>
<th>p-value</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean VWF:Ag (U/mL)</td>
<td>1.01 (0.65-1.46) ± 0.33</td>
<td>0.59 (0.47-0.93) ± 0.17</td>
<td>&lt; 0.001</td>
<td>Mann-Whitney</td>
</tr>
<tr>
<td>Mean VWF:RCo (range)</td>
<td>0.69 (0.61-1.22) ± 0.18 (n=36)</td>
<td>0.38 (0.21-0.58) ± 0.09</td>
<td>&lt; 0.001</td>
<td>Mann-Whitney</td>
</tr>
<tr>
<td>Mean FVIII (range)</td>
<td>1.34 (0.71-1.49) ± 0.45 (n=36)</td>
<td>0.71 (0.47-0.93) ± 0.13</td>
<td>&lt; 0.001</td>
<td>Mann-Whitney</td>
</tr>
<tr>
<td>Blood group 0 (%)</td>
<td>15 (40)</td>
<td>16 (80)</td>
<td>0.001</td>
<td>Chi-square</td>
</tr>
<tr>
<td>Mean BS (range)</td>
<td>1.2 (0 to 4) ± 1.3</td>
<td>10 (4-17) ± 4.2</td>
<td>&lt; 0.001</td>
<td>Mann-Whitney</td>
</tr>
<tr>
<td>Mean BS (range)</td>
<td>1.5 (0 to 4) ± 1.4</td>
<td>11 (5-20) ± 4.0</td>
<td>&lt; 0.001</td>
<td>Mann-Whitney</td>
</tr>
</tbody>
</table>

* 2 control subjects were excluded due to sample thaw.
3.1.2 Gender distribution

From Table 1 significant gender skewing is obvious. While gender distribution in the control group was almost even, in the affected group significantly more females participated in the study than males. This is reflective of the clinic population at Kingston General Hospital as there are many more females diagnosed than males and therefore available for recruitment.

3.1.3 Subject age

Mean ages for both the control and affected populations were not significantly different. There was no upper age restriction imposed and therefore there was a range of 54 years in the control population and 41 years in the affected population.

3.1.4 VWF antigen levels

Subjects in the control group all had normal VWF:Ag (greater than 0.5 U/mL) Subjects in the affected group had a significantly lower level of VWF:Ag than subjects in the control group. This is expected based on our inclusion criteria of a previous diagnosis of type 1 VWD. The mean VWF:Ag in the affected group was not less than 0.5 U/mL however, because our criteria for Type 1 VWD was VWF:Ag and/or VWF:RCo between 0.05 and 0.50 IU/mL. For the affected subjects, the baseline level was used which was the level first recorded in our clinic.
3.1.5 VWF:RCo activity

VWF:RCo was significantly lower in the affected group than in the control group, similarly to the VWF:Ag and FVIII:C. This is reflective of the “proportional decrease” in lab levels that is often seen in type 1 VWD. The mean VWF:RCo/VWF:Ag for the control group was 0.77 while the mean ratio for the affected group was 0.67.

3.1.6 FVIII:C levels

Subjects in the control group had a normal mean FVIII:C (greater than 0.50 U/mL). The subjects in the affected group had a significantly lower FVIII:C than those in the control group. The mean FVIII:C was higher than the mean VWF:Ag levels in both groups which can occur when VWF synthesis is decreased.

3.1.7 ABO blood group

The prevalence of blood group O in the control population is reflective of the Canadian population as a whole (46%)⁹. There were significantly more individuals with type O blood in the affected group. This is because those with type O blood generally have a 25-35% decrease in VWF:Ag levels when compared with other blood types is therefore generally increased in a group of type 1 VWD individuals. The antigen structure in blood group O is thought to promote increased clearance of VWF, and thus results in lower circulating levels²⁹.
3.1.8 Bleeding score correlations by version

**Table 2.** ICC and difference between ISTH BAT and Self-BAT scores, versions 1-4.

<table>
<thead>
<tr>
<th>Version</th>
<th>Subjects (n)</th>
<th>ICC</th>
<th>Differences between scores (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>0.484</td>
<td>0.233</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>0.794</td>
<td>0.635</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>0.809</td>
<td>0.123</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>0.869</td>
<td>0.605</td>
</tr>
</tbody>
</table>

Subjects in the affected group had a significantly higher mean bleeding score on the Self-BAT and on the ISTH BAT (**Table 1, Figure 1**). There was no significant difference found between the scores obtained on the Self-BAT and on the ISTH BAT for any version (both controls and affected)(Mann-Whitney, SPSS). The ICC between scores obtained on the Self-BAT and on the ISTH BAT was poor for the first version, but steadily improved after each major revision for a final ICC of 0.869, which represents excellent correlation.
3.1.9 Agreement analysis

Figure 2. Bleeding scores using the ISTH BAT and Self BAT (n=58) with line of equality.

Overall ICC of 0.878.
The Bland-Altman plot suggests reasonable agreement overall, but that there are some discrepancies at higher values of bleeding assessment, which can also be seen in Figure 2.
3.1.10 Test re-test reliability

Ten of the affected subjects were asked to complete the Self-BAT again (Version 4), anywhere from 5-8 months after completing their first questionnaire. The test re-test reliability, calculated with the intraclass correlation coefficient (SPSS) was found to be 0.95.

Figure 4. Test re-test reliability. The ICC of the Self BAT # 1 scores and Self BAT # 2 scores was found to be 0.95.
3.2 Phase 2

3.2.1 Population demographics and bleeding scores

Demographic information from the subject data form (Appendix C and D) was compiled into an SPSS database. Differences in age and gender distribution were compared between control and affected groups. Mean VWF antigen levels, FVIII levels and VWF ristocetin cofactor activity were determined for the control and affected group. ABO blood group was also determined for each group in addition to the mean bleeding scores and ranges. In the control group for Phase 2, 6 of the samples were excluded due to the accidental sample thaw.

| Table 3. Population demographics, laboratory levels and bleeding scores (Phase 2). |
|-------------------------------|---------------------------------|-------|-----------------|
|                              | Control (n=27)                  | Affected (n=23) | p-value       |
| Gender (M/F)                  | 10/17                           | 3/21          | 0.200          | Chi-square |
| Mean age in years (range)     | 44 (19 to 91)                   | 38 (18 to 62) | 0.342          | Mann-Whitney |
| Laboratory Values             |                                 |                 |                |
| Mean VWF:Ag (U/mL) (range) ± SD | 0.87 (0.6-1.4) ± 0.31 (n = 21) | 0.49 (0.31-0.73) ± 1.7 | < 0.001       | Mann-Whitney |
| Mean VWF:RCo (range) ± SD     | 0.66 (0.57-0.83) ± 0.11 (n = 21)* | 0.35 (0.13-0.55) ± 0.12 | < 0.001       | Mann-Whitney |
| Mean FVIII:C (range) ± SD     | 0.90 (0.6-1.48) ± 0.25 (n = 21)* | 0.71 (0.3-1.49) ± 0.36 | < 0.001       | Mann-Whitney |
| Blood group 0 (%)             | 12 (44%)                        | 18 (78%)      | 0.001          | Chi-square |
| Mean BS (range) for Self BAT ± SD | 1.5 (0 to 4) ± 1.4              | 9.7 (2 to 16) ± 4.0 | 0.001          | Mann-Whitney |

* 6 control subjects were excluded due to sample thaw.
3.2.2 Gender distribution

Gender distribution in Phase 2 was found to be quite similar to that of Phase 1. There were significantly more females in the affected population when compared to the control population.

3.2.3 Subject age

There was no significant difference found between the mean age of the control population when compared to the affected population. There was a greater age range in Phase 2, especially in the control population when compared to Phase 1.

3.2.4 VWF antigen levels

VWF antigen level was found to be significantly higher in the control population when compared to the affected population. Mean antigen level was considered normal in the control population (0.93 U/mL) and abnormal in the affected population (0.49 U/mL). While some affected subjects were found to have a normal antigen level (greater than 0.50 U/mL), they were all previously confirmed to have type 1 VWD according to our study definition.

3.2.5 VWF Ristocetin cofactor activity

Affected subjects had significantly lower ristocetin cofactor activity than the control subjects. Similar to Phase 1, these concordant decreases are typical of a type 1 VWD cohort. The mean VWF:RCo was normal for the control group (> 0.50 U/mL) and abnormal for the affected group. The mean VWF:RCo/VWF:Ag ratio for the control group was 0.89 while the mean ratio for the affected group was 0.84.
3.2.6 FVIII:C levels

FVIII:C levels in the affected group were significantly lower than those in the control group. The mean FVIII:C in the affected group was in the normal range, which is not surprising because in type 1 VWD, the FVIII:C is usually higher than the VWF:Ag.

3.2.7 Bleeding scores

The bleeding scores obtained on the Self-BAT in the affected population were significantly higher than those obtained in the control population. There was one affected subject who had a normal score of 2. This subject was a female who only reported mild bruising and blood in the stool with no apparent cause, not requiring treatment. This patient had a VWF:Ag on the lower side of normal (VWF:Ag = 0.55 U/mL), a VWF:RCo of 0.36 and a FVIII:C of 0.91 U/mL.
3.3 Category-total correlation

The Pearson correlation between the score for each category on the Self-BAT and the total score was calculated for each affected subject (Table 4). A low category-total correlation (< 0.3) represents a category that contributes little to the cumulative score. A high category-total correlation (>0.9) represents a category that contributes a large amount to the cumulative score.

The GI bleeding, hematoma, hemarthrosis and “other” categories had a category-total correlation of < 0.3. In general, this means that these categories contribute less to the cumulative scores than the other. However, in this study, because type 1 VWD patients tend to not experience symptoms in these categories, the correlation is low because the symptoms did not appear enough in the answers to the Self-BAT.

Table 4. Correlation between each category and cumulative bleeding scores (Phase 2).

<table>
<thead>
<tr>
<th>Category</th>
<th>Correlation (Pearson)</th>
<th>Significance (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nosebleeds</td>
<td>0.521</td>
<td>0.009</td>
</tr>
<tr>
<td>Bruising</td>
<td>0.456</td>
<td>0.025</td>
</tr>
<tr>
<td>Minor wounds</td>
<td>0.686</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Blood in urine</td>
<td>0.319</td>
<td>0.129</td>
</tr>
<tr>
<td>GI bleeding</td>
<td>0.001</td>
<td>0.998</td>
</tr>
<tr>
<td>Oral cavity bleeding</td>
<td>0.379</td>
<td>0.068</td>
</tr>
<tr>
<td>Dental extractions</td>
<td>0.707</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Post-surgical bleeding</td>
<td>0.476</td>
<td>0.019</td>
</tr>
<tr>
<td>Menorrhagia</td>
<td>0.562</td>
<td>0.004</td>
</tr>
<tr>
<td>Postpartum bleeding</td>
<td>0.613</td>
<td>0.001</td>
</tr>
<tr>
<td>Hematoma</td>
<td>0.237</td>
<td>0.264</td>
</tr>
<tr>
<td>Hemarthrosis</td>
<td>0.226</td>
<td>0.288</td>
</tr>
<tr>
<td>“Other”</td>
<td>0.269</td>
<td>0.240</td>
</tr>
</tbody>
</table>
3.4 Category-category correlation

The Pearson correlation between the scores for each category was measured against each other. A low correlation (<0.3) indicates that the categories being compared are measuring different things while a higher correlation may indicate category redundancy. Each of the 13 categories were measured against each other and no correlations of greater than 0.9 were found, indicating that there were no redundancies amongst categories.

There were some significant correlations found between categories in the affected group as seen below in Table 5.

Table 5. Significant correlations between categories.

<table>
<thead>
<tr>
<th>Category 1</th>
<th>Category 2</th>
<th>Correlation (Pearson)</th>
<th>Significance (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical attention for epistaxis</td>
<td>Treatment for minor wounds</td>
<td>0.652</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Medical attention for bruising</td>
<td>Treatment for minor wounds</td>
<td>0.617</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Medical attention for bruising</td>
<td>Medical attention for oral cavity bleeding</td>
<td>0.550</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Medical attention for bruising</td>
<td>Postpartum bleeding</td>
<td>0.550</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Medical attention for dental extractions</td>
<td>Treatment for minor wounds</td>
<td>0.422</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
3.5 Chi square analysis

Each item in the Self-BAT questionnaire was analyzed for differences between control and affected responses by using a chi square analysis (SPSS) (Table 6). A significant difference between control and affected response to an item would mean that the item was “discriminatory” in that it could accurately differentiate between control and affected status. Out of a total of 67 items on the questionnaire, 7 were found to be discriminatory (p = < 0.05).

Table 6. Items identified as “discriminatory” using chi-square analyses.

<table>
<thead>
<tr>
<th>Questionnaire Item</th>
<th>Significance (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Were you ever given medical attention for your nosebleeds?”</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>“How long do you usually bleed after a small cut?”</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>“How often do you have bleeding from a small cut?”</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Bleeding in the urine without identifiable cause</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>“Were you ever given medical attention for bleeding after a tooth was removed?”</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>“Did you have to stay home from work or school more than 2 times per year because of heavy bleeding?”</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>“Were you ever given medical attention for heavy periods?”</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
3.6 ABO blood group

3.6.1 ABO blood group and VWF antigen

There was no significant difference in the distribution of VWF antigen levels across blood groups (Mann-Whitney, SPSS) in contrast to the literature, where individuals with blood group O may have up to a 25-35% reduction in VWF antigen levels\(^30\). This may simply be a reflection of sample size.

3.6.2 ABO blood group and bleeding score

There was no significant difference in the distribution of bleeding scores across blood groups (Mann-Whitney, SPSS).

3.7 Gender-specific bleeding

Bleeding specific to women including menorrhagia and postpartum bleeding was analyzed for differences in distribution across the control and affected groups using Mann-Whitney tests for significance. It was found that the affected groups reported significantly more bleeding related to menorrhagia than the control group. However, no significant difference was found between postpartum bleeding and treatment between control and affected groups.
Chapter 4

Discussion
4.1 Optimization of the Self-BAT

There were four versions of the Self-BAT in total throughout the process of turning the ISTH BAT into a tool that subjects could administer themselves. The revisions took into account the feedback from the focus groups. Changes were only considered once they had been suggested by more than one person and on more than one occasion. The first major change that occurred early in the process was the change of each question stem to exclude the word “problem”. In the first version, each question stem began with a question about whether the subject had a problem which a specific hematologic symptom. This lack of objectivity was causing confusion among study participants. “What quantifies a problem?” was a question that almost each participant raised in the first focus group. The question stems were re-worded to simply ask if the symptom had ever occurred. The questions following each stem are detailed enough that if the subject actually does have a problem in that particular category, it is confirmed through their answers to the rest of the questions.

The second version of the questionnaire was much more appealing to the focus groups. However, some of the medical terms that remained in the Self-BAT from the ISTH BAT began to pose a problem. While the questionnaire was, for the most part, created for a grade 4 reading level, there was still some terminology that had to be changed. The next major change consisted of finding replacement vocabulary for medical terms such as “subdural” and “hematoma” or providing detailed descriptions, which resulted in Version 3.

The third and final change was two-fold to produce the final version, Version 4. The questionnaire was first split into “undiagnosed” and “previously diagnosed” versions. The “previously diagnosed” version was then split into a “before diagnosis” and “after diagnosis” category for each symptom. The decision to split the questionnaire was made because of the need
to obtain more information from those who had been previously diagnosed. The bleeding scores from those who had been treated prophylactically before being exposed to a hemostatic challenge would not be accurate unless there was a place on the questionnaire to note that they had been treated. Of course, this does not apply to those who are undiagnosed in most cases and would not only confuse those subjects, but lengthen the administration time for them as well. By splitting the questionnaire it allowed for more information to be collected regarding their treatment and more accurate scores. In addition, we found that when the questionnaire was split into before and after diagnosis categories, it gave subjects a frame of reference. In older subjects, this was especially helpful as it allowed them to remember more of the hemostatic challenges they had gone through in the past. As the study progresses into Phase 3, the validation phase, the “undiagnosed” version of the questionnaire will be administered since the subjects who will be recruited will not have been diagnosed with a bleeding disorder at the time of the study.
4.2 The item-reduction phase

The goal of Phase 2 was to use statistical analysis to identify the discriminatory questions in the Self-BAT in order to create the most efficient and concise tool possible.

4.2.1 Category-total correlation

Category-total correlations for gastrointestinal bleeding, hematomas, hemarthrosis and the “other” category were found to be less than 0.3. In some cases, this would mean that these categories could be removed, as they do not contribute as much as the others. However, in the type 1 VWD population, these categories represent symptoms that do not typically occur in this form of the disease. These particular symptoms are more typical of type 2 and 3 VWD. Rather than classifying these categories as “non-contributive”, the low correlations indicate that there were not enough subjects in our population to allow these symptoms to contribute. Therefore, they were kept and not eliminated. Another point to consider is that each category can potentially accrue a wealth of information. While the Self-BAT should be succinct and efficient, it should also not ignore large amount of potentially valuable patient information.

4.2.2 Significant category-category correlations

In the affected group, there were significant correlations found between several of the categories. A significant correlation was found between seeking medical attention for a nosebleed and requiring medical attention for prolonged bleeding for a small wound. Seeking medical attention for extensive bruising was significantly correlated to seeking medical attention for a small wound, requiring medical attention for oral cavity bleeding and postpartum bleeding. Finally, requiring medical attention after a dental extraction was significantly correlated to
requiring treatment for small wounds. These findings are expected as bruising, prolonged bleeding from small wounds and requiring medical attention after a dental extraction are some of the most common symptoms that present in type 1 VWD. The correlation between bruising and postpartum bleeding is interesting and while the answer to one category is not quite predictive of the other, it could be an important parallel should the relationship strengthen in the final phase of the study. It should be noted that there was no correlation found between menorrhagia and postpartum bleeding or bleeding after dental extractions and post-surgical bleeding as would be expected. These correlations have presented in the literature in the past, and therefore are taken into consideration when it comes to managing patients clinically\textsuperscript{16,31}. Therefore, women who present with menorrhagia may be treated prophylactically before childbirth in addition to those who had bleeding after a dental extraction. In addition, many of our affected subjects had not yet given birth at the time of the study, which may explain part of the lack of correlation.

**4.2.3 Discrimination analysis**

In total, 7 of the items on the Self-BAT were found to be discriminatory (as seen in Table 4). This list of items was not at all surprising, as they are the most common symptoms experienced by those with type 1 VWD. The exception to that was blood present in the urine without an identifiable cause. While this symptom is not common in type 1 VWD, it is even less common in the general population. If the Self-BAT were to be reduced to only these 7 discriminatory items, rather than the full questionnaire there are many instances where this would be a valuable tool. However, the ultimate goal of the Self-BAT is to discriminate between unaffected and affected. By eliminating the majority of the questions there is the risk of losing important information in making a diagnosis.
4.2.4 Statistical evidence did not support reduction

In summary of the statistical analysis, the reduction of the questionnaire was not supported. There was not enough evidence to reduce the questionnaire by removing categories or items. However, if the same study were to be performed on a larger sample size, this could change. Our sample size was restricted to the affected individuals who were willing to participate in our study out of the clinic population at Kingston General Hospital. As the study progresses into the third phase, at some point reduction may become more practical.

4.2.5 Quality criteria of the Self BAT

Many of the quality criteria as suggested by Terwee et al\textsuperscript{32} were evaluated during Phase 2 of the Self BAT study. The target populations (undiagnosed and previously diagnosed) for each version of the Self-BAT were clearly defined and relevant to the questionnaire. Discriminatory items were defined and justified and while item-reduction did not occur, statistical evidence was provided in support of that decision. In addition, the readability of the Self BAT is a grade 4 reading level and appropriately tailored to our target populations. Internal consistency was evaluated with category-category correlations to ensure that no redundancy was occurring. The reproducibility of the questionnaire was excellent, when evaluated with test re-test reliability. The timeframe for this was appropriate and justified. The agreement between the Self BAT and the ISTH BAT was analyzed with a Bland-Altman plot which suggested reasonable agreement overall with some discrepancies with higher bleeding scores. The reliability of the questionnaire was excellent, with an ICC of 0.878, which is higher than the recommended cut-off for adequacy. In summary, the Self BAT performed well when evaluated for quality criteria with some room for improvement in the agreement analysis.
4.2.6 Determining a new reference range for bleeding scores

A final supporting argument for not reducing the Self-BAT arises from the scoring system. Since the Self-BAT was correlated to the ISTH BAT, both of which have the same categories – if we were to remove categories or questions, the range of possible scores would change. The normal and abnormal range of scores arises from a number of previously validated studies and if we were to change it, we would have to define the new “normal” and “abnormal” range of scores. By doing this, the scores collected in the first two phases of the studies would no longer be relatable to the new, reduced questionnaire.
4.3 Laboratory analysis

4.3.1 ABO blood group

The literature has shown that plasma VWF:Ag levels (and FVIII levels) can be significantly affected by ABO blood group. Individuals with type O blood can have up to a 35% reduction in plasma VWF level and are consistently found to have the lowest levels of VWF:Ag when compared to the other blood groups. The ABO blood group system consists of A, B and H antigens respectively. Individuals with blood group A, B or AB are able, through glycotransferases, to convert the H antigen (the precursor) into the A or B structure. Those with group O blood however, lack the transferase enzyme and express only the H structure. Little is known about VWF protein clearance but it is suspected that those with blood group O, as a result of carbohydrate structure have an increased clearance, and therefore lower levels of VWF:Ag\textsuperscript{29,30}.

