A Mixed Methods Study of Adherence to Prophylactic Treatment Among Young People With Haemophilia

Sandra Barbara van Os

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Abstract

Introduction

Haemophilia is an inherited bleeding disorder caused by a deficiency in one of the coagulation or blood clotting factors in the blood. When injured someone with haemophilia does not bleed more intensely than a person without haemophilia, but they tend to bleed for a much longer time. For people affected by severe haemophilia, the deficiency in coagulation factor can cause spontaneous internal bleeding in joints and muscles, as well as intracranial bleeding, and bleeding in soft tissues (e.g. nosebleeds or bleeding gums). The most common form is Haemophilia A which is caused by a deficiency in factor VIII. Haemophilia B is caused by a deficiency of factor IX and tends to be less severe than haemophilia A.

Haemophilia is treated by replacing the deficient coagulation factor in the blood through intravenous injections of factor concentrate. Treatment can be on-demand, where medication is used to treat a bleeding episode; or preventative, where factor replacement treatment is used to increase the concentration of coagulation factor in the blood to prevent bleeding. Most young people with severe haemophilia in the UK follow a preventative treatment regimen (prophylactic treatment or prophylaxis). Patients with severe haemophilia A usually take 3 or 4 injections per week on alternate days, whereas patients with severe haemophilia B usually take 2 or 3 injections per week.

There is good evidence that prophylaxis reduces bleeds and joint damage, whilst also improving quality of life. Therefore it is imperative for future health and functioning that young people with haemophilia (YPH) follow the prophylactic regimen they agreed with their haemophilia team. However, reported adherence levels among YPH vary widely (17 - 93%). Additionally, drivers of (non)adherence among YPH specifically have not been evidenced.

Aims

The overall aim of the research described in this thesis was to gain a better understanding of the extent to which YPH adhere to their prophylactic treatment, and better understand what drives their (non-)adherence.

The aims of the quantitative questionnaire study were to measure levels of adherence among YPH, and to assess whether psychosocial factors that have been shown to be associated with adherence among young people with other chronic illnesses, such as self-efficacy and social support, are also associated with adherence among YPH.

Based on previous research on adherence and social cognitive models of illness, it was hypothesised that:

- there would be differences between adolescents and young adults in relation to psychosocial correlates of adherence.
- higher perceptions of pain and impact of pain would be associated with better adherence (De Moerloose, Urbancik, Van Den Berg, & Richards, 2008; Treil, Rice, & Leissinger, 2007).
- higher perceptions of chronicity, consequences and treatment control would be predictive of higher adherence (Chilcot et al., 2010; Horne & Weinman, 2002).
- greater perception of necessity of prophylaxis would be predictive of higher adherence whereas concerns about prophylaxis would not be predictive (de Thurah, Nørgaard, Harder, & Stengaard-Pedersen, 2010; Horne et al., 2013; Horne & Weinman, 1999; Llewellyn, Miners, Lee, Harrington, & Weinman, 2003; Wileman et al., 2014).
- greater negative mood would be associated with lower adherence scores (Cox & Hunt, 2015; Helgeson, Siminerio, Escobar, & Becker, 2009; Snell, Fernandes, Bujoreanu, & Garcia, 2014).

In addition, based on evidence that lower adherence results in worse disease outcomes (Berntorp, 2009; M. J. Manco-Johnson et al., 2007), it was anticipated that non-adherence to prophylaxis would be associated with higher numbers of bleeds and hospital visits.

The aims of the qualitative interview studies with YPH, parents of YPH, and haemophilia healthcare professionals were to examine perceptions and experiences in relation to prophylaxis and how they make sense of these experiences. It was anticipated that this would provide evidence to gain a better understanding of the complexities surrounding prophylaxis and of the barriers and facilitators to adherence among YPH.

Methods

Questionnaire study

90 patients (aged 12-25, diagnosed with severe haemophilia, and on a prophylactic regimen) were recruited from 13 haemophilia centres across England and Wales. One further participant was recruited through the Haemophilia Society. Participants were invited to complete a questionnaire (on paper or online) which included questions in relation to: self-reported adherence (VERITAS-Pro; N. Duncan, Kronenberger, Roberson, & Shapiro, 2010), illness perceptions (Brief Illness Perceptions Questionnaire; Broadbent,

Petrie, Main, & Weinman, 2006), beliefs about medicines (Beliefs about Medicines Questionnaire; Horne, Weinman, & Hankins, 1999), mood (The Positive Affect and Negative Affect Schedule; Watson, Clark, & Tellegen, 1988)); social support, self-efficacy, and outcome expectations. Clinical information in relation to the number of bleeds and hospital visits each participant had during the previous 6 months were collected from their medical notes.

Qualitative interview studies

Participants for the first study were YPH who follow a prophylactic treatment regimen. Participants for the second study were parents of YPH who follow a prophylactic regimen, and participants for the third study were haemophilia healthcare professionals (HP). Interview participants were recruited from five haemophilia centres across England and Wales. To protect confidentiality parents of YPH who took part in the interview study with YPH were excluded from taking part. .The interviews were transcribed verbatim and analysed using Interpretative Phenomenological Analysis (IPA).

Results

The quantitative findings of this study suggest that overall adherence among young people with haemophilia (YPH) is generally good. The qualitative findings confirm this, and suggest the support provided by haemophilia centres is likely to contribute to these high levels of adherence. The good relationship and regular contact between the clinical team and their patients appears to enable healthcare professionals to identify and address potential issues (such as non-adherence) early.

The quantitative study found that non-adherence was more likely to be due to forgetting than skipping. It is likely that young peoples' busy lifestyles are partially responsible for this. However, findings from the qualitative studies also indicate that patients may find it easier to admit to forgetting than skipping. This may be because they are more likely to be 'told off' if they admit to intentionally skipping injections, whereas they get a more understanding response when they admit to sometimes forgetting injections.

Interestingly, comparison of clinical outcomes (number of bleeds and hospital visits) indicated that adherent participants had more bleeds and hospital visits during the previous six months in comparison to non-adherent participants. Comparison of age groups indicated that there were no significant differences in adherence scores between adolescents and young adults. In relation to psychosocial predictors of adherence, the findings suggest that better social support, greater belief in the necessity and efficacy of prophylaxis, fewer concerns about this treatment and more negative feelings (such as

fear, anxiety or anger) about haemophilia are the most important factors associated with better adherence among young people with haemophilia.

The findings of the three qualitative interview studies suggest that YPH may experience a tension between their desire to live a 'normal' life on the one hand and managing their haemophilia successfully on the other. This is because prophylaxis is a demanding treatment, but also because self-management revolves around 'managing risk' to prevent bleeding episodes, which can interfere with YPH lifestyles. Both parents and YPH felt it is ok to miss occasional injections. However they agreed that the gaps between injections should not be too long and that treatment should always be taken in preparation of physical activity.

As a result of the increasingly flexible and personalised approach to prophylaxis in the UK it is much more challenging to define and assess adherence. It also appears that some patients 'get away' with non-adherence without suffering bleeds. In reality this means that HP often focus their efforts on those patients who are struggling (e.g. who are presenting with bleeds), or those who have clearly become disengaged (e.g. not attending clinical appointments, not responding to letters or telephone messages, not completing treatment logs, etc.).

The main barriers to adherence suggested by YPH and parents were broadly in line and included: lifestyle (fitting treatment in with other priorities such as school or work); being out of normal routine (e.g. on holiday); treatment being time-consuming and unpleasant; not wanting to be 'different'; issues around venous access; and psychological issues (such as anxiety and stress). HP added some additional barriers including: difficulty in engaging YPH during adolescence; absence of symptoms may reduce motivation to take prophylaxis; lack of knowledge about haemophilia and prophylaxis; and challenging family dynamics (e.g. lack of parental support; chaotic lifestyle, etc.).

The key finding from all three interview studies is that support from the haemophilia centre is an important facilitator to adherence. It appears that the current approach that haemophilia centres follow is helping patients to keep on track with their treatment and self-management more generally.

Conclusion

This programme of research is the first large nationwide study to examine adherence to prophylaxis among YPH specifically. It is also the first to utilise a mixed methodology, combining rigorous quantitative assessment of adherence with in-depth qualitative analysis of the complexities around adherence among YPH. Based on the findings of this

programme of research a new framework for understanding adherence among YPH is put forward. This framework proposes that, due to the increasingly flexible approach to prophylaxis in the UK, adherence should be considered in combination with the key clinical outcome (bleeds) and health-related quality of life (QoL). By considering an individual patient's adherence, QoL, and bleeding together one can truly understand what is driving outcomes for this patient. This will in turn allow clinicians to understand which patients are in most need of help, and in what way they are most likely to achieve improvements for individual patients.

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Chapter 1: Introduction to Haemophilia

1.1 What is Haemophilia?

Haemophilia is an inherited bleeding disorder caused by a deficiency in one of the coagulation factors in the blood. The normal blood clotting process involves as many as 20 different plasma proteins, known as coagulation or blood clotting factors (Lee, Berntorp, & Hoots, 2005). These factors interact with other chemicals in the body to form fibrin, which is necessary to maintain a scab and stop the bleeding. Someone with haemophilia does not bleed more intensely than a person without haemophilia, but they tend to bleed for a much longer time. This is because after a blood vessel is injured in someone with haemophilia, the amount of fibrin that is formed is insufficient to main a robust clot.

The most common form is Haemophilia A which is caused by a deficiency in factor VIII. Haemophilia B (also known as Christmas disease) is caused by a deficiency of factor IX and tends to be less severe than haemophilia A (Online Mendelian Inheritance in Man®, 2014). Haemophilia occurs mostly in males and females were historically considered asymptomatic carriers. However, more recently there is a move to recognise females with symptoms as having mild haemophilia. It is very rare for women to have severe or even moderate haemophilia, unless there is an additional genetic abnormality (e.g. Turner's syndrome). Bleeding disorders among females may cause special challenges because of the bleeding associated with menstruation and childbirth.

Factor XI deficiency (also known as Haemophilia C in some parts of the world) is a rare inherited bleeding disorder. It affects men and women as its inheritance is autosomal (not x-linked as haemophilia A and B), and is most common among people of Ashkenazi Jewish descent. Haemophilia C differs from haemophilia A and B in that the majority of cases are mild and that bleeding in joints and muscles is very rare (Seligsohn & Bolton-Maggs, 2010).

Acquired haemophilia is a rare condition that is not caused by inherited gene mutations, but instead results from autoantibodies that attack and disable coagulation factor VIII. In some cases the production of these antibodies is related to pregnancy, autoimmune diseases such as rheumatoid arthritis, cancer, or as a reaction to certain medications. However, in approximately half of cases the reason for the antibody production is never found (Delgado, Jimenez-Yuste, Hernandez-Navarro, & Villar, 2003).

Haemophilia A affects 1 in 5,000 to 1 in 10,000 male live births, which is five times more common than haemophilia B (Online Mendelian Inheritance in Man®, 2014). There are just under 10,000 people in the UK who have been diagnosed with haemophilia, of which approximately 5,900 with Haemophilia A and 1,200 with Haemophilia B (UKHCDO Annual Report, 2014). The remainder

have been diagnosed with factor XI deficiency or acquired haemophilia. Despite relatively few patients, haemophilia healthcare represents a significant cost to the NHS. Total estimated lifetime costs for one patient following a prophylactic (preventative) treatment regimen for severe haemophilia are £5.98million for haemophilia A, and £2.47million for haemophilia B (Miners, 2009).

1.2 Symptoms

Haemophilia A and B are classified as mild, moderate or severe (table 1.1). This classification predicts patients' bleeding risk and outcome, and guides clinicians towards the best treatment strategy. Patients' tendency to bleed is correlated with the concentration of the deficient factor in the blood, which is measured through a blood test.

Table 1.1: Classification of haemophilia A and B (Bolton-Maggs & Pasi, 2003)

Concentration of factor measured through blood test	Classification	Patients in UK, N (%)*		Symptoms
		Haemophilia A	Haemophilia B	
< 1% of normal	Severe	2002 (35%)	410 (34%)	Spontaneous joint and muscle bleeding; excessive bleeding after injuries, accidents and surgery.
1 – 5% of normal	Moderate	512 (9%)	249 (21%)	Bleeding into joints and muscles after minor injuries; excessive bleeding after surgery or dental extractions.
5 – 40% of normal	Mild	3172 (56%)	546 (45%)	Spontaneous bleeding does not occur; bleeding after surgery, dental extractions and accidents.

*UKHCDO Annual report (Bleeding disorder statistics for April 2013 to March 2014)

For people affected by severe haemophilia, the deficiency in coagulation factor can cause spontaneous internal bleeds in joints and muscles, as well as nosebleeds and bleeding gums. In severe cases even minor injuries can result in blood loss lasting days or weeks, which in some cases never heal completely. Intracranial bleeding is another important, albeit less common, complication which can be life threatening or permanently debilitating. People affected by moderate haemophilia can also experience spontaneous bleeds, although most of their bleeds tend to be due to (minor) injuries, surgery or dental extractions. In mild cases spontaneous bleeding does not occur, but treatment is usually required to stop severe bleeding following accidents, surgery or dental extractions.

Haemophilia symptoms manifest along a spectrum between mild and severe bleeding, and vary between patients identified as having the same numerical levels of clotting factor deficiency. This is why in clinical practice there is often a focus on an individual patient's tendency to bleed, referred to as bleeding phenotype, rather than what would be expected based on their classification.

Internal bleeds usually begin with a tingling feeling and mild pain in the affected area. If a bleed is not treated, it can lead to severe pain, stiffness and the site of the bleed becoming hot, swollen and tender. The most common muscle bleeds occur in the upper and forearm, groin area (psoas muscle which runs down the back of the abdomen hidden from view), calf and thigh. The most commonly affected joints are the knee, ankle and elbow. Recurring bleeding into a joint can damage it, lead to formation of a 'target joint' (a joint with recurring bleeding) and ultimately lead to Haemophilic arthropathy (a chronic form of arthritis). This can be very painful and cause disability. It is estimated that approximately 50% of people with haemophilia will develop arthropathy (Madhok,York, & Sturrock, 1991), which often requires joint repair or joint replacement surgery.

Young boys with severe haemophilia are likely to experience bleeds from a very early age, most commonly as they start to learn to crawl and walk. The majority of patients will experience a significant bleed in the first 2 years of life. If severe haemophilia is untreated from early childhood, a patient is likely to be significantly disabled by the end of their first decade (if they are still alive).

Joint damage is more common in older adults with severe haemophilia because preventative treatment (prophylaxis) was not available to them when they were young (a description of treatment options will be outlined below). Thanks to modern treatments children growing up with haemophilia today may be less likely to develop severe joint damage in future.

Complications of haemophilia are much more common among patients with moderate or severe haemophilia. These can be caused directly by the condition itself (such as arthropathy as a result of repeated bleeding in a joint), through its treatment (such as Hepatitis C and HIV infections acquired through contaminated blood), or through inhibitors, which are immune system reactions to treatment (K. Fischer, Valentino, Ljung, & Blanchette, 2008). In the past men with haemophilia were likely to

die in their youth. However, thanks to advances in diagnosis and development of effective and safe recombinant (non-plasma derived) treatment, affected individuals can now enjoy a normal life expectancy.

1.3 Aetiology of Haemophilia

Both Haemophilia A and B are X-linked recessive conditions, which means that they are usually passed down through the x chromosome. Females can inherit the defective gene from either their mother or father. It is very rare for a female to inherit haemophilia, as she would need to be the daughter of a mother who is a carrier and a father with haemophilia.

A male with haemophilia will always pass the affected gene to his daughters (making them a so-called 'obligate carrier'), whereas his sons will not inherit the gene. All children of a female who is a carrier of the gene have a 1 in 2 chance to be affected, meaning that daughters have a 50% chance to be a carrier, and sons have a 50% chance to be affected by haemophilia. However, not in all cases of haemophilia there is a preceding family history, approximately a third of all cases of haemophilia are caused by spontaneous genetic mutations (Bowen, 2002).

1.4 Diagnosis of Haemophilia

Severe haemophilia is often diagnosed during the first year of life. This can be shortly after birth, particularly if there is marked bruising or a haematoma (a collection of blood) caused by the delivery. But usually diagnosis happens once babies start crawling or walking, when small bumps or falls can cause heavy bruising. Milder forms of haemophilia are often not diagnosed until a person experiences abnormal blood loss following an operation, accident or dental extraction. As the bleeding patterns and problems caused by haemophilia A and B are the same, only a blood test can confirm which type of the disorder a person has. This blood test is crucial, as the treatment for haemophilia A and B are completely different.

Daughters of female carriers (who therefore have a 50% chance to be a carrier too), can chose to be tested before they reach child bearing age to check if they carry the gene. As daughters of males with haemophilia always inherit the gene this test is not usually carried out for them, as the test would essentially be a paternity test. However, in many cases clinicians would simply check their levels of clotting factor through a blood test (particularly if they experience any symptoms). Recent developments in prenatal testing now allow female carriers to have their children tested before they are born. Thanks to new methods it is now possible to test foetal DNA from peripheral blood of the mother (making more invasive testing such as Chorionic Villus Sampling, which takes a sample

from the placenta, unnecessary). Prenatal diagnosis is possible from as early as 10 weeks into pregnancy (R. C. Ljung, 1996; Peyvandi, 2005).

1.5 Treatment

Haemophilia is treated by replacing the deficient coagulation factor in the blood through intravenous injection of factor concentrate. Treatment for haemophilia A contains Factor VIII, whereas treatment for haemophilia B contains Factor IX. Factor concentrate treatment can be either on-demand, where medication is used to treat a bleeding episode; or preventative, where medication is used to increase the concentration of coagulation factor in the blood to prevent bleeding. This preventative treatment is often referred to as prophylactic treatment or prophylaxis (Manco-Johnson, et al., 2007).

Up to the mid-1980s treatment was made from human blood (plasma-derived), which put patients at significant risk of infection with blood-borne viruses such as hepatitis C and HIV. Many of the patients who were infected with HIV died as a result. The risk of contaminated blood products was significantly reduced by the introduction of recombinant products (factor concentrates that are manufactured using genetically engineered cells that carry a human factor gene, which are treated to inactivate or remove blood-borne viruses). The latest recombinant products use no human or animal-derived proteins in the manufacturing process at all, virtually eliminating the risk of transmission of infection. Recombinant products are concentrated into a powder form that is mixed with sterile water before it is injected. Factor concentrates are measured in units, with one unit being the equivalent of the amount of factor activity found in 1 cc or 1 ml of fresh plasma. Factor treatment is delivered in glass vials with labels indicating the number of units per vial. Treatment comes in different vial sizes, but patients may need to mix more than one vial to add up to the approximate number of units they require. Administering treatment can be time consuming as it involves several steps including: preparation (clearing and cleaning a space to do the injection); making up treatment (mixing the sterile water and powder together to make up the dose and get the treatment into the syringe ready for injection); preparing the skin (often with an antiseptic wipe); injecting the treatment into the vein; taking out the needle and applying pressure on the puncture wound to stop the bleeding; disposing of the needle and other materials; logging the treatment on the treatment log (Haemtrack).