In order to confirm this relationship, ABO blood group was determined for each subject using DNA extract from whole blood. It was found that 44% of the control population and 78% of the affected population were group O. This reflects the Canadian population with respect to blood group. No significant difference was found in the distribution of VWF antigen levels across the different blood groups in the control or affected group. In addition, there was no significant difference in the distribution of bleeding scores across blood groups in either group. Both might simply reflect the sample size in our study being too small to detect these effects.
4.4 Gender-specific bleeding

The prevalence of menorrhagia in bleeding disorders has been widely discussed in the literature. In a patient survey of 99 women with type 1 VWD, 71% of patients had sought medical attention for heavy periods with 13 patients receiving a hysterectomy solely for the purpose of controlling their menorrhagia. It was also found that significantly more women reported postpartum hemorrhaging than in the control group. The results of the Self-BAT study reinforce the claims regarding menorrhagia. In our affected group significantly more women reported heavy periods, having to seek medical attention for their periods and requiring treatment. However, we did not find that significantly more women with type 1 VWD sought medical treatment for postpartum bleeding which is consistent with the lack of correlation found between menorrhagia and postpartum bleeding. These results may have important clinical implications, especially for the undiagnosed affected patient. While bleeding disorders as a whole affected up to 2% of the population it has been reported that between 10-20% of women with objectively documented menorrhagia are affected. With women presenting with complaints of menorrhagia, the Self-BAT could be especially useful to discriminate between those who need further investigation for a bleeding disorder and those who don’t.
4.5 The Self-Pediatric Bleeding Questionnaire (Self-PBQ)

Based on the success of the Self-BAT study, a pediatric-specific (separate) study has recently been initiated across Canada. An important criticism of bleeding assessment tools to date is that there are no applicable pediatric versions. A tool for assessing pediatric bleeding is inherently different than assessing bleeding in adults. Children often are not old enough to have undergone the same hemostatic challenges that adults have, and therefore identifying a mild bleeding disorder is especially difficult. Children are also typically more active than adults and tend to bruise themselves easily, making distinguishing between normal bleeding and abnormal bleeding also especially difficult.

The Self-PBQ study began with the translation of the expert-administered Pediatric Bleeding Questionnaire\textsuperscript{20} to a grade four reading level using the same methods as the Self-BAT study. Parents completed the Self-PBQ for children under the age of 12 while children ages 12 and older completed the questionnaire on their own, provided they could read at a grade 4 reading level. Focus groups were also conducted with the parents and children present. From these focus groups, we were able to carry one of the suggestions over to the Self-BAT study for the final version of the questionnaire. A question stem page (Appendix A) was added to the beginning of the questionnaire in order to improve efficiency and minimize administration time.
4.6 Limitations

It is important to note some of the limitations that were present throughout the Self-BAT study. While laboratory levels for VWF:Ag, FVIII and VWF:RCo from the affected subjects were previously determined and recorded by the core lab at Kingston General Hospital, all the lab work for the control subjects was performed in our research lab. While the laboratory procedures for each assay are standardized, a few of the plasma samples were accidentally thawed and as a result, the values obtained for the FVIII:C and VWF:RCo were skewed. Therefore, those samples were excluded from the lab analyses.

One of the limitations of previously validated bleeding questionnaires, and a limitation that is still present in the Self-BAT is the issue of “questionnaire saturation”. Severity of symptoms still takes precedence over the frequency and therefore subjects that have had severe symptoms (i.e. requiring blood transfusions) on multiple occasions still attain the same score as a subject that only required said treatment on one occasion. However, because the abnormal cumulative score cut-off is 4, both of the above subjects would still receive an abnormal score and would be investigated accordingly. Attempts were made in the ISTH-BAT to account for bleeding frequency, although proof of success of the inclusion of a measure of bleeding frequency are currently lacking. Certainly, if BATs are to be used to assess disease severity, this issue needs to be addressed. One possibility, in addressing this issue, would be to create a revised scoring system for bleeding severity and test it among patients with various bleeding disorders in a study much like this one. There is no clinical imperative to use BATs as a screening tool in the setting of a severe bleeding disorder as clearly diagnostic laboratory testing exists (i.e.: a FVIII level of < 0.01 IU/mL clearly makes the diagnosis of severe Hemophilia A).

A final criticism of the Self-BAT is that the questionnaire is more relevant for women. Because women are more frequently diagnosed with a bleeding disorder, in that they often
undergo more hemostatic challenges earlier in life than men, there are more women available for
study. In addition, many of the men who participated in the study scored very low, with some
scoring within the normal range. If a man has yet to undergo surgery, trauma or dental
extractions, it can be difficult to identify an affected male unless they have undergone nosebleeds
or excessive bleeding earlier in life. If women are consistently in need of a tool like the Self-BAT
then maybe it is appropriate that the questionnaire be more tailored to women. An effort will be
made in Phase 3 to recruit more males so that we have enough information to be able to
distinguish between affected and unaffected males as effectively as possible.

4.7 Phase 3

The next and final phase of the Self-BAT study will be Phase 3, the validation phase. In
order to validate the questionnaire, the Self-BAT will be administered to individuals referred to a
tertiary care facility for bleeding symptoms but who have yet to be diagnosed. We will then be
able to evaluate how well the Self-BAT acts as a screening tool to predict the diagnosis of type 1
VWD as well as other mild bleeding disorders.
4.8 Application to other bleeding disorders

At the present time, we have only studied the Self-BAT in type 1 VWD. There are other bleeding disorders that are prevalent in the community that may benefit from a tool such as the Self-BAT. These possible applications to other bleeding disorders will be explored in the validation phase of the study.

4.8.1 Hemophilia

Mild Hemophilia A can present similarly to VWD, without hemarthrosis and unprovoked bleeding\(^3^5\). In cases like these, it could be beneficial to have a tool like the Self-BAT. While the Self-BAT would be unlikely to distinguish between Hemophilia A and VWD if no hemarthrosis or unprovoked bleeding were present, if the Self-BAT could distinguish the patient as “abnormal” the patient would receive further laboratory investigation and the diagnosis would become clear. Plans to analyze the effectiveness of the Self-BAT in distinguishing symptomatic Hemophilia A carriers (women who carry the gene for Hemophilia A and have problems with bleeding) from asymptomatic carriers are in the near future.

4.8.2 Platelet Function Disorders

PFDs present in a very similar way to type 1 VWD, the Self-BAT would undoubtedly be of use in identifying those affected individuals, simply because it is capable of distinguishing between normal and abnormal bleeding.
4.9 Conclusions and future directions

The Self-BAT has proven to be an effective self-administered version of the ISTH BAT. Administration time for unaffected subjects was 5-10 minutes while administration time for affected subjects ranged from 5-20 minutes. We have shown that the scores obtained on the Self-BAT are tightly correlated to the ISTH BAT and that there is excellent test re-test reliability. We believe that the Self-BAT will emerge from Phase 3 as an efficient and accurate method of distinguishing between those who are affected with type 1 VWD and those who are not. Above all, the tool will be appropriate for concerned individuals to complete at home, at the request of their physician or hopefully on the Internet.

4.9.1 Item-reduced version

As was mentioned previously, the item-reduced version of the Self-BAT (with only the discriminatory questions) may have different but equally important uses in the community. This condensed, 7-question tool could potentially be used as a screening tool to be administered before surgical procedures, childbirth or immediately after trauma. It is our hope that by using this as a screening tool, physicians will be more aware of the potential for bleeding and thus be more prepared, improving patient outcome.
References


Appendix A

Consent Form (Control)
PATIENT INFORMATION AND CONSENT FORM

Title of Study: Generation and Validation of the Self-Bleeding Assessment Tool (BAT)

Principal Investigator: Dr. Paula James, MD, FRCPC
Associate Professor, Department of Medicine
Queen’s University, Kingston, ON
Tel: (613) 533-2946
FAX: (613) 533-6855
Email: jamesp@queensu.ca

We invite you to participate in a research study to test how well a bleeding questionnaire works as a screening tool for inherited bleeding disorders. We have previously published a bleeding questionnaire that can help to identify those adults who need follow up testing for problems with bleeding and/or bruising. This questionnaire has to be administered by an expert. We would like to turn this questionnaire into a tool that people could fill in themselves. First, we need to know if this questionnaire is understandable. Second, we need to know if it can work as well as the original at identifying people who do and do not have problems with bleeding and/or bruising. You have not experienced problems with bleeding or bruising. This study has been reviewed for ethical compliance by the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board.
**Background Information:**
Inherited bleeding disorders that cause bleeding from the skin or mucous membranes can be difficult to diagnose. Such disorders include von Willebrand disease (VWD), platelet function disorders (PFD) or deficiencies of clotting factors. We have developed a bleeding questionnaire called the Condensed MCMD1-VWD Bleeding Questionnaire which has shown to be helpful in deciding which patients need further specialized testing when they are seen in their family doctor’s office, and we are interested in creating a version that can be self-administered. By doing so we hope to provide an accurate summary of a great deal of clinical information about an individual patient, aiding in communication between clinicians and prioritizing laboratory testing. The self-administered questionnaire will also act as an important self-identification tool for patients debating seeking the help of specialists in the hemostasis field.

**Purpose of the Study:**
We hope to validate our bleeding questionnaire for self-administered use.

**Description of the Research**
If you are interested in participating, a research assistant will help you complete a Bleeding Questionnaire, which is a standardized form that asks a number of questions about a variety of bleeding and bruising symptoms. You will also complete a self-administered version on a separate visit. We will ask you to provide us with four tubes of blood that will be drawn at your first visit. The blood will be used to extract your DNA for genetic testing for inherited bleeding disorders in addition to ABO blood group and laboratory values for coagulation factors. The samples will be kept in a secure freezer for the duration of the study. In addition to the above requirements, subjects will participate in a focus group consisting of 5-10 participants to discuss opinions regarding the questionnaires. This focus group session will be recorded using an audio recording device. At the end of this consent form, we will ask you a series of questions about your wishes regarding your DNA.

**Risks**
There is a risk of pain associated with the blood tests, and a small risk of developing a bruise or infection at the needle site.

If you are a First Nations person, or an indigenous person and you have contact with spiritual “elders” you may want to talk with them before you agree to participate in this study. Elders have reservations about genetic research.

**Benefits**

It is unlikely that you will benefit directly from this study. However, an improvement of our knowledge of the genetics of bleeding disorders may help other patients in the future.

**Inclusion/Exclusion**

You are eligible for this study if you are ≥ 18 years old and have not been previously diagnosed with a bleeding or platelet disorder and have not reported problems with bleeding or bruising. You are not eligible if you are pregnant.

**Confidentiality**

All information obtained during the course of this study is strictly confidential and your anonymity will be protected at all times. All documents containing your name will be kept in locked files and will only be available to study personnel. This includes Dr. James and the research assistant(s) who will help you complete the Bleeding Questionnaire, and the technologists who will be performing the blood tests. You will be assigned a unique identifying code that will be used in the Excel spreadsheet where we will maintain the study data. Study data will also be maintained in hard copy form in locked files. You will not be identified in any publications resulting from this study.
Voluntary Nature of Study
Your participation in this study is voluntary. You may withdraw at any time and your withdrawal will not affect your future medical care with your Hematologist or at this hospital.

Consent
I have read and understand the consent form for this study. I acknowledge that the study has been explained to me and that any questions that I have asked have been answered to my satisfaction. I am voluntarily signing this form. I will receive a copy of this consent form for my information.

By signing this consent form, I do not waive my legal rights nor release the investigator(s) and sponsors from their legal and professional responsibilities.

___________________________  ______________________________
Name of Patient (print)      Name of person obtaining consent (print)

___________________________  ______________________________
Signature               Signature

____________________
Date

Additional Research Questions:
My medical record (including health card number) may be accessed in order to confirm details of my medical history (if necessary) and to obtain the results of the tests ordered by my Hematologist today.

YES NO ___________ / ________________
Initials Date

Given that this study involves your DNA, there are several more options for you to consider. You can choose all, some, or none of them. Please provide an answer for each option.

I agree that the study investigators can share my DNA and relevant health records with other researchers for studies on inherited bleeding disorders, while maintaining my confidentiality.

YES NO ___________ / ________________
Initials Date

I agree that the study investigators can share my DNA and relevant health records with other researchers for studies on disorders other than inherited bleeding disorders, while maintaining my confidentiality.

YES NO ___________ / ________________
Initials Date

I agree to be contacted in the future for additional research purposes directly related to the present project.
If research with your DNA reveals some other medical condition relating to you (when possible):

do you wish to be informed?

YES  NO  __________ / ______________
Initials  Date

do you wish your family doctor to be informed?

YES  NO  __________ / ______________
Initials  Date

If you have any questions about the research you may contact:

Dr. Paula James  Dr. John McCans, Head
Department of Medicine  Department of Medicine
Rm 2025, Etherington Hall  OR  Rm 3041, Etherington Hall
Queen’s University  Queen’s University
Kingston, ON  K7L 2V6  Kingston, ON  K7L 2V6
Tel: (613) 533-2946  Tel: (613) 533-6327

If you have any questions about your rights as a research subject, you may contact:

Dr. Albert Clark
Chair, Research Ethics Board
Queen’s University Health Sciences and Affiliated Teaching Hospitals
Office of Research Services
Fleming Hall, Jemmett Wing
Queen’s University
Kingston, ON K7L 3N6
Tel: (613) 533-6081
Appendix B

Consent Form (Affected)
We invite you to participate in a research study to test how well a bleeding questionnaire works as a screening tool for inherited bleeding disorders. We have previously published a bleeding questionnaire that can help to identify those adults who need follow up testing for problems with bleeding and/or bruising. This questionnaire has to be administered by an expert. We would like to turn this questionnaire into a tool that people could fill in themselves. First, we need to know if this questionnaire is understandable. Second, we need to know if it can work as well as the original at identifying people who do and do not have problems with bleeding and/or bruising. You are being invited to participate because you have been previously diagnosed a clotting or platelet disorder or you have been referred to a Hematologist for problems with bleeding or bruising. This study has been reviewed for ethical compliance by the Queen’s University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board.
Background Information:
Inherited bleeding disorders that cause bleeding from the skin or mucous membranes can be difficult to diagnose. Such disorders include von Willebrand disease (VWD), platelet function disorders (PFD) or deficiencies of clotting factors. We have developed a bleeding questionnaire called the Condensed MCMDM1-VWD Bleeding Questionnaire which has shown to be helpful in deciding which patients need further specialized testing when they are seen in their family doctor’s office, and we are interested in creating a version that can be self-administered. By doing so we hope to provide an accurate summary of a great deal of clinical information about an individual patient, aiding in communication between clinicians and prioritizing laboratory testing. The self-administered questionnaire will also act as an important self-identification tool for patients debating seeking the help of specialists in the hemostasis field.

Purpose of the Study:
We hope to validate our bleeding questionnaire for self-administered use.

Description of the Research
If you are interested in participating, a research assistant will help you complete a Bleeding Questionnaire, which is a standardized form that asks a number of questions about a variety of bleeding and bruising symptoms. You will also complete a self-administered version on a separate visit. We will ask you to provide us with four tubes of blood that will be drawn at your first visit. The blood will be used to extract your DNA for genetic testing for inherited bleeding disorders in addition to ABO blood group and laboratory values for coagulation factors. The samples will be kept in a secure freezer for the duration of the study. In addition to the above requirements, subjects will participate in a focus group consisting of 5-10 participants to discuss opinions regarding the questionnaires. This focus group session will be recorded using and audio recording device. At the end of this consent form, we will ask you a series of questions about your wishes regarding your DNA.

Risks
There is a risk of pain associated with the blood tests, and a small risk of developing a bruise or infection at the needle site.

If you are a First Nations person, or an indigenous person and you have contact with spiritual “elders” you may want to talk with them before you agree to participate in this study. Elders have reservations about genetic research.

**Benefits**

It is unlikely that you will benefit directly from this study. However, an improvement of our knowledge of the genetics of bleeding disorders may help other patients in the future.

**Inclusion/Exclusion**

You are eligible for this study if you are ≥ 18 years old and have been previously diagnosed with a bleeding or platelet disorder or you have been referred to a Hematologist because of a problem with bleeding or bruising. You are not eligible if you are pregnant.

**Confidentiality**

All information obtained during the course of this study is strictly confidential and your anonymity will be protected at all times. All documents containing your name will be kept in locked files and will only be available to study personnel. This includes Dr. James and the research assistant(s) who will help you complete the Bleeding Questionnaire, and the technologists who will be performing the blood tests. You will be assigned a unique identifying code that will be used in the Excel spreadsheet where we will maintain the study data. Study data will also be maintained in hard copy form in locked files. You will not be identified in any publications resulting from this study.

**Voluntary Nature of Study**

Your participation in this study is voluntary. You may withdraw at any time and your withdrawal will not affect your future medical care with your Hematologist or at this hospital.
Consent

I have read and understand the consent form for this study. I acknowledge that the study has been explained to me and that any questions that I have asked have been answered to my satisfaction. I am voluntarily signing this form. I will receive a copy of this consent form for my information.

By signing this consent form, I do not waive my legal rights nor release the investigator(s) and sponsors from their legal and professional responsibilities.

___________________________  ________________________________
Name of Patient (print)       Name of person obtaining consent (print)

___________________________  ________________________________
Signature                   Signature

_____________
Date

Additional Research Questions:

My medical record (including health card number) may be accessed in order to confirm details of my medical history (if necessary) and to obtain the results of the tests ordered by my Hematologist today.
Given that this study involves your DNA, there are several more options for you to consider. You can choose all, some, or none of them. Please provide an answer for each option.

I agree that the study investigators can share my DNA and relevant health records with other researchers for studies on **inherited bleeding disorders**, while maintaining my confidentiality.

YES  NO   __________ / _______________
      Initials  Date

I agree that the study investigators can share my DNA and relevant health records with other researchers for studies on **disorders other than inherited bleeding disorders**, while maintaining my confidentiality.

YES  NO   __________ / _______________
      Initials  Date

I agree to be contacted in the future for additional research purposes directly related to the present project.

YES  NO   __________ / _______________
      Initials  Date
If research with your DNA reveals some other medical condition relating to you (when possible):

do you wish to be informed?

YES  NO  

________________________ / ________________________

Initials  Date

do you wish your family doctor to be informed?