In some parts of the developing world on-demand treatment with Fresh Frozen Plasma (FFP) is still the only option for people with haemophilia. In addition to the risk of viral contamination, there are other considerable problems associated with the use of FFP in the treatment of haemophilia leading to much worse prognosis for patients unable to access modern treatment. Most notably, because the factor in FFP is much less concentrated, large volumes of plasma must be transfused. This in

turn can lead to a complication called circulatory overload which is associated with increased in-hospital mortality and longer lengths of stay in hospital and intensive care (Murphy et al., 2013).

1.5.1 On-demand treatment

When a bleeding episode occurs people with haemophilia usually require immediate factor replacement treatment to stop the bleeding. This treatment is referred to as on-demand treatment, and should be administered as quickly as possible after the bleeding has started to prevent long-term damage. Bleeding usually stops when enough coagulation factor reaches the bleeding site. Many patients with severe haemophilia follow a regular prophylactic treatment regimen, described in the next section, to prevent bleeds. The majority of patients with mild and moderate haemophilia only use on-demand treatment if and when a bleed occurs.

Initially patients (or their parents if they are young) are encouraged to telephone the haemophilia centre whenever they are experiencing a serious bleed, so that the clinical team can advise on how to treat it. Over time parents and then the individual boy/young man become confident about how to treat their bleeds at home early, without the need to contact their haemophilia team or attend the hospital. The majority of patients in the UK record their prophylaxis, bleeding episodes and on-demand treatment through an online portal, Haemtrack. This allows the haemophilia team to review how patients are doing without needing to contact them, and highlights potential issues that may need attention from the haemophilia team (e.g. recurring bleeding, non-adherence, etc.). Haemtrack can also be a useful conversation starter during check-up appointments, as it allows patients and the haemophilia team to jointly review what has happened since the last check-up appointment in terms of treatment and bleeding episodes.

The required dose to treat a bleed is calculated based on a number of factors including the severity of the bleed; body weight; the patient's bleeding phenotype (their individual tendency to bleed); the baseline level of factor in the patient's blood; and the estimated level of factor to be achieved to stop the bleeding. Severe bleeds usually require several injections over a number of days. Those who follow a prophylactic treatment regimen may take on-demand treatment in addition to their regular prophylactic injections. Many clinicians recommend that after patients have administered their on-demand treatment, they apply RICE (Rest, Ice, Compression and Elevation) to the affected area. This helps to reduce swelling and tissue damage, and is an important supplement to the factor therapy.

For people with haemophilia, dental extractions and surgery have to be planned in advance. It is vital that the haemophilia team is involved from the start to ensure that the patient receives additional treatment to protect them from bleeding complications. In cases of mild haemophilia or very small procedures people may be given Tranexamic acid alone (a medicine that is used in

treating and preventing bleeding problems and usually comes in tablet form), or Desmopressin (also known as DDAVP, a synthetic hormone which stimulates the release of endogenous factor VIII and is usually given by injection). For people with more severe forms of haemophilia and for more invasive procedures, additional factor treatment is usually required to provide protection during and after the procedure. This is sometimes referred to as short-term prophylaxis. Many haemophilia centres in the UK are situated in or are affiliated to large hospitals; this is to ensure that the haemophilia teams are on-hand to deal with potential complications that may arise during or after surgery.

1.5.2 Prophylactic treatment

Most young people with severe haemophilia in the UK follow a preventative treatment regimen (prophylactic treatment or prophylaxis). The purpose of prophylaxis is to increase the concentration of coagulation factor in the patient's blood to a level which protects them from spontaneous bleeding episodes in joints and muscles (often brought on by activities), bleeding in response to minor trauma (bumps and scratches), and intracranial bleeding. This is achieved by raising the baseline concentration of residual coagulation factor in the blood to levels similar to those of people with mild or moderate

haemophilia, recognising that as the baseline levels of clotting factor rise, spontaneous and/or serious bleeding episodes become less common (Ahlberg, 1965; R. Ljung, 2009). Patients with severe haemophilia A in the UK usually take 3 or 4 injections per week on alternate days, whereas patients with severe haemophilia B usually take 2 or 3 injections per week.

Prophylactic treatment has revolutionised haemophilia treatment, particularly for people with severe haemophilia. There is good evidence that it reduces joint bleeds and resulting joint damage (K. Fischer, 2002; M. J. Manco-Johnson et al., 2007) as well as intracranial bleeds (R. Ljung, 2009; Witmer et al., 2011), whilst also improving quality of life (Richards et al., 2010). According to a joint statement made by the World Health Organisation (WHO) and the World Federation for Haemophilia (WFH), initiating prophylaxis at an early age is the optimal form of treatment for people with severe haemophilia (Coppola, Di Capua, & De Simone, 2008).

In the UK, prophylaxis is often initiated shortly after diagnosis of severe haemophilia, either before or at the time of the first joint bleed (so called primary prophylaxis). Regular prophylaxis may require the insertion of a permanent indwelling intravenous catheter (e.g. Port-a-cath) to enable infusions.

Parents are trained by the haemophilia team to give the injections to their child at home, however in some cases a nurse may visit the family at home to help with the treatment, or treatment may be

administered by a nurse in the hospital. This tends to only be during the first few weeks or months of training a family to get competent and confident with home treatment.

There are many different potential issues surrounding initiating prophylaxis for young children (such as difficulty in finding babies' or infants' veins because they are so small or their arm is "chubby", parents and/or children may have or develop needle phobia, or parents' lifestyle or personal circumstances may not be ideal for administration of regular intravenous treatment, etc.). These difficulties in turn can have a detrimental effect on treatment adherence.

Children are usually encouraged to help with the treatment from a young age (e.g. to mix up the treatment ready for the injection, clean the skin, etc.), and are then slowly trained to gradually take over the responsibility for their injections. Haemophilia teams generally aim for their patients to do their own injections by the time they start senior school. However, the age at which patients become responsible for their own treatment varies widely, with some children able to do the injection independently from a young age, whereas others prefer someone else (usually a parent) to do their injections for as long as possible. In some cases a port-a-cath or an external catheter (called a Hickman line or Broviac) can be surgically inserted into a vein, making it easier to give regular factor treatment or draw blood for tests. The use of such catheters can be complicated by infection and blockage and they have to be used with great care.

In previous decades prophylactic regimens often required patients to do their injections in the morning on set days each week. Most patients were directed to do their injections on Monday, Wednesday and Friday morning, which left them unprotected on Sundays and did not take their individual activities into account. In recent years regimens have become more flexible and tailored to individuals, and it appears that many clinicians now encourage patients to adjust their treatment according to their lifestyle and planned activities. This means that patients should take their treatment on days they are planning to be active and on some occasions top up with an additional injection if they feel their usual regimen will not afford them enough protection. Equally, if they are planning to be inactive on a day they usually take their treatment, it may be more sensible to bring the treatment forward or back. However, it is important to highlight that it is not clear from the literature how widespread this more flexible approach is in paediatric and adult practice.

Usually patients are encouraged to continue taking prophylaxis into adulthood, and in many cases for the rest of their lives. However in some cases it may be possible to change to an on-demand regimen, as some people with severe haemophilia are able to live the lifestyle they want without the need for prophylaxis. However, these patients are usually encouraged to attend regular check-ups in the hospital, and to consider switching back to prophylaxis if they start to experience bleeding problems.

There is currently no consensus on how prophylaxis should be managed for patients with severe haemophilia once they reach adolescence and young adulthood. However, results from one study suggest that a significant proportion of patients with severe haemophilia may not require intensive prophylaxis for the rest of their lives. In their study of a cohort of 218 patients registered at 19 haemophilia centres across Europe, Richards et al. (2007) found that approximately half had successfully reduced or stopped prophylaxis when they reached adolescence, and that only 28% of the patients who had stopped had to reintroduce prophylaxis due to an increase in bleeding. However, further studies are currently being undertaken across Europe to gather more evidence to inform future practice.

1.5.3 Inhibitors

In some cases the body responds to factor replacement treatment by producing antibodies that inhibit or interfere with the function of the treatment and make it much harder to prevent and treat bleeds. These antibodies are known as inhibitors and occur in approximately 30-35 percent of people with severe haemophilia A, and are much less common in severe Haemophilia B (K. Fischer et al., 2008).

When a patient develops inhibitors, more intensive or alternative treatment may be required to control bleeds and try and eliminate inhibitors. Most inhibitors are temporary and often appear during the first year of treatment. People with moderate to severe inhibitors are often prescribed a treatment called immune tolerance therapy (ITT), which aims to manipulate the immune system and involves a course of daily injections of recombinant factor treatment that last between 6 and 24 months. If the treatment is successful the immune system will start to recognise the blood clotting factors as "self" and stop producing inhibitors. ITT is estimated to be successful in approximately 80% of cases (Hay, 2012) .

In the event of a bleed people with inhibitors have to use a medication called a bypass agent, which is a separate product that can be used to stop bleeding by ‘bypassing’ the inhibitor. Those patients for whom ITT doesn't work may need to use bypass agents for the rest of their lives. Bypass agents can be used as prophylaxis, but are not as effective at preventing bleeds as prophylaxis with factor concentrate. For these patients it will therefore be less likely that their haemophilia will be well controlled, and they are therefore more likely to suffer joint damage. People who develop inhibitors face a higher mortality rate, and the cost of their treatment rises significantly. Although much progress has been made in the treatment of inhibitors, they remain a significant problem in the management of haemophilia today.

1.5.4 Multidisciplinary haemophilia care

In the UK haemophilia care is provided by NHS haemophilia centres and haemophilia comprehensive care centres (CCC). Haemophilia centres are usually smaller and not able to provide a complete range of specialist treatment. CCC are usually larger (looking after patients from a wider geographic area) and have the resources to cope with more complex treatment issues as well as routine care. There are currently 22 CCC and 64 haemophilia centres in the UK (UKHCDO annual report, 2014).

Many patients with severe haemophilia receive their care from CCC where they are usually looked after by a multidisciplinary team that in addition to doctors and nurses may include physiotherapists, psychologists, play specialists, and social workers. In these teams nurses in particular take a prominent role in liaising with patients and looking after their treatment. Similarly physiotherapists have a key role in assessment, rehabilitation and education of patients and their families.

1.6 Self-management

People with haemophilia are encouraged to take an active role in monitoring and managing their condition from childhood. Responsibility for managing their condition increases gradually with age and maturity, with most patients becoming fully self-sufficient by late adolescence. For people with a severe bleeding phenotype (most people with severe haemophilia and some with moderate haemophilia) this includes many self-management behaviours, of which the most important are shown in table 1.2.

Patients who are on prophylaxis (most patients with severe haemophilia, and patients with moderate haemophilia with a severe bleeding phenotype) are encouraged to attend routine check-up appointments every 3 to 4 months during childhood, and then every 6 months as an adult. Patients with mild or moderate haemophilia who are not on prophylaxis generally only attend one annual check-up appointment.

All people with haemophilia, even those who are not on prophylaxis, need to consider the risks associated with their condition, particularly in relation to medical procedures and emergencies. Haemophilia centres (or CCC) encourage all patients to contact the centre in the case of medical emergencies or in preparation of planned medical procedures.

Table 1.2: Haemophilia self-management behaviours for people with a severe bleeding phenotype

Day-to-day management:

- Manage stock of factor treatment and associated materials (such as needles). Most people with severe haemophilia in the UK receive regular home deliveries of treatment.
- Take treatment, this includes working out dose and frequency based on planned activities.
- Complete treatment log to record time and dose of treatment. Many patients now use Haemtrack, an online treatment log which includes smart phone functionality.
- Monitor and treat bleeds, including liaising with the haemophilia centre, and attending hospital if required.
- Ensure treatment is available at school/college/university or work, and carry emergency treatment when away from home.

Contact with haemophilia centre:

- Book and attend check-up appointments.
- Attend physiotherapy and occupational therapy appointments.
- Contact the haemophilia centre when a bleeding episode occurs to receive advice and guidance on how to treat it, and attend the hospital for assessment and treatment if required.
- Inform the haemophilia centre of any planned medical procedures or dental work.

Lifestyle considerations:

- Avoid medications that can interfere with coagulation (such as aspirin and NSAIDs).
- Avoid activities and sports that increase risk of bleeding.
- Wear medical alert bracelet and/or carry medical alert card.
- Ensure there is always someone around who knows what to do in an emergency.
- Take out additional travel insurance for trips abroad and avoid countries where adequate emergency treatment is not available.

1.7 Prognosis

Life expectancy varies with the severity of haemophilia and availability of adequate treatment. Before effective treatment became available in the 1960s the average life expectancy for someone with haemophilia in the UK was 11 years (Jones, 1991). By the 1980s life expectancy for those receiving appropriate treatment increased to 50-60 years, and today someone who receives optimal treatment can expect a life expectancy that is very similar of those who are not affected by haemophilia (Rodriguez-Merchan, 2010).

Before the advent of recombinant factor concentrates patients were at significant risk of infection with HIV and Hepatitis C through contaminated treatment. A study published in 1998 (AIDS Group of the United Kingdom Haemophilia Centre Directors) reported that HIV antibodies were found in 41% of people with haemophilia A and 6% of those with haemophilia B. These percentages increased to 59% and 11% respectively for those affected by severe haemophilia. Many men with haemophilia alive today who received treatment in the 1970s and 1980s are infected with both Hepatitis C and HIV, resulting in a much worse prognosis (Wilde, 2004).

An important advance in the search for better treatment and a cure for haemophilia is gene therapy. In summary, this involves the transfer of a normal copy of a gene to an individual who has a mutation in that gene (Ponder, 2006). Gene therapy research trials are ongoing in both animals and humans, and studies have been published showing the first durable gene therapy in severe haemophilia B (Nathwani et al., 2014; Nathwani et al., 2011). Gene therapy trials for haemophilia A are lagging behind a little but the first human trials are currently underway in the UK. It is anticipated that gene therapy may eventually help people with haemophilia to produce their own coagulation factor, reducing or even removing their need to inject factor treatment on a regular basis.

1.8 Impact of Haemophilia

1.8.1 Impact on patient

Young people with haemophilia (YPH), even those with severe bleeding phenotypes, are usually able to live a relatively normal life. Studies in the US, Netherlands, and Australia found that haemophilia A did not appear to impact academic achievements (Drake et al., 2010; Plug et al., 2008; Talaulikar, Shadbolt, McDonald, & Pidcock, 2006), although some studies suggest that people with severe haemophilia may participate less in full-time work (Plug et al., 2008; Talaulikar et al., 2006), and that discrimination at school and work still exists (J. Barlow, Stapley, Ellard, & Gilchrist, 2007; J. H. Barlow, Stapley, & Ellard, 2007). In addition to the demanding treatment regimen and general practicalities of managing a chronic health condition, there are some specific issues for people living with haemophilia.

Exercise

People with haemophilia are generally encouraged to be active and exercise, as it can help develop strong bones and muscles and therefore protect against damage caused by bleeds (Von Mackensen, 2007). However, they are advised to avoid contact sports such as rugby and boxing and other activities that increase the risk of bleeding. Haemophilia teams in the UK tend to work

closely with patients and their parents to assess individual circumstances and consider a wide range of criteria before advising patients on the sports and activities that are safe and best suited for them. These criteria include personal bleeding history, the associated risk level and contact level of the sport, and the benefits it may bring (such as muscle strengthening and stretching). Many haemophilia centres employ specialist haemophilia physiotherapists, who work with patients on existing injuries and suggest strategies they can employ to prevent future injuries.

Medication

Certain medications, including widely available painkillers and cold remedies (such as aspirin and ibuprofen), can interfere with blood clotting. Parents of children with haemophilia are taught to be very cautious with medication, and to always check with the haemophilia centre if they are unsure. Many haemophilia nurses and doctors remind their patients of the dangers of some medications regularly.

As haemophilia is a fairly rare disorder, some doctors and nurses who work in different specialties are unaware of the risks of inappropriate treatment, which can sometimes lead to life-threatening complications (J. H. Barlow et al., 2007; Talaulikar et al., 2006). To avoid such complications, patients are encouraged to always contact the haemophilia centre about any non-haemophilia related medical issues they are seeking treatment for. During routine check-ups many clinicians will also ask patients if they have any medical treatments planned to ensure that involvement from the haematology team is arranged if needed. People with haemophilia are also encouraged to have a medical alert card/bracelet on them at all times to ensure that in the case of an emergency medical assistance is sought.

Psychosocial impact

Physical or functional limitations caused by haemophilia can make young people feel shy, insecure or embarrassed. Visible joint damage, needle marks and decreased muscle tone can result in young people developing poor body image. For some this may mean that they do not want to expose the affected area to others (avoiding activities such as swimming and wearing clothes that cover them at all times), while for others it may lead to psychological issues that can manifest themselves in many ways including low self-esteem and anxiety. These psychological issues are likely to influence social interaction, quality of life, and can have a detrimental impact on treatment adherence.

The current literature suggests that even today people with haemophilia may experience stigma or judgement, including discrimination at work or school (J. H. Barlow et al., 2007; Cassis, Querol,

Forsyth, & Iorio, 2012). Some CCC employ a specialist social worker or psychologist to support patients with the psychological, social and practical challenges of living with haemophilia. Other centres refer patients to external support services.

1.8.2 Impact on family

Over the decades it has been documented that there is a social impact of living with haemophilia (Beeton, Neal, Watson, & Lee, 2007; Boon & Roberts, 1970; Cassis et al., 2012). This is not just the case for the patient themselves, but also for their families and wider social environment. In particular carrier mothers may be affected, as in addition to the day-to-day worry about their child they may feel guilty about passing the condition onto him. Some studies suggest that mothers are more likely to suffer from anxiety and depression that is related to their child's haemophilia than fathers (Bottos, Zanon, Sartori, & Girolami, 2007; Saviolo-Negrin et al., 1999).

In most cases parents are responsible for the management of haemophilia during childhood; they have to learn to recognise the onset of bleeds and administer the intravenous treatment; decide which activities their child can take part in (and manage the difficulties associated with stopping their child from participating in activities they enjoy); and decide who to inform of their child's haemophilia. Finding a balance between safeguarding a son with haemophilia without over protecting him is often reported as a specific issue (Beeton et al., 2007). It is likely that the way in which parents respond to living with a child with haemophilia, and manage the condition during his childhood, may form the foundation for the child's behaviour and perceptions in relation to their condition into adulthood (Canclini et al., 2003).

Treatment and healthcare provisions have improved significantly in recent decades, leading to a much better situation for people with haemophilia and their families. However, having a child with haemophilia can still impact on family life and family dynamics (Wiedebusch, Pollmann, Siegmund, & Muthny, 2008). Unaffected siblings may find it difficult to understand why they need to be more careful around their brother because of his haemophilia, especially following a bleed. Situations in which a family activity has to be cancelled because of a bleeding episode affects siblings as well as the boy with haemophilia. And of course there are the many hospital visits, special arrangements to accommodate the child with haemophilia, and other issues that are likely to take parents' time and attention away from their other children, who may or may not have haemophilia as well. Managing these situations and balancing the needs of affected and unaffected children is likely to cause additional stress for parents.

The challenges associated with raising a child with haemophilia may even influence couples' reproductive choices. After having a child with haemophilia some parents decide not to have any subsequent children or opt for prenatal diagnosis with the option to terminate the pregnancy,

whereas others may use pre-implantation genetic diagnosis or non-invasive sex determination to ensure they have a female child (Kadir, Economides, Braithwaite, Goldman, & Lee, 1997; Knol, Voskuilen, Holterman, Kluin-Nelemans, & Meijer, 2011). Pre-implantation genetic diagnosis is a very expensive procedure with a relatively low success rate; resulting in pregnancy for approximately 17% of women (Nicolle, Talks, & Hanley, 2004). Natural conception followed by antenatal diagnosis increases the chance of successful pregnancy, and is far more cost-effective. However, it is associated with a potentially high psychological costs (in case of termination of an affected pregnancy) and considerable ethical implications.

In the UK and many other European countries, families who are (potentially) affected by bleeding disorders have access to genetic counselling. In the UK this is usually provided by a haemophilia centre. The aim of this counselling is to provide carriers and their partners with sufficient information to consider implications for themselves and potential children, and support them through the subsequent decision making process. Genetic counselling should ideally take place before conception, to allow couples to consider and plan their options without any time pressure (Chi & Kadir, 2009; Lee et al., 1998).

1.9 Haemophilia treatment in the context of this research

The availability of safe and routine prophylaxis has revolutionised haemophilia treatment in this country, in particular for those with severe haemophilia. Quality of Life, life-expectancy and long-term outcomes have improved immensely, and allow most people with haemophilia to live a full and productive life. However, patients' adherence to their prophylactic treatment regimen has a considerable influence on its efficacy. Adherence in this context is the extent to which a patient follows the treatment regimen they agreed with their haemophilia team. Non-adherence (i.e. not keeping to the agreed frequency and/or dosing and/or timing of prophylactic injections) increases the risk of spontaneous bleeds (Hacker, Geraghty, & Manco-Johnson, 2001), which increases treatment costs (Panicker, Warrier, Thomas, & Lusher, 2003), and may result in joint damage leading to poorer physical and emotional wellbeing (Marilyn J Manco-Johnson et al., 2007; Treil et al., 2007). In addition to the immediate costs associated with treating bleeds (on-demand treatment, potential hospitalisation, clinic visits, etc.), they may also lead to increased future care-costs due to disability. Because of the very high costs, the cost-benefit for prophylaxis correlates strongly with treatment adherence (M. J. Manco-Johnson et al., 2007; Thornburg & Pipe, 2006). Even low levels of non-adherence can result in significant medical problems and permanent disability (Treil et al., 2007).

Levels of adherence to prophylaxis reported in the existing literature vary widely from 80-87% in a study conducted across 6 European countries (De Moerloose et al., 2008) to 44% in a single centre UK study (Llewellyn et al., 2003), and reasons for non-adherence among YPH are not evidenced. In addition, reported adherence levels among adolescents and young adults are predominately based on estimations made by healthcare professionals and/or parents rather than young people themselves (Geraghty et al., 2006; Hacker et al., 2001).

Despite the wide variation in reported levels of adherence, many of the North American and European studies suggest that patients may need additional support to help them keep to their treatment regimen during adolescence (Geraghty; Dunkley, Harrington, Lindvall, Maahs & Sek, 2006; Breakey, Blanchette, & Bolton-Maggs, 2010), as they go through the transition from paediatric to adult care and are expected to become responsible for their own treatment. The literature suggests that adherence is unlikely to improve into young adulthood, and may indeed reduce further, particularly if transition was problematic or unsuccessful (Breakey, Blanchette, & Bolton-Maggs, 2010; Geraghty et al., 2006). For this reason, this programme of research will aim to assess the levels of adherence to prophylactic treatment among YPH who are aged 12-25, and explore their reasons for (non-)adherence.

This will be done using a mixed methods approach involving quantitative and qualitative studies. The quantitative part of this research aims to assess levels of adherence and psychosocial factors that have been shown to be associated with treatment adherence among young people with other chronic health conditions (such as diabetes). The qualitative studies aim to examine personal experiences YPH have in relation to prophylactic treatment, and how they make sense of these experiences. The qualitative work will also include the perspectives of parents and healthcare professionals. Before going on to describe these studies, an introduction is provided for theories and empirical evidence on adherence in order to (a) highlight its importance in maintaining optimum health and (b) identify factors (from theory or research) that may influence adherence in order to provide a starting point for the research that follows. Below follows a short description of each of the following chapters.

Chapter 2: Introduction to treatment adherence and theoretical models of adherence.

Chapter 3: Review of literature in relation to adherence among young people with chronic health conditions, with a focus on haemophilia. This chapter concludes with a rationale for the methods used and a summary or these methods.

Chapter 4: Cross-sectional analysis of adherence to prophylaxis and psychosocial factors of adherence among young people with haemophilia.

Chapter 5: Approach and methodology for three qualitative interview studies.

Chapter 6: Interpretative Phenomenological Analysis of patients' accounts of prophylaxis and their adherence to this treatment.

Chapter 7: Interpretative Phenomenological Analysis of parents' accounts of prophylaxis and their sons' adherence to this treatment.

Chapter 8: Interpretative Phenomenological Analysis of haemophilia healthcare professionals' accounts of adherence to prophylactic treatment.

Chapter 9: Discussion of qualitative interview studies.

Chapter 10: General discussion.

Chapter 2: Introduction to treatment adherence

An extensive literature now exists in relation to treatment adherence, particularly for chronic health conditions. In the last two decades a number of comprehensive reviews have been published (M. DiMatteo, 1994; M. R. DiMatteo, 2004; R. Haynes, McDonald, Garg, & Montague, 2003; R. B. Haynes, Ackloo, Sahota, McDonald, & Yao, 2008; Kripalani, Yao, & Haynes, 2007; Osterberg & Blaschke, 2005; Vermeire, Hearnshaw, Van Royen, & Denekens, 2001), including a report by the World Health Organisation (Sabaté, 2003).

However, studies investigating adherence have based their research on various theories or models of health behaviour and adherence. Therefore this chapter will start with a brief definition of adherence, followed by an overview of theoretical models that have been used to try and explain (non)adherence to treatment for chronic health conditions.

2.1 Definition of adherence

The existing literature often uses the terms ‘adherence’ and ‘compliance’ interchangeably. However it is important to differentiate between these two terms, as compliance implies that patients should keep to their prescribed treatment regimen, whereas adherence implies that patients have a choice to follow the treatment regimen that they have agreed with their doctor. Adherence in this context is defined as the extent to which a patient’s behaviour matches agreed recommendations from the prescriber (Horne, 2006; G. J. Treharne, Lyons, Hale, Douglas, & Kitas, 2006).

Current prophylaxis regimen for haemophilia are often individualised, with a clear focus on concordance between healthcare professional (HP) and patient. Concordance in this context means that treatment decisions are agreed jointly between the haemophilia team and patient (and parent/caregiver where appropriate). Concordance is subsequently considered an important tool to improve patient engagement and adherence, rather than an outcome in itself (Horne, 2006). Therefore, this programme of research will use the term ‘adherence’ throughout.

The existing literature suggests that treatment adherence is multidimensional and determined by a number of interacting factors. Different theories and research studies emphasize different dimensions, but most agree that the key factors involved in adherence relate to patient characteristics (e.g. demographics, self-efficacy, attitudes and perceptions, cognitive factors, socio-economic status); clinical characteristics (e.g. complexity of regimen, severity of symptoms, level of disability and co-morbidities); social environment (availability of social support, family dynamics, school or work environment); and the health care provider (e.g. relationship between patient and doctor, resources available to support patients, practicalities around medication collection/delivery).

Research in other chronic conditions has made a useful distinction between intentional non-adherence and unintentional non-adherence (M. J. Johnson, 2002; Lehane & McCarthy, 2007). Unintentional non-adherence (forgetting) can usually be addressed with simple interventions, such reminders on a calendar or diary, telephone or text message reminders (Pop-Eleches et al., 2011) or visual prompts (putting medication in a highly visible place such as the kitchen counter). However, intentional non-adherence (skipping) is often driven by complex psychological processes and is therefore more challenging to address. Research in haemophilia has thus far not made this distinction, nor has it investigated the complex psychological processes that are likely to underlie non-adherence to prophylaxis.

2.2 Theoretical models of adherence

Various theoretical models and frameworks for explaining variations in health-related behaviour have been used to try and explain and predict treatment adherence, including Social Cognition Models (SCM), such as the health belief model, Stage Models and Self-Regulatory Theory.

2.2.1 Social Cognition Models

Social Cognition Models (SCM) propose that peoples' beliefs and attitudes, which are derived socially, influence their interpretation of information and experiences and are a key determinant in behaviour (Conner & Norman, 2005). These models share the common core assumption that people carry out a cost-benefit analysis, weighing up their beliefs about the necessity of medications against their concerns about the potential adverse effects of taking them.

2.2.1.1 Health Belief Model

One of the most influential SCM to attempt to explain health behaviour is the health belief model (HBM, Rosenstock, 1966). The model was initially applied to explain preventative health behaviours, but was later developed further and applied to other health behaviours including treatment adherence (Becker & Maiman, 1975).

The HBM has been described as an 'expectancy-value' decision-making model as it is based on the assumption that individuals adopt health behaviours only after evaluating and comparing the perceived health threats and perceived cost-benefits of all alternatives (Christensen, 2004; Janis, 1984). Revised versions of the model include the additional components *health motivation* (Becker, Haefner & Maiman, 1977b) and *cues to action* (Mattson, 1999).

In the context of treatment adherence HBM suggests that before making the rational decision to take their treatment an individual is likely to assess the health threat by evaluating their perceived susceptibility (e.g. of experiencing side effects from medication or developing symptoms due to not taking their treatment) and perceived severity (e.g. severity of those side effects or symptoms), followed by weighing up the benefits (e.g. reduction in symptoms as a result of taking medication) against the perceived barriers (e.g. the time it would cost to take the medication). Internal cues to action (e.g. experiencing a symptom) or external cues (e.g. being encouraged to adhere to their treatment by a doctor) are suggested to play an important role in maintaining or improving treatment adherence.

The HBM has been used to investigate medication adherence across a number of chronic illnesses including diabetes (Alogna, 1980; Brownlee-Duffeck et al., 1987); hypertension (Nelson, Stason, Neutra, Solomon, & McArdle, 1978); and renal disease (Cummings, Becker, Kirscht, & Levin, 1982; Hartman & Becker, 1978). These studies have typically found that adherence was predicted by various combinations of components of the HBM, rather than the precise interaction of all dimension specified by the model (Home, Weinman, Myers, & Midence, 1998). This mixed pattern of findings may be explained by limitations of the HBM. One limitation is its failure to include an intention stage between beliefs and behaviour, and that it does not include social factors such as subjective norm (Sheeran & Abraham, 1996). Another limitation is that the HBM does not specify the beliefs that underlie broad constructs such as perceived benefits and barriers (Horne, 1997; Horne & Weinman, 1994). In the context of adherence to treatment for chronic illness, a key limitation of the HBM is that it implies that health-behaviours arise from a single rational decision that is based on a one-off cost-benefit analysis. The model does not present a framework that explains maintenance of adherence to long-term treatment regimens, or specific illness perceptions involved in chronic illness (Horne, 1997; Leventhal, Diefenbach, & Leventhal, 1992; Sheeran & Abraham, 1996).

2.2.1.2 Beliefs about Medicines

The Beliefs about Medicines Questionnaire (BMQ, Horne et al., 1999) is an extension to the HBM which directly addresses the cost-benefit analysis of perceived benefits and barriers of taking medication. It aims to quantify patients' personal beliefs about the necessity of their prescribed medication and their concerns about taking it, and to assess associations between these beliefs and adherence. The cost-benefit analysis in which individuals weigh up their beliefs about their treatment can be quantified using the BMQ (*necessity* total score minus *concerns* total score), this is sometimes referred to as the necessity-concern framework or differential (Emilsson et al., 2011; Menckeberg et al., 2008; Tibaldi et al., 2009).

Horne (1999) used the BMQ to investigate adherence in a sample of asthmatic, cardiac, renal, and oncology patients, and found that specific medication beliefs explained 15-20% of the variance in adherence. Studies in rheumatoid arthritis suggest that perceptions in relation to the *necessity* of medication are most important (Thurah, Nørgaard, Harder, & Stengaard-Pedersen, 2010; G. Treharne, Lyons, & Kitas, 2004), whereas studies in osteoporosis suggest that it is *concerns* about medication that play a more important role (Desai, Sonone, & Bhasme, 2005). In a study of 65 UK males with haemophilia (aged 12 years or older) Llewellyn et al. (2003) found that patients who had a greater perception of treatment *necessity* were significantly more likely to adhere to their treatment and that *concerns* about treatment were not significantly associated with adherence. It is not surprising that beliefs differ between different illness groups, as the characteristics of both illness and treatment can vary greatly. In some adherence research, the BMQ has been used to extend the Self-Regulation Model (see below) to provide a more comprehensive view of patients' perceptions in relation to their health condition as well as their treatment. (Horne & Weinman, 2002; Rees, Leong, Crowston, & Lamoureux, 2010; Ross, Walker, & MacLeod, 2004).

2.2.1.3 Theory of Reasoned Action and Theory of Planned Behaviour

The Theory of Reasoned Action (TRA, Ajzen & Fishbein, 1980) is a more general theory of human behaviour, which is based on the assumption that behavioural intentions are strong predictors of behaviour change and that these intentions are influenced by an individual's attitudes towards the behaviour and their perceived subjective norms. From the TRA perspective, attitudes include the expected consequences of the behaviour and the importance of those consequences. Perceived subjective norms refer to what an individual believes others expect or want them to do in relation to a particular behaviour. This component distinguishes the TRA from the HBM and other expectancy-based models of health-related behaviour. In the context of adherence, the TRA predicts that someone is most likely to form an intention to adopt a particular behaviour (e.g. keep to their treatment regimen) when the expected consequences are relatively beneficial (e.g. reduction in symptoms as a result of taking treatment), the expected consequences are important (e.g. the reduction in symptomology is valued), and the behaviour is in line with subjective norms (e.g. significant others would prefer the individual to take their treatment). The intention to adhere to treatment leads to the behaviour (i.e. adhering to treatment).

The Theory of Planned Behaviour (TPB, Ajzen, 1988) is an extension of the TRA, which builds on Bandura's (1977) work on self-efficacy and control. In addition to the attitudinal components and subjective norm of the earlier model, the TPB considers an individual's perceived degree of volitional control over the behaviour. This is influenced by the individual's belief that they have access to the resources and skills needed to carry out the behaviour successfully.

In the model an individual's intention to perform the behaviour is the single most predictive factor of behaviour (Ajzen, 1991). Behavioural intention is influenced by three factors: an individual's attitudes (beliefs about the behaviour and perceived consequences), their perceptions in relation to subjective norm (individual assesses if significant others think they should adopt the behaviour or not), and their perceived behavioural control (self-efficacy). Perceived behavioural control may also predict behaviour directly as it is unlikely that an individual will adopt a behaviour if they feel they are not capable of carrying it out, even if their intention is high.

A number of studies have used the theory of planned behaviour to explain preventive health behaviours such as exercise and smoking cessation (Abraham, Sheeran & Johnston 1998; Armitage & Conner, 2001), but studies that have explicitly evaluated it in relation to adherence to treatment for chronic illness are much less common. However, there is broad support for the assertion that behavioural intentions are influenced by attitudes and subjective norms, although the strength of the relationship between intentions and behaviour varies across studies and between behaviours (Connor & Sparks 1996). Experimental evidence suggests that changing intentions has little effect on changing behaviour (Chatzisarantis & Hagger, 2005), and that interventions based on the TPB can sometimes be effective at changing behaviour without changing any of the components of the model (Sniehotta, 2009).

Studies using SCM to explore adherence in chronic illness have produced a mixed pattern of findings. For instance, in studies utilizing the HBM, adherence was typically predicted by various combinations of components of the model, rather than the precise interaction of all dimensions specified by the model (Home et al., 1998). Findings of studies that utilized theories of reasoned action and planned behaviour support the suggestion that behavioural intentions are influenced by attitudes and subjective norms. Although the strength of the association between intentions and behaviour varies between studies and behaviours (Conner & Sparks, 1996), a meta-analysis by Webb and Sheeran (2006) showed that medium-to-large change in intention is likely to lead to a small-to-medium change in behaviour.

2.2.2 Stages of Health Behaviour

One key criticism of SCMs is that they do not address the dynamic nature of cognitions and behaviour, which are likely to change over time and interact in different ways depending on the situation. It has been suggested that health behaviour may proceed in stages, and that the importance of different cognitions fluctuates depending on the stage. Weinstein (1988) suggests that interventions to promote health behaviour are likely to be more effective if they are targeted at the particular cognitions which characterise the stage that the individual has reached in their

consideration or implementation of the behaviour. Several stage models of health behaviour have been proposed in which health behaviours occur as the result of several stages of cognition.

The Transtheoretical Model, or Stages of Change Model (TM, Prochaska & DiClemente, 1994; Prochaska, DiClemente, & Norcross, 1992) proposes that adoption and maintenance of a health behaviour occurs in five progressive stages of change (*Pre-contemplation, Contemplation, Preparation, Action and Maintenance*). In instances where the behaviour change is aimed at stopping problematic behaviour (such as smoking) a sixth stage, *Termination,* may occur when the goal has been reached (e.g. smoking cessation). It is likely that an individual may follow a cyclical route through the first five stages, which may be characterised by many brief or partially successful attempts before behaviour change is established. In general successful progression depends on a positive decisional balance (perceived advantages of the behaviour need to outweigh the negatives), self-efficacy and strategies that can help to make and maintain the behaviour change (referred to as processes of change). The TM has been successfully applied to a variety of situations, including smoking cessation (Carlo C. DiClemente et al., 1991); diet and weight control (Curry et al., 1992); stress management (Evers et al., 2006); adherence to antihypertensive medication (S. S. Johnson, Driskell, Johnson, Prochaska, et al., 2006) and lipid-lowering drugs (S. S. Johnson, Driskell, Johnson, Dyment, et al., 2006); and exercise (Marcus et al., 1992).