YES  NO  

________________________ / ________________________

Initials  Date

If you have any questions about the research you may contact:

Dr. Paula James  
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Tel: (613) 533-6327

If you have any questions about your rights as a research subject, you may contact:

Dr. Albert Clark  
Chair, Research Ethics Board  
Queen’s University Health Sciences and Affiliated Teaching Hospitals  
Office of Research Services  
Fleming Hall, Jemmett Wing
Appendix C

Self BAT Version # 1
SELF-BLEEDING ASSESSMENT TOOL:

Patient Information
Name ____________________________________________________________
Address __________________________________________________________
______________________________________________________________
Phone Number ___________________ Email __________________________
Gender Male ☐ Female ☐
Age ___________ Date of Birth ___________ (DD/MO/YYYY)
Ethnic Background ________________________________________________
Presenting complaint of bleeding or bruising today Yes ☐ No ☐
Personal history of bleeding or bruising Yes ☐ No ☐
Ever been diagnosed with a bleeding disorder? Yes ☐ No ☐
Diagnosis: _______________________________________________________
Immediate or extended family history of bleeding? Yes ☐ No/ Unsure ☐
Relation of family member with bleeding: ___________________________
What was the diagnosis? _________________________________________

Have you been diagnosed with any other medical conditions? ________________________________________________________________

Are you currently taking Oral Contraceptive Pills? Yes ☐ No ☐
If yes, brand name _____________________________________________
Are you pregnant? ________ Gestation time __________

Specify any herbals and/or medications that you have taken in the past 30 days:
Name: __________________ Last time taken: ____________________
_________________________________________________________________
_________________________________________________________________
1. Have you ever had a problem with nosebleeds?  [ ] Yes  [ ] No (skip to 2)

1.1 Please check all of the reasons that have caused your nosebleeds.
- an injury [ ]
- picking your nose [ ]
- dry air [ ]
- a stuffy nose (cold, allergy) [ ]
- taking an aspirin [ ]
- no reason, my nosebleeds just start on their own [ ]

1.2 How long do your nosebleeds usually last?  [ ] less than 1 minute
[ ] 1 - 10 minutes
[ ] more than 10 minutes

1.3 How often do you have nosebleeds?  [ ] 1 - 5 times per year
[ ] more than 5 times per year

1.4 Have you ever talked to a doctor about your nosebleeds?  [ ] Yes  [ ] No (skip to 2)

1.5 Have you ever been given medical treatment for your nosebleeds?  [ ] Yes  [ ] No (skip to 2)

If yes, please check all of the treatments that you have had.
- my nose was cauterized or packed at least once [ ]
- I was on a medication (liquid or pills) at least once [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once [ ]
- I was given a medication in a nose spray at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment, but don’t know what it was [ ]
| 2. Are you an easy bruiser? | [ ] Yes | [ ] No (skip to 3) |
| 2.1 Please check all the types of bruising you have had. | |
| - petechiae, i.e. small (1-2 mm) red or purple spots on the skin | [ ] |
| - a bruise | [ ] |
| - a hematoma, i.e. a bruise that has a hard lump | [ ] |
| - I don’t know | [ ] |
| 2.2 How large are your bruises usually? | |
| - the size of a pea or smaller | [ ] |
| - between the size of a pea and an orange | [ ] |
| - the size of an orange or larger | [ ] |
| 2.3 How often do you get bruises? | [ ] 1 - 4 times per year |
| | [ ] 5 times per year or more |
| 2.4 Where do you usually get bruises? | |
| - on the arms and legs only | [ ] |
| - on the chest, back and stomach only | [ ] |
| - all over your body | [ ] |
| If you get small red-purple spots (petechiae), where do you usually see them? | |
| - on the legs only | [ ] |
| - on your face only | [ ] |
| - all over your body | [ ] |
| 2.5 Have you ever talked to a doctor about your bruising? | [ ] Yes |
| | [ ] No (skip to 3) |
2.6 Have you ever been given medical treatment for your bruising?  
[ ] Yes  [ ] No (skip to 3)  
If yes, please check all of the treatments that you have had.  
- I was treated with medications at least once [ ]  
- I was given a blood transfusion at least once [ ]  
- I was given a treatment but don’t know what it was [ ]

3. Have you ever had a problem with bleeding from a small cut, for example, from a paper cut or from shaving?  
[ ] Yes  [ ] No (skip to 4)  
3.1 How long do you usually bleed after a small cut?  
[ ] less than 1 minute  
[ ] 1 to 10 minutes  
[ ] more than 10 minutes  
3.2 How often do you have bleeding from a small cut?  
[ ] 1 - 5 times per year  
[ ] more than 5 times per year  
3.3 Have you ever talked to a doctor about bleeding from a small cut?  
[ ] Yes  [ ] No (skip to 4)  
3.4 Have you ever been given medical treatment for a small cut?  
[ ] Yes  [ ] No (skip to 4)  
If yes, please check all of the treatments that you have had.  
- I had stitches at least once [ ]  
- I was given a medication intravenously (IV), or with a needle under the skin at least once [ ]  
- I was given a blood transfusion at least once [ ]  
- I was given a treatment, but don’t know what it was [ ]
4. **Have you ever seen blood in your urine?** (If you are a female, this does NOT include when you have had your period.)

- [ ] Yes
- [ ] No (skip to 5)

4.1 Please check all of the causes of blood in the urine that you have had.

- [ ] kidney stones
- [ ] infection
- [ ] another kidney or bladder disease
- [ ] no reason that I know

4.2 Have you ever talked to a doctor about unexplained blood in your urine?

- [ ] Yes
- [ ] No (skip to 5)

4.3 Have you ever been given medical treatment for unexplained blood in your urine?

- [ ] Yes
- [ ] No (skip to 5)

If yes, please check all of the treatments that you have had.

- [ ] I had surgery at least once to stop the bleeding
- [ ] I was on treatment with iron at least once
- [ ] I was given a medication intravenously (IV), or with a needle under the skin at least once
- [ ] I was given a blood transfusion at least once
- [ ] I was given antibiotics at least once
- [ ] I was given a treatment but don’t know what it was
5. Have you ever had a problem with bleeding from your stomach or bowel? [ ] Yes [ ] No (skip to 6)

5.1 Have you ever
- vomited red blood, or what looked like coffee grounds [ ]
- passed black, tarry stools while you were not taking iron supplements [ ]
- passed red blood in or with your stools [ ]

5.2 Please check all of the causes of this bleeding that you have had
- an ulcer [ ]
- liver disease [ ]
- abnormal and fragile blood vessels in the bowel (angiodysplasia) [ ]
- hemorrhoids, 'piles' [ ]
- another identifiable cause [ ]
- for no reason [ ]

5.3 Have you ever talked to a doctor about unexplained bleeding from your stomach or bowel? [ ] Yes [ ] No (skip to 6)

5.4 Have you ever been given medical treatment for unexplained bleeding from your stomach or bowel? [ ] Yes [ ] No (skip to 6)

If yes, please check all of the treatments that you have had.
- I had surgery to stop the bleeding at least once [ ]
- I was on a medication (liquid or pills) at least once [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don't know what it was [ ]
6. Have you ever had a problem with bleeding from the mouth? (This does NOT include tooth extraction at the dentist.)

[ ] Yes  [ ] No (skip to 7)

6.1 Please check all of the causes of bleeding from the mouth that you have had.
- new teeth coming in or tooth loss
- brushing/flossing
- bite on lip, tongue or cheek
- cleaning at the dentist's
- another cause

Please specify:

6.2 How long does this bleeding usually last?
[ ] less than 1 minute
[ ] 1 to 10 minutes
[ ] more than 10 minutes

6.3 Have you ever talked to a doctor or dentist about bleeding from the mouth?
[ ] Yes  [ ] No (skip to 7)

6.4 Have you ever been given medical treatment for bleeding from the mouth?
[ ] Yes  [ ] No (skip to 7)

If yes, please check all of the treatments that you have had.
- I had dental packing, cauterization or had stitches to stop the bleeding at least once
- I was on a medication (liquid or pills) at least once
- I was given a medication intravenously (IV), or with a needle under the skin at least once
- I was given a blood transfusion at least once
- I was given a treatment but don't know what it was
7. **Have you ever had a problem with bleeding after having a tooth taken out at the dentist?**

   [ ] Yes  [ ] No (skip to 8)

### 7.1 Please check what kind of tooth was taken out.

- baby tooth  [ ]
- adult tooth  [ ]
- wisdom tooth  [ ]

### 7.2 Have you ever talked to a doctor or dentist about this bleeding?

   [ ] Yes  [ ] No (skip to 8)

### 7.3 Have you ever been given medical treatment for bleeding after a tooth was taken out?

   [ ] Yes  [ ] No (skip to 8)

If yes, please check all of the treatments that you have had.

- I had dental packing or had stitches to stop the bleeding, at least once  [ ]
- I was on a medication (liquid or pills) at least once  [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once  [ ]
- I was given a blood transfusion at least once  [ ]
- I was given a treatment but don’t know what it was  [ ]
8. Have you ever had a problem with bleeding during or after surgery? [ ] Yes [ ] No (skip to 9)

8.1 Please check what kind of surgery you had
- tonsils/adenoids taken out [ ]
- other surgery of the nose or throat [ ]
- surgery of the chest [ ]
- surgery of the womb or ovaries, including caesarian section, removal of the womb [ ]
- other surgery of the stomach or belly [ ]
- other surgeries Please specify:

8.2 Have you ever talked to a doctor about the bleeding you had after surgery? [ ] Yes [ ] No (skip to 9)

8.3 Have you ever been given medical treatment for bleeding after surgery? [ ] Yes [ ] No (skip to 9)

If yes, please check all of the treatments that you have had.
- I had packing or stitches to stop the bleeding, at least once [ ]
- I was on a medication (liquid or pills) at least once [ ]
- I was given a medication intravenously (IV), with a needle under the skin, at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]
If you are a male, please skip to 11 now.

<table>
<thead>
<tr>
<th>9.</th>
<th>Have you ever had a problem with heavy periods?</th>
<th>[ ] Yes</th>
<th>[ ] No (skip to 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.1</td>
<td>Please check all that applies to the heaviest period you ever had</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- I had to change my pad/tampon more often than every 2 hours</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- the period lasted for more than 7 days</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- I passed clots and had flooding</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>9.2</td>
<td>Have you stayed at home from work/school more than twice a year because of heavy bleeding?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>9.3</td>
<td>Have your periods been heavy from the get-go?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>9.4</td>
<td>How long have you had a problem with heavy periods?</td>
<td>[ ] 1 year or less</td>
<td>[ ] more than 1 year</td>
</tr>
<tr>
<td>9.5</td>
<td>Have you ever been on a birth control pill?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td></td>
<td>If yes, have your periods become better since?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>9.6</td>
<td>Have you ever talked to a doctor about your heavy periods?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 10)</td>
</tr>
<tr>
<td>9.7</td>
<td>Have you ever been given medical treatment for heavy periods?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 10)</td>
</tr>
</tbody>
</table>
If yes, please check all of the treatments that you have had.

- I was on iron or on other medications (liquid or pills) at least once
- I was given the birth control pill because of heavy periods
- I was given the birth control pill as well as on other pills
- I had surgery to stop the bleeding at least once (e.g. removal of the womb, burning (ablation) or scraping (curettage) of the lining of the womb)
- I was given a medication intravenously (IV), or with a needle under the skin at least once
- I was given a blood transfusion at least once
- I was admitted to hospital at least once
- I was given a treatment but don’t know what it was
If you have NEVER had a baby, please skip to 11 now.

<table>
<thead>
<tr>
<th></th>
<th>10. Have you ever had a problem with bleeding after having a baby?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ ] Yes</td>
</tr>
</tbody>
</table>

10.1 How many times did you give birth by vaginal delivery?

10.2 When did the problems with vaginal bleeding occur?

|   | within the first 24 hours after delivery | [ ] between 24 hours and 6 weeks after delivery | [ ] all of the above |

10.3 How long did the vaginal discharge last?

|   | less than 6 weeks | [ ] more than 6 weeks |

10.4 Did you have to stay in the hospital longer because of this bleeding?

|   | Yes | [ ] No |

10.5 Have you ever talked to a doctor about this bleeding?

|   | Yes | [ ] No (skip to 11) |

10.6 Have you ever been given medical treatment for bleeding after having a baby?

|   | Yes | [ ] No (skip to 11) |
10.7 If yes, please check all of the treatments that you have had.

- I was given a medication intravenously (IV) to induce contraction of the womb at least once [ ]
- I was put on iron or other pills at least once [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once [ ]
- I was given a blood transfusion at least once [ ]
- I had an examination and/or packing of the womb while I was put asleep at least once [ ]
- I had surgery (eg. removing the womb, tying off the bleeding vessels,…) at least once [ ]
- I was in the intensive care unit (ICU) at least once [ ]
- I was given a treatment but don’t know what it was [ ]
11. Have you ever had bleeding into a muscle? (This would look like a bruise on the skin, but it would be hard and hurt a lot more.)

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No (skip to 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.1 Was this bleeding caused by an injury?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.2 Have you ever talked to a doctor about your bleeding into a muscle?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.3 Have you ever been given medical treatment for bleeding into a muscle?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If yes, please check all of the treatments that you have had.

- I had surgery to take away the blood at least once [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once [ ]
- I was given clotting factors at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]
12. Have you ever had bleeding into a joint? [ ] Yes [ ] No (skip to 13)

12.1 Was the bleeding caused by an injury? [ ] Yes [ ] No

12.2 Have you ever talked to a doctor about bleeding into a joint? [ ] Yes [ ] No (skip to 13)

12.3 Have you ever been given medical treatment for bleeding into a joint? [ ] Yes [ ] No (skip to 13)

If yes, please check all of the treatments that you have had.

- I had surgery to take away the blood at least once [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once [ ]
- I was given clotting factors at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]
13. Have you ever had bleeding into the head (brain) or spine? [ ] Yes [ ] No (skip to 14)

13.1 Where was the bleeding?
- subdural [ ]
- intracerebral [ ]
- I don’t know [ ]

13.2 Please check all of the treatments that you have had.
- I had surgery to take away the blood [ ]
- I had surgery to have a shunt put in [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]
### 14 Other types of bleeding. Please ask your mom or dad for help with these because many of these other types of bleeding would have happened when you were a baby.

14.1 Have you ever had any of the following?

- A problem with bleeding from the umbilical stump at birth  [ ]

- Cephalohematoma, i.e. a collection of blood under the scalp as a newborn, presenting as a soft swelling at the back of the head  [ ]

- Bleeding upon suctioning of the mouth and nose at birth  [ ]

- Bleeding into your cheek, caused by sucking during bottle or breastfeeding  [ ]

- A problem with bleeding during or after the surgery to remove the foreskin of a penis (circumcision)  [ ]

- A problem with bleeding from a needle poke when blood was drawn  [ ]

- Bleeding in the white of your eye  [ ]
14.2 Have you ever talked to a doctor about any of those bleeding symptoms?  [ ] Yes  [ ] No

14.3 Have you ever been given medical treatment for any of these bleeding symptoms?  [ ] Yes  [ ] No

For each of these symptoms separately, please check the treatments that you have had.

- I was on a medication (liquid or pills) at least once
- I had surgery to stop the bleeding or had stitches at least once
- I was given a medication intravenously (IV), with a needle under the skin, at least once
- I was given a blood transfusion at least once
- I was given a treatment but don’t know what it was

If you have had problems with any other bleeding symptoms that were not included in this questionnaire, please comment on these here.
Appendix D

Self BAT Version # 2
SELF-BLEEDING ASSESSMENT TOOL:

Patient Information
Name __________________________________________________________
Address __________________________________________________________
 ________________________________________________________________
Phone Number ___________________ Email __________________________
Gender  Male ☐ Female ☐
Age ____________ Date of Birth ____________ (DD/MO/YYYY)
Ethnic Background ________________________________________________

Presenting complaint of bleeding or bruising today  Yes ☐ No ☐
Personal history of bleeding or bruising  Yes ☐ No ☐
Ever been diagnosed with a bleeding disorder?  Yes ☐ No ☐
Diagnosis: _____________________________________________
Immediate or extended family history of bleeding?  Yes ☐ No/ Unsure ☐
Relation of family member with bleeding: ______________________________
What was the diagnosis? ____________________________________________

Have you been diagnosed with any other medical conditions?
_________________________________________________________________
_________________________________________________________________

Are you currently taking Oral Contraceptive Pills?  Yes ☐ No ☐
If yes, brand name _______________________________________________
Are you pregnant? _______ Gestation time ___________

Specify any herbals and/or medications that you have taken in the past 30 days:
Name: __________________ Last time taken: __________________
_________________________________________________________________
_________________________________________________________________
1. **Have you ever experienced nosebleeds?**

   - [ ] Yes
   - [ ] No (skip to 2)

1.1 Please check all of the reasons that have caused your nosebleeds.

   - [ ] an injury
   - [ ] picking your nose
   - [ ] dry air
   - [ ] a stuffy nose (cold, allergy)
   - [ ] taking an aspirin
   - [ ] no reason, my nosebleeds just start on their own

1.2 How long do your nosebleeds usually last?

   - [ ] less than 1 minute
   - [ ] 1 - 10 minutes
   - [ ] more than 10 minutes

1.3 How often do you have nosebleeds?

   - [ ] 1 - 5 times per year
   - [ ] more than 5 times per year

1.4 Have you ever talked to a doctor about your nosebleeds?

   - [ ] Yes
   - [ ] No (skip to 2)

1.5 Have you ever been given medical treatment for your nosebleeds?

   - [ ] Yes
   - [ ] No (skip to 2)

   If yes, please check all of the treatments that you have had.

   - [ ] my nose was cauterized or packed at least once
   - [ ] I was on a medication (liquid or pills) at least once
   - [ ] I was given a medication intravenously (IV), or with a needle under the skin at least once
   - [ ] I was given a medication in a nose spray at least once
   - [ ] I was given a blood transfusion at least once
   - [ ] I was given a treatment, but don’t know what it was

Comments:

______________________________________________________________________

____________________________________________________________
2. Are you an easy bruiser?  

2.1 Please check all the types of bruising you have had.  
   - petechiae, i.e. small (1-2 mm) red or purple spots on the skin  
     [ ]  
   - a bruise  
     [ ]  
   - a hematoma, i.e. a bruise that has a hard lump  
     [ ]  
   - I don’t know  
     [ ]

2.2 How large are your bruises usually?  
   - the size of a pea or smaller  
     [ ]  
   - between the size of a pea and an orange  
     [ ]  
   - the size of an orange or larger  
     [ ]  

2.3 How often do you get bruises?  
   [ ] 1 - 4 times per year  
   [ ] 5 times per year or more

2.4 Where do you usually get bruises?  
   - on the arms and legs only  
     [ ]  
   - on the chest, back and stomach only  
     [ ]  
   - all over your body  
     [ ]

If you get small red-purple spots (petechiae), where do you usually see them?  
   - on the legs only  
     [ ]  
   - on your face only  
     [ ]  
   - all over your body  
     [ ]  

2.5 Have you ever talked to a doctor about your bruising?  
   [ ] Yes  
   [ ] No (skip to 3)
2.6 Have you ever been given medical treatment for your bruising? [ ] Yes [ ] No (skip to 3)

If yes, please check all of the treatments that you have had.

- I was treated with medications at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>3.</td>
<td><strong>Have you ever had a problem with bleeding from a small cut, for example, from a paper cut or from shaving?</strong></td>
<td>[ ] Yes [ ] No (skip to 4)</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td>3.1</td>
<td><strong>How long do you usually bleed after a small cut?</strong></td>
<td>[ ] less than 1 minute [ ] 1 to 10 minutes [ ] more than 10 minutes</td>
</tr>
<tr>
<td></td>
<td></td>
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</tr>
<tr>
<td>3.2</td>
<td><strong>How often do you have bleeding from a small cut?</strong></td>
<td>[ ] 1 - 5 times per year [ ] more than 5 times per year</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3.3</td>
<td><strong>Have you ever talked to a doctor about bleeding from a small cut?</strong></td>
<td>[ ] Yes [ ] No (skip to 4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.4</td>
<td><strong>Have you ever been given medical treatment for a small cut?</strong></td>
<td>[ ] Yes [ ] No (skip to 4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>If yes, please check all of the treatments that you have had.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- I had stitches at least once [ ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- I was given a medication intravenously (IV) or with a needle under the skin at least once [ ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- I was given medication orally at least once [ ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- I was given a blood transfusion at least once [ ]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- I was given a treatment, but don’t know what it was [ ]</td>
<td></td>
</tr>
</tbody>
</table>
4. Have you ever seen blood in your urine? (If you are a female, this does NOT include when you have had your period.)

[ ] Yes  [ ] No (skip to 5)

4.1 Please check all of the causes of blood in the urine that you have had.

- kidney stones  [ ]
- infection  [ ]
- another kidney or bladder disease  [ ]
- no reason that I know  [ ]

4.2 Have you ever talked to a doctor about unexplained blood in your urine?

[ ] Yes  [ ] No (skip to 5)

4.3 Have you ever been given medical treatment for unexplained blood in your urine?

If yes, please check all of the treatments that you have had.

- I had surgery at least once to stop the bleeding  [ ]
- I was on treatment with iron at least once  [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once  [ ]
- I was given a blood transfusion at least once  [ ]
- I was given antibiotics at least once  [ ]
- I was given a treatment but don’t know what it was  [ ]
5. **Have you ever had a problem with bleeding from your stomach or bowel?**  
   [ ] Yes  [ ] No (skip to 6)

5.1 Have you ever:
   - vomited red blood, or what looked like coffee grounds  
     [ ]
   - passed black, tarry stools while you were not taking iron supplements  
     [ ]
   - passed red blood in or with your stools  
     [ ]

5.2 Please check all of the causes of this bleeding that you have had:
   - an ulcer  
     [ ]
   - liver disease  
     [ ]
   - abnormal and fragile blood vessels in the bowel (angiodysplasia)  
     [ ]
   - hemorrhoids, 'piles'  
     [ ]
   - another identifiable cause  
     [ ]
   - for no reason  
     [ ]

5.3 **Have you ever talked to a doctor about unexplained bleeding from your stomach or bowel?**  
   [ ] Yes  [ ] No (skip to 6)

5.4 **Have you ever been given medical treatment for unexplained bleeding from your stomach or bowel?**  
   [ ] Yes  [ ] No (skip to 6)
   If yes, please check all of the treatments that you have had:
   - I had surgery to stop the bleeding at least once  
     [ ]
   - I was on a medication (liquid or pills) at least once  
     [ ]
   - I was given a medication intravenously (IV), or with a needle under the skin at least once  
     [ ]
   - I was given a blood transfusion at least once  
     [ ]
   - I was given a treatment but don’t know what it was  
     [ ]
6. Have you ever noticed bleeding from the mouth? (This does NOT include tooth extraction at the dentist.)

[ ] Yes [ ] No (skip to 7)

6.1 Please check all of the causes of bleeding from the mouth that you have had.

- new teeth coming in or tooth loss [ ]
- brushing/flossing [ ]
- bite on lip, tongue or cheek [ ]
- cleaning at the dentist’s [ ]
- another cause [ ]

Please specify:__________________

6.2 How long does this bleeding usually last?

[ ] less than 1 minute
[ ] 1 to 10 minutes
[ ] more than 10 minutes

6.3 Have you ever talked to a doctor or dentist about bleeding from the mouth?

[ ] Yes [ ] No (skip to 7)

6.4 Have you ever been given medical treatment for bleeding from the mouth?

[ ] Yes [ ] No (skip to 7)

If yes, please check all of the treatments that you have had.