One of the key criticisms of stage models (and indeed SCM) is that they do not fully address how motivation to continue a health behaviour is maintained. There is an implicit assumption that the main cognitive barrier to maintenance is low self-efficacy. Therefore, if an individual is confident that their medication works, believe that they are capable of adhering to their treatment regimen, and are motivated to do so, the model assumes that they will continue to take their treatment.

Another criticism of the TM is that it is a pseudo-stage model, where each different stage reflects a different level of intention rather than being qualitatively different from the other stages (Conner et al., 2002; Sutton, 2001). In their critique of the model Littell and Girvin (2002) suggest that although it may present some potentially helpful ways of considering how people grow and change, its explanations of people and processes are not especially true or generalizable. They propose that the search for a generic underlying structure of behaviour change does not consider that successful change processes may vary depending on the complexity and features of the intended behaviour change, external facilitators and barriers, cultural context, and potential other issues an individual may be experiencing. Little experimental evidence exists to support the effectiveness of interventions aimed at behaviour change based on the Transtheoretical model, and its empirical support has been questioned by findings of several systematic reviews (e.g. Cahill, Lancaster, & Green, 2010; Littell & Girvin, 2002; Riemsma et al., 2003; Whitelaw, Baldwin, Bunton, & Flynn, 2000).

2.2.3 Self-Regulation Model

Leventhal and colleagues (1993) suggest that once self-efficacy and outcome efficacy is in place, continued behaviour depends on continued motivation. In an attempt to explain the dynamic interaction between cognitions, motivation and behaviour, Leventhal and colleagues (Leventhal, Meyer, & Nerenz, 1980) developed the Self-Regulatory Theory as a framework for understanding illness behaviour. This is often referred to as Leventhal's Self-Regulatory Model (SRM). The SRM views the patient as an active problem solver, whose health-related behaviour is an attempt to close the perceived gap between current health status and a future health goal. Patients respond to illness in a dynamic way based on their interpretation and evaluation of the illness. In this context adherence is considered one of a number of behaviours the patient adopts to cope with their illness (based on and influenced by their perceptions)

According to the SRM, a patient will select coping strategies based on their interpretation and evaluation of their illness. These coping behaviours are then appraised and the effectiveness of these strategies is fed back into the patient's model of the illness, and used to shape future coping responses (Leventhal, Nerenz, & Purse, 1984; Meyer, Leventhal, & Gutmann, 1985). The model proposes that these three stages of processing (interpretation of the illness; coping with the illness and associated symptoms; and appraisal of the coping strategies used) occur in parallel at a cognitive and emotional level, and that a mediational relationship exists between illness representations, coping strategies and illness outcome, whereby coping mediates the relationship between illness representations and illness outcome (Carlisle, John, Fife-Schaw, & Lloyd, 2005). According to the SRM, people form common-sense models of their illness which are organised around five broad dimensions (Table 3). Therefore the SRM is sometimes referred to as the Common-Sense Model of self-regulation.

Table 2.1: Illness Representations of the Self-Regulatory Model

Illness representation	**Definition**
Identity	The illness label or diagnosis and the associated symptoms
Consequences	The expected effects that the illness may have on the patient's life
Timeline	The expected duration of the illness (acute or chronic)
Control/cure	Perceptions of the extent to which the illness can be controlled or cured through treatment or behaviour
Cause	The factors that the patient believed caused the illness

Later versions of the model include additional dimensions which represent perceptions in relation to illness coherence (patients' understanding of their illness); the cyclical nature of illness (symptoms may be acute, cyclical or chronic), and emotional responses (Moss-Morris, Weinman, Petrie, Horne, Cameron, & Buick, 2002).

These dimensions provide a framework which enables patients to make sense of their illness and symptoms, assess their health risk, and direct action and coping. Each dimension represents one aspect of the illness and together they provide the individual's coherent view of their condition (Weinman, Petrie, Moss-Morris, Horne, 1996). It is likely

that illness representations are influenced by cultural context (Landrine & Klonoff, 1992) and by other factors such as subjective norm and past experience (Leventhal et al., 1992).

Ongoing research has shown that patient behaviour is influenced by illness representations, and that illness representations form a useful basis for self-regulatory interventions in acute and chronic illnesses (Petrie, Broadbent, & Meechan, 2003). Hagger & Orbell (2003) conducted a meta-analysis of the intercorrelations between the components of the SRM and found significant relationships between some of the illness representations and certain categories of coping strategies, and also between certain illness representations and illness outcomes. However, they reported that the role of outcome appraisals had remained untested in the literature. This may be because positive appraisal of coping may be a coping strategy in itself, whereas maladaptive coping may cause negative appraisal (Carlisle et al., 2005).

A number of studies have investigated illness perceptions in relation to adherence to treatment in chronic illness, with variable results. Llewellyn, Miners, Lee, Harrington & Weinman (2003) measured adherence to prophylactic treatment among people with severe haemophilia and found that only illness identity (symptomatology) and necessity of medications (measured by the BMQ) significantly predicted non-adherence. Horne & Weinman (2002) found that for asthma patients symptomatology played a key role in adherence to prophylactic treatment. In this study patients who were symptom-free were less likely to take their preventer medication compared to those who perceived their illness to be chronic and have potentially serious consequences. In other studies Chilcot, Wellsted & Farrington (2010) found among patients with end-stage renal disease that a perception of consequences as being less serious predicted non-adherence to fluid restrictions. Ross, Walker & MacCleod (2004) found that less personal control and lower emotional reaction predicted non-adherence to hypertension medication. In other studies, illness identity, which is based upon symptoms, has been shown to be important in the regulation of the response to illness.

However, it is important to consider that aetiology, experience and treatment of different chronic health conditions are quite disparate, which may lead to the development of different illness representations. For example, people with severe haemophilia are generally diagnosed at a very

young age, and tend to be involved with (or responsible for) regular preventative treatment from a young age. People with end-stage renal disease on the other hand will generally be older at onset and less aware of how to manage treatment until they develop some experience.

Horne (2003) suggests that a symbiotic relationship exists between the SRM or common-sense model of self-regulation and the necessity-concern framework (as assessed by the Beliefs about Medicines Questionnaire) in explaining variations in treatment uptake and adherence. He proposes that treatment perceptions and the necessity-concerns framework can be used to extend the explanatory power of the CSM in relation to treatment adherence (Horne, 1997; Horne & Weinman, 2002), and equally the CSM can contribute to the understanding of the process by which treatment perceptions influence adherence.

The review of studies that have used the SRM to examine treatment adherence shows the majority of these studies were cross-sectional studies, and as a result were unable to look at the changes that are likely to occur as individuals with chronic illness progress from diagnosis to self-management.

2.2.4 Efficacy beliefs

In relation to adherence, beliefs about self-efficacy (e.g. I am confident that I am able to take my treatment) and outcome efficacy (e.g. taking my treatment will reduce my symptoms) can play an important role. Self-efficacy beliefs are influenced by an individual's assessment of their own behaviour, the behaviour of others and feedback they receive about their own behaviour from significant others (Albert Bandura, 1997). Perceived self-efficacy has been shown to be associated with adherence to health-related behaviours such as smoking cessation (Carlo C DiClemente, Prochaska, & Gibertini, 1985) and exercise programmes (Kaplan, Atkins, & Reinsch, 1984), and has been proven to be an effective basis for interventions aimed at improving self-management and clinical outcomes in a number of chronic health conditions such as arthritis, lung disease and heart disease (K. Lorig et al., 1986; Kate Lorig & Holman, 1993; K. R. Lorig, Mazonson, & Holman, 1993; K. R. Lorig et al., 1999). Self-efficacy has also been shown to be related with diabetes self-management and glycaemic control in adolescents with type I diabetes, (Griva, Myers, & Newman, 2000; Grossman, Brink, & Hauser, 1987; Ott, Greening, Palardy, Holderby, & DeBell, 2000).

Although positive self-efficacy can encourage adherence on its own, it has been shown to have a stronger influence when combined with positive outcome expectations in adults (Williams & Bond, 2002) and adolescents with type I diabetes (Iannotti et al., 2006) . These findings support Bandura's (1997) original suggestion that individuals are most likely to adopt a health behaviour if they perceive themselves to be capable of doing so, and if they expect this behaviour to have mainly

positive consequences (more positive outcome expectations and fewer negative outcome expectations).

According to Bandura (1994; 1997) efficacy beliefs are developed and influenced by four main sources. Firstly, personal successes (or mastery experiences) can build an individual's belief in their efficacy, particularly if they have had to overcome some obstacles in order to achieve success. On the other hand failures or easy successes can undermine perceived self-efficacy. Secondly, vicarious experiences through social models can also influence efficacy beliefs (positively or negatively), with models who are perceived to be the most similar to an individual having the biggest influence. Thirdly, social persuasion can encourage people to try harder and persist for longer in trying to succeed, which in turn can promote skills development and a sense of self-efficacy. However it can also persuade people that they lack capabilities, which in turn can undermine motivation and self-efficacy, and lead to avoidance of challenging activities. Fourthly, an individual's state of mind and their physical and emotional responses to challenges (such as stress or physically demanding activities) also influences their efficacy beliefs.

The inclusion of efficacy beliefs in SCMs such as the TPB has improved their ability to predict preventative health behaviours, including medication adherence (Barnhoorn & Adriaanse, 1992; Schwarzer & Fuchs, 1996). Beliefs about self-efficacy and outcome efficacy (outcome expectations) may be influenced by previous experience and other cognitions.

2.2.5 Social Support

In addition to the above models, there is also evidence to support the association between adherence and social support (DiMatteo, 2004; Owen, Friesen, Roberts, & Flux, 1985). DiMatteo (2004) suggested that support and help from friends and family promotes adherence by providing a buffer for illness-related stress, encouraging optimism and self-esteem, reducing anxiety and depression and giving practical assistance. In his 2004 meta-analysis DiMatteo found that practical support with treatment was most strongly associated with adherence, although adherence was also found to be related to emotional support, family cohesiveness and conflict, marital status, and living arrangements. In research with adolescents with type I diabetes (Annette M. La Greca et al., 1995; Annette M La Greca & Bearman, 2002) support from family and friends were both found to be significantly associated with better adherence and/or self-management.

2.2.6 Summary of theories of adherence

The existing literature in relation to adherence to long-term therapies for chronic illness suggest that it is multidimensional and determined by a number of interacting factors including patient characteristics; clinical characteristics; social environment; and the health care provider. Studies using SCM to explore adherence in chronic illness have produced some evidence to support sections of models and frameworks such as the HBM and TPB, however there is no evidence to support the precise interaction of all dimensions specified by these models. Illness representations, beliefs about medicines, self-efficacy and perceived availability and quality of social support have been shown to be important correlates of treatment adherence and self-management in chronic health conditions, and together they may provide a more rounded explanation of adherence to long-term therapies such as prophylaxis. The research described in this thesis will therefore combine these correlates into a framework for understanding adherence to prophylaxis among YPH. The next chapter will provide an overview of the literature in relation to treatment adherence among adolescents and young adults with chronic health conditions, with a focus on haemophilia.

Chapter 3: Adherence among adolescents and young adults with chronic health conditions, with a focus on haemophilia

The aim of this chapter is to give a comprehensive overview of the literature surrounding treatment adherence among young people who are affected by chronic health conditions, with a particular focus on adolescents and young adults with haemophilia. The chapter will guide the reader towards an understanding of the specific issues that influence adherence to prophylactic treatment among young people with haemophilia (YPH).

3.1 Levels of adherence among young people affected by chronic health conditions

Adherence is an important factor in the efficacy of all medical treatments, in fact adherent patients are almost three times more likely to have a good outcome in comparison to non-adherent patients (Robin DiMatteo, Giordani, Lepper, & Croghan, 2002). Levels of adherence reported among adolescents with chronic illnesses such as diabetes, juvenile rheumatoid arthritis (JVA) and asthma vary widely, from 10% to almost 90% (Alvin, Rey, & Frappier, 1995; Michaud, Frappier, & Pless, 1991; P. Michaud, J. Suris, & R. Viner, 2004; Rapoff & Barnard, 1991).

For instance, non-adherence rates among adolescents have been reported to be approximately 28% for medication for epilepsy (Asadi-Pooya, 2005); 25% to insulin injections for diabetes (S. B. Johnson et al., 1992; Weissberg-Benchell et al., 1995); 29% for blood glucose monitoring and 81% for diet recommendations in diabetes (S. B. Johnson et al., 1992); between 17% and 90% for inhaled medication in asthma (Bender et al., 2000; Coutts, Gibson, & Paton, 1992; Lemanek, 1990); and 45% for oral medication in juvenile rheumatoid arthritis (JRA, Litt & Cuskey, 1981).

3.2 Measurement of adherence

Measurement of adherence is challenging, and may vary depending on the self-management behaviour that is being assessed. For instance, it is likely that adherence to a diet or exercise regimen will be assessed differently from adherence to taking medication or attending clinic appointments. The way in which good adherence is defined also influences how adherence may be assessed. For instance, for some treatments good adherence may be indicated by a certain level of the medication in the bloodstream, whereas for other treatments the level of adherence may be determined by the number of times that treatment is taken. The most common ways to assess adherence are described below.

3.2.1 Self-report data

One commonly use method to assess adherence in research is to ask patients to indicate their own adherence using a questionnaire or diary. There are many validated questionnaires to assess adherence to specific treatments or self-management behaviours, such as the VERITAS-Pro (Duncan, Kronenberger, Roberson & Shapiro, 2010) which assesses adherence to prophylactic treatment for haemophilia. Many adherence self-report questionnaires are validated against treatment logs to check how well they assess adherence. However, a key challenge is that some patient may not report their adherence accurately or truthfully. This may be because they do not want to admit to sub-optimal adherence or do not remember the exact timing and/or dose of their last treatment.

3.2.2 Treatment logs

Many patients with chronic illnesses are invited (or required) to complete a treatment log every time they take their treatment. Patients who follow a prophylactic treatment regimen for their haemophilia are required to log all the treatments they take (including any additional treatments taken to treat bleeds) on Haemtrack. This is an online treatment log with smartphone functionality that can be accessed by the haemophilia team, enabling them to monitor adherence of individual patients remotely. As with self-report questionnaires and diaries, this method relies on patients completing the information accurately and timely.

3.2.3 Pharmacy data

Adherence to medication that is dispensed by a pharmacist may be assessed by checking repeat prescriptions, looking at how much medication a patient has received from the pharmacy and if this would be enough to keep to their agreed treatment regimen. If a patient is not ordering (or receiving) sufficient medication from the pharmacy, it is likely that their adherence is suboptimal. This method is often just an estimate, as it only shows how much treatment a patient has received and not how much treatment they have actually taken. For instance, it is possible that a patient has received enough treatment from the pharmacy, but does not actually take it.

3.2.4 Blood tests

Some medications can be detected in the blood using a blood test, where the level of medication in a patient's blood stream gives a good indication of how well they adhere to their treatment (e.g. Methotrexate, a medication used by patients with rheumatoid arthritis). In other conditions a blood

test can give an indication of how well someone is managing their condition (e.g. a HbA1c blood test indicates how well blood glucose levels are controlled in someone with diabetes). However, this method requires a patient to come to the hospital or surgery to have a blood test and relies on the healthcare provider having enough resource to take the blood test and analyse it.

3.2.5 Electronic monitoring

For medication that is taken through an oral capsule or pill, it is possible to assess adherence by recording the date and time that the cap of the pill bottle is opened. This method only gives an indication, as of course it is possible that a patient simply opens and closes the pill bottle without taking their treatment.

Due to the limitations associated with these different ways to assess adherence it can be useful to combine several methods. For instance, one may use data from treatment logs to validate self-report questionnaire data, or combine pharmacy data or electronic monitoring with treatment logs. Although combining data from several sources is likely to increase the cost of research, it is also likely to improve data quality and validity of the research.

3.3 Levels of adherence to prophylactic treatment among young people with haemophilia

Due to the rarity of haemophilia research samples tend to be small and few studies have been published. A recent systematic review on the determinants of adherence to prophylaxis in haemophilia (Schrijvers, Uitslager, Schuurmans, & Fischer, 2013) identified just five articles in relation to barriers and motivators of adherence to prophylactic treatment in haemophilia, which were all published in the period of 2001-2008. After critical appraisal using the STROBE statement (von Elm et al., 2008) and criteria for quality of evidence developed by the Dutch Cochrane Centre (Offringa, Assendelft, & Scholten, 2008), two of these five studies were considered as the best evidence available. The first study (De Moerloose et al., 2008) was a survey of adherence in six European countries, and the second study (Llewellyn et al., 2003) was a UK single-centre survey study. The three other studies (du Treil, Rice, & Leissinger, 2007; Geraghty et al., 2006; Hacker et al., 2001) were excluded from the review because of small sample sizes, concerns about selection bias, use of unvalidated questionnaires, and not measuring adherence (instead asking healthcare professionals or parents to estimate adherence). The review authors (Schrijvers et al., 2013) suggest that the motivators of adherence are: experience of symptoms, a positive belief of necessity of treatment and a good relationship with the healthcare provider. Important barriers identified by the review are: infrequent or absence of symptoms and increasing age.

Levels of adherence reported in the current vary widely. Although the two studies included in the above review broadly agreed in relation to the drivers of adherence, they reported very different levels of adherence. In their survey of adherence in six European countries (De Moerloose et al., 2008) found that adherence to prophylaxis across their entire sample (patients of all ages over 2) was 93% and overall adherence (to prophylaxis and on-demand treatment) among adolescents (aged 12-19) was 98%. A key limitation of this study is that, although the total sample was large (N=180), data was collected in six countries which each contributed just 30 participants. Practice patterns across these countries are, in some cases significantly, different. Therefore the overall findings of this study do not provide insight into local circumstances in each of the six countries, whereas the local samples of 30 participants in each country are not sufficiently large enough to evidence local levels of adherence and drivers of adherence.

In their UK single-centre survey study (Llewellyn et al., 2003) found that 34% of patients (patients of all ages over 11) were fully adherent to frequency of prophylactic injections, and 44% of patients were fully adherent to the recommended dose of their prophylactic injections. A key limitation of this study is the small sample (N=65), which included patients who follow a prophylactic treatment regimen as well as people following an on-demand regimen, and consisted of participants aged 12 years and older. Due to the significant differences in haemophilia treatment (and resulting issues such as HIV infection as a result of contaminated blood) during the previous decades, haemophilia-related experiences of older people in the sample would have been completely different from younger participants. As the findings are based on the average scores of the total sample, they may not be particularly helpful to understand either older patients with significant haemophilia-related issues or younger patients who have very few health issues.

The levels reported by the 3 studies that were excluded from the review also vary considerably. In their single-centre study in the US du Treil et al. (2007) found that only 17% of participants on prophylaxis had high adherence (defined as 67-100% of treatments taken as prescribed), whereas 45% of patients on on-demand treatment had high adherence. Hacker et al. (2001) suggested that 58.8% of responders (mostly mothers of patients aged 18 or younger) in their single-centre study in the US reported excellent adherence to prophylaxis (giving 75-100% of prescribed injections). Geraghty et al. (2006) sent The Haemophilia A Practice Patterns Survey (PPS 2003) to 274 haemophilia centres worldwide and received responses from haemophilia nurses in 19 countries. Nurses estimated that adherence to prophylaxis would be highest among the 0-12 age group, with 59% of patients achieving an adherence rate over 90%. Nurses estimated that the percentage of patients achieving this high rate of adherence among the other age groups would be considerably lower (13% of 13-18 year olds, 6% of 19-28 year olds, and 17% of patients aged 29 and older).

Findings from a multi-centre study across Denmark, Norway and Sweden, (Lindvall et al., 2006) indicate that 41% of their 108 respondents (aged between 13 and 25 years old) had not always kept

to their prescribed treatment regimen, but because this study did not specifically investigate adherence it was not clear if these were longer periods of non-adherence or one-off situations.

The large variation in reported adherence levels may be explained by the fact that the practice patterns across the different countries in which the studies were carried out are significantly different. A survey of haemophilia care in 19 European countries (O'Mahony, Noone, Giangrande, & Prihodova, 2011) found enormous variation in relation to the availability of factor concentrates, per capita usage of factor treatment, brands of factor concentrates prescribed, and availability of home treatment (and home delivery of treatment). Treatment protocols also appear to differ significantly between different countries. For instance, in Sweden prophylactic regimen are based on the high-dose Malmö protocol, with injections of 25-40 International Units (IU) per kg of bodyweight, whereas Dutch regimen are based on the intermediate-dose Utrecht protocol, with injections of 15-30 IU/kg.

Another reason may be the different measures that were used to assess adherence (self-report, estimations by clinical staff and/or parents, pharmacological data, and treatment logs) but also different definitions of adherence. Despite the variation in reported adherence levels, many of the North American and European studies agree that additional support may be needed to help patients keep to their treatment regimen during transition from childhood into adulthood (Breakey et al., 2010; Geraghty et al., 2006). This is because most of these studies found that adherence levels reduce during this period, and that adolescent patients are more challenging to engage with treatment.

3.4 Factors associated with adherence to long-term treatment among adolescents and young adult with chronic health conditions

A substantial evidence base now exists in relation to factors that are associated with (non)adherence among young people affected by a chronic illness (Bosley, Fosbury, & Cochrane, 1995; Fielding & Duff, 1999; Fotheringham & Sawyer, 1995; Krasnegor, Epstein, Johnson, Yaffe, & Epstein, 2013; H. A. KyngÄs, Kroll, & Duffy, 2000; Ivan Barry Pless et al., 1994; Rogers, Miller, Murphy, Tanney, & Fortune, 2001; D. L. Roter et al., 1998; Vermeire et al., 2001). However findings are inconsistent, which is not surprising considering the fact that each situation and each treatment differs, and that it is therefore challenging to identify one or more factors which can reliably explain or predict adherence in the majority of patients and situations.

However, the literature recognises that there are specific factors that may be associated with adherence, and indeed may explain or predict (non)adherence among chronically ill young people. These factors can be grouped according to the following themes: developmental issues; medical and demographic factors; cognitive-emotional and motivational factors; family and peer support;, and the quality of the interaction between the patient and healthcare provider (H. A. KyngÄs et al.,

2000). These will be addressed in turn below, both in terms of adherence to chronic conditions in general as well as, where it exists, evidence that is relevant to adherence to prophylaxis in haemophilia.

3.4.1 Developmental issues

Adolescent development can be divided into three stages: early, middle and late adolescence. Each of these stages is characterised by rapid biological, social and psychological changes, which are highly inter-related. Chronic illness can potentially influence these developmental processes, and equally physiological change and psychosocial adjustments can have an impact on the disease. The developmental changes that characterise (and are unique to) adolescence result in specific disease patterns, unusual symptom presentations, and unique challenges in relation to disease management and communication between HP, parents, and patients. As a result of the growing body of research in this area, these issues are increasingly recognised by health professionals (Jessop & Stein, 1994; Newacheck & Halfon, 1998; Newacheck & Taylor, 1992), and indeed young people themselves (Beresford & Sloper, 2003).

Individuals' perceptions and beliefs in relation to medication and health in more general are often formed during adolescence (P. A. Michaud, J. C. Suris, & R. Viner, 2004). HP working with young people who are affected by chronic illness are therefore not only managing the current situation, but also laying a foundation for disease (self-) management in later life.

Rates of adherence among adolescents and young adults are not necessarily always lower than among adults (Dunbar-Jacob, Burke, & Puczynski, 1995), however young people with chronic illness face specific challenges that are related to biological, psychological and social development. Adolescence is characterised by rapid changes in physical appearance and increased comparisons of physical attributes with peers. This may heighten awareness of potential physical and social side effects of treatment and may lead to young patients questioning the necessity and benefits of their treatment (H. A. KyngÄs et al., 2000).

Identity, self-image, and ego-development can be affected by chronic illness, particularly when illness is more severe (Hauser, Jacobson, Noam, & Powers, 1983; Jacobson et al., 1997; Silver, Bauman, Coupey, Doctors, & Boeck, 1990). This may explain why young people with chronic illness are more likely to have a negative body image, or higher body dissatisfaction (Choquet, Du Pasquier Fediaevsky, & Manfredi, 1997; Manworren, 1996), particularly in cases where orthopaedic or neuromuscular defects result in disability.

In order to achieve independence from parental influence, it is common for adolescents to spend more time with peers, and to adopt new norms and values (Anderson, Ho, Brackett, Finkelstein, &

Laffel, 1997; Suris, Michaud, & Viner, 2004). Adolescents with a chronic illness may value the liberating social interaction and acceptance of friends more than their, sometimes restrictive, treatment regimen (Keller & Nicolls, 1990; Seiffge-Krenke, 1990). Woodgate (1998a, 1998b) suggests that adolescents may experience more restriction, pain and additional worries because of chronic illness. There is also evidence that adolescents who suffer from invisible conditions (such as epilepsy and haemophilia) may find it more difficult to accept and discuss their condition (Ivan B Pless & Roghmann, 1971), and some may avoid disclosing their condition altogether. This can place them in difficult situations such as having to find alternative reasons for not participating in peer activities, or placing others in a difficult position when they experience unexpected medical situations.

There is some evidence to suggest that adolescents and young adults affected by chronic illness arrange and attend fewer medical appointments in comparison to other age groups (Marcell, Klein, Fischer, Allan, & Kokotailo, 2002; Settertobulte & Kolip, 1997).The demands of managing a chronic illness and the restrictions on lifestyle inherent in many conditions increase dependence on the family and carers at a time when this usually decreases (Eiser & Berrenberg, 1995). Supportive relationships with peers may help young people to break away from their parents or caregivers, and engage in their individuation process. This process can be encouraged by the healthcare team by providing opportunities for young patients to interact with each other, such as peer support groups or social outings.

Treatment adherence requires personal organisation, cognitive ability, and a belief that treatment is necessary and beneficial (Sabaté, 2003; Vermeire et al., 2001). In their review KyngÄs and colleagues (2000) suggest that during adolescence abstract thinking is often not fully developed yet, which can manifest itself as an inability to understand future consequences of today's behaviour; young people thinking of themselves as invincible or bullet proof; and relatively poor ability to plan and prepare for difficult situations. They argue that as a result of these cognitive issues, the prevention of long term complications of illness may be a poor motivator for treatment adherence, which may explain poor adherence levels among adolescents with chronic illnesses.

Empirical findings of developmental issues that affect adherence to prophylactic treatment among young people with haemophilia

Transition from childhood into adulthood has implications for treatment and healthcare provision for most YPH in the UK. Transition from paediatric to adult care, and the way in which most patients gradually take responsibility for their own treatment can be seen as a developmental process. P Petrini and Seuser (2009) suggest that adherence to prophylaxis is likely to reduce during adolescence because the pressures involved with learning self-management often coincide with the

simultaneous physical, psychological, social and sexual developmental changes that characterise adolescence (e.g. achieving independence from parents and building new relationships and social networks). Several studies have found that adherence to prophylaxis was very high among children and significantly worse among adolescents (Kathelijn Fischer et al., 2007; Geraghty et al., 2006), however these studies did not provide clear evidence for the suggested reasons for non-adherence among adolescents.

The marks and scars left by regular intravenous injections may impact on young people's body image and confidence. Particularly during the development phase when they start to take control of their changing (maturing) body, comparison to peers who do not have haemophilia may highlight differences and decrease body confidence (Lee et al., 2005; Seuser, 2009).

Although physical activity is an important part of self-management for YPH, restrictions in relation to which physical activities they can take part in at school may highlight that they are different, which in turn may also affect their confidence (Groen, Takken, Van Der Net, Helders, & Fischer, 2011; Lee et al., 2005; Petrini & Seuser, 2009).

3.4.2 Medical and demographic factors

Chronic illnesses and their symptomatology may affect adherence themselves, as patients may keep to their treatment regimen simply because they know that non-adherence will have serious consequences.

Disease-related factors are thought to play an important role in treatment adherence. Lower adherence has been found to be associated with longer disease duration, earlier age of onset, later referral to a specialist, fewer clinical visits, and shorter disease duration among adolescents with Juvenile Rheumatoid Arthritis (Litt & Cuskey, 1981), and absence of daily symptoms among adolescents with asthma (Dekker, Dieleman, Kaptein, & Mulder, 1993).

Medication side effects have also been shown to affect adherence among adolescents with chronic illnesses (Catz, Kelly, Bogart, Benotsch, & McAuliffe, 2000; Nevins, 2002; Price, 1996; Rogers et al., 2001). The nature and complexity of treatment is also an important determinant of adherence. For instance, adherence to the demanding physical exercise regimen recommended for JRA appears to be significantly lower than adherence to medication in the same patient group (Hayford & Ross, 1988). Among young people with type I diabetes adherence to diet recommendation and blood glucose monitoring has been found to be significantly higher than adherence to insulin injections (S. B. Johnson et al., 1992; Weissberg-Benchell et al., 1995).

Empirical findings of medical and demographic factors that affect adherence to prophylactic treatment among young people with haemophilia

The regular intravenous injections make prophylaxis a demanding treatment regimen. Studies have suggested that the time consuming nature of the treatment and issues in relation to the actual injection (such as venous access) are important barriers to adherence (Geraghty et al., 2006; Hacker et al., 2001). In the UK many patients are encouraged to take their treatment in the morning, so that it provides them with cover during the day. Having to fit a time-consuming treatment into the morning routine can be challenging as young people have to get ready to leave the house early to go to school or work.

The prophylactic injections require technical skills and confidence, which make it a more challenging than taking a tablet or using an inhaler. The current literature suggests that patient education plays an important role in ensuring that patients have adequate knowledge and skills before they take over full responsibility for their prophylactic treatment (J. Barlow et al., 2007; K. Fischer et al., 2008). In their multi-centre Scandinavian study Lindvall et al. (2006) found that the average age at which patients took responsibility for the management and treatment of their haemophilia was 14.1 years. Comparable data are not available YPH in the UK.

As many YPH in the UK started prophylaxis at an early age they may not have experienced many (or any) serious bleeds, and are therefore unfamiliar with the resulting joint damage. They do not know what life would be like without prophylaxis, and therefore may not appreciate the importance of adhering to their treatment (Hacker et al., 2001). However, the findings from a UK single-centre qualitative study (K. Khair, Gibson, & Meerabeau, 2012) suggest that adherence tends to be good among boys with haemophilia because they generally recognise that prophylaxis offers them protection from bleeding. In addition, older (and sportier) boys who took part in this interview study understood the need for tailored prophylaxis around risky activities such as sport or events away from home. Khair and colleagues suggest that adherence often improves when treatment frequency increases to daily, as the injections become part of the daily routine.

3.4.3 Cognitive-emotional and motivational factors

Adolescents are most likely to adhere to their treatment if they believe it will be effective (H. A. KyngÄs et al., 2000). Studies in different chronic illnesses (Carbone, Zebrack, Plegue, Joshi, & Shellhaas, 2013; Koster, Philbert, Winters, & Bouvy, 2015) have found that understanding and knowledge about illness and treatment are important for adherence, and that understanding is likely to follow a developmental progression (Berry, Hayford, Ross, Pachman, & Lavigne, 1993).

The Department of Health National Framework for Children (2003) suggests that children have a right to be involved in treatment decisions, and that communication must be tailored to children's level of understanding and developmental stage. Tailoring information based on the constantly evolving and changing developmental factors during childhood and adolescence can be challenging for HP, and as a result in some cases information is still directed to parents rather than young patients themselves (Tates & Meeuwesen, 2001; van Dulmen, 1998).

Decreased emotional well-being, low self-esteem and social dependence are more common among young people with chronic illnesses in comparison to healthy peers (Bosley et al., 1995; Chigier, 1992; CHRISTIE, 1990; Eiser, 1990). These in turn may have a negative impact on adherence. Litt et al (1982) found that adolescents with JRA who were adherent also had greater self-esteem and felt more autonomous in comparison to those with lower adherence.

Empirical findings of Cognitive-emotional and motivational factors that affect adherence to prophylactic treatment among young people with haemophilia

As mentioned above, one important factor that may reduce adherence among YPH is their (lack of) experience of bleeding and the resulting joint damage, as adherence is often driven by the motivation to reduce or prevent symptomatology (Geraghty et al., 2006). In the absence of this motivation it may be challenging to convince young people to keep to their treatment regimen, particularly as prophylaxis is demanding and time-consuming.

The findings from a large Dutch study (Triemstra et al., 1998) suggest that psychological characteristics (anxiety, depression, anger, and optimism) are strong predictors of adaptation to haemophilia, well-being and level of disability.

The current literature also suggests that poor knowledge and disease understanding may have a detrimental influence on adherence during adolescence and young adulthood (Kate Khair, 2013; Lindvall et al., 2006). Lindvall et al. (2010) suggest that haemophilia teams should regularly discuss topics such as type and severity of haemophilia, treatment issues (including adherence), genetic inheritance knowledge and bleed management with patients, as this would lead to a better understanding of the risks of complications, benefits of treatment and importance of self-care. In addition, current more flexible approaches to prophylaxis treatment regimens engage patient in treatment decision making, leading to greater concordance (Khair et al, 2013). The combination of better understanding of treatment and involvement in clinical decision-making helps patients to plan treatment around their normal day-to-day activities, which in turn is likely to improve treatment uptake (Khair et al, 2012).

3.4.4 Social support (peer and family support)

An individual's social situation influences the way in which they experience their illness, and manage their health (Burroughs, Pontious, & Santiago, 1993). Family and peers are important sources of support for young people in managing their chronic health condition. Family support often consists of practical and tangible help with disease and treatment management, whereas peer support often centres around social interaction and emotional support. Research in young people with diabetes and JRA has found that positive family climate, parental supervision, family cohesion and open relationships within the family are associated with good adherence, whereas poor relationships, conflicts, and behavioural problems within the family seem to be related to poor adherence (Chaney & Peterson, 1989; Degotardi, Revenson, & Ilowite, 1999; H. Kyngäs, Hentinen, & Barlow, 1998; Weissberg-Benchell et al., 1995).

Many young people who are affected by chronic illness feel different from their peers, which can lead to them feeling socially restricted. Some research suggests that this in turn can affect adherence (H. Kyngäs et al., 1998; Seiffge-Krenke, 1990). Emotional peer support can help them feel more accepted (H. A. KyngÄs et al., 2000), but friends can also help them keep to their treatment (e.g. by reminding them when to take their medication or encouraging them to look after themselves).

However, friends and social contacts can also exert a negative influence on adherence. Not wanting to be different, or miss out on activities with friends, can make it challenging for young people to follow their treatment regimen as recommended (H. Kyngäs et al., 1998).

Empirical findings of the association between social support and adherence to prophylactic treatment among young people with haemophilia

In their review article Petrini and Seuser (2009) suggest that the most important factor that influences compliance is support from parents, peers and caregivers. They emphasize that social support encourages young people to look after their haemophilia and is crucial to help patients through challenging periods. Lindvall et al. (2006) suggest that frequent contact and visits to the haemophilia centre can foster familiarity between the doctors and nurses and the patient and their family, which in turn facilitates open communication can help the haemophilia team to tailor their approach to the individual patient.

3.4.5 Quality of the interaction between the patient and healthcare provider

The quality of the interaction between patient and doctor has been shown to affect adherence in various chronic illnesses (Bartlett et al., 1984; M Robin DiMatteo & DiNicola, 1982; D. Roter & Hall, 2006). A good relationship between the patient and health care provider can improve adherence (M Robin DiMatteo & DiNicola, 1982; Karlsson, Holmes, & Lang, 1988; H. Kyngäs et al., 1998; Thorne, 1990), whereas conflicts between patients and healthcare providers are likely to be associated with poor adherence (Karlsson et al., 1988).

Adolescents and young adults who are encouraged to actively participate in treatment decisions may be more committed to the resulting treatment regimen, and as a result show higher levels of adherence (Berry et al., 1993).

Empirical findings of patient-healthcare provider relationship and adherence to prophylactic treatment among young people with haemophilia

As described above, members of the haemophilia team can play an important role in informing and educating patients about their haemophilia and treatment, which in turn can improve adherence and self-management (Kate Khair, 2013; Lindvall, Colstrup, Loogna, Wollter, & Gronhaug, 2010; Lindvall et al., 2006). However, no studies were found that directly examined the role that the relationship between patient and HP plays in adherence to prophylaxis.

3.5 Conclusion of literature review and justification for this programme of research

A haemophilia research steering committee with members representing haemophilia healthcare providers, members of the Haemophilia Society and patients highlighted that adherence to prophylaxis among young people in the UK is a key concern that is shared by these stakeholders. The committee agreed that there is a lack of knowledge about the drivers of (non-)adherence among YPH, and that research in this area should be prioritised. The existing adherence in haemophilia literature is very small with only a handful of publications in the world, and it offers very little evidence in relation to levels of adherence among YPH. Other limitations of the current literature are that most of the studies were conducted outside of the UK in countries where haemophilia healthcare is organised in a different way, and that studies do not provide sufficient evidence for the suggested barriers and facilitators to adherence. Additionally, the increasing flexibility and personalisation of prophylactic regimen in this country, which are likely to influence adherence, have thus far not received much attention in the literature.