- I had dental packing, cauterization or had stitches to stop the bleeding at least once [ ]
- I was on a medication (liquid or pills) at least once [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]
### 7. Have you ever had a tooth/teeth taken out at the dentist?  

[ ] Yes    [ ] No (skip to 8)

#### 7.1 Please check what kind of tooth was taken out and note how many of each

- baby tooth [ ] _______
- adult tooth [ ] _______
- wisdom tooth [ ] _______

#### 7.2 Did you experience any abnormal bleeding after any of these extractions?  

[ ] Yes    [ ] No (skip to 8)

#### 7.3 Have you ever talked to a doctor or dentist about this bleeding?  

[ ] Yes    [ ] No (skip to 8)

#### 7.4 Have you ever been given medical treatment for bleeding after a tooth was taken out?

If yes, please check all of the treatments that you have had.

- I had dental packing or had stitches to stop the bleeding, at least once [ ]
- I was on a medication (liquid or pills) at least once [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]
<table>
<thead>
<tr>
<th>8. Have you ever had surgery or a major trauma (e.g. car accident)?</th>
<th>[ ] Yes</th>
<th>[ ] No (skip to 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.1 Please check what kind of surgery/trauma you had</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- tonsils/adenoids taken out</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- other surgery of the nose or throat</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- surgery of the chest</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- surgery of the womb or ovaries, including caesarian section, removal of the womb</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- other surgery of the stomach or belly</td>
<td>[ ]</td>
<td></td>
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<tr>
<td>- other surgeries</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>Please specify: ____________________</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.2 Did you experience any abnormal bleeding during or after any of these surgeries?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 9)</td>
</tr>
<tr>
<td>8.3 Have you ever talked to a doctor about the bleeding during or after you had surgery?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 9)</td>
</tr>
<tr>
<td>8.4 Have you ever been given medical treatment for bleeding during or after surgery?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 9)</td>
</tr>
<tr>
<td>If yes, please check all of the treatments that you have had.</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- I had packing or stitches to stop the bleeding, at least once</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- I was on a medication (liquid or pills) at least once</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- I was given a medication intravenously (IV), with a needle under the skin, at least once</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- I was given a blood transfusion at least once</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- I was given a treatment but don’t know what it was</td>
<td>[ ]</td>
<td></td>
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</tbody>
</table>
If you are a male, please skip to 11 now.

### 9. Have you ever had a problem with heavy periods?

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.0</td>
<td>Would you consider your periods to be regular?</td>
<td></td>
</tr>
<tr>
<td>9.1</td>
<td>Please check all that applies to the heaviest period you ever had</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- I had to change my pad/tampon more often than every 2 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- the period lasted for more than 7 days</td>
<td></td>
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<tr>
<td></td>
<td>- I passed clots and had flooding</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Spotting mid-cycle</td>
<td></td>
</tr>
<tr>
<td>9.2</td>
<td>Have you stayed at home from work/school more than twice a year because of heavy bleeding?</td>
<td></td>
</tr>
<tr>
<td>9.3</td>
<td>Have your periods been heavy from the get-go?</td>
<td></td>
</tr>
<tr>
<td>9.4</td>
<td>How long have you had a problem with heavy periods?</td>
<td></td>
</tr>
<tr>
<td>9.5</td>
<td>Have you ever been on a birth control pill?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If yes, have your periods become better since?</td>
<td></td>
</tr>
<tr>
<td>9.6</td>
<td>Have you ever talked to a doctor about your heavy periods?</td>
<td></td>
</tr>
</tbody>
</table>


9.7 Have you ever been given medical treatment for heavy periods?

[ ] Yes  [ ] No (skip to 10)

If yes, please check all of the treatments that you have had.

- I was on iron or on other medications (liquid or pills) at least once
- I was given the birth control pill because of heavy periods
- I was given the birth control pill as well as on other pills
- I had surgery to stop the bleeding at least once (e.g. removal of the womb, burning (ablation) or scraping (curettage) of the lining of the womb)
- I was given a medication intravenously (IV), or with a needle under the skin at least once
- I was given a blood transfusion at least once
- I was admitted to hospital at least once
- I was given a treatment but don’t know what it was
- I was given medication for pain associated with cramping

Comments:
_________________________________________________________________
9.7 Have you ever been given medical treatment for heavy periods? [ ] Yes [ ] No (skip to 10)

If yes, please check all of the treatments that you have had.

- I was on iron or on other medications (liquid or pills) at least once  [ ]
- I was given the birth control pill because of heavy periods  [ ]
- I was given the birth control pill as well as on other pills  [ ]
- I had surgery to stop the bleeding at least once (e.g. removal of the womb, burning (ablation) or scraping (curettage) of the lining of the womb)  [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once  [ ]
- I was given a blood transfusion at least once  [ ]
- I was admitted to hospital at least once  [ ]
- I was given a treatment but don’t know what it was  [ ]
- I was given medication for pain associated with cramping  [ ]

Comments: ___________________________________________
<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>10. Have you ever been pregnant?</strong></td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 11)</td>
</tr>
<tr>
<td><strong>10.1 Have you ever been pregnant but not carried the baby to term?</strong></td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 10.5)</td>
</tr>
<tr>
<td>If so, how many times?</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>10.2 Was it associated with excessive bleeding?</strong></td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td><strong>10.3 Did you seek medical attention?</strong></td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td><strong>10.4 If yes, please check all of the treatments that you have had:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- I was given a medication intravenously (IV) to induce contraction of the womb at least once</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- I was put on iron or other pills at least once</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- I was given a medication intravenously (IV), or with a needle under the skin at least once</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- I was given a blood transfusion at least once</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- I had an examination and/or packing of the womb while I was put asleep at least once</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- I had surgery (e.g. removing of the womb, tying off the bleeding vessels,…) at least once</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- I was in the intensive care unit (ICU) at least once</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>- I was given a treatment but I don't know what it was</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>Question</td>
<td>Options</td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------------------------------------</td>
<td>----------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>10.5 Have you ever given birth by vaginal delivery? (If no, skip to 11)</td>
<td>[ ] Yes [ ] No</td>
<td></td>
</tr>
<tr>
<td>How many times?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10.6 Did you experience problems with bleeding during the pregnancy or after the birth? (If no, skip to 11)</td>
<td>[ ] Yes [ ] No</td>
<td></td>
</tr>
<tr>
<td>10.7 When did the problems with vaginal bleeding occur?</td>
<td>[ ] within the first 24 hours after delivery [ ] between 24 hours and 6 weeks after delivery [ ] all of the above</td>
<td></td>
</tr>
<tr>
<td>10.4 How long did the vaginal discharge last?</td>
<td>[ ] less than 6 weeks [ ] more than 6 weeks</td>
<td></td>
</tr>
<tr>
<td>10.5 Did you have to stay in the hospital longer because of this bleeding?</td>
<td>[ ] Yes [ ] No</td>
<td></td>
</tr>
<tr>
<td>10.6 Have you ever talked to a doctor about this bleeding?</td>
<td>[ ] Yes [ ] No (skip to 11)</td>
<td></td>
</tr>
</tbody>
</table>
10.7 Have you ever been given medical treatment for bleeding after having a baby?  
[ ] Yes  [ ] No (skip to 11)

10.8 If yes, please check all of the treatments that you have had.

- I was given a medication intravenously (IV) to induce contraction of the womb at least once  
[ ]

- I was put on iron or other pills at least once  
[ ]

- I was given a medication intravenously (IV), or with a needle under the skin at least once  
[ ]

- I was given a blood transfusion at least once  
[ ]

- I had an examination and/or packing of the womb while I was put asleep at least once  
[ ]

- I had surgery (eg. removing the womb, tying off the bleeding vessels,...) at least once  
[ ]

- I was in the intensive care unit (ICU) at least once  
[ ]

- I was given a treatment but don’t know what it was  
[ ]
11. Have you ever had bleeding into a muscle? (This would look like a bruise on the skin, but it would be hard and hurt a lot more.)  

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No (skip to 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.1</td>
<td>Was this bleeding caused by an injury?</td>
<td>[ ] Yes</td>
</tr>
<tr>
<td>11.2</td>
<td>Have you ever talked to a doctor about your bleeding into a muscle?</td>
<td>[ ] Yes</td>
</tr>
<tr>
<td>11.3</td>
<td>Have you ever been given medical treatment for bleeding into a muscle?</td>
<td>[ ] Yes</td>
</tr>
</tbody>
</table>

If yes, please check all of the treatments that you have had.

- I had surgery to take away the blood at least once
- I was given a medication intravenously (IV), or with a needle under the skin at least once
- I was given clotting factors at least once
- I was given a blood transfusion at least once
- I was given a treatment but don’t know what it was
12. **Have you ever had bleeding into a joint?**

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No (skip to 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.1 Was the bleeding caused by an injury?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>12.2 Have you ever talked to a doctor about bleeding into a joint?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 13)</td>
</tr>
<tr>
<td>12.3 Have you ever been given medical treatment for bleeding into a joint?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 13)</td>
</tr>
</tbody>
</table>

If yes, please check all of the treatments that you have had.

- I had surgery to take away the blood at least once
- I was given a medication intravenously (IV), or with a needle under the skin at least once
- I was given clotting factors at least once
- I was given a blood transfusion at least once
- I was given a treatment but don’t know what it was
### 13. Have you ever had bleeding into or out of the head, brain or spine?

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No (skip to 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### 13.1 Where was the bleeding?

- Scalp [ ]
- Under the skill and around the brain [ ]
- Within the brain tissue [ ]
- I don’t know [ ]

#### 13.2 Please check all of the treatments that you have had.

- I had surgery to take away the blood [ ]
- I had surgery to have a shunt put in [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]

Comments:

__________________________________________________________________

__________________________________________________________________
14 Other types of bleeding. Some of these other types of bleeding would have happened shortly after birth.

14.1 Have you ever had any of the following?

- A problem with bleeding from the umbilical stump at birth [ ] Yes [ ] No [ ] Unsure
- cephalohematoma, i.e. a collection of blood under the scalp as a newborn, presenting as a soft swelling at the back of the head [ ] Yes [ ] No [ ] Unsure
- bleeding upon suctioning of the mouth and nose at birth [ ] Yes [ ] No [ ] Unsure
- bleeding into your cheek, caused by sucking during bottle or breastfeeding [ ] Yes [ ] No [ ] Unsure
- a problem with bleeding during or after the surgery to remove the foreskin of the penis (circumcision) [ ] Yes [ ] No [ ] Unsure
- a problem with bleeding from a needle poke when blood was drawn [ ] Yes [ ] No [ ] Unsure
- bleeding in the white of your eye [ ] Yes [ ] No [ ] Unsure
- bleeding after sexual intercourse [ ] Yes [ ] No [ ] Unsure

14.2 Have you ever talked to a doctor about any of those bleeding symptoms? [ ] Yes [ ] No

14.3 Have you ever been given medical treatment for any of these bleeding symptoms? [ ] Yes [ ] No
For each of these symptoms separately, please check the treatments that you have had.

- I was on a medication (liquid or pills) at least once [ ]
- I had surgery to stop the bleeding or had stitches at least once [ ]
- I was given a medication intravenously (IV), with a needle under the skin, at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]

If you have had problems with any other bleeding symptoms that were not included in this questionnaire, please comment on these here.

______________________________________________________________________
______________________________________________________________________
Appendix E

Self BAT Version # 3
SELF-BLEEDING ASSESSMENT TOOL:

Patient Information

Name _______________________________________________________

Address ______________________________________________________

______________________________________________________________

Phone Number ___________________ Email _________________________

Gender  Male  □  Female  □

Age __________ Age __________  Date of Birth ____________ (DD/MO/YYYY)

Ethnic Background _________________________________

Presenting complaint of bleeding or bruising today  Yes  □  No  □

Personal history of bleeding or bruising  Yes  □  No  □

Ever been diagnosed with a bleeding disorder?  Yes  □  No  □

Diagnosis: __________________________________________

Immediate or extended family history of bleeding?  Yes  □  No/ Unsure  □

Relation of family member with bleeding:_____________________________

What was the diagnosis? _________________________________________

Please describe any other diagnosed medical conditions, past or present:

____________________________________________________________________

____________________________________________________________________

____________________________________________________________________

Are you currently on birth control?  □ Yes  □ No

If yes, please list the type and brand name (ex. IUD, Mirena):

____________________________________________________________________

____________________________________________________________________

____________________________________________________________________

Are you pregnant? __________  Gestation time __________

Specify any herbals and/or medications that you have taken in the past 30 days:

Name:  Last time taken:

____________________________________________________________________

____________________________________________________________________

____________________________________________________________________

____________________________________________________________________

____________________________________________________________________
1. Have you ever experienced nosebleeds?  
   [ ] Yes  [ ] No (skip to 2)

1.1 Please check all of the reasons that have caused your nosebleeds.
   - an injury  [ ]
   - picking your nose  [ ]
   - dry air  [ ]
   - a stuffy nose (cold, allergy)  [ ]
   - taking an aspirin  [ ]
   - no reason, my nosebleeds just start on their own  [ ]

1.2 How long do your nosebleeds usually last?
   [ ] 10 minutes or less
   [ ] more than 10 minutes

1.3 How often do you have nosebleeds?
   [ ] 5 times per year or less
   [ ] more than 5 times per year

1.4 Have you ever talked to a doctor about your nosebleeds?
   [ ] Yes  [ ] No (skip to 2)

1.5 Have you ever been given medical treatment for your nosebleeds?
   [ ] Yes  [ ] No (skip to 2)
   If yes, please check all of the treatments that you have had.
   - my nose was cauterized or packed at least once  [ ]
   - I was on a medication (liquid or pills) at least once  [ ]
   - I was given a medication intravenously (IV), or with a needle under the skin at least once  [ ]
   - I was given a medication in a nose spray at least once  [ ]
   - I was given a blood transfusion at least once  [ ]
   - I was given a treatment, but don’t know what it was  [ ]

Comments: ____________________________________________________________
______________________________________________________________________
2. Have you ever had unexplained bruises or bruises that are bruises that are larger than you think they should be? [ ] Yes [ ] No (skip to 3)

2.1 Please check all the types of bruising you have had.
- petechiae, i.e. small (1-2 mm) red or purple spots on the skin [ ]
- a bruise [ ]
- a hematoma, i.e. a bruise that has a hard lump [ ]
- I don’t know [ ]

2.2 How large are your bruises usually?
- the size of a pea or smaller [ ]
- between the size of a pea and an orange [ ]
- the size of an orange or larger [ ]

2.3 How often do you get bruises? [ ] 5 times per year or less [ ] more than 5 times per year

2.4 Where do you usually get bruises?
- on the arms and legs only [ ]
- on the chest, back and stomach only [ ]
- all over your body [ ]

If you get small red-purple spots (petechiae), where do you usually see them?
- on the legs only [ ]
- on your face only [ ]
- all over your body [ ]
2.5 Have you ever talked to a doctor about your bruising?
   [ ] Yes  [ ] No (skip to 3)

2.6 Have you ever been given medical treatment for your bruising?
   [ ] Yes  [ ] No (skip to 3)

   If yes, please check all of the treatments that you have had.
   - I was treated with medications at least once  [ ]
   - I was given a blood transfusion at least once  [ ]
   - I was given a treatment but don't know what it was  [ ]
<p>| | | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>3. Have you ever had bleeding from a small cut?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 4)</td>
</tr>
<tr>
<td>3.1 How long do you usually bleed after a small cut?</td>
<td>[ ] 10 minutes or less</td>
<td>[ ] more than 10 minutes</td>
</tr>
<tr>
<td>3.2 How often do you have bleeding from a small cut?</td>
<td>[ ] 5 times per year or less</td>
<td>[ ] more than 5 times per year</td>
</tr>
<tr>
<td>3.3 Have you ever talked to a doctor about bleeding from a small cut?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 4)</td>
</tr>
<tr>
<td>3.4 Have you ever been given medical treatment for a small cut?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 4)</td>
</tr>
<tr>
<td>If yes, please check all of the treatments that you have had.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- I had stitches at least once</td>
<td>[ ]</td>
</tr>
<tr>
<td></td>
<td>- I was given a medication intravenously (IV) or with a needle under the skin at least once</td>
<td>[ ]</td>
</tr>
<tr>
<td></td>
<td>- I was given medication orally at least once</td>
<td>[ ]</td>
</tr>
<tr>
<td></td>
<td>- I was given a blood transfusion at least once</td>
<td>[ ]</td>
</tr>
<tr>
<td></td>
<td>- I was given a treatment, but don’t know what it was</td>
<td>[ ]</td>
</tr>
</tbody>
</table>
4. Have you ever seen blood in your urine? (If you are a female, this does NOT include when you have had your period.)

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No (skip to 5)</th>
</tr>
</thead>
</table>

4.1 Please check all of the causes of blood in the urine that you have had.
- kidney stones
- infection
- another kidney or bladder disease
- no reason that I know

4.2 Have you ever talked to a doctor about unexplained blood in your urine?

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No (skip to 5)</th>
</tr>
</thead>
</table>

4.3 Have you ever been given medical treatment for unexplained blood in your urine?

If yes, please check all of the treatments that you have had.
- I had surgery at least once to stop the bleeding
- I was on treatment with iron at least once
- I was given a medication intravenously (IV), or with a needle under the skin at least once
- I was given a blood transfusion at least once
- I was given antibiotics at least once
- I was given a treatment but don’t know what it was
5. Have you ever had bleeding inside your intestines, stomach or bowel? [ ] Yes [ ] No (skip to 6)

5.1 Have you ever:
- vomited red blood, or what looked like coffee grounds [ ]
- passed black, tarry stools while you were not taking iron supplements [ ]
- passed red blood in or with your stools [ ]

5.2 Please check all of the causes of this bleeding that you have had
- an ulcer [ ]
- liver disease [ ]
- abnormal and fragile blood vessels in the bowel (angiodysplasia) [ ]
- hemorrhoids, 'piles' or anal fissures [ ]
- another identifiable cause [ ]
- for no reason [ ]

5.3 Have you ever talked to a doctor about unexplained bleeding from your stomach or bowel? [ ] Yes [ ] No (skip to 6)

5.4 Have you ever been given medical treatment for unexplained bleeding from you stomach or bowel? [ ] Yes [ ] No (skip to 6)

If yes, please check all of the treatments that you have had.
- I had surgery to stop the bleeding at least once [ ]
- I was on a medication (liquid or pills) at least once [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]
6. Have you ever noticed bleeding from the mouth? (This does NOT include tooth extraction at the dentist.)

   [ ] Yes  [ ] No (skip to 7)

6.1 Please check all of the causes of bleeding from the mouth that you have had.

   - new teeth coming in or tooth loss
   - brushing/flossing
   - bite on lip, tongue or cheek
   - cleaning at the dentist’s
   - another cause

   [ ]

   Please specify:

6.2 How long does this bleeding usually last?

   [ ] 10 minutes or less
   [ ] more than 10 minutes

6.3 Have you ever talked to a doctor or dentist about bleeding from the mouth?

   [ ] Yes  [ ] No (skip to 7)

6.4 Have you ever been given medical treatment for bleeding from the mouth?

   [ ] Yes  [ ] No (skip to 7)

   If yes, please check all of the treatments that you have had.

   - I had dental packing, cauterization or had stitches to stop the bleeding at least once
   - I was on a medication (liquid or pills) at least once
   - I was given a medication intravenously (IV), or with a needle under the skin at least once
   - I was given a blood transfusion at least once
   - I was given a treatment but don’t know what it was

   [ ]
7. Have you ever had a tooth/teeth taken out at the dentist? [ ] Yes [ ] No (skip to 8)

7.1 Please check what kind of tooth was taken out and note how many of each
- baby tooth [ ] _______
- adult tooth [ ] _______
- wisdom tooth [ ] _______

7.2 Did you experience any abnormal bleeding after any of these extractions? [ ] Yes [ ] No (skip to 8)

7.3 Have you ever talked to a doctor or dentist about this bleeding? [ ] Yes [ ] No (skip to 8)

7.4 Have you ever been given medical treatment for bleeding after a tooth was taken out?
If yes, please check all of the treatments that you have had.
- I had dental packing or had stitches to stop the bleeding, at least once [ ]
- I was on a medication (liquid or pills) at least once [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]
8. Have you ever had surgery or a major trauma (e.g. car accident)?

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No (skip to 9)</th>
</tr>
</thead>
</table>

8.1 Please check what kind of surgery/trauma you had

- tonsils/adenoids taken out [  ]
- other surgery of the nose or throat [  ]
- surgery of the chest [  ]
- surgery of the womb or ovaries, including caesarian section, removal of the womb [  ]
- other surgery of the stomach or belly [  ]
- other surgeries [  ]
- trauma [  ]

Please specify: ____________________

8.2 Did you experience any abnormal bleeding during or after any of these surgeries?

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No (skip to 9)</th>
</tr>
</thead>
</table>

8.3 Have you ever talked to a doctor about the bleeding during or after you had surgery?

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No (skip to 9)</th>
</tr>
</thead>
</table>

8.4 Have you ever been given medical treatment for bleeding during or after surgery?

If yes, please check all of the treatments that you have had.