With this in mind, and considering how the particular research questions of this study may best be addressed, it was decided to adopt a mixed methodology approach. This approach has the

advantage of combining objective and rigorous assessment of quantifiable phenomena (such as treatment adherence) and in-depth and detailed study of phenomena that are not easily quantifiable (such as patients' experiences in relation to prophylactic treatment and the way they make meaning of those experiences). It is anticipated that the qualitative and quantitative findings will complement each other, and allow the researcher to present a comprehensive study of adherence to prophylactic treatment among YPH in the UK, and the strengths and weaknesses in current healthcare provisions for this patient group.

3.6 Rationale for a mixed methods approach

The way in which individuals make sense of their health-related issues is central to many of the health psychology models described in the previous chapter. Combining quantitative instruments such as the Beliefs about Medicines Questionnaire (Horne et al., 1999) and Brief Illness Perceptions Questionnaire (Broadbent et al., 2006), with qualitative interviews based on Interpretative Phenomenological Analysis (IPA, Jonathan A Smith, 2010), may contribute towards an understanding of the way in which patients make sense of their health-related experiences, and the way this may influence their health-related behaviour (Hanson, Creswell, Clark, Petska, & Creswell, 2005; Tashakkori & Teddlie, 1998; Teddlie & Tashakkori, 2009). In the context of this programme of research it is anticipated that the combination of detailed qualitative analysis of young peoples' experiences in relation to prophylaxis and the way in which they make meaning of these experiences, and quantitative analysis of their treatment-related perceptions, beliefs and behaviour, could lead to an enhanced understanding of adherence to prophylaxis in this patient group, barriers and facilitators to their adherence, and psychosocial factors that may be associated with their self-management.

3.7 Rationale for Interpretative Phenomenological Analysis (IPA)

The aim of the qualitative element of this study was to examine personal experiences of YPH, parents of YPH, and haemophilia HP in relation to prophylactic treatment, and how they make sense of these experiences. IPA was the chosen approach because it has an idiographic focus, which combines psychological, interpretative and idiographic components. It aims to offer insights into how a given person, in a given context, makes sense of a given phenomenon (Jonathan A Smith, 2010). Therefore its focus is on '*exploring experience in its own terms'*, without reducing it down to *'predefined or overly abstract categories'* (Jonathan A Smith, 2010). IPA employs a "double hermeneutic" in which the researcher tries to make sense of the participant trying to make sense of their experiences (Smith and colleagues, 2003; 2009) . IPA studies usually employ a fairly homogenous sample, drawing on the accounts of a small number of people who have certain

experiences in common (Reid, Flowers, & Larkin, 2005). Data were collected through face-to-face semi-structured interviews which were audio-recorded. The researcher tried to use as few prompts as possible, to encourage participants to tell their story in their own words, and in their own time. The interviews were transcribed verbatim and then analysed using IPA (Jonathan A. Smith, 2003; J. A. Smith, & Osborn, M. , 2008). A detailed description of the IPA methodology used will be described in chapter five.

3.8 Rationale for Quantitative questionnaire

The aim of the quantitative element of this study was to assess levels of adherence among YPH, and psychosocial factors that the current adherence literature suggests may be important correlates or even predictors of adherence. The study employed a questionnaire that mainly consisted of widely used validated scales which are grounded in health psychology theory. Using these scales will allow the researcher to test current adherence theory, and compare the findings with other research studies. Variables for which no appropriate validated scales were available were assessed using newly constructed scales which were based on existing scales from research in other chronic health conditions (such as diabetes). Several open questions were included to offer participants the opportunity to describe their experiences in their own words. A detailed description of the quantitative methodology will be described in chapter 5.

3.9 Recruitment

Haemophilia centres

Severe haemophilia is rare with approximately 5,900 people with Haemophilia A, and 1,200 with Haemophilia B in the UK. Following discussions facilitated by the Haemophilia Research Steering Committee, and based on initial estimates of the number of young people who are affected by severe haemophilia in the UK (provided by members of the committee), it was decided that we would aim to recruit approximately 100 questionnaire participants and 20 interview participants from across the 3 large haemophilia centres in London (the Royal Free Hospital, Guy's and St Thomas' Hospital, and the Royal London Hospital).

However, a more accurate (and considerably lower) estimate provided by the UK Haemophilia Centres Doctors' Organisation (UKHCDO) database highlighted that there were only 473 people in England and Wales who met the inclusion criteria for the studies (diagnosed with severe haemophilia, aged 12-25, and following a prophylactic treatment regimen). Additionally, after several months the Royal Free Hospital decided they were unable to take further part in the study. It

was therefore decided to try and recruit participants in all large haemophilia centres across England and Wales, making this a nationwide programme of research.

The research received external peer reviewed funding from the Bayer Haemophilia Awards Programme (Caregiver Award awarded to the author), making it eligible for adoption onto the National Institute of Health Research (NIHR) Clinical Research Network (CRN) Portfolio. The research was discussed at a national NIHR CRN Non-Malignant Haematology Specialty Group meeting, and was prioritised for support throughout the network of haemophilia centres across England and Wales. Thanks to this support the study was given access to local networks of dedicated skilled research staff (including research nurses and allied health professionals), who were able to help with identifying eligible patients, arranging consent to participate in the study, and data collection. Many of the centres that agreed to take part in this study were enthusiastic, and keen to take part. However, the prioritisation by the specialty group helped enormously, as it highlighted the importance of the research. Haemophilia centres were invited (and encouraged) to take part in the study personally by the Chair of the specialty group Professor Collins, and remunerated by the NIHR CRN Portfolio for each participant they recruited into the study.

Participants

The 13 centres that agreed to take part in the questionnaire study look after approximately 150 of the 473 eligible patients in England and Wales. As many of these 150 patients as possible were approached face-to-face while they attended an outpatient appointment in the haemophilia centre. After they were given the opportunity to read the information sheet and ask questions about the study, 108 of the 125 patients who were invited to take part in the questionnaire study agreed to participate, although 18 did not return the questionnaire or later withdrew. An additional 47 members of the Haemophilia Society were invited to complete the questionnaire online, which resulted in one additional response. Analysis was thus performed on 91 participants, which is approximately 19% of the total population, making this is a substantial sample.

Five of the haemophilia centres involved with the questionnaire study also agreed to take part in the interview studies. In these centres potential participants were given information about both the questionnaire and interview study in advance of their routine check-up appointment at the haemophilia centre, and it was explained that they could take part in either the questionnaire or the interview study. During their appointment they had the opportunity to ask any questions about the studies, before being invited to consent to either one of the studies. Participants who agreed to take part in the questionnaire study were invited to complete the consent form and questionnaire immediately after their appointment, before leaving the haemophilia centre. Some participants took the questionnaire home and posted it back to the haemophilia centre once they had completed it.

Participants who agreed to be interviewed were invited to complete the consent form and asked to provide contact details so that the researcher could contact them at a later time to arrange the interview time and location.

3.10 Summary of methods used

In order to provide a complete and comprehensive evaluation of adherence to prophylaxis among YPH, a number of studies were carried out. Firstly, levels of adherence and psychosocial predictors of adherence were assessed in a large multicentre cross-sectional questionnaire study. In order to better understand the drivers of (non-)adherence, qualitative interview studies were conducted with patients, parents and haemophilia HP. Interpretative Phenomenological Analysis of the interview data, with a specific focus on personal experiences and perceptions in relation to prophylaxis, identified key themes in relation to adherence to prophylaxis among YPH, including barriers and facilitators to adherence.

Chapter 4: Cross-sectional analysis of adherence to prophylaxis and psychosocial factors of adherence among young people with haemophilia

4.1 Introduction

Chapter one discussed the significant burden of self-management on young people with haemophilia (YPH) and their families. Patients are required to attend outpatient appointments, keep to a demanding treatment regimen, avoid activities that increase the risk of bleeding, and manage bleeds if and when they occur. There is strong evidence that early and sustained prophylactic treatment with factor replacement therapy reduces joint bleeds and resulting arthropathy (K. Fischer, 2002; M. J. Manco-Johnson et al., 2007) whilst also improving quality of life (Richards et al., 2010). However, the benefits of prophylaxis can be difficult to perceive for patients aged 25 and younger as many do not know what life would have been like without prophylaxis, whereas they often perceive the treatment burden as high (Hacker et al., 2001).

Patients' adherence to prophylaxis has a considerable influence on its efficacy. Non-adherence increases the risk of spontaneous bleeds (Hacker et al., 2001), which increase treatment costs (Panicker et al., 2003), and may result in joint damage leading to poorer physical and emotional wellbeing (Marilyn J Manco-Johnson et al., 2007; Treil et al., 2007). In addition to the immediate costs associated with treating bleeds (e.g. on-demand treatment), they may also lead to increased future care-costs due to disability. Levels of adherence to prophylaxis reported in the existing literature vary widely (De Moerloose et al., 2008; Treil et al., 2007), and reasons for non-adherence are not evidenced. In addition, reported adherence levels among adolescents and young adults are predominately based on estimations made by healthcare professionals (HP) and parents, rather than young people themselves (Geraghty et al., 2006; Hacker et al., 2001). For these reasons this study will focus on adherence to prophylaxis among YPH.

Chapter two discussed that non-adherence can be intentional, where a deliberate decision is made not to take treatment or unintentional which is usually due to forgetting. It is likely that there are different causes and effects of these different types of adherence, but they have not been reliably separated in the literature. Although a thorough review by Clifford, Barber & Horne (2008) demonstrated the importance of differentiating between the two, few researchers have consistently and reliably measured and reported the differences in their research, particularly in haemophilia. Therefore, this study will use the VERITAS-Pro, a validated measure of self-reported adherence to prophylaxis, which assesses the different dimensions of adherence through separate subscales. Chapter two also discussed the social cognition models that have been shown to be important correlates of treatment adherence and self-management in chronic health conditions. It is

anticipated that, in combination with self-reported adherence and clinical information in relation to bleeding episodes and hospital visits, these models may provide a more rounded explanation of adherence to prophylaxis among YPH.

4.2 Aims and hypotheses

The first aim of this study is to assess self-reported levels of adherence to prophylaxis using the VERITAS-Pro questionnaire (Validated Hemophilia Regimen Treatment Adherence Scale—Prophylaxis; Duncan, Kronenberger, Roberson & Shapiro, 2010).

The second aim is to provide evidence of the psychosocial factors of adherence to prophylaxis based on a large sample of young haemophilia patients, which is currently lacking in the literature. This will be done by assessing the key psychosocial factors that have been shown to be associated with adherence among young people with various chronic illnesses as described in the literature review (illness perceptions, self-efficacy, beliefs about medicines, outcome expectations, mood and social support). In addition, clinical data in relation to bleeds and hospital visits will be collected to establish the effects of non-adherence on these clinical outcomes.

Based on previous research on adherence and social cognitive models of illness, it is hypothesised that there will be differences between adolescents and young adults in relation to psychosocial correlates of adherence:

1) Unintentional non-adherence is anticipated to be higher among young adults because they tend to have less parental involvement and help with their treatment, and are more likely to experience life events that may interfere with adherence (e.g. leaving home, university life, first job, starting a family, etc.).

2) Intentional non-adherence is anticipated to be higher among adolescents because of rapid biological, psychological and social changes that characterise this developmental stage (e.g. difficulty in understanding future repercussions of today's actions, asserting independence from parents, etc.).

3) Factors of the social cognition models are anticipated to differ between adolescents and young adults because of differing experiences of managing haemophilia (e.g. differences in parental influence and relationships with doctors/nurses, and fewer long-term issues associated with recurring bleeding).

There has been a large amount of previous research on the effects that social cognitive models of illness have on adherence on which the following hypotheses are based for the entire sample:

4) Pain; higher perceptions of pain and impact of pain will be associated with better adherence (De Moerloose et al., 2008; Treil et al., 2007).

5) Illness perceptions; higher perceptions of chronicity, consequences and treatment control will be predictive of higher adherence (Chilcot et al., 2010; Horne & Weinman, 2002).

6) Beliefs about medications; higher perceptions of necessity of prophylaxis will be predictive of higher adherence whereas concerns about prophylaxis will not be predictive (de Thurah et al., 2010; Horne et al., 2013; Horne & Weinman, 1999; Llewellyn et al., 2003; Wileman et al., 2014).

7) Mood: patients with greater negative mood are anticipated to have lower adherence scores ((Cox & Hunt, 2015; Helgeson et al., 2009; Snell et al., 2014).

Based on evidence that lower adherence results in worse disease outcomes (Berntorp, 2009; M. J. Manco-Johnson et al., 2007) the following hypothesis was generated:

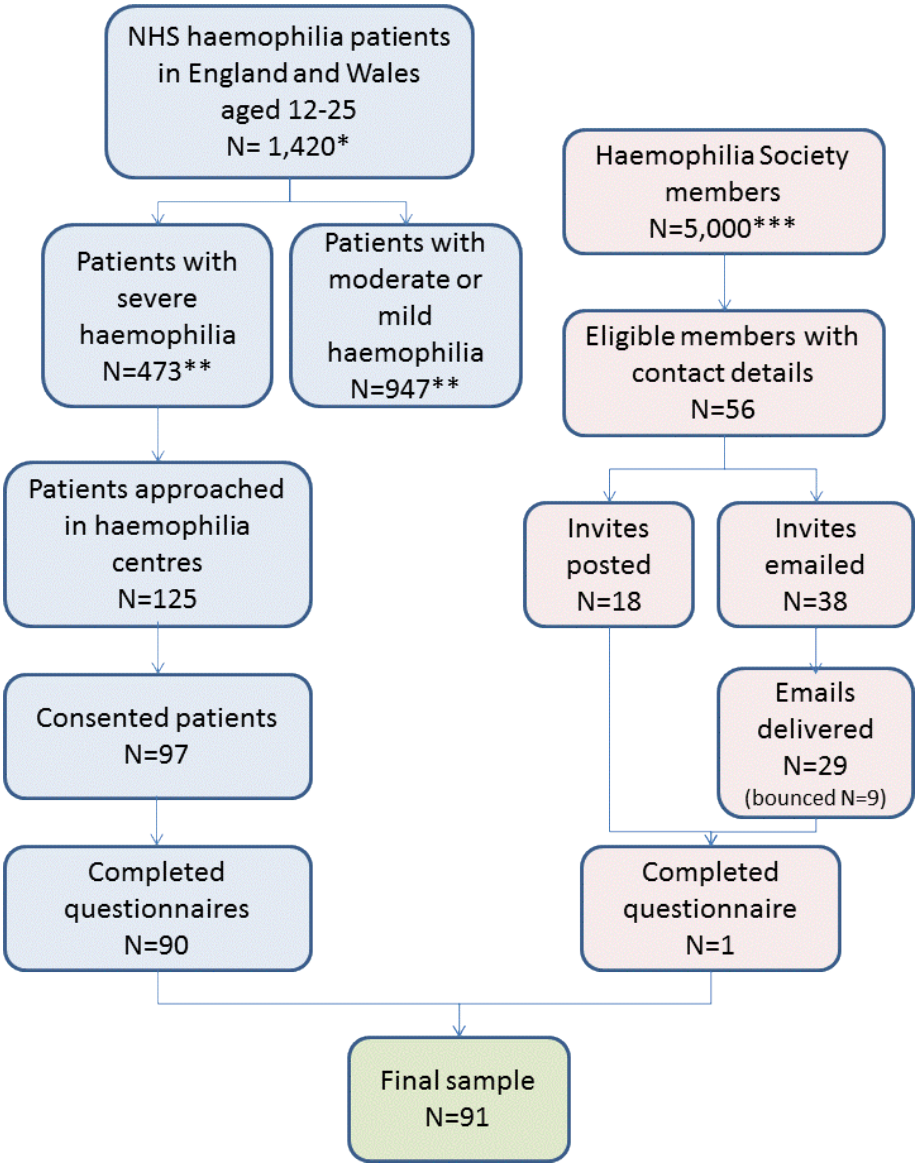
8) Non-adherence to prophylaxis will be related to higher numbers of bleeds and hospital visits.

4.3 Methodology

4.3.1 Participants

In total, 473 people in England and Wales met the inclusion criteria for this study (diagnosed with severe haemophilia, aged 12-25, and following a prophylactic treatment regimen). The 13 centres that agreed to take part in this study look after approximately 150 of these patients. The recruitment target was to invite as many of these 150 patients as possible. Eligible patients were approached face-to-face while they attended an outpatient appointment in the haemophilia centre. Of the 125 patients who were invited 108 agreed to participate, although 18 did not return the questionnaire or later withdrew. An additional 47 members of the Haemophilia Society were invited to complete the questionnaire online, which resulted in one additional response. Analysis was thus performed on 91 participants, which at approximately 19% of the total population is a substantial sample.

Figure 4.1 shows the recruitment process. The mean age was 18.83 (SD=5.00). Demographic and clinical details for the whole sample are shown in Table 4.2 on page 62.



**National Haemophilia Database: 30 – 09 – 2012*

***UKHCDO annual report 2010*

****Haemophilia Society Annual report 2014*

Figure 4.1: Recruitment flow-chart questionnaire study

4.3.2 Materials and procedure

All consecutive patients aged 12 to 25 years old (inclusive) diagnosed with severe haemophilia and currently on prophylaxis in 13 hospitals across England and Wales were invited to participate. In order to recruit patients in the specific age groups, dedicated clinics were targeted for recruitment and postal and email invites were also sent to eligible members of the Haemophilia Society. Written consent (and parental consent where relevant) was obtained before patients completed the questionnaires by themselves in the clinic or at home. The majority of questionnaires were completed on paper (n = 80), with the remainder being completed online (n = 11). A number of clinical variables were collected from the notes of patients who consented to the study including; number of hospital visits during the last 6 months, number of spontaneous bleeds and traumatic bleeds (caused by trauma or injury to the body) during the last 6 months. All data were confidential and assigned an anonymous participant identification number. The data were subject to double data entry to ensure there were no errors. The study was approved by the Yorkshire & The Humber - South Yorkshire NRES Committee (13/YH/0143) and all data handling conformed to Good Clinical Practice Guidelines (McGraw, George, Shearn, Hall, & Haws, 2010).

The full questionnaire is shown in Appendix 4.1 and described in more detail below. The questions were reviewed by a panel of patients, haemophilia doctors and nurses and a health psychologist who specialises in haemophilia. The questionnaire was then piloted with five patients to ensure validity. The final questionnaire consisted of questions assessing self-reported adherence (VERITAS-Pro), Haemophilia-related pain and impact of this pain, Illness Perceptions (Brief IPQ; Broadbent et al., 2006), Beliefs about Medications (BMQ; Horne et al., 1999), Self-efficacy and outcome expectations, Positive Affect and Negative Affect (Watson et al., 1988), and Social support.

Validated Hemophilia Regimen Treatment Adherence Scale-Prophylaxis (VERITAS-Pro)

The VERITAS-Pro (N. Duncan et al., 2010) is a validated measure of self-reported adherence to prophylactic treatment among people with haemophilia. The 24-item scale consists of six sub-scales which examine the extent to which participants take their injections at the recommended time (time), use the recommended dose (dose), plan ahead to ensure they have enough factor treatment and supplies (plan), remember to take their injections (remember), skip injections (skip) and communicate with the haemophilia centre appropriately (communicate). All questions are scored on a 5 point Likert scale with lower scores demonstrating better adherence.