- I had packing or stitches to stop the bleeding, at least once [  ]
- I was on a medication (liquid or pills) at least once [  ]
- I was given a medication intravenously (IV), with a needle under the skin, at least once [  ]
- I was given a blood transfusion at least once [  ]
- I was given a treatment but don't know what it was [  ]
If you are a male, please skip to 11 now.

<table>
<thead>
<tr>
<th>9. Have you ever had a period?</th>
<th>[ ] Yes</th>
<th>[ ] No (skip to 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are you:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>☐ Pre-menopausal</td>
<td></td>
<td>☐ Post-menopausal</td>
</tr>
<tr>
<td><em>If you are post-menopausal, please answer the following questions to the best of your ability</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

9.1 Were/are your periods regular?  
Please check all that applies to the heaviest period you ever had:
- [ ] I had to change my pad/tampon more often than every 2 hours
- [ ] the period lasted for more than 7 days
- [ ] I passed clots and had flooding
- [ ] Spotting mid-cycle

9.2 Have you stayed at home from work/school more than twice a year because of heavy bleeding?

9.3 Have your periods been heavy from the get-go?

9.4 How long have you had a problem with heavy periods?
- [ ] 1 year or less
- [ ] more than 1 year

9.5 Have you ever talked to a doctor about your heavy periods?
- [ ] Yes
- [ ] No
Have you ever been given medical treatment for heavy periods?

If yes, please check all of the treatments that you have had.

- I was on iron or on other medications (liquid or pills) at least once
- I was given the birth control pill because of heavy periods
- I was given the birth control pill as well as on other pills
- I had surgery to stop the bleeding at least once (e.g. removal of the womb, burning (ablation) or scraping (curettage) of the lining of the womb)
- I was given a medication intravenously (IV), or with a needle under the skin at least once
- I was given a blood transfusion at least once
- I was admitted to hospital at least once
- I was given a treatment but don’t know what it was
- I was given medication for pain associated with cramping

Comments: ________________________________
<table>
<thead>
<tr>
<th>10. Have you ever been pregnant?</th>
<th>[ ] Yes</th>
<th>[ ] No (skip to 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.1 Have you ever been pregnant but not carried the baby to term?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 10.5)</td>
</tr>
<tr>
<td>If so, how many times?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10.2 Was it associated with excessive bleeding?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>10.3 Did you seek medical attention?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>If yes, please check all of the treatments you have had:</td>
<td></td>
<td></td>
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<tr>
<td>- I was given a medication intravenously (IV) to induce contraction of the womb at least once</td>
<td>☐</td>
<td></td>
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<tr>
<td>- I was put on iron or other pills at least once</td>
<td>☐</td>
<td></td>
</tr>
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</tr>
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<td>☐</td>
<td></td>
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<tr>
<td>- I had an examination and/or packing of the womb while I was put asleep at least once</td>
<td>☐</td>
<td></td>
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<tr>
<td>- I had surgery (eg. removing the womb, tying off the bleeding vessels,…) at least once</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>- I was in the intensive care unit (ICU) at least once</td>
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<td>- I was given a treatment but don’t know what it was</td>
<td>☐</td>
<td></td>
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<td>- Other or non-applicable</td>
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<tr>
<td>Question</td>
<td>Response Options</td>
<td></td>
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<td>------------------------------------------------------------------------</td>
<td>------------------------------------------------------</td>
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</tr>
<tr>
<td>Have you ever given birth by vaginal delivery? (If no, skip to 11)</td>
<td>[ ] Yes  [ ] No (skip to 11)</td>
<td></td>
</tr>
<tr>
<td>How many times?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did you experience problems with bleeding during the pregnancy or</td>
<td>[ ] Yes  [ ] No</td>
<td></td>
</tr>
<tr>
<td>after the birth? (If no, skip to 11)</td>
<td></td>
<td></td>
</tr>
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<td>When did the problems with vaginal bleeding occur?</td>
<td>[ ] within the first 24 hours after delivery</td>
<td></td>
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<tr>
<td></td>
<td>[ ] between 24 hours and 6 weeks after delivery</td>
<td></td>
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<tr>
<td></td>
<td>[ ] all of the above</td>
<td></td>
</tr>
<tr>
<td>How long did the vaginal discharge last?</td>
<td>[ ] less than 6 weeks</td>
<td></td>
</tr>
<tr>
<td></td>
<td>[ ] more than 6 weeks</td>
<td></td>
</tr>
<tr>
<td>Did you have to stay in the hospital longer because of this bleeding?</td>
<td>[ ] Yes  [ ] No</td>
<td></td>
</tr>
<tr>
<td>Have you ever talked to a doctor about this bleeding?</td>
<td>[ ] Yes  [ ] No (skip to 11)</td>
<td></td>
</tr>
</tbody>
</table>
10.7 Have you ever been given medical treatment for bleeding after having a baby? 
[ ] Yes  [ ] No (skip to 11)

10.8 If yes, please check all of the treatments that you have had.
- I was given a medication intravenously (IV) to induce contraction of the womb at least once
- I was put on iron or other pills at least once
- I was given a medication intravenously (IV), or with a needle under the skin at least once
- I was given a blood transfusion at least once
- I had an examination and/or packing of the womb while I was put asleep at least once
- I had surgery (eg. removing the womb, tying off the bleeding vessels,...) at least once
- I was in the intensive care unit (ICU) at least once
- I was given a treatment but don’t know what it was
11. Have you ever had bleeding into a muscle? (This would look like a bruise on the skin, but it would be hard and hurt a lot more.)  

[ ] Yes  
[ ] No (skip to 12)

11.1 Was this bleeding caused by an injury?  

[ ] Yes  
[ ] No

11.2 Have you ever talked to a doctor about your bleeding into a muscle?  

[ ] Yes  
[ ] No (skip to 12)

11.3 Have you ever been given medical treatment for bleeding into a muscle?  

If yes, please check all of the treatments that you have had.

- I had surgery to take away the blood at least once  
- I was given a medication intravenously (IV), or with a needle under the skin at least once  
- I was given clotting factors at least once  
- I was given a blood transfusion at least once  
- I was given a treatment but don’t know what it was  

[ ]  
[ ]  
[ ]  
[ ]  
[ ]
12. Have you ever had bleeding into a joint? [ ] Yes [ ] No (skip to 13)

12.1 Was the bleeding caused by an injury? [ ] Yes [ ] No

12.2 Have you ever talked to a doctor about bleeding into a joint? [ ] Yes [ ] No (skip to 13)

12.3 Have you ever been given medical treatment for bleeding into a joint? [ ] Yes [ ] No (skip to 13)

If yes, please check all of the treatments that you have had.

- I had surgery to take away the blood at least once [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once [ ]
- I was given clotting factors at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]
13. Have you ever had bleeding into or out of the head, brain or spine?  
[ ] Yes  [ ] No (skip to 14)

13.1 Where was the bleeding?
   - Scalp  [ ]
   - Under the skull and around the brain  [ ]
   - Within the brain tissue  [ ]
   - I don’t know  [ ]

13.2 Please check all of the treatments that you have had.
   - I had surgery to take away the blood  [ ]
   - I had surgery to have a shunt put in  [ ]
   - I was given a blood transfusion at least once  [ ]
   - I was given a treatment but don’t know what it was  [ ]

Comments:

______________________________________________________________________
______________________________________________________________________
14 Other types of bleeding. Some of these other types of bleeding would have happened shortly after birth.

14.1 Have you ever had any of the following?

- A problem with bleeding from the umbilical stump at birth
- Cephalohematoma, i.e., a collection of blood under the scalp as a newborn, presenting as a soft swelling at the back of the head
- Bleeding upon suctioning of the mouth and nose at birth
- Bleeding into your cheek, caused by sucking during bottle or breast feeding
- A problem with bleeding during or after the surgery to remove the foreskin of the penis (circumcision)
- A problem with bleeding from a needle poke when blood was drawn
- Bleeding in the white of your eye
- Bleeding after sexual intercourse

[ ] Yes [ ] No [ ] Unsure

14.2 Have you ever talked to a doctor about any of those bleeding symptoms?

[ ] Yes [ ] No
14.3 Have you ever been given medical treatment for any of these bleeding symptoms?

[ ] Yes [ ] No

For each of these symptoms separately, please check the treatments that you have had.

- I was on a medication (liquid or pills) at least once
- I had surgery to stop the bleeding or had stitches at least once
- I was given a medication intravenously (IV), with a needle under the skin, at least once
- I was given a blood transfusion at least once
- I was given a treatment but don’t know what it was

If you have had problems with any other bleeding symptoms that were not included in this questionnaire, please comment on these here.

______________________________________________________________________
______________________________________________________________________
Appendix F

Self BAT Version # 4 (Undiagnosed)
SELF ADMINISTERED BLEEDING TOOL (SELF-BAT)

START TIME: _____________

- If answer [✓] Yes to ANY of the questions below, please complete those sections of the attached questionnaire.
- If answer [✓] No to ALL of the questions below, please complete section 14.0 of the attached questionnaire.

| 1.0 | Have you ever had a nosebleed? | [ ] Yes | [ ] No |
| 2.0 | Have you ever had a bruise? | [ ] Yes | [ ] No |
| 3.0 | Have you ever had bleeding from a small cut, for example, from a paper cut or shaving? | [ ] Yes | [ ] No |
| 4.0 | Have you ever seen blood in the urine? (If you are a female, this does NOT mean from a period.) | [ ] Yes | [ ] No |
| 5.0 | Have you ever had bleeding from the stomach or bowel? | [ ] Yes | [ ] No |
| 6.0 | Have you ever had bleeding from the mouth? (This does NOT include tooth extraction at the dentist.) | [ ] Yes | [ ] No |
| 7.0 | Have you ever had a tooth pulled by the dentist? | [ ] Yes | [ ] No |
| 8.0 | Have you ever had surgery? | [ ] Yes | [ ] No |

*If the research participant is a MALE or a female that has NEVER had a period, please skip to 11.0 now

| 9.0 | Have you ever had a period? | [ ] Yes | [ ] No |
| 10.0 | Have you ever had a baby or been pregnant? | [ ] Yes | [ ] No |
| 11.0 | Have you ever had bleeding into a muscle? | [ ] Yes | [ ] No |
| 12.0 | Have you ever had bleeding into a joint? | [ ] Yes | [ ] No |
| 13.0 | Have you ever had bleeding into the head (brain) or spine? | [ ] Yes | [ ] No |

Please complete section 14.0 of the attached questionnaire.
SELF-BLEEDING ASSESSMENT TOOL:

Patient Information

Name __________________________________________________________

Address _______________________________________________________

Phone Number ___________________ Email ________________________

Gender  Male  □  Female  □

Age ___________  Date of Birth _____________ (DD/MO/YYYY)

Ethnic Background _____________________________________________

Presenting complaint of bleeding or bruising today  Yes □  No □

Personal history of bleeding or bruising  Yes □  No □

Ever been diagnosed with a bleeding disorder?  Yes □  No □

Diagnosis: __________________________________

Immediate or extended family history of bleeding?  Yes □  No/ Unsure □

Relation of family member with bleeding:_____________________________

What was the diagnosis? _________________________________

Please describe any other diagnosed medical conditions, past or present:

_____________________________________________________________________

Are you currently on birth control?  □ Yes  □ No

If yes, please list the type and brand name (ex. IUD, Mirena):

_____________________________________________________________________

Are you pregnant? ___________  Gestation time ____________

Specify any herbals and/or medications that you have taken in the past 30 days:

Name: ___________________________________________ Last time taken:

_____________________________________________________________________

_____________________________________________________________________

_____________________________________________________________________

_____________________________________________________________________

_____________________________________________________________________

_____________________________________________________________________

138
1. **Have you ever experienced nosebleeds?**

   [ ] Yes  [ ] No (skip to 2)

1.1 Please check all of the reasons that have caused your nosebleeds.

   - [ ] an injury
   - [ ] picking your nose
   - [ ] dry air
   - [ ] a stuffy nose (cold, allergy)
   - [ ] taking an aspirin
   - [ ] no reason, my nosebleeds just start on their own

1.2 How long do your nosebleeds usually last?

   [ ] 10 minutes or less
   [ ] more than 10 minutes

1.3 How often do you have nosebleeds?

   [ ] 5 times per year or less
   [ ] more than 5 times per year

1.4 Have you ever talked to a doctor about your nosebleeds?

   [ ] Yes  [ ] No (skip to 2)

1.5 Have you ever been given medical treatment for your nosebleeds?

   [ ] Yes  [ ] No (skip to 2)

   If yes, please check all of the treatments that you have had.

   - [ ] my nose was cauterized or packed at least once
   - [ ] I was on a medication (liquid or pills) at least once
   - [ ] I was given a medication intravenously (IV), or with a needle under the skin at least once
   - [ ] I was given a medication in a nose spray at least once
   - [ ] I was given a blood transfusion at least once
   - [ ] I was given a treatment, but don’t know what it was

Comments:

______________________________________________________________________

______________________________________________________________________

2
2. **Have you ever had unexplained bruises or bruises that are bruises that are larger than you think they should be?**

   [ ] Yes [ ] No (skip to 3)

### 2.1 Please check all the types of bruising you have had.

- petechiae, i.e. small (1-2 mm) red or purple spots on the skin [ ]
- a bruise [ ]
- a hematoma, i.e. a bruise that has a hard lump [ ]
- I don’t know [ ]

### 2.2 How large are your bruises usually?

- the size of a pea or smaller [ ]
- between the size of a pea and an orange [ ]
- the size of an orange or larger [ ]

### 2.3 How often do you get bruises?

[ ] 5 times per year or less
[ ] more than 5 times per year

### 2.4 Where do you usually get bruises?

- on the arms and legs only [ ]
- on the chest, back and stomach only [ ]
- all over your body [ ]

If you get small red-purple spots (petechiae), where do you usually see them?

- on the legs only [ ]
- on your face only [ ]
- all over your body [ ]
2.5 Have you ever talked to a doctor about your bruising? [ ] Yes [ ] No (skip to 3)

2.6 Have you ever been given medical treatment for your bruising? [ ] Yes [ ] No (skip to 3)

If yes, please check all of the treatments that you have had.
- I was treated with medications at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]
3. **Have you ever had bleeding from a small cut?**

- [ ] Yes
- [ ] No (skip to 4)

3.1 How long do you usually bleed after a small cut?

- [ ] 10 minutes or less
- [ ] more than 10 minutes

3.2 How often do you have bleeding from a small cut?

- [ ] 5 times per year or less
- [ ] more than 5 times per year

3.3 Have you ever talked to a doctor about bleeding from a small cut?

- [ ] Yes
- [ ] No (skip to 4)

3.4 Have you ever been given medical treatment for a small cut?

- [ ] Yes
- [ ] No (skip to 4)

If yes, please check all of the treatments that you have had.

- [ ] I had stitches at least once
- [ ] I was given a medication intravenously (IV) or with a needle under the skin at least once
- [ ] I was given medication orally at least once
- [ ] I was given a blood transfusion at least once
- [ ] I was given a treatment, but don’t know what it was
4. **Have you ever seen blood in your urine?** *(If you are a female, this does NOT include when you have had your period.)*

   [ ] Yes  [ ] No  (skip to 5)

4.1 Please check all of the causes of blood in the urine that you have had.

   - kidney stones
   - infection
   - another kidney or bladder disease
   - no reason that I know

4.2 **Have you ever talked to a doctor about unexplained blood in your urine?**

   [ ] Yes  [ ] No  (skip to 5)

4.3 **Have you ever been given medical treatment for unexplained blood in your urine?**

   If yes, please check all of the treatments that you have had.

   - I had surgery at least once to stop the bleeding
   - I was on treatment with iron at least once
   - I was given a medication intravenously (IV), or with a needle under the skin at least once
   - I was given a blood transfusion at least once
   - I was given antibiotics at least once
   - I was given a treatment but don’t know what it was
5. Have you ever had bleeding inside your intestines, stomach or bowel?  
[ ] Yes  [ ] No (skip to 6)

5.1 Have you ever:
- vomited red blood, or what looked like coffee grounds  
- passed black, tarry stools while you were not taking iron supplements  
- passed red blood in or with your stools

5.2 Please check all of the causes of this bleeding that you have had
- an ulcer  
- liver disease  
- abnormal and fragile blood vessels in the bowel (angiodyplasia)  
- hemorrhoids, 'piles' or anal fissures  
- another identifiable cause  
- for no reason

5.3 Have you ever talked to a doctor about unexplained bleeding from your stomach or bowel?  
[ ] Yes  [ ] No (skip to 6)

5.4 Have you ever been given medical treatment for unexplained bleeding from your stomach or bowel?  
[ ] Yes  [ ] No (skip to 6)

If yes, please check all of the treatments that you have had.
- I had surgery to stop the bleeding at least once
- I was on a medication (liquid or pills) at least once
- I was given a medication intravenously (IV), or with a needle under the skin at least once
- I was given a blood transfusion at least once
- I was given a treatment but don’t know what it was
6. Have you ever noticed bleeding from the mouth? (This does NOT include tooth extraction at the dentist.)

[ ] Yes  [ ] No (skip to 7)

6.1 Please check all of the causes of bleeding from the mouth that you have had.

- new teeth coming in or tooth loss  [ ]
- brushing/flossing  [ ]
- bite on lip, tongue or cheek  [ ]
- cleaning at the dentist’s  [ ]
- another cause  [ ]

Please specify:

6.2 How long does this bleeding usually last?

[ ] 10 minutes or less
[ ] more than 10 minutes

6.3 Have you ever talked to a doctor or dentist about bleeding from the mouth?

[ ] Yes  [ ] No (skip to 7)

6.4 Have you ever been given medical treatment for bleeding from the mouth?

[ ] Yes  [ ] No (skip to 7)

If yes, please check all of the treatments that you have had.

- I had dental packing, cauterization or had stitches to stop the bleeding at least once  [ ]
- I was on a medication (liquid or pills) at least once  [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once  [ ]
- I was given a blood transfusion at least once  [ ]
- I was given a treatment but don’t know what it was  [ ]
7. Have you ever had a tooth/teeth taken out at the dentist?  [ ] Yes  [ ] No (skip to 8)

7.1 Please check what kind of tooth was taken out and note how many of each
   - baby tooth  [ ] ______
   - adult tooth  [ ] ______
   - wisdom tooth  [ ] ______

7.2 Did you experience any abnormal bleeding after any of these extractions?  [ ] Yes  [ ] No (skip to 8)

7.3 Have you ever talked to a doctor or dentist about this bleeding?  [ ] Yes  [ ] No (skip to 8)

7.4 Have you ever been given medical treatment for bleeding after a tooth was taken out?
   If yes, please check all of the treatments that you have had.
   - I had dental packing or had stitches to stop the bleeding, at least once  [ ]
   - I was on a medication (liquid or pills) at least once  [ ]
   - I was given a medication intravenously (IV), or with a needle under the skin at least once  [ ]
   - I was given a blood transfusion at least once  [ ]
   - I was given a treatment but don’t know what it was  [ ]
8.  Have you ever had surgery or a major trauma (e.g. car accident)? [ ] Yes  [ ] No (skip to 9)

8.1 Please check what kind of surgery/trauma you had
   - tonsils/adenoids taken out [ ]
   - other surgery of the nose or throat [ ]
   - surgery of the chest [ ]
   - surgery of the womb or ovaries, including caesarian section, removal of the womb [ ]
   - other surgery of the stomach or belly [ ]
   - other surgeries [ ]
   - trauma

   Please specify: __________________________

8.2 Did you experience any abnormal bleeding during or after any of these surgeries? [ ] Yes  [ ] No (skip to 9)

8.3 Have you ever talked to a doctor about the bleeding during or after you had surgery? [ ] Yes  [ ] No (skip to 9)

8.4 Have you ever been given medical treatment for bleeding during or after surgery? [ ] Yes  [ ] No (skip to 9)

   If yes, please check all of the treatments that you have had.
   - I had packing or stitches to stop the bleeding, at least once [ ]
   - I was on a medication (liquid or pills) at least once [ ]
   - I was given a medication intravenously (IV), with a needle under the skin, at least once [ ]
   - I was given a blood transfusion at least once [ ]
   - I was given a treatment but don’t know what it was [ ]
If you are a male, please skip to 11 now.

9. Have you ever had a period?

[ ] Yes  [ ] No (skip to 10)

Are you:

☐ Pre-menopausal  ☐ Post-menopausal

*If you are post-menopausal, please answer the following questions to the best of your ability

9.1 Were/are your periods regular?

[ ] Yes  [ ] No

Please check all that applies to the heaviest period you ever had:

- I had to change my pad/tampon more often than every 2 hours  [ ]
- the period lasted for more than 7 days  [ ]
- I passed clots and had flooding  [ ]
- Spotting mid-cycle  [ ]

9.2 Have you stayed at home from work/school more than twice a year because of heavy bleeding?

[ ] Yes  [ ] No

9.3 Have your periods been heavy from the get-go?

[ ] Yes  [ ] No

9.4 How long have you had a problem with heavy periods?

[ ] 1 year or less  [ ] more than 1 year

9.5 Have you ever talked to a doctor about your heavy periods?

[ ] Yes  [ ] No
9.7 Have you ever been given medical treatment for heavy periods?  