As the scale was developed and validated in the US, it was necessary to rewrite some of the questions to make them appropriate for patients in the UK. For example the word ‘infusions’ was changed to ‘injections’. The rewritten scale was reviewed and tested by a panel of patients,

haemophilia doctors and nurses and a health psychologist who specialises in haemophilia. The members of the panel agreed that the dosing subscale, which aims to gauge whether patients keep to the recommended dosing, was not relevant for patients in the UK. This is because many patients in the UK are encouraged to tailor the dosing around their physical activity level, increasing the dose or frequency of treatment to provide cover for activities. This means that patients who do not keep to an agreed treatment schedule are not necessarily non-adherent. In addition, the VERITAS-Pro was developed in the US where funding for haemophilia care, and in particular prophylaxis, is often limited. The scale was based on previous US studies which suggest that concerns in relation to cost/affordability of prophylaxis are important barriers to adherence. This situation is not relevant in the UK where patients receive prophylaxis for free through the National Health Service. Appendix 4.2 highlights the changes that were made to the VERITAS-Pro scale.

Scores on each VERITAS-Pro subscale can range from 4 to 20, with higher scores indicating poorer adherence. Adherence sum scores for this study can therefore range from 20 to 100. The original validation studies (N. Duncan et al., 2010; N. Duncan, Shapiro, Ye, Epstein, & Luo, 2012) put forward a cut-off on the VERITAS-Pro total score as a threshold for non-adherence. Adherence was dichotomised into an adherent and non-adherent group using this 52-point cut-off for some of the analysis to enable comparison with other studies and between adherers and non-adherers. It also allowed the researcher to ascertain the proportion of participants with scores above the cut-off indicating they are non-adherent. However, this study relies primarily on the VERITAS-Pro scores as continuous because (i) this allows for testing of associations between level of adherence and outcomes rather than a coarse adherence/non-adherence dichotomy, (ii), this makes it possible to examine different types of non-adherence (i.e. forgetting and skipping), and (iii) the cut-off score has not yet been validated or applied in a patient population.

Clinical information.

The number of bleeds a patient experiences, and the frequency of their hospital visits, can be an indication of how well they manage their condition. Therefore the number of hospital visits and bleeds during the last 6 months was collated from medical notes for each patient. Bleed data was split into bleeds that were caused by accidents or injuries (traumatic bleeds) and breakthrough bleeds (spontaneous bleeds).

Self-Regulatory Model, Brief Illness perceptions Questionnaire

The Brief Illness Perception Questionnaire (Broadbent et al., 2006) was designed to provide a quicker way to assess the cognitive and emotional representations of illness that are included in the

Illness Perception Questionnaire-Revised (Moss-Morris et al., 2002). It is a 9-item questionnaire which uses a single-item scale approach to assess perceptions on a 0-10 response scale. The Brief IPQ comprises 6 items on cognitive representations of illness perception: consequences (of the condition), timeline (is the condition acute or chronic), personal control (patients' ability to influence symptoms), treatment control (extent to which treatment reduces symptoms), coherence (understanding of the illness), and identity (extent to which patients experience symptoms). There are 2 items on emotional representation: concern (about the condition) and emotional responses (extent to which the condition affects the patients feelings). The last item is on the perceived cause of illness; in which respondents list the most important causal factors in their illness.

Beliefs about Medicines Questionnaire

The Beliefs about Medicines Questionnaire (BMQ, Horne & Weinman, 1999) consists of two sections; beliefs about medicines in general (BMQ General) and beliefs about the specific medication prescribed for a given condition (BMQ Specific). For the purpose of this study only the BMQ Specific was included, which consists of two subscales; *Concerns* and *Necessity*. The Concerns subscale includes five questions referring to concerns patients might have about taking prophylaxis. The Necessity subscale includes five questions related to patients' perceptions about the necessary to take prophylaxis in order to stay well. In all cases, questions were scored on a 5 point Likert scale with higher scores on the Concerns subscale indicating more concerns and higher scores on the Necessity subscale indicating stronger beliefs in the necessity of prophylaxis.

Self-efficacy

In accordance with Bandura's (1997) situation-specific behaviour-based model, two self-efficacy scales were used. The first scale assessed self-efficacy in relation to haemophilia self-management and the second looked at self-efficacy in relation to prophylactic treatment specifically. As no appropriate existing scales were found, new scales were devised using Bandura's guide for constructing self-efficacy scales (Bandura, 2006). The content of the scales was informed by previous research looking at self-efficacy, outcome expectations and adherence among young people with type I diabetes (Chlebowy & Garvin, 2006; Iannotti et al., 2006). In addition a pilot study was undertaken with the aim to identify key haemophilia self-management behaviours and difficulties that young people experience in relation to their treatment. This information was then used to generate items in relation to self-efficacy and outcome expectations. Participants for the pilot (10 adolescents and 10 young adults with severe haemophilia) were recruited through the haemophilia society. They completed multiple choice and open questions via an online questionnaire.

These new scales were then reviewed by the panel and piloted with five patients.

The haemophilia-related self-efficacy scale consisted of three subscales: Communication (3 items assessing confidence in communicating about haemophilia); Taking prophylaxis (7 items assessing confidence in relation to all actions that are involved in taking prophylaxis); and Your health (2 items assessing confidence in managing health in general and preventing/dealing with haemophilia-related issues). Each item was scored on a 0-10 response scale.

To assess prophylaxis-related self-efficacy participants were invited to rate how confident they were that they could take their prophylaxis in 10 situations that were identified as challenging by the pilot study (e.g. when I am tired, when I'm busy, when I am away from home/on holiday, etc.). Each item was scored on a 0-10 response scale.

Outcomes expectations

The Outcome expectations scale was devised using the same literature and pilot data as the self-efficacy scales. Each of the 10 items was a potential answer to the question: 'If I always did everything I am supposed to do to manage my haemophilia, it would.....'. Patients were invited to rate how much they agreed with each answer using a 0-10 response scale. Five of the answers represented positive outcome expectations (e.g. keep me healthy), and 5 represented negative outcome expectations (e.g. be too time consuming).

Social support

Based on research with young people diagnosed with type I diabetes (Bearman & La Greca, 2002; Iannotti et al., 2006; Annette M. La Greca et al., 1995; Skinner, John, & Hampson, 2000) and previous research in haemophilia (P. Petrini, 2007; P Petrini & Seuser, 2009), a number of potential sources of social support in relation to prophylaxis were identified. After careful review and discussion, the panel agreed the most important ways in which YPH may be supported in relation to their prophylactic treatment. This resulted in an 8-item scale which assesses support in relation to being reminded to take treatment; others appreciating how hard it is to take prophylaxis; being told off for missing injections; being praised for taking treatment; receiving help with bleeds; having someone that listens to concerns and worries; receiving encouragement; and someone showing understanding. The design of the questionnaire is based on the widely used The Diabetes Family Behavior Checklist (Schafer, McCaul, & Glasgow, 1986). Participants were invited to rate how often they receive support in each of the above categories using a 0 to 5- scale (never, less than twice a month, twice a month, once a week, several times a week, at least once a day). They were then asked to indicate how satisfied they are with this support using a -1 to 3 scale (Unhelpful or NOT

supportive, neutral, A little helpful or supportive, Helpful/ supportive, Very supportive). The overall social support score is obtained by multiplying the frequency score by the satisfaction score.

Positive and Negative Affect Schedule (PANAS)

The Positive and Negative Affect schedule (PANAS; Watson et al., 1988) is a valid and reliable self-report measure of both negative and positive mood states. This scale was selected over other widely used scales, such as the PHQ-9, after extensive discussions with the steering committee. Members of the committee felt it was important to assess both positive and negative affect, and in particular clinicians felt that it would be inappropriate to use a scale that includes sensitive questions (e.g. about suicide ideation). The PANAS consists of two 10-item mood scales asking participants to rate specific feelings and emotions associated with positive affect (e.g., enthusiasm) and negative affect (e.g., afraid) experienced during a given time. Participants were invited to rate the extent to which they experienced each emotion during the current week. Individuals responded to each item on the following scale: (1) very slightly or not at all, (2) a little, (3) moderately, (4) quite a bit, and (5) very much.

In summary, all measures included in this research were psychometrically valid and selected on the basis of prior use in research about adherence among young people with chronic illness. And they were all reviewed and amended by a panel and the steering committee (which included young people with haemophilia, members of the haemophilia society, specialist nurses, haematologists and academics) to ensure relevance and appropriateness.

4.3.3 Statistical analyses

Sum scores for each adherence subscale (as continuous measures) and psychosocial factors were generated for each patient. Tests of normality were undertaken. In addition to univariate analyses, Pearson's correlation was used to assess bivariate associations between adherence, clinical outcomes and psychosocial factors. To establish the predictive ability of the psychosocial factors to explain variation in adherence scores, linear multiple regression analyses were carried out. Sensitivity analysis confirmed that the regression models were not unduly affected by multicollinearity, bias or outliers. All significance testing used an α level of 0.05.

To test potential differences between adherent and non-adherent patients, the sample was dichotomised into two groups (adherent and non-adherent) using the 51-point cut-off on the VERITAS-Pro total score put forward as the threshold for non-adherence in the original validation study (N. Duncan et al., 2010).

Differences in clinical outcomes and psychosocial factors between adolescents and young adults and the two adherence groups were tested using independent t-tests. Bootstrapping was performed to reduce the impact of bias. Differences between categorical variables were tested using $א^2$.

Analyses reported in the main section of this thesis were carried out using listwise deletion for systematically missing data and means imputation for randomly missing data. In addition analyses were also carried out using means imputation for all missing data, which are shown in the appendices (www.missingdata.org.uk).

4.4 Results

4.4.1 Statistical power

Power analyses were undertaken using GPower, version 3.1.9.2 (Faul, Erdfelder, Lang, & Buchner, 2007). The findings of power calculations for analyses testing the difference of means (t-test) are presented in appendix 4.4.a.

The hypotheses that this study aimed to test were mostly 1-tailed, indicating that a certain outcome (such as skipping) or determinant of adherence (such as greater belief in the necessity of prophylaxis) would be greater in one group of participants compared to another group (e.g. adolescents versus young adults). The outcome of the power calculations indicate that based on an effect size between 10% and 15% the t-tests that were carried out had a statistical power around 80%. As a result we can assume that the sample size was sufficient to test 1-tailed hypotheses with reasonable confidence.

The power calculations for linear multiple regression analyses are presented in appendix 4.4b, and indicate that based on an effect size of approximately 20% the sample size was sufficient to achieve a statistical power of at least 80%.

4.4.2 Data screening

Missing data was at an acceptable level for most questionnaires (ranging from 0 – 5%). However, there were larger numbers of missing responses for some of the adherence questions (ranging from 2 to 17%), questions investigating satisfaction about social support (10 to 16%) and the concerns about prophylaxis subscale of the BMQ (3 to 12%).

Closer inspection indicated that a significant proportion of the missing responses to VERITAS-Pro adherence questions were due to patients answering ‘not applicable’. This appeared to be particularly the case for questions that assume that patients take treatment according to a pre-agreed schedule that does not allow for flexibility (e.g. I do injections according to the schedule that

was given to me by my doctor or nurse). This reflects the fact that the VERITAS-Pro was constructed and validated in the US, and perhaps does not reflect the more flexible and personalised way in which many YPH in the UK manage their haemophilia treatment.

The scoring instructions provided by the authors of the VERITAS-Pro include the following guidance on how to treat missing data:

> If a subscale is missing one item, you may extrapolate a value for that item using the average of the other three items on the subscale.
>
> a. Any subscale missing more than one answer is considered invalid and cannot be scored.
> b. Any total scale missing more than two answers is considered invalid and cannot be scored.

After implementing this guidance any remaining missing data was addressed by applying listwise deletion for the analyses of VERITAS-Pro data.

In relation to the social support questions the reason for the missing responses was likely to be that patients were not sure how to answer the questions due to the potentially confusing lay-out of the questionnaire. Patients were asked to indicate how often they received a particular type of social support, as well as the extent to which they were satisfied with this support. On reflection it may have been better to separate the frequency and satisfaction into separate sections.

Further investigation of the original copies of the completed questionnaires showed that at one of the study centres the questionnaires were printed incorrectly, which meant that the last two questions of the concerns subscale of the BMQ were missing. Apart from the data issues described above, most of the data were shown to be randomly missing. It was therefore possible to replace the majority of missing values with a suitable substitute (the mean value). However, the VERITAS-Pro data were analysed with list-wise deletion (as directed by the authors of the scale).

Boxplots for the frequency distribution of the VERITAS-pro subscales and adherence sum scores are presented in appendix 4.3. The boxplots indicate that the Timing, Planning and Skipping subscales are likely to be positively skewed an each contain outliers. Further data screening revealed that several of the variables measured by the questionnaire, including the adherence subscales mentioned above, were skewed and contained outliers. So as not to violate the assumption of normality which is necessary for many of the statistical analyses that were carried out, positively skewed variables were log transformed. For negatively skewed data square transformations were performed. Log transformation of Social support (frequency*satisfaction) and Spontaneous bleeds did not improve skew, therefore original values were used in their non-parametric analyses.

Further inspection of the raw data did not show any obvious inaccuracies, indicating that outliers were unlikely to be due to gross errors or mistakes. Therefore, the skews in the data suggest that the majority of patients adhere to their treatment with only a small group regularly forgetting or skipping injections. For all of the scales that were positively skewed a low score indicates a positive outcome (few concerns, few negative outcome expectations few negative feelings, and better adherence), whereas for the scales that were negatively skewed higher scores indicate a positive outcome (positive outcome expectations, positive feelings, high self-efficacy and a positive belief in the necessity of prophylaxis). The adherence *Communicating* subscale was the only exception with a negative skew (indicating low adherence). However, it could be argued that several items included in this scale may not be appropriate for patients in the UK who follow a more flexible treatment regimen. For instance, one of the questions asks patients if they make decisions about their treatment themselves, without calling the Haemophilia Centre. In the original scale this behaviour would be classed as non-adherent.

However, many UK patients are now encouraged to tailor their treatment around their activities on a week-by-week basis, and are not expected to call the centre for each adjustment to their treatment. This supports the suggestion made above that for future research it would be useful to improve validity of the VERITAS-Pro and that analysis should be carried out separately on the forgetting and skipping subscales in addition to adherence sum scores.

Clinical information (number of bleeds and hospital visits) was only available for 83% of patients. However, there is no reason to believe that cases are missing in a systematic way and so for analyses list-wise deletion was employed.

4.4.3 Reliability of scales use

The internal reliability of the sub-scales used to measure adherence was good as indicated by Cronbach's α in Table 4.1. The internal reliability of the Timing, Remembering and Communicating subscales improved (albeit not significantly) after missing data was imputed.

Of the remainder of the scales, only the Beliefs about Medicines Concerns sub-scale had a reliability score that was lower than ideal ($\alpha = 0.69$), albeit still acceptable. None of the 5 items in this subscale appeared particularly problematic (item-total correlations were all above 0.3).

Table 4.1: Internal consistency shown by Cronbach's α for each questionnaire subscale

Scale	Cronbach's α
Veritas-Pro Questionnaire	
Timing	0.82
Planning	0.68
Remembering	0.83
Skipping	0.88
Communicating	0.71
Self-efficacy	
Haemophilia-related	0.81
Prophylaxis-related	0.92
Beliefs about Medicines Questionnaire	
Necessity	0.80
Concerns	0.69
Positive Affect Negative Affect Scale	
Positive Affect	0.91
Negative Affect	0.85
Social Support	
Frequency	0.86
Satisfaction	0.88

4.4.4 Adherence in the sample

Demographics for the sample are presented in table 4.2. Information about ethnicity was not collected. The mean age was 18.99 (SD=4.11). The majority of participants were in school (33%), college/university (20.9%) or fulltime work (25.3%). Many participants still lived at home with their parents (78%), and only 19.8% of participants have a sibling who is also affected by haemophilia. 70% of participants do their prophylactic injections entirely themselves. As described above on page 50, the sample of 91 participants makes up approx. 19% of the total population of young people with haemophilia who follow a prophylactic regimen in England and Wales. Although this is a large sample it is difficult to confirm the extent to which this sample is representative of the population, as we were not permitted to collect information about patients who decided not to take part or patients who were not approached. As the questionnaire was completely anonymous it was not possible to compare participants to non-participants.

Adherence in the sample appeared to be good, as indicated by the total sample mean scores (table 4.2). However the relatively large standard deviation suggests that scores were dispersed widely.

When the sample was dichotomised into two adherence groups (adherence sum scores ≥ 51 indicating non-adherence), just 16% of the sample had scores indicating they were non-adherent. Both intentional non-adherence (skipping sub-scale scores ≥ 11) and unintentional non-adherence

(*Remembering* sub-scale scores ≥ 11) were low. Only eight patients (9%) had *Skipping* scores above the cut-off point that indicated intentional non-adherence and only 13 patients (14%) had *Remembering* scores above the cut-off point that indicated unintentional non-adherence. Of these 21 patients there were six patients (7%) that were both intentionally and unintentionally non-adherent.

The *Communicating* sub-scale was the only sub-scale on which a majority of patients (59%) had a score above the cut-off indicating non-adherence (scores ≥10). This may be because some of the questions in this subscale appear to lack content validity, as described in the data screening section above.

Comparison of adherence levels among young people who live at home and those who live independently were not found to be significantly different: $F(2, 84) = 1.64$, $P = 0.199$, and young people who receive help with taking their treatment were not found to be more adherent than those who do their injections entirely themselves: $F(3, 83) = 2.33$, $P = 0.080$. This may suggest that higher levels of adherence among adolescents may not be due to parental involvement and support. However, it could also suggest that the self-report measures do not accurately assess parental support and levels of adherence.