[ ] Yes  [ ] No (skip to 10)

If yes, please check all of the treatments that you have had.

- I was on iron or on other medications (liquid or pills) at least once  
- I was given the birth control pill because of heavy periods  
- I was given the birth control pill as well as on other pills  
- I had surgery to stop the bleeding at least once (e.g. removal of the womb, burning (ablation) or scraping (curettage) of the lining of the womb)  
- I was given a medication intravenously (IV), or with a needle under the skin at least once  
- I was given a blood transfusion at least once  
- I was admitted to hospital at least once  
- I was given a treatment but don’t know what it was  
- I was given medication for pain associated with cramping

Comments: ________________________________
10. Have you ever been pregnant? [ ] Yes [ ] No (skip to 11)

10.1 Have you ever been pregnant but not carried the baby to term? [ ] Yes [ ] No (skip to 10.5)

If so, how many times? ______

10.2 Was it associated with excessive bleeding? [ ] Yes [ ] No

10.3 Did you seek medical attention? [ ] Yes [ ] No

If yes, please check all of the treatments you have had:

- I was given a medication intravenously (IV) to induce contraction of the womb at least once

- I was put on iron or other pills at least once

- I was given a medication intravenously (IV), or with a needle under the skin at least once

- I was given a blood transfusion at least once

- I had an examination and/or packing of the womb while I was put asleep at least once

- I had surgery (eg. removing the womb, tying off the bleeding vessels,…) at least once

- I was in the intensive care unit (ICU) at least once

- I was given a treatment but don’t know what it was

- Other or non-applicable
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<th>Question</th>
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<tbody>
<tr>
<td>10.5</td>
<td>Have you ever given birth by vaginal delivery? (If no, skip to 11)</td>
<td>[ ] Yes [ ] No (skip to 11)</td>
</tr>
<tr>
<td></td>
<td>How many times?</td>
<td>[ ] Yes [ ] No</td>
</tr>
<tr>
<td></td>
<td>Did you experience problems with bleeding during the pregnancy or after the birth? (If no, skip to 11)</td>
<td>[ ] Yes [ ] No</td>
</tr>
<tr>
<td>10.6</td>
<td>When did the problems with vaginal bleeding occur?</td>
<td>[ ] within the first 24 hours after delivery [ ] between 24 hours and 6 weeks after delivery [ ] all of the above</td>
</tr>
<tr>
<td>10.8</td>
<td>How long did the vaginal discharge last?</td>
<td>[ ] less than 6 weeks [ ] more than 6 weeks</td>
</tr>
<tr>
<td>10.9</td>
<td>Did you have to stay in the hospital longer because of this bleeding?</td>
<td>[ ] Yes [ ] No</td>
</tr>
<tr>
<td>10.10</td>
<td>Have you ever talked to a doctor about this bleeding?</td>
<td>[ ] Yes [ ] No (skip to 11)</td>
</tr>
</tbody>
</table>
10.7 Have you ever been given medical treatment for bleeding after having a baby?

- [ ] Yes
- [ ] No (skip to 11)

10.8 If yes, please check all of the treatments that you have had.

- I was given a medication intravenously (IV) to induce contraction of the womb at least once
- I was put on iron or other pills at least once
- I was given a medication intravenously (IV), or with a needle under the skin at least once
- I was given a blood transfusion at least once
- I had an examination and/or packing of the womb while I was put asleep at least once
- I had surgery (eg. removing the womb, tying off the bleeding vessels,...) at least once
- I was in the intensive care unit (ICU) at least once
- I was given a treatment but don't know what it was
Have you ever had bleeding into a muscle? (This would look like a bruise on the skin, but it would be hard and hurt a lot more.)

<table>
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<th>Question</th>
<th>Yes</th>
<th>No (skip to 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.1 Was this bleeding caused by an injury?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.2 Have you ever talked to a doctor about your bleeding into a muscle?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.3 Have you ever been given medical treatment for bleeding into a muscle?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If yes, please check all of the treatments that you have had.

- Had surgery to take away the blood at least once
- Was given a medication intravenously (IV), or with a needle under the skin at least once
- Was given clotting factors at least once
- Was given a blood transfusion at least once
- Was given a treatment but don’t know what it was
<table>
<thead>
<tr>
<th>12.</th>
<th><strong>Have you ever had bleeding into a joint?</strong></th>
<th>[ ] Yes</th>
<th>[ ] No (skip to 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.1</td>
<td>Was the bleeding caused by an injury?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>12.2</td>
<td>Have you ever talked to a doctor about bleeding into a joint?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 13)</td>
</tr>
<tr>
<td>12.3</td>
<td>Have you ever been given medical treatment for bleeding into a joint?</td>
<td>[ ] Yes</td>
<td>[ ] No (skip to 13)</td>
</tr>
</tbody>
</table>

If yes, please check all of the treatments that you have had.

- I had surgery to take away the blood at least once [ ]
- I was given a medication intravenously (IV), or with a needle under the skin at least once [ ]
- I was given clotting factors at least once [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don’t know what it was [ ]
13. Have you ever had bleeding into or out of the head, brain or spine?  
[ ] Yes  
[ ] No (skip to 14)

13.1 Where was the bleeding?
- Scalp [ ]
- Under the skull and around the brain [ ]
- Within the brain tissue [ ]
- I don't know [ ]

13.2 Please check all of the treatments that you have had.
- I had surgery to take away the blood [ ]
- I had surgery to have a shunt put in [ ]
- I was given a blood transfusion at least once [ ]
- I was given a treatment but don't know what it was [ ]

Comments:
____________________________________________________________________
____________________________________________________________________
<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Unsure</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.1 Have you ever had any of the following?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- A problem with bleeding from the umbilical stump at birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- cephalohematoma, i.e. a collection of blood under the scalp as a newborn, presenting as a soft swelling at the back of the head</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- bleeding upon succioning of the mouth and nose at birth</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- bleeding into your cheek, caused by sucking during bottle or breastfeeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- a problem with bleeding during or after the surgery to remove the foreskin of the penis (circumcision)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- a problem with bleeding from a needle poke when blood was drawn</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- bleeding in the white of your eye</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- bleeding after sexual intercourse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.2 Have you ever talked to a doctor about any of those bleeding symptoms?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
14.3 Have you ever been given medical treatment for any of these bleeding symptoms?  
[ ] Yes  [ ] No

For each of these symptoms separately, please check the treatments that you have had.

- I was on a medication (liquid or pills) at least once  
[ ]

- I had surgery to stop the bleeding or had stitches at least once  
[ ]

- I was given a medication intravenously (IV), with a needle under the skin, at least once  
[ ]

- I was given a blood transfusion at least once  
[ ]

- I was given a treatment but don’t know what it was  
[ ]

If you have had problems with any other bleeding symptoms that were not included in this questionnaire, please comment on these here.

____________________________________________________________________
____________________________________________________________________
Appendix G

Self BAT Version # 4 (Previously Diagnosed)
**SELF ADMINISTERED BLEEDING TOOL (SELF-BAT)**

**START TIME:** _____________

- If answer [✓] Yes to ANY of the questions below, please complete those sections of the attached questionnaire.
- If answer [✓] No to ALL of the questions below, please complete section 14.0 of the attached questionnaire.

<table>
<thead>
<tr>
<th></th>
<th>Question</th>
<th>[ ] Yes</th>
<th>[ ] No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>Have you ever had a nosebleed?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>Have you ever had a bruise?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.0</td>
<td>Have you ever had bleeding from a small cut, for example, from a paper cut or shaving?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>4.0</td>
<td>Have you ever seen blood in the urine? (If you are a female, this does NOT mean from a period.)</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>5.0</td>
<td>Have you ever had bleeding from the stomach or bowel?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>6.0</td>
<td>Have you ever had bleeding from the mouth? (This does NOT include tooth extraction at the dentist.)</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>7.0</td>
<td>Have you ever had a tooth pulled by the dentist?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>8.0</td>
<td>Have you ever had surgery?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
</tbody>
</table>

*If the research participant is a MALE or a female that has NEVER had a period, please skip to 11.0 now*

<table>
<thead>
<tr>
<th></th>
<th>Question</th>
<th>[ ] Yes</th>
<th>[ ] No</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.0</td>
<td>Have you ever had a period?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10.0</td>
<td>Have you ever had a baby or been pregnant?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>11.0</td>
<td>Have you ever had bleeding into a muscle?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>12.0</td>
<td>Have you ever had bleeding into a joint?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
<tr>
<td>13.0</td>
<td>Have you ever had bleeding into the head (brain) or spine?</td>
<td>[ ] Yes</td>
<td>[ ] No</td>
</tr>
</tbody>
</table>

Please complete section 14.0 of the attached questionnaire.
SELF-BLEEDING ASSESSMENT TOOL:

Patient Information

Name _______________________________________________
Address _____________________________________________
_____________________________________________________
Phone Number _____________________  Email __________________
Gender  Male □  Female □
Age ___________  Date of Birth ___________ (DD/MO/YYYY)
Ethnic Background _________________________________

Presenting complaint of bleeding or bruising today  Yes □  No □
Personal history of bleeding or bruising  Yes □  No □
Ever been diagnosed with a bleeding disorder?  Yes □  No □
Diagnosis: _________________________________________________
Immediate or extended family history of bleeding?  Yes □  No/ Unsure □
Relation of family member with bleeding:_______________________________
What was the diagnosis? ___________________________________________
Please describe any other diagnosed medical conditions, past or present:
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
Are you currently on birth control? □ Yes □ No
If yes, please list the type and brand name (ex. IUD, Mirena):
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
Are you pregnant? ___________  Gestation time ___________
Specify any herbals and/or medications that you have taken in the past 30 days:
Name:  Last time taken:
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
1. **Have you ever had a nosebleed?**  
   [ ] Yes  
   [ ] No (skip to 2)

### Before Diagnosis

Please check all of the reasons that caused you to have nosebleeds:

- [ ] An injury
- [ ] Picking your nose
- [ ] Dry air
- [ ] A stuffy nose (cold, allergies)
- [ ] Taking an aspirin
- [ ] No reason, my nosebleeds just start on their own

How long did your nosebleeds usually last?

- [ ] 10 minutes or less
- [ ] More than 10 minutes

How often did you have nosebleeds?

- [ ] 5 times per year or less
- [ ] More than 5 times per year

Did you ever talk to a doctor about your nosebleeds?

- [ ] Yes  
  - [ ] No

Were you ever given medical treatment for your nosebleeds?

- [ ] Yes  
  - [ ] No

If yes, please check all of the treatments that you had:

- [ ] My nose was cauterized or packed at least once
- [ ] I was on a medication (liquid or pills) at least once

### After Diagnosis

Please check all of the reasons that cause you to have nosebleeds:

- [ ] An injury
- [ ] Picking your nose
- [ ] Dry air
- [ ] A stuffy nose (cold, allergies)
- [ ] Taking an aspirin
- [ ] No reason, my nosebleeds just start on their own

How long do your nosebleeds usually last?

- [ ] 10 minutes or less
- [ ] More than 10 minutes

How often do you have nosebleeds?

- [ ] 5 times per year or less
- [ ] More than 5 times per year

Do you ever talk to a doctor about your nosebleeds?

- [ ] Yes  
  - [ ] No (skip to 2)

Were you ever given medical treatment for your nosebleeds?

- [ ] Yes  
  - [ ] No (skip to 2)

If yes, please check all of the treatments that you had:

- [ ] My nose was cauterized or packed at least once
- [ ] I was on a medication (liquid or pills) at least once
☐ I was given a medication in a nose spray at least once
☐ I was given a blood transfusion at least once
☐ I was given a treatment but I don’t know what it was

☐ I was given a medication in a nose spray at least once
☐ I was given a blood transfusion at least once
☐ I was given a treatment but I don’t know what it was
2. Have you ever had bruises or other bleeding into/under the skin? (we are interested in any bruise or other skin bleeding you have had)

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Please check all of the types of bleeding into the skin that you had:</td>
<td>Please check all of the types of bleeding into the skin that you had:</td>
</tr>
<tr>
<td>☐ Petechiae, i.e. small (1-2 mm) red or purple spots on the skin</td>
<td>☐ Petechiae, i.e. small (1-2 mm) red or purple spots on the skin</td>
</tr>
<tr>
<td>☐ A regular bruise</td>
<td>☐ A regular bruise</td>
</tr>
<tr>
<td>☐ A hematoma, i.e. a firm, painful lump from bleeding into/under the skin</td>
<td>☐ A hematoma, i.e. a firm, painful lump from bleeding into/under the skin</td>
</tr>
<tr>
<td>☐ I don’t know</td>
<td>☐ I don’t know</td>
</tr>
<tr>
<td>How large were your bruises usually?</td>
<td>How large are your bruises usually?</td>
</tr>
<tr>
<td>☐ The size of a pea or smaller</td>
<td>☐ The size of a pea or smaller</td>
</tr>
<tr>
<td>☐ Between the size of a pea and an orange</td>
<td>☐ Between the size of a pea and an orange</td>
</tr>
<tr>
<td>☐ The size of an orange or larger</td>
<td>☐ The size of an orange or larger</td>
</tr>
<tr>
<td>How often did you get bruises?</td>
<td>How often do you get bruises?</td>
</tr>
<tr>
<td>☐ 5 times per year or less</td>
<td>☐ 5 times per year or less</td>
</tr>
<tr>
<td>☐ More than 5 times per year</td>
<td>☐ More than 5 times per year</td>
</tr>
<tr>
<td>Where did you usually get bruises?</td>
<td>Where do you usually get bruises?</td>
</tr>
<tr>
<td>☐ Arms and legs only</td>
<td>☐ Arms and legs only</td>
</tr>
<tr>
<td>☐ Chest, back and stomach only</td>
<td>☐ Chest, back and stomach only</td>
</tr>
<tr>
<td>☐ All over your body</td>
<td>☐ All over your body</td>
</tr>
</tbody>
</table>

If you got small red-purple spots (petechiae), where did you usually see them?
<p>| If you got small red-purple spots (petechiae), where do you usually see them? |
|------------------|------------------|
| ☐ Legs only | ☐ Legs only |
| ☐ Face only | ☐ Face only |
| ☐ All over your body | ☐ All over your body |</p>
<table>
<thead>
<tr>
<th>Did you ever talk to a doctor about your bruising?</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Yes □ No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Were you ever given medical treatment for your bruising?</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Yes □ No</td>
</tr>
</tbody>
</table>

If yes, please check all of the treatments that you had:

- □ I was treated with medications at least once
- □ I was given a blood transfusion at least once
- □ I was given a treatment but I don’t know what it was

---

<table>
<thead>
<tr>
<th>Do you ever talk to a doctor about your bruising?</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Yes □ No (skip to 3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Are you ever given medical treatment for your bruising?</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Yes □ No (skip to 3)</td>
</tr>
</tbody>
</table>

If yes, please check all of the treatments that you had:

- □ I was treated with medications at least once
- □ I was given a blood transfusion at least once
- □ I was given a treatment but I don’t know what it was
3. Have you ever had bleeding from a small cut? (i.e.: shaving or while cutting food)  
[ ] Yes  [ ] No (skip to 4)

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>How long did you usually bleed after a small cut?</strong></td>
<td><strong>How long do you usually bleed after a small cut?</strong></td>
</tr>
<tr>
<td>- 10 minutes or less</td>
<td>- 10 minutes or less</td>
</tr>
<tr>
<td>- More than 10 minutes</td>
<td>- More than 10 minutes</td>
</tr>
<tr>
<td><strong>How often did you have bleeding from a small cut?</strong></td>
<td><strong>How often do you have bleeding from a small cut?</strong></td>
</tr>
<tr>
<td>- 5 times per year or less</td>
<td>- 5 times per year or less</td>
</tr>
<tr>
<td>- More than 5 times per year</td>
<td>- More than 5 times per year</td>
</tr>
<tr>
<td><strong>Did you ever talk to a doctor about bleeding from a small cut?</strong></td>
<td><strong>Do you ever talk to a doctor about bleeding from a small cut?</strong></td>
</tr>
<tr>
<td>- Yes  - No</td>
<td>- Yes  - No</td>
</tr>
<tr>
<td><strong>Were you ever given medical treatment for a small cut?</strong></td>
<td><strong>Are you ever given medical treatment for a small cut?</strong></td>
</tr>
<tr>
<td>- Yes  - No</td>
<td>- Yes  - No</td>
</tr>
<tr>
<td><strong>If yes, please check all of the treatments you had:</strong></td>
<td><strong>If yes, please check all of the treatments you had:</strong></td>
</tr>
<tr>
<td>- I had stitches at least once</td>
<td>- I had stitches at least once</td>
</tr>
<tr>
<td>- I was given medication intravenously (IV) or with a needle under the skin at least once</td>
<td>- I was given medication intravenously (IV) or with a needle under the skin at least once</td>
</tr>
<tr>
<td>- I was given a blood transfusion at least once</td>
<td>- I was given a blood transfusion at least once</td>
</tr>
<tr>
<td>- I was given a treatment, but I don’t know what it was</td>
<td>- I was given a treatment, but I don’t know what it was</td>
</tr>
</tbody>
</table>
4. Have you ever seen blood in your urine?  [ ] Yes  [ ] No (skip to 5)
   (If you are a female, this does NOT include when you have your period.)

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Please check all of the causes of blood in the urine that you had:</strong></td>
<td><strong>Please check all of the causes of blood in the urine that you had:</strong></td>
</tr>
<tr>
<td>□ Kidney stones</td>
<td>□ Kidney stones</td>
</tr>
<tr>
<td>□ Infection</td>
<td>□ Infection</td>
</tr>
<tr>
<td>□ Another kidney or bladder disease</td>
<td>□ Another kidney or bladder disease</td>
</tr>
<tr>
<td>□ No reason that I know of</td>
<td>□ No reason that I know of</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Did you ever talk to your doctor about unexplained blood in your urine?</th>
<th>Did you ever talk to your doctor about unexplained blood in your urine?</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Yes  □ No</td>
<td>□ Yes  □ No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Were you ever given medical treatment for unexplained blood in your urine?</th>
<th>Were you ever given medical treatment for unexplained blood in your urine?</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Yes  □ No</td>
<td>□ Yes  □ No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>If yes, please check all of the treatments you had:</th>
<th>If yes, please check all of the treatments you had:</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ I had surgery at least once to stop the bleeding</td>
<td>□ I had surgery at least once to stop the bleeding</td>
</tr>
<tr>
<td>□ I was on treatment with iron at least once</td>
<td>□ I was on treatment with iron at least once</td>
</tr>
<tr>
<td>□ I was given a medication intravenously (IV), or with a needle under the skin at least once</td>
<td>□ I was given a medication intravenously (IV), or with a needle under the skin at least once</td>
</tr>
<tr>
<td>□ I was given a blood transfusion at least once</td>
<td>□ I was given a blood transfusion at least once</td>
</tr>
<tr>
<td>□ I was given antibiotics at least once</td>
<td>□ I was given antibiotics at least once</td>
</tr>
<tr>
<td>□ I was given a treatment but I don’t know what it was</td>
<td>□ I was given a treatment but I don’t know what it was</td>
</tr>
</tbody>
</table>
5. Have you ever had bleeding inside your intestines, stomach or bowel?  
[ ] Yes  [ ] No (skip to 6)

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Did you ever:</strong></td>
<td><strong>Do you ever:</strong></td>
</tr>
<tr>
<td>☐ Vomit red blood, or what looked like coffee grounds</td>
<td>☐ Vomit red blood, or what looked like coffee grounds</td>
</tr>
<tr>
<td>☐ Pass black, tarry stools while you weren’t taking iron supplements</td>
<td>☐ Pass black, tarry stools while you weren’t taking iron supplements</td>
</tr>
<tr>
<td>☐ Pass red blood in or with your stools</td>
<td>☐ Pass red blood in or with your stools</td>
</tr>
</tbody>
</table>

Please check all of the causes of this bleeding that you have had:

☐ An ulcer  
☐ Liver disease  
☐ Abnormal and fragile blood vessels in the bowel (angiodysplasia)  
☐ Hemorrhoids, ‘piles’ or anal fissures  
☐ Another identifiable cause  
☐ For no reason

**Did you ever talk to a doctor about unexplained bleeding from your stomach or bowel?**

☐ Yes  ☐ No

**Were you ever given medical treatment for unexplained bleeding from your stomach or bowel?**

☐ Yes  ☐ No

If yes, please check all of the treatments you had:

☐ Surgery to stop the bleeding  
☐ Medication (liquid or pills)  
☐ Medication given intravenously (IV), or with a needle under the skin  
☐ Blood transfusion  
☐ Unknown treatment

**Are you ever given medical treatment for unexplained bleeding from your stomach or bowel?**

☐ Yes  ☐ No

If yes, please check all of the treatments you had:

☐ Surgery to stop the bleeding  
☐ Medication (liquid or pills)  
☐ Medication given intravenously (IV), or with a needle under the skin  
☐ Blood transfusion  
☐ Unknown treatment
6. Have you ever noticed bleeding from your gums or inside the mouth? (This does NOT include tooth extraction at the dentist.)