Table 4.2: Demographics for the entire sample and adherence groups

	Total sample (n=91)	Adherent (n=64)	Non-adherent (n=14)
Age Mean (SD)	18.99 (4.11)	19.00 (4.22)	18.94 (3.75)
min/max	12/25	12/25	13/24
skewness	-0.119	-0.091	-0.32
kurtosis	-1.283	-1.321	-1.169
	n (%)	**n (%)**	**n (%)**
Education/Work			
School	30 (33%)	19 (29.7%)	3 (21.4%)
College/university	19 (20.9%)	15 (23.4%)	3 (21.4%)
Other full-time education	1 (1.1%)	0	1 (7.1%)
Part-time work	8 (8.8%)	7 (10.9%)	0
Full-time work	23 (25.3%)	16 (25.0%)	5 (35.7%)
Don't work	6 (6.6%)	4 (6.3%)	2 (14.3%)
Other	2 (2.2%)	2 (3.1%)	0
Missing	2 (2.2%)	1 (1.63%)	0
Living arrangements			
I live with my parents	71 (78%)	49 (76.6%)	11 (78.6%)
I live independently alone	4 (4.4%)	2 (3.1%)	2 (14.3%)
I live independently with others	15 (16.5%)	13 (20.3)	1 (7.1%)
Missing	1 (1.1%)	0	0
Responsibility for prophylaxis			
Someone else does injections for me	8 (8.8%)	7 (10.9%)	0
They are done by someone else, and I help	10 (11%)	6 (9.4%)	1 (7.1%)
They are mostly done by me with help from someone else	8 (8.8%)	6 (9.4%)	0
I do them entirely myself	64 (70.3%)	45 (70.3%)	12 (85.8%)
Missing	1 (1.1%)	0	1 (7.1%)
Siblings with Haemophilia			
Yes	18 (19.8%)	14 (21.9%)	4 (28.6%)
No	71 (78%)	50 (78.1%)	10 (71.4%)
Missing	2 (2.2%)	0	0

Ethnicity was not collected. There were no significant differences between adherers and non-adherers in relation to any of the demographics (highest chi-square F=4.39, lowest p value = 0.11).

4.4.5 Differences between adolescents and young adults.

Table 4.3 presents the differences in adherence and clinical outcomes between adolescents and young adults. It was hypothesized that unintentional non-adherence would be higher among young adults, and that intentional non-adherence would be higher among adolescents. However, there were no significant differences between the age groups in relation to adherence scores and clinical outcomes.

Table 4.3: Adherence and clinical outcomes for adolescents and young adults.

	Adolescents (n=41)							Young adults (n=50)						
	N	Mean	SD	Min	Max	Skewness	Kurtosis	N	Mean	SD	Min	Max	Skewness	Kurtosis
Age	41	15	1.88	12	18	0	-1.09	50	22.26	1.97	19	25	-0.09	-1.17
Self-reported adherence (VERITAS-Pro)														
Timing	36	7.53	3.75	4	16	1.03	0.18	47	7.57	2.93	4	17	0.95	1.28
Log Timing	36	6.75	1.59	4	16	0.39	-1.02	47	7.05	1.47	4	17	0.39	-1.02
Planning	36	7.16	3.31	4	16	1.04	0.26	48	7.39	3.33	4	16	1.07	0.66
Log Planning	36	6.54	1.54	4	16	0.44	-0.95	48	6.75	1.53	4	16	0.32	-0.86
Remembering	34	8.05	3.28	4	14	0.41	-1.04	47	8.4	2.92	4	17	0.76	1.14
Skipping	34	5.59	2.05	4	12	1.52	1.79	47	5.79	2.64	4	15	1.94	3.82
Log skipping	34	5.24	1.38	4	12	1.031	-0.004	47	5.37	1.45	4	15	1.17	0.6
Communicating	37	11.53	4.16	4	20	0.08	-0.9	48	12.95	4.07	4	19	-0.5	-0.31
Sum	33	40.38	12.26	23	73	0.88	0.44	46	42.35	9.16	20	60	0.21	-0.15
Clinical information														
Pain severity	37	2.73	5.58	0	6	0.26	-0.99	49	3.08	1.41	0	6	0.31	-0.87
Impact of pain	39	2.23	1.33	0	5	0.98	-0.2	49	2.12	1.39	0	5	1.02	-0.35
Spontaneous bleeds	32	2.16	5.31	0	26	3.71	14.45	43	1.21	2.77	0	13	2.93	9.1
Log spontaneous bleeds	32	2.33	2.91	0	26	1.24	0.68	43	3.01	2.51	0	13	0	-1.22
Traumatic bleeds	32	1.34	2.39	0	12	3.13	12.42	43	0.72	1.42	0	8	3.56	16.24
Log Traumatic bleeds	32	1.55	1.84	0	12	0.61	1.84	43	1.55	1.84	0	8	1.44	2.07
Hospital visits	30	4.73	5.58	0	19	1.39	1.12	44	3.07	3.37	0	17	2.26	6.17
Log Hospital visits	30	3.38	2.93	0	19	0.19	-1.52	44	2.27	2.28	0	17	0.7	-0.56

Where transformation has been undertaken the geometric mean and SD are shown. Independent t-tests did not detect any significant differences between adolescents and young adults.

Table 4.4 presents the differences in psychosocial factor scores between adolescents and young adults. It was hypothesized that there would be differences in many of the psychosocial factors.

Young adults had greater beliefs in the necessity of treatment (mean difference -1.967, BCa 95% CI [-3.513, -0.421], t(89) = -2.528, p=0.013), and had greater necessity/concern differential scores (mean difference -2.488, BCa 95% CI [-4.550, -0.427], t(89) = -2.398, p=0.019) indicating that their belief in the necessity of treatment outweighs their concerns about treatment.

Young adults perceived themselves to have more personal control over their symptoms (mean difference -1.202, BCa 95% CI [-2.209, -.196], t(89) = -2.374, p=0.02), and had greater self-efficacy scores in relation to haemophilia in general (mean difference -6.720, BCa 95% CI [-12.602, -.838], t(89) = -2.270, p=0.026), and prophylaxis specifically (mean difference -8.431, BCa 95% CI [-16.363, -.499], t(89) = -2.112, p=0.037). They also had fewer negative outcome expectations (mean difference 4.820, BCa 95% CI [1.128, 8.513], t(89) = 2.594, p=0.011). In relation to social support young adults reported to receive significantly less social support than adolescents (mean difference 9.273, BCa 95% CI [5.225, 13.321], t(89) = 4.551, p=0.0001), although their satisfaction with the social support they receive was not significantly different (mean difference 3.059, BCa 95% CI [0.031, 6.088], t(89) = 2.007, p=0.048).

Table 4.4: Psychosocial scores for adolescents and young adults.

	Adolescents (n=41)						Young adults (n=50)					
	Mean	SD	Min	Max	Skewness	Kurtosis	Mean	SD	Min	Max	Skewness	Kurtosis
Beliefs about medicines												
Concern	11.06	3.23	5	18	0.25	-0.56	10.54	3.98	5	18	0.11	-1.29
Necessity	18.74	4.25	8	24	-0.73	0.04	20.71	3.17	13	25	-0.60	-0.24
Differential	7.69	5.00	-7	15	-0.77	0.67	10.18	4.86	-1	20	-0.13	-0.14
Self-regulatory Model (Brief IPQ)												
Consequences	6.14	2.95	0	10	-0.56	-0.49	5.68	3.20	0	10	-0.21	-1.15
Timeline	9.48	1.04	5	10	-2.66	8.14	9.70	0.84	6	10	-3.04	9.21
Squared Timeline	9.54	4.14	5	10	-2.22	5.04	9.74	3.77	6	10	-2.835	7.519
Personal Control	6.02	2.63	0	9	-1.29	0.72	7.22	2.21	0	10	-1.07	1.25
Squared Personal Control	6.55	4.90	0	9	-0.42	-0.55	7.54	5.26	0	10	-0.18	-0.64
Treatment Control	8.87	1.35	5	10	-1.30	1.46	8.84	1.57	3	10	-1.70	3.29
Squared Treatment Control	8.97	4.66	5	10	-0.92	0.13	8.98	4.90	3	10	-1.12	0.60
Identity	5.75	2.45	0	10	-0.53	0.00	5.20	2.54	0	10	-0.93	-0.80
Concerns	4.71	2.89	0	10	0.21	-0.90	4.63	3.12	0	10	0.09	-1.01
Coherence	8.53	1.45	5	10	-0.82	-0.32	8.56	1.53	5	10	-0.82	-0.45
Emotional Representations	4.60	2.91	0	10	0.07	-0.69	3.70	3.09	0	10	0.26	-1.20
Self-efficacy and Outcome expectations												
Haemophilia-related Self-efficacy	100.00	14.03	73	118	-0.48	-0.86	106.72	14.06	54	120	-1.76	3.63
Squared Haemophilia-related Self-efficacy	100.96	52.18	73	118	-0.29	-1.07	107.62	51.79	54	120	-1.30	1.53
Prophylaxis-related Self-efficacy	76.38	21.00	27	100	-0.84	-0.34	84.81	17.10	35	100	-1.33	1.25
Squared Prophylaxis-related Self-efficacy	79.15	53.70	27	100	-0.44	-1.01	86.49	50.48	35	100	-0.90	-0.17
Positive Outcome expectations	38.22	11.23	6	60	-0.54	0.24	35.91	10.45	8	60	-0.09	0.97
Negative Outcome expectations	18.33	9.62	4	40	0.28	-0.93	13.51	8.11	4	29	0.43	-1.06
Mood (PANAS)												
Positive affect	30.96	9.76	11	49	-0.51	-0.19	31.69	10.15	10	50	-0.51	-0.25
Negative affect	10.65	4.29	7	23	1.44	1.32	12.56	5.44	7	32	1.36	2.26
Log Negative affect	9.97	1.42	7	23	0.90	-0.14	11.59	1.49	7	32	0.41	-0.50
Social Support												
Frequency	24.03	8.71	10	40	0.18	-1.16	14.75	10.39	0	40	0.78	-0.24
Satisfaction	12.14	7.19	-2	24	-0.10	-0.78	9.08	7.27	-7	24	0.12	-0.46
Frequency*Satisfaction^{T}	38.69	27.79	-3	96	0.82	-0.27	26.75	29.76	-7	120	1.74	3.05

Where transformation has been undertaken the geometric mean and SD are shown. ^{T} Log transformation of social support frequency*satisfaction did not improve skew, therefore this variable was only included in non-parametric analyses and original values are shown above .

4.4.6 Adherence and clinical outcomes

Correlation analyses (table 4.5) did not show any significant associations between clinical outcomes (bleeds and hospital visits) and adherence sum scores. However, the planning subscale showed a significant correlation with pain severity and the impact of this pain over the previous 4 weeks. This suggests that pain (or potential anxiety caused by pain) may act as a prompt for patients to plan around their treatment.

Table 4.5: Pearson's correlation between adherence and clinical outcomes.

	VERITAS-Pro adherence subscales					
	Log Timing	Log Planning	Remembering	Log Skipper	Communicating	Adherence Sum
Pain severity^{T}	.017	**.239***	.124	.147	-.110	.103
Pain impact^{T}	-.101	**.263***	.008	.155	-.127	.054
Spontaneous bleeds^{T}	.335	-.314	.186	-.011	-.299	-.124
Traumatic bleeds^{T}	.050	.121	-.026	-.070	-.109	.019
Log Total bleeds^{T}	-.035	-.037	.023	.065	-.126	-.110
Hospital visits^{T}	-.383	.463	-.338	.029	-.122	-.107

* p<0.05, ** p<0.001, ^{T} during previous 4 weeks, ^{TT} during previous 6 months.

Listwise N=79

Despite the lack of significant correlations between adherence sum and clinical outcomes, when the sample was dichotomised into adherent/non-adherent (Table 4.6), there were significant differences in the number of total bleeds (mean difference -2.71, BCa 95% CI [-4.226, -1.209], t(74) = -3.593, p=0.001), and hospital visits (mean difference -0.507, BCa 95% CI [-0.972, -0.041], t(64) = -2.235, p=0.034).

Interestingly, adherent patients experienced more bleeds and visited the haemophilia centre more frequently than non-adherent patients. This contradicts the hypothesis that predicted that adherent patients would experience less bleeds and would visit the haemophilia centre less frequently. It was also hypothesized that higher perceptions of pain and impact of pain would be associated with better adherence; however adherers did not appear to experience significantly less severe pain or impact of pain.

Table 4.6: Clinical outcomes of adherent and non-adherent patients.

	Adherent (n=65)							Non-adherent (n=14)						
	N	Mean	SD	Min	Max	Skewness	Kurtosis	N	Mean	SD	Min	Max	Skewness	Kurtosis
Age	65	19.34	4.01	12	25	-0.15	-1.27	14	19.5	3.44	14	24	-0.27	-1.07
Self-reported adherence (VERITAS-Pro)														
Timing	65	6.51	2.25	4	12	0.54	-0.48	14	12.48	3.22	7	17	-0.23	-1.12
Log Timing	65	6.14	1.41	4	12	0.06	-1.23	14	12.06	1.32	7	17	-0.61	-0.61
Planning	65	6.75	2.92	4	16	1.19	1.12	14	10.67	3.4	6	16	0.31	-1.13
Log Planning	65	6.22	1.49	4	16	0.47	-0.79	14	10.16	1.39	6	16	-0.14	-0.95
Remembering	65	7.28	2.27	4	11	0.01	-1.15	14	12.38	2.59	8	17	-0.05	-0.37
Skipping	65	5.27	1.96	4	15	2.48	8.53	14	7.71	3.31	4	14	0.49	-0.78
Log Skipping	65	5.01	1.35	4	12	-0.08	-1.31	14	7.06	1.56	4	14	-0.08	-1.31
Communicating	65	12.07	4.14	4	20	-0.13	-0.67	14	15.26	2.65	9	18	-1.17	1.02
Sum	65	37.87	7.24	20	51	-0.17	-0.35	14	58.5	5.6	53	73	1.8	2.88
Clinical information														
Pain severity	62	2.94	1.41	0	6	0.3	-0.87	13	3.15	1.73	0	6	0.07	-1.42
Impact of pain	64	2.16	1.25	0	5	1.05	0.08	13	2.46	1.71	0	6	0.66	-1.14
Spontaneous bleeds	53	2.23	4.69	0	26	3.43	13.58	14	0.07	0.27	0	1	3.74	14
Traumatic bleeds	53	0.96	1.58	0	8	2.28	6.59	14	0.64	0.93	0	3	1.53	2.03
Log Traumatic bleeds	53	1.87	1.92	0	8	1.27	-0.11	14	1.35	1.62	0	3	1.27	-0.11
Total bleeds	60	3.37	5.41	0	26	2.42	6.21	14	0.71	1.14	0	4	2.11	4.99
Log Total bleeds	60	3.34	2.69	0	26	0.35	-0.876	14	1.41	1.79	0	4	1.53	1.43
Hospital visits	54	4.09	4.7	0	19	1.77	2.83	12	2.25	2.09	0	8	2.1	5.29
Log Hospital visits	49	2.82	2.62	0	19	0.46	-1.12	11	1.95	1.95	0	8	0.85	0.47

Where transformation has been undertaken the geometric mean and SD are shown. Difference between adherent and non-adherent (*p<0.05, **P<0.001) as measured by independent t-test.

4.4.7 Psychosocial factors and adherence

Table 4.7 shows the Pearson's correlations between the adherence subscales and psychosocial factors.

Better adherence sum scores were significantly associated with greater beliefs in the necessity of prophylaxis, fewer concerns about prophylaxis, and therefore a greater necessity/concern differential, which indicates that the necessity of prophylaxis outweighs concerns about this treatment.

In relation to illness perceptions, greater emotional representations (negative feelings such as fear, anger or distress) were associated with better adherence, indicating that haemophilia-related fear or anxiety may encourage better adherence.

Better adherence was also associated with greater positive outcome expectations and social support (frequency and satisfaction). This suggests that patients who believe that taking their treatment will result in more positive outcomes, and patients with better social support are more likely to adhere to their treatment.

Drilling down into the results deeper shows some significant associations between the different adherence subscales and psychosocial factors. Greater concerns about prophylaxis treatment were associated with worse scores on the timing, remembering and skipping subscales, whereas greater beliefs in the necessity of treatment were associated with better scores on the timing subscale.

In relation to illness perceptions, the results suggest that patients who have greater concerns, better coherence and more emotional representations in relation to their haemophilia are more likely to contact the haemophilia centre. Patients with greater coherence are also more likely to plan better in relation to their treatment (e.g. ensuring they do not run out of factor treatment and supplies).

Positive outcome expectations were shown to be associated with better planning and less forgetting, whereas negative outcome expectations were associated with more skipping. Haemophilia-related self-efficacy was not associated with any of the adherence subscales. However, prophylaxis-related self-efficacy was significantly associated to better adherence in relation to timing of treatment.

More frequent social support was associated with better scores on the communicating subscale and better adherence sum scores. Greater satisfaction with social support was associated with better adherence in relation to remembering treatments and communicating with the haemophilia team.

Table 4.7: Pearson's correlation between adherence subscales and psychosocial factors

	Log Timing	Log Planning	Remembering	Log Skipping	Communicating	Adherence Sum
Beliefs about Medicines (BMQ)						
BMQ Concern	**.248***	.124	**.290****	**.359****	-.033	**.262***
BMQ necessity	**-.325****	-.124	-.090	-.057	-.148	**-.249***
Differential	**-.414****	-.178	**-.265***	**-.286***	-.090	**-.366****
Self-regulatory model (IPQ)						
Consequences	-.081	.125	-.038	.046	-.092	-.019
Squared Timeline	-.021	.083	.196	-.082	.015	.086
Squared Personal Control	.017	.119	.132	.085	.146	.161
Squared Treatment Control	.120	.029	.190	-.087	-.084	.057
Identity	-.016	.208	.005	.053	-.096	.047
Concerns	.023	-.070	.025	.081	**-.244***	-.098
Coherence	-.125	**-.229***	-.058	.181	**-.320****	-.206
Emotional representations	-.112	-.126	-.061	.025	**-.348****	**-.223***
Outcome expectations and Self-efficacy						
Positive outcome expectations	-.145	**-.456****	**-.285***	-.183	-.124	**-.363****
Negative outcome expectations	.148	-.008	.157	**.293****	-.181	.087
Squared Haemophilia-related Self efficacy	-.092	-.147	.008	-.147	.018	-.107
Squared Prophylaxis-related Self efficacy	**-.254***	-.199	-.154	-.198	.093	-.188
Mood (PANAS)						
Positive affect	-.075	-.159	-.090	-.025	-.045	-.128
Log Negative affect	-.057	-.004	.028	.191	-.061	.007
Social support						
Frequency	-.123	-.160	-.191	-.048	**-.400****	**-.297****
Satisfaction	-.153	-.105	**-.232***	-.165	**-.334****	**-.301****

* p<0.05, ** p<0.001, ^{T} during previous 4 weeks, ^{TT} during previous 6 months. Listwise N=79

Table 4.8 compares the psychosocial factor scores of adherent and non-adherent participants. Non-adherent participants had significantly lower BMQ Necessity scores (mean difference -2.494, BCa 95% CI [-4.4423, -0.564], t(89) = -2.568, p=0.12), BMQ Necessity/Concern Differentials (mean difference -4.219, BCa 95% CI [-6.723, -1.715], t(89) = -3.348, p=0.001), Prophylaxis-related self-efficacy scores (mean difference -1865.226, BCa 95% CI [-3260.590, -469.860], t(89) = -2.656, p=0.009), and Social support scores (frequency*satisfaction