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you ever noticed bleeding from your gums or inside the mouth?</td>
<td>[ ] Yes [ ] No (skip to 7)</td>
</tr>
<tr>
<td>Please check all of the causes of bleeding from the mouth that you have had:</td>
<td>Please check all of the causes of bleeding from the mouth that you have had:</td>
</tr>
<tr>
<td>- New teeth coming on or tooth loss</td>
<td>- New teeth coming on or tooth loss</td>
</tr>
<tr>
<td>- Brushing or flossing</td>
<td>- Brushing or flossing</td>
</tr>
<tr>
<td>- Bite on the lip, tongue or cheek</td>
<td>- Bite on the lip, tongue or cheek</td>
</tr>
<tr>
<td>- Cleaning at the dentist</td>
<td>- Cleaning at the dentist</td>
</tr>
<tr>
<td>- Another cause:</td>
<td>- Another cause:</td>
</tr>
<tr>
<td>How long did the bleeding usually last?</td>
<td>How long does the bleeding usually last?</td>
</tr>
<tr>
<td>- 10 minutes or less</td>
<td>- 10 minutes or less</td>
</tr>
<tr>
<td>- More than 10 minutes</td>
<td>- More than 10 minutes</td>
</tr>
<tr>
<td>Did you ever talk to a doctor or dentist about bleeding from the mouth?</td>
<td>Have you ever talked to a doctor or dentist about bleeding from the mouth?</td>
</tr>
<tr>
<td>- Yes</td>
<td>- Yes</td>
</tr>
<tr>
<td>- No</td>
<td>- No</td>
</tr>
<tr>
<td>Were you ever given medical treatment for bleeding from the mouth?</td>
<td>Are you ever given medical treatment for bleeding from the mouth?</td>
</tr>
<tr>
<td>- Yes</td>
<td>- Yes</td>
</tr>
<tr>
<td>- No</td>
<td>- No</td>
</tr>
<tr>
<td>If yes, please check all of the treatments you had:</td>
<td>If yes, please check all of the treatments you have had:</td>
</tr>
<tr>
<td>- Dental packing, cauterization or stitches</td>
<td>- Dental packing, cauterization or stitches</td>
</tr>
<tr>
<td>- Medication (liquid or pills) at least once</td>
<td>- Medication (liquid or pills) at least once</td>
</tr>
<tr>
<td>- Medication given intravenously (IV), or with a needle under the skin at least once</td>
<td>- Medication given intravenously (IV), or with a needle under the skin at least once</td>
</tr>
<tr>
<td>- Blood transfusion</td>
<td>- Blood transfusion</td>
</tr>
<tr>
<td>- Unsure of treatment</td>
<td>- Unsure of treatment</td>
</tr>
</tbody>
</table>
7. Have you ever had a tooth/teeth pulled by a dentist? [ ] Yes [ ] No (skip to 8)

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Please check what kind of tooth was taken out and note how many of each:</strong></td>
<td><strong>Please check what kind of tooth was taken out and note how many of each:</strong></td>
</tr>
<tr>
<td>☐ Baby teeth</td>
<td>☐ Baby teeth</td>
</tr>
<tr>
<td>☐ Adult teeth</td>
<td>☐ Adult teeth</td>
</tr>
<tr>
<td>☐ Wisdom teeth</td>
<td>☐ Wisdom teeth</td>
</tr>
<tr>
<td><strong>Did you experience any abnormal bleeding after any of these extractions?</strong></td>
<td><strong>Did you experience any abnormal bleeding after any of these extractions?</strong></td>
</tr>
<tr>
<td>☐ Yes</td>
<td>☐ Yes</td>
</tr>
<tr>
<td>☐ No</td>
<td>☐ No</td>
</tr>
<tr>
<td><strong>Did you ever talk to a doctor or dentist about the bleeding?</strong></td>
<td><strong>Did you ever talk to a doctor or dentist about the bleeding?</strong></td>
</tr>
<tr>
<td>☐ Yes</td>
<td>☐ Yes</td>
</tr>
<tr>
<td>☐ No</td>
<td>☐ No</td>
</tr>
<tr>
<td><strong>Were you ever given medical treatment for bleeding after a tooth was taken out?</strong></td>
<td><strong>Were you ever given medical treatment for bleeding after a tooth was taken out?</strong></td>
</tr>
<tr>
<td>☐ Yes</td>
<td>☐ Yes</td>
</tr>
<tr>
<td>☐ No</td>
<td>☐ No</td>
</tr>
<tr>
<td><strong>If yes, please check all of the treatments you had:</strong></td>
<td><strong>If yes, please check all of the treatments you had:</strong></td>
</tr>
<tr>
<td>☐ Dental packing, cauterization or stitches</td>
<td>☐ Dental packing, cauterization or stitches</td>
</tr>
<tr>
<td>☐ Medication (liquid or pills) at least once</td>
<td>☐ Medication (liquid or pills) at least once</td>
</tr>
<tr>
<td>☐ Medication given intravenously (IV), or with a needle under the skin at least once</td>
<td>☐ Medication given intravenously (IV), or with a needle under the skin at least once</td>
</tr>
<tr>
<td>☐ Blood transfusion</td>
<td>☐ Blood transfusion</td>
</tr>
<tr>
<td>☐ Unsure of treatment</td>
<td>☐ Unsure of treatment</td>
</tr>
</tbody>
</table>
8. Have you ever had surgery or a major trauma (e.g. car accident)?

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Please check what type of surgery or trauma you had:</strong></td>
<td><strong>Please check what type of surgery or trauma you had:</strong></td>
</tr>
<tr>
<td>☐ Tonsil/ adenoid removal</td>
<td>☐ Tonsil/ adenoid removal</td>
</tr>
<tr>
<td>☐ Other nose/ throat surgery</td>
<td>☐ Other nose/ throat surgery</td>
</tr>
<tr>
<td>☐ Chest surgery</td>
<td>☐ Chest surgery</td>
</tr>
<tr>
<td>☐ Surgery of the womb or ovaries (including caesarean section or removal of womb)</td>
<td>☐ Surgery of the womb or ovaries (including caesarean section or removal of womb)</td>
</tr>
<tr>
<td>☐ Other surgery of the stomach or belly</td>
<td>☐ Other surgery of the stomach or belly</td>
</tr>
<tr>
<td>☐ Other surgery: __________________</td>
<td>☐ Other surgery: __________________</td>
</tr>
<tr>
<td>☐ Trauma: ______________________</td>
<td>☐ Trauma: ______________________</td>
</tr>
<tr>
<td><strong>Did you experience any abnormal bleeding during or after any of these surgeries or trauma?</strong></td>
<td><strong>Did you experience any abnormal bleeding during or after any of these surgeries or trauma?</strong></td>
</tr>
<tr>
<td>☐ Yes</td>
<td>☐ Yes</td>
</tr>
<tr>
<td>☐ No</td>
<td>☐ No</td>
</tr>
<tr>
<td><strong>Did you ever talk to a doctor about the bleeding during or after your surgery or trauma?</strong></td>
<td><strong>Did you ever talk to a doctor about the bleeding during or after your surgery or trauma?</strong></td>
</tr>
<tr>
<td>☐ Yes</td>
<td>☐ Yes</td>
</tr>
<tr>
<td>☐ No</td>
<td>☐ No</td>
</tr>
<tr>
<td><strong>Were you given medical treatment for bleeding during or after surgery or trauma?</strong></td>
<td><strong>Were you given medical treatment for bleeding during or after surgery or trauma?</strong></td>
</tr>
<tr>
<td>☐ Yes</td>
<td>☐ Yes</td>
</tr>
<tr>
<td>☐ No</td>
<td>☐ No</td>
</tr>
<tr>
<td>If yes, please check all of the treatments you received:</td>
<td><strong>If yes, please check all of the treatments you received:</strong></td>
</tr>
<tr>
<td>☐ Packing or stitches to stop the bleeding</td>
<td>☐ Packing or stitches to stop the bleeding</td>
</tr>
<tr>
<td>☐ Medication (liquid or pills) at least once</td>
<td>☐ Medication (liquid or pills) at least once</td>
</tr>
<tr>
<td>[ ] Yes</td>
<td>[ ] No (skip to 9)</td>
</tr>
<tr>
<td>Medication given intravenously (IV), or with a needle under the skin at least once</td>
<td>Blood transfusion</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td></td>
<td>Unsure of treatment</td>
</tr>
</tbody>
</table>
If you are a male, please skip to 11 now.

9. With regards to your menstrual periods:

<table>
<thead>
<tr>
<th>Are you:</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Still having your periods</td>
</tr>
</tbody>
</table>

* If you are post-menopausal, please answer the following questions to the best of your ability

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Were your periods regular?</td>
<td></td>
</tr>
<tr>
<td>☐ Yes ☐ No</td>
<td></td>
</tr>
<tr>
<td>Please check all that applies to the heaviest period you had:</td>
<td></td>
</tr>
<tr>
<td>☐ I had to change my pad/tampon more often than every 2 hours</td>
<td></td>
</tr>
<tr>
<td>☐ My period lasted more than 7 days</td>
<td></td>
</tr>
<tr>
<td>☐ I passed clots or had flooding</td>
<td></td>
</tr>
<tr>
<td>☐ I spotted mid-cycle</td>
<td></td>
</tr>
<tr>
<td>Did you stay at home from work/school more than twice a year because of heavy bleeding?</td>
<td></td>
</tr>
<tr>
<td>☐ Yes ☐ No</td>
<td></td>
</tr>
<tr>
<td>Had your periods been heavy from the get-go?</td>
<td></td>
</tr>
<tr>
<td>☐ Yes ☐ No</td>
<td></td>
</tr>
<tr>
<td>How long did you have a problem with heavy periods?</td>
<td></td>
</tr>
<tr>
<td>☐ 1 year or less</td>
<td></td>
</tr>
<tr>
<td>☐ More than 1 year</td>
<td></td>
</tr>
<tr>
<td>Did you talk to a doctor about your heavy periods?</td>
<td></td>
</tr>
<tr>
<td>☐ Yes ☐ No</td>
<td></td>
</tr>
<tr>
<td>Are your periods regular?</td>
<td></td>
</tr>
<tr>
<td>☐ Yes ☐ No</td>
<td></td>
</tr>
<tr>
<td>Please check all that applies to the heaviest period you had:</td>
<td></td>
</tr>
<tr>
<td>☐ I had to change my pad/tampon more often than every 2 hours</td>
<td></td>
</tr>
<tr>
<td>☐ My period lasted more than 7 days</td>
<td></td>
</tr>
<tr>
<td>☐ I passed clots or had flooding</td>
<td></td>
</tr>
<tr>
<td>☐ I spotted mid-cycle</td>
<td></td>
</tr>
<tr>
<td>Do you stay at home from work/school more than twice a year because of heavy bleeding?</td>
<td></td>
</tr>
<tr>
<td>☐ Yes ☐ No</td>
<td></td>
</tr>
<tr>
<td>How long did you have a problem with heavy periods?</td>
<td></td>
</tr>
<tr>
<td>☐ 1 year or less</td>
<td></td>
</tr>
<tr>
<td>☐ More than 1 year</td>
<td></td>
</tr>
<tr>
<td>Do you talk to a doctor about your heavy periods?</td>
<td></td>
</tr>
<tr>
<td>☐ Yes ☐ No</td>
<td></td>
</tr>
</tbody>
</table>
Were you ever given medical treatment for heavy periods?

- [ ] Yes
- [ ] No

If yes, please check all of the treatments that you had:

- [ ] I was on iron or other medications (liquid or pills) at least once
- [ ] I was given the birth control pill because of heavy periods
- [ ] I had surgery to stop the bleeding at least once (e.g. removal of womb, burning (ablation) or scraping (curettage) of the lining of the womb)
- [ ] I was given a medication intravenously (IV), or with a needle under the skin
- [ ] Blood transfusion
- [ ] I was admitted to the hospital
- [ ] Unsure of treatment
- [ ] Medication for pain associated with cramping
10. Have you ever been pregnant? [ ] Yes [ ] No (skip to 11)

How many times have you been pregnant? (include all pregnancies)

________

How many pregnancies resulted in live births?

________

How many pregnancies were not carried to term (either miscarriage or abortion)?

________

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Was/were the miscarriage(s) or abortion(s) associated with excessive bleeding?</strong></td>
<td><strong>Was/were the miscarriage(s) or abortion(s) associated with excessive bleeding?</strong></td>
</tr>
<tr>
<td>□ Yes □ No</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td><strong>Did you seek medical attention?</strong></td>
<td><strong>Did you seek medical attention?</strong></td>
</tr>
<tr>
<td>□ Yes □ No</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td><strong>If yes, please check all of the treatments you received:</strong></td>
<td><strong>If yes, please check all of the treatments you received:</strong></td>
</tr>
<tr>
<td>□ I was given a medication intravenously (IV) to induce contraction of the womb</td>
<td>□ I was given a medication intravenously (IV) to induce contraction of the womb</td>
</tr>
<tr>
<td>□ I was on iron or other medications (liquid or pills) at least once</td>
<td>□ I was on iron or other medications (liquid or pills) at least once</td>
</tr>
<tr>
<td>□ I had surgery to stop the bleeding at least once (e.g. removal of womb, tying off blood vessels)</td>
<td>□ I had surgery to stop the bleeding at least once (e.g. removal of womb, tying off blood vessels)</td>
</tr>
<tr>
<td>□ I was given a medication intravenously (IV), or with a needle under the skin</td>
<td>□ I was given a medication intravenously (IV), or with a needle under the skin</td>
</tr>
<tr>
<td>□ Blood transfusion</td>
<td>□ Blood transfusion</td>
</tr>
<tr>
<td>□ I was in the intensive care unit (ICU) at least once</td>
<td>□ I was in the intensive care unit (ICU) at least once</td>
</tr>
</tbody>
</table>
How many times have you been pregnant? (include all pregnancies)

________

For the live births, how many were vaginal?

________

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did you experience problems with bleeding during the vaginal delivery or after the birth?</td>
<td>Did you experience problems with bleeding during the vaginal delivery or after the birth?</td>
</tr>
<tr>
<td>□ Yes □ No</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>When did the problems with vaginal bleeding occur?</td>
<td>When did the problems with vaginal bleeding occur?</td>
</tr>
<tr>
<td>□ In the delivery room</td>
<td>□ In the delivery room</td>
</tr>
<tr>
<td>□ Within the first 24 hours after delivery</td>
<td>□ Within the first 24 hours after delivery</td>
</tr>
<tr>
<td>□ Within the first 6 weeks after delivery</td>
<td>□ Within the first 6 weeks after delivery</td>
</tr>
<tr>
<td>How long did the vaginal bleeding last?</td>
<td>How long did the vaginal bleeding last?</td>
</tr>
<tr>
<td>□ Less than 6 weeks</td>
<td>□ Less than 6 weeks</td>
</tr>
<tr>
<td>□ More than 6 weeks</td>
<td>□ More than 6 weeks</td>
</tr>
<tr>
<td>Did you have to stay in the hospital longer because of the bleeding?</td>
<td>Did you have to stay in the hospital longer because of the bleeding?</td>
</tr>
<tr>
<td>□ Yes □ No</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>Did you talk to a doctor about this bleeding?</td>
<td>Did you talk to a doctor about this bleeding?</td>
</tr>
<tr>
<td>□ Yes □ No</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>Were you given medical treatment for bleeding during/after a vaginal delivery?</td>
<td>Were you given medical treatment for bleeding during/after a vaginal delivery?</td>
</tr>
<tr>
<td>□ I was given a treatment but I don’t know what it was</td>
<td>□ I was given a treatment but I don’t know what it was</td>
</tr>
</tbody>
</table>
If yes, please check all of the treatments that you have had:

- [ ] I was given a medication intravenously (IV) to induce contraction of the womb at least once
- [ ] I was put on iron or other pills at least once
- [ ] I was given a medication intravenously (IV), or with a needle under the skin at least once
- [ ] I was given a blood transfusion at least once
- [ ] I had an examination and/or packing of the womb while I was put asleep at least once
- [ ] I had surgery (e.g. removing of the womb, tying off blood vessels) at least once
- [ ] I was in the intensive care unit (ICU) at least once
- [ ] I was given a treatment but I don’t know what it was

If yes, please check all of the treatments that you have had:

- [ ] I was given a medication intravenously (IV) to induce contraction of the womb at least once
- [ ] I was put on iron or other pills at least once
- [ ] I was given a medication intravenously (IV), or with a needle under the skin at least once
- [ ] I was given a blood transfusion at least once
- [ ] I had an examination and/or packing of the womb while I was put asleep at least once
- [ ] I had surgery (e.g. removing of the womb, tying off blood vessels) at least once
- [ ] I was in the intensive care unit (ICU) at least once
- [ ] I was given a treatment but I don’t know what it was
<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Was the bleeding caused by an injury?</strong></td>
<td><strong>Was the bleeding caused by an injury?</strong></td>
</tr>
<tr>
<td>□ Yes □ No</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td><strong>Did you ever talked to a doctor about your bleeding into a muscle?</strong></td>
<td><strong>Have you ever talked to a doctor about your bleeding into a muscle?</strong></td>
</tr>
<tr>
<td>□ Yes □ No</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td><strong>Did you ever receive medical treatment for bleeding into a muscle?</strong></td>
<td><strong>Have you ever been given medical treatment for bleeding into a muscle?</strong></td>
</tr>
<tr>
<td>□ Yes □ No</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td><strong>If yes, please check all of the treatments that you had:</strong></td>
<td><strong>If yes, please check all of the treatments that you had:</strong></td>
</tr>
<tr>
<td>□ I had surgery to take away the blood at least once</td>
<td>□ I had surgery to take away the blood at least once</td>
</tr>
<tr>
<td>□ I was given a medication intravenously (IV), or with a needle under the skin at least once</td>
<td>□ I was given a medication intravenously (IV), or with a needle under the skin at least once</td>
</tr>
<tr>
<td>□ I was given clotting factors at least once</td>
<td>□ I was given clotting factors at least once</td>
</tr>
<tr>
<td>□ I was given a blood transfusion at least once</td>
<td>□ I was given a blood transfusion at least once</td>
</tr>
<tr>
<td>□ I was given a treatment but I don’t know what it was</td>
<td>□ I was given a treatment but I don’t know what it was</td>
</tr>
<tr>
<td>Before Diagnosis</td>
<td>After Diagnosis</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------</td>
</tr>
<tr>
<td><strong>12. Have you ever had bleeding into a joint?</strong></td>
<td></td>
</tr>
<tr>
<td>[ ] Yes [ ] No</td>
<td></td>
</tr>
</tbody>
</table>

**Was the bleeding caused by an injury?**
- [ ] Yes [ ] No

**Did you ever talk to a doctor about your bleeding into a joint?**
- [ ] Yes [ ] No

**Did you ever receive medical treatment for bleeding into a joint?**
- [ ] Yes [ ] No

If yes, please check all of the treatments that you had:
- [ ] I had surgery to take away the blood at least once
- [ ] I was given a medication intravenously (IV), or with a needle under the skin at least once
- [ ] I was given clotting factors at least once
- [ ] I was given a blood transfusion at least once
- [ ] I was given a treatment but I don’t know what it was

**Was the bleeding caused by an injury?**
- [ ] Yes [ ] No

**Did you ever talk to a doctor about your bleeding into a joint?**
- [ ] Yes [ ] No

**Did you ever receive medical treatment for bleeding into a joint?**
- [ ] Yes [ ] No

If yes, please check all of the treatments that you had:
- [ ] I had surgery to take away the blood at least once
- [ ] I was given a medication intravenously (IV), or with a needle under the skin at least once
- [ ] I was given clotting factors at least once
- [ ] I was given a blood transfusion at least once
- [ ] I was given a treatment but I don’t know what it was
### 13. Have you ever had bleeding into or out of the head, brain or spine?

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Where was the bleeding?</strong></td>
<td><strong>Where was the bleeding?</strong></td>
</tr>
<tr>
<td>- Scalp</td>
<td>- Scalp</td>
</tr>
<tr>
<td>- Under the skull and around the brain</td>
<td>- Under the skull and around the brain</td>
</tr>
<tr>
<td>- Within the brain tissue</td>
<td>- Within the brain tissue</td>
</tr>
<tr>
<td>- I don’t know</td>
<td>- I don’t know</td>
</tr>
</tbody>
</table>

**Please check all of the treatments you received:**

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>- I had surgery to take away the blood</td>
<td>- I had surgery to take away the blood</td>
</tr>
<tr>
<td>- I had surgery to have a shunt put in</td>
<td>- I had surgery to have a shunt put in</td>
</tr>
<tr>
<td>- I was given a blood transfusion at least once</td>
<td>- I was given a blood transfusion at least once</td>
</tr>
<tr>
<td>- I was given a treatment but I don’t know what it was</td>
<td>- I was given a treatment but I don’t know what it was</td>
</tr>
</tbody>
</table>

**Comments:**

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

---

179
14 Other types of bleeding. Some of these other types of bleeding would have happened shortly after birth.

<table>
<thead>
<tr>
<th>Before Diagnosis</th>
<th>After Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Please check if you have had any of the following. If unsure, leave it blank:</td>
<td>Please check if you have had any of the following. If unsure, leave it blank:</td>
</tr>
<tr>
<td>☐ A problem with bleeding from the umbilical stump after birth</td>
<td>☐ A problem with bleeding from the umbilical stump after birth</td>
</tr>
<tr>
<td>☐ Cephalohematoma, i.e. a collection of blood under the scalp as a newborn, presenting as a soft swelling at the back of the head</td>
<td>☐ Cephalohematoma, i.e. a collection of blood under the scalp as a newborn, presenting as a soft swelling at the back of the head</td>
</tr>
<tr>
<td>☐ Bleeding upon suctioning of the mouth and nose at birth</td>
<td>☐ Bleeding upon suctioning of the mouth and nose at birth</td>
</tr>
<tr>
<td>☐ Bleeding into your cheek, caused by sucking during bottle or breastfeeding</td>
<td>☐ Bleeding into your cheek, caused by sucking during bottle or breastfeeding</td>
</tr>
<tr>
<td>☐ A problem with bleeding during or after the surgery to remove the foreskin of the penis (circumcision)</td>
<td>☐ A problem with bleeding during or after the surgery to remove the foreskin of the penis (circumcision)</td>
</tr>
<tr>
<td>☐ A problem with bleeding from a needle poke when blood was drawn</td>
<td>☐ A problem with bleeding from a needle poke when blood was drawn</td>
</tr>
<tr>
<td>☐ Bleeding in the whites of your eyes</td>
<td>☐ Bleeding in the whites of your eyes</td>
</tr>
<tr>
<td>☐ Bleeding after sexual intercourse</td>
<td>☐ Bleeding after sexual intercourse</td>
</tr>
</tbody>
</table>

Have you ever talked to a doctor about any of these bleeding symptoms?

☐ Yes ☐ No

Have you ever been given medical treatment for any of these bleeding symptoms?

☐ Yes ☐ No

Have you ever been given medical treatment for any of these bleeding symptoms?

☐ Yes ☐ No
For each of these symptoms separately, please check the treatments that you have had:

- [ ] I was on a medication (liquid or pills) at least once
- [ ] I had surgery to stop the bleeding or had stitches at least once
- [ ] I was given a medication intravenously (IV), with a needle under the skin, at least once
- [ ] I was given a blood transfusion at least once
- [ ] I was given a treatment but I don’t know what it was

For each of these symptoms separately, please check the treatments that you have had:

- [ ] I was on a medication (liquid or pills) at least once
- [ ] I had surgery to stop the bleeding or had stitches at least once
- [ ] I was given a medication intravenously (IV), with a needle under the skin, at least once
- [ ] I was given a blood transfusion at least once
- [ ] I was given a treatment but I don’t know what it was

If you have had problems with any other bleeding symptoms that were not included in this questionnaire, please comment on these here.

________________________________________________________________________
___________________
_____________________________________________________
________________________________________________
________________________
Appendix H

Focus Group Transcripts
M.D.: I have a couple of questions I would like to ask about both questionnaires and if anyone has any questions or comments, please feel free to add. Was everyone able to easily understand all of the questions on the questionnaire? Were there questions that were unclear?

**Subject:** Talking about bruising on top of your skin, I have no idea what that is.

M.D.: Subcutaneous?

**Subject:** Yeah, that part.

*(Passes out blank Self-BAT questionnaires to all subjects for review)*

**Subject:** Yeah here. Number 11. Have you ever had bruising into skin? I wasn’t completely sure if that’s ever happened to me. I didn’t really understand that.

**P.J.:** I think what we were trying to get at is that everyone bruises if you hit us. What we sometimes see with patients with inherited bleeding disorders, they actually get bleeding into their skin, which turns into a raised lump. We wouldn’t have expected anyone who is part of the control to have had that. We were trying to distinguish between a regular bruise that’s flat and a raised bruise.

**Subject:** I have a question about the part with bleeding into the head or bleeding into the spine.

**Subject:** I didn’t understand subdural or cerebral.

**P.J.:** Maybe we should take out the medical terms.

**Subject:** I had nosebleeds when I was a six-year old but I don’t have them anymore, there’s nowhere to say that it’s not ongoing.

**P.J.:** That’s actually very common that people only have nosebleeds as a child and then improve into adulthood.
M.D.: I think we were just trying to figure out, when they were at their worst, how many nosebleeds were you having, but you’re right.

P.J.: Would you have liked a couple of lines to write some notes?

Subjects: Yeah.

M.D.: What did everyone think of the length of the questionnaire?

Subject: It looks kind of intimidating with a lot of pages but I said no to a lot of questions so it only took me 5 to 10 minutes.

M.D.: Was it easy to follow? Was everything in a logical place?

Subject: Some of the boxes don’t match up.

M.D.: We’re still working on the formatting.

P.J.: Yes you’re right, we have heard that before.

Subject: Maybe you could put pictures as an example for the different types of bruising.

M.D.: Are there any words in particular that you would like to see defined?

Julie: What about petechiae? Did everyone understand that?

Subjects: No, not really

P.J.: That could look like a lot of things, that’s a good suggestion. What did they guys think about the questionnaire? Was it an issue to skip the parts that were only relevant for women?

Subject (male): No it was pretty clear, pretty straightforward

P.J.: What did the women think about the parts that were gynecologic or obstetric? Was it clear what we were trying to get at? Any suggestions?

Subject (female): I think it was clear

M.D.: Everyone felt comfortable answering the questions?

Subjects: Yeah

M.D.: Any questions or topics that you think we missed that should be added?
**Subject**: Family history of bleeding? Like, immediate family members

**M.D.**: We could clarify how far we want you to think back on the subject info page

**P.J.**: I’m going to step out and let you guys finish. Thanks again everyone

**M.D.**: Does anyone have any other comments?

**Subject**: I wasn’t quite sure what was considered a problem, sometimes my gums bleed a little when I’m brushing my teeth but I don’t think it’s a problem. I felt like I needed to explain it

**M.D.**: That’s an issue that’s been raised before; people seem to share the same opinion

**Subject**: Maybe you should clarify what is considered a problem

**Julie**: We might want to add a section there for comments so people can clarify. Any comments or questions about the consent form?

**Subject**: I thought that was pretty good, I remember.

**Subject**: I found that things came to mind a lot easier on the expert version when someone was prompting me.

**M.D.**: Do you think that’s because it was your second time answering the questionnaire?

**Subject**: Yah that could be it, I remembered more.

**Subject**: I need someone to tell me what is a problem and what isn’t, or else I think I have a problem.

**Subject**: What is the intended age range for this questionnaire? I don’t think children would be able to understand some of it.

**M.D.**: Adults, over the age of 18. There will be a separate questionnaire for children.

**M.D.**: Any other comments?

**M.D.**: Thanks everyone, help yourself to coffee and donuts. After blood work you’re free to go.
Focus Group # 2 Transcript (Control Group)

M.D.: We’re looking for any an all feedback that you have. I have some brief questions I want to go over to get the ball rolling first. Was everyone able to easily understand all the questions?

Subject: Question number 1 with nosebleeds. Have you ever had a problem with nosebleeds? I took that to be did my nose ever bleed. So I answered yes to that but then I changed it to no afterwards. I was confused. I think that question could be worded better.

M.D.: Do you think we should add the word spontaneous to the question? Would that make it clearer?

Subject: I understand where you were heading but only after the whole page. Let me think about it.

Subject: It seems pretty indecisive.

M.D.: Any other wording that wasn’t clear?

Subject: There are a couple words in here that weren’t provided with a definition.

M.D.: Which words?

Subject: Subdural and intracerebral.

M.D.: We’re trying to think of alternatives to that medical terminology, it has been brought up before.

P.J.: The problem is that bleeding in the head can be in different areas. Even if you didn’t know what it meant, was the word subdural a word that you had heard before?

Subjects: No.

P.J.: Was it clear that we were talking about bleeding inside of your skull?

Subjects: Yes.
P.J.: The other thing that we often hear from people is that nosebleeds are more often a problem when they’re kids and everyone tends to outgrow them to a certain degree. People wanted a few lines to explain about their nosebleeds, would you guys also like that?

Subjects: Yes.

M.D.: Any questions that you couldn’t answer because you couldn’t understand what we were getting at?

Subject: Are you keeping track of the notes we write down in the side columns?

M.D.: Yes, as we go through the questionnaires we will be recording the feedback and taking it into consideration.

M.D.: What did you think of the length of the questionnaire? Did you think we needed to add in anything?

Subject: I think it could be a bit more specific.

M.D.: Okay, any particular areas that you think could be more specific?

Subject: I’m not sure exactly which one.

M.D.: Someone did bring up in the last group that they would appreciate a few lines here and there so that they could explain themselves a little bit better. Which areas do you think you would like a few lines to write an explanation?

Subject: The surgery section and the “other” section.

M.D.: So maybe a line or two at the end of each section just in case?

Subjects: Yeah.

M.D.: What about the order of the questionnaire? Was it logical?

Subject: I thought it was well organized, for me anyways.

M.D.: Are there any topics that you think should be added that relate to bleeding?

Subject: What about family history?
M.D.: There is a space to write family history on the first page of the questionnaire but people have commented that they want us to be more specific as to whom exactly we want them to write down.

Subject: I find that with a lot of quizzes and tests there isn’t a lot of consistency. I think that a few directions could go a long way.

Subject: Question 8 with respect to surgery – I was only asked about bleeding after surgery but I got two units of blood during surgery and I had nowhere to put that.

M.D.: That’s a great point, we will correct that.

Subject: Forgive my ignorance but hasn’t everyone in the world had surgery?

M.D.: No.

P.J.: No actually, there are people who haven’t. It can make diagnosis especially difficult when I have a male who hasn’t had his clotting system challenged.

M.D.: Any other comments?

Subjects: I had one. We will you be continuing the study? Do you want more volunteers?

M.D.: Absolutely, have them call the recruiting phone number.
Focus Group # 3 Transcript (Control Group)

M.D.: We’d like any and all feedback. The more you tell us, the easier it is for us to make the questionnaire better. The first question I wanted to ask was how did you find the questionnaire overall?

Subject: The dentistry one. Please check what kind of tooth was taken out and how many. I put 3 but then had to go back and change it because I realized you were talking about removals not just teeth falling out. Also I think I got into the habit of skipping to the next section.

M.D.: But once you went back you were able to understand what we were asking?

Subject: Yes

P.J.: Ideally we’d like to have this be an online questionnaire so the skips would be clearer in that situation.

Subject: Ok

M.D.: What about the language? Any words that you would change?

Subject: Everything was very easy to understand.

Subject: Other types of bleeding after birth – that was confusing

M.D.: Those are on there more so we can prove that they shouldn’t be on there. We don’t expect anyone to know if they had bleeding at their own birth.

Subject: Oh okay.

Subject: The one that says specifies “herbals and medications”, how many do you want?

M.D.: I think we’re more concerned about the prescription medication but anything that you can remember you are taking would be great.

M.D.: Was the flow logical?

Subject: Yes I think so.
Subjects: Is there a reason no one mentioned abortions or miscarriages?

P.J.: That’s actually really important.

M.D.: I guess I would put abortion under the surgery section but it doesn’t really say, we should clarify.

P.J.: Certainly women who have had a miscarriage and have a bleeding disorder usually have it worse.

M.D.: Is there anything else that we might have omitted that we should be including?

Subject: After the pregnancy section, do you want the number of times you’re given medication for a C-section? Is that something you want?

M.D.: We do have some comment sections in the revised version that we’ve done based off the feedback the previous groups had given us but we’re trying to move away from that just because when it does end up on the computer, it probably won’t be able to process comments.

Subject: What about pictures?

M.D.: We’re in the process of trying to find pictures we could add for the bruising categories.

M.D.: Any other last comments or suggestions?

M.D.: Thank you for all your contributions.
Focus Group # 4 Transcript (Control Group)

M.D.: We’d like any and all feedback about anything you might not have understood or anything you think we should add. Please don’t hesitate to mention anything.

Subjects: I think I elaborated more the second time I answered the questions.

P.J.: Is there anything you think we can do to draw the answers out of you the first time?

M.D.: Any comments to begin with?

Subject: How do you define an “easy-bruiser”?

M.D.: We’ve had that question a lot and we’re working to try and re-word it. We’re going to make it as specific as possible. Any other parts where you didn’t understand what we were talking about?

Julie: I think we need to add something about medical history.

M.D.: Yes, we need to add that section.

Subject: I also had to add in the last time I took the medication.

P.J.: That’s a really good idea, that’s exactly what we want to know about.

Subject: The word problem is getting to me. I’m not sure what’s qualifies as a problem.

Subject: I think that depends on how concerned you are with your health.

P.J.: It sounds like we need to take the qualifying information out of the question stem and make the decision ourselves.

M.D.: We’ve actually made the change for the next version of the questionnaire.

M.D.: Any other words or phrasing you didn’t understand?

Subject: How would I know if I had bleeding into my joint?

M.D.: Your doctor would have told you, usually you would know – it’s extremely painful.

P.J.: It’s especially common in those with Hemophilia.
Subject: What about the bleeding into the head/spine?

M.D.: That has been fixed for the next version. We took the medical terminology out. We changed it to bleeding out of the scalp, into the skull or into the brain tissue.

Subject: Oh okay.

Subject: What about bleeding from the ears?

Julie: We should probably include that in the other category, it can be a sign of bleeding in the head.

Subject: With respect to the nosebleeds, does the timing and frequency really help?

M.D.: Yes, it lets us evaluate what is normal and what is not.

M.D.: Any other comments?

M.D.: Thank you everyone for your feedback – we appreciate it!
Focus Group # 5 Transcript (Control Group)

M.D.: What we’re trying to get form you guys is any and all feedback about the questionnaire that you filled out on your own. Any comments are appreciated.

Subject: I’m 72 and I found it hard to remember details about my pregnancies. I didn’t know whether it was relevant or not for the questionnaire.

P.J.: It’s definitely relevant. Usually people who have trouble and require medical treatment such as a blood transfusion they remember it thought.

Subject: Yes that’s true.

M.D.: Were there any parts that were unclear?

Subject: One thing I noticed is the time frame about the nosebleeds. Why is the cut-off 10 minutes?

P.J.: That’s because bleeding during a nosebleed for more than 10 minutes has been shown to be clinically significant.

Subject: What about people with low literacy? Will the expert version disappear?

P.J.: No, definitely not. We will always ask the questions in our clinic when a patient comes in, especially if they have difficulties. There wouldn’t be a way around that in someone who was illiterate. An expert would have to be involved. In that case it could be a tool for the family physician, for example.

Subject: Not everyone would know what angiodysplasia is.

M.D.: It’s hard to find a replacement for the medical terminology so we put the explanation in brackets.

Subject: I would hope that online wouldn’t be the only way to do this questionnaire.

Subject: I would like some pictures put in as well.
M.D.: Yes, that’s been mentioned before so we’re trying to track some down.

Subject: What does surgery of the belly include?

M.D.: We should probably be more specific and list examples.

Subject: In question 9 it asks about birth control pills but not about the other forms of birth control.

P.J.: What we really want to know is if you had been on anything with estrogen in it.

M.D.: We could just ask what type of birth control.

Subject: Yeah.

Subject: The morning-after pill should also be included.

Subject: And hormone replacement

M.D.: That’s true. We should definitely expand that section. Any other language you didn’t understand?

Subject: Am I really expected to remember the stuff in the “other” section?

M.D.: No definitely not and we’ve heard the same opinion from everyone else as well.

M.D.: Any other comments?

Subject: Why does it ask about medication in the last 30 days?

M.D.: We’re trying to gauge if you had taken anything that might interfere with your blood work.

M.D.: Thanks everyone so much for coming.
Focus Group # 6 Transcript (Control Group)

M.D.: Basically what we want is to get an idea of any feedback or any questions that you would change or that you didn’t understand.

Subject: I wasn’t sure if the medical conditions on the front page included existing conditions or past conditions. I wasn’t sure what was relevant.

M.D.: Whatever you can remember is helpful for us, just maybe put a note whether it’s ongoing or not.

P.J.: We pretty much want to know everything, anything that may be significant.

Subject: In the periods section there was nowhere to put that I was post-menopausal.

M.D.: That’s definitely in our next group of changes, it was mentioned previously as well.

Subject: I had a question about the bruising. What is easily bruised?

M.D.: This has actually been brought up each time. We are trying to get an idea of whether you think you are an easy-bruiser or whether it concerns you.

Angie: What about a question like “do you ever have unexplained bruising?”

P.J.: Yeah that’s something typical that we hear from people with inherited bleeding disorders.

M.D.: Maybe we should phrase it exactly like that then.

P.J.: Yeah.

Subject: You should ask to specify what type of trauma in the trauma section.

M.D.: Yeah we could do that.

M.D.: Anything else you didn’t understand? Someone mentioned in the last group that not everyone would understand “abnormal and fragile vessels in the bowel”. Would everyone understand blood vessels or bowel?

Subject: Yes I think so.
Subject: I think that if you had it you would know.

M.D.: Okay.

Subject: I had to add anal fissures in.

M.D.: That’s a good one we will add that in. Any other unclear areas?

Subject: I didn’t understand “bleeding from your stomach”. Like into what?

M.D.: We should probably make that distinction. We were trying to get at “bleeding in the stomach” I think, as in ulcers.

Subject: That would make more sense.

M.D.: Anything you think we left out?

M.D.: Thanks everyone so much for coming.
Focus Group # 7 Transcript (Affected Group)

M.D.: We’d love to hear anything you have to say about how the questionnaire was to answer, or any questions you may have.

Subject: I’ve never gone to term but I’ve also never lost a baby, my babies were premature but there’s nowhere to put that.

P.J.: Yeah we need to put a place for that for sure.

Subject: There’s nowhere to put whether the symptoms were before or after diagnosis.

P.J.: There are versions around that are separated but that would essentially double the administration time, how would you guys feel about that?

Subject: Yah I think it’s important to be able to put that.

M.D.: Yah that’s probably a good idea.

Subject: Then there would be space for pre-treatment too.

Subject: We should definitely put a spot for pre-treatment before surgery. I wrote it as a note beside it.

M.D.: Okay, so that’s a good idea.

Subject: It should be clearer in the period part where I am in my period, like whether I am still menstruating.

M.D.: Yes, that’s something that’s been mentioned before and has been included in the next version.

M.D.: Any other sections that were unclear?

Subject: Obviously I don’t remember anything about bleeding around the time of my birth and neither does my mother so that section isn’t really applicable for me.
M.D.: That’s okay. We’re just trying to show that we should take them off – everyone feels the same way.

Subject: I would suggest that you put a place for I.V. iron.

M.D.: Yeah that’s great, we can add that in.

Subject: I have a comment about the nosebleed. I was given thrombin in powder form to snort when I had a nosebleed and there is nowhere to put that.

P.J.: You know we forgot about that because it’s actually not available anymore. We will definitely add that in though.

M.D.: Any other comments?

M.D.: Thanks everyone for coming.
M.D.: When you were filling out the questionnaire on your own, did you find that anything was difficult to understand?

Subject: I found it confusing.

M.D.: What part was confusing?

Subject: The part that said “before and after”, I haven’t had anything done after my diagnosis.

M.D.: Okay, do you think we should have included maybe an instructional paragraph in the beginning?

Subject: It needs something along those lines.

M.D.: Okay so you were just confused where to put what then?

Subject: Yes, the same questions were on both sides.

M.D.: We just want you to think about when you had each procedure done, and put them in the right category. So we can tell if you had treatment before or not.

Subject: So a lot of it would depend on the age at diagnosis.

M.D.: Right. We know that it may be hard to remember what to put where, but it’s important to us to know as much as possible about the timeline.

M.D.: What did you think of the length? Was it too long to fill out both sides?

Subject: It was a little long but you’re still gathering information right now.

P.J.: That’s exactly right, we don’t know which questions are going to be the most useful right now.

M.D.: Any other comments?

M.D.: Great, thank you everyone.
Focus Group # 9 (Affected Group)

M.D.: If you could just let us know how it was to fill out the questionnaire or if there were any areas that were confusing that would be really appreciated.

Subject: The only thing I noticed was that because I was diagnosed later in life was that there wasn’t much on the “after diagnosis” side.

M.D.: We have heard that before and we know that your answers and timeline will vary based on when you were diagnosed, but it really helps us when we get an idea of whether or not you had been diagnosed prior to answer each question.

Subject: I think it’s a great idea.

Angie: Was there anything that we maybe missed in the questionnaire?

Subject: Can you outgrow it?

P.J.: Yes, actually your clotting factors rise as you get older so some people do grow out of it.

M.D.: Were there any parts that were unclear?

Subject: The joint part. I didn’t understand it if it’s happened to me.

P.J.: You would have gone to the ER if it happened to you because it’s really painful, it’s really more for those with Haemophilia.

M.D.: Any other areas that were confusing?

Subject: Are there male-specific questions that would show symptoms of VWD? Like how women get a period?

M.D.: I’m not sure. P.J.?

P.J.: Some men can have bleeding in the urine or bleeding after sex if they have Haemophilia.

M.D.: Any other comments?

Subject: I thought it was pretty good.
M.D.: Did you think it was really long?

Subject: No, I thought it would be worse.

M.D.: Well thank you everyone for all your input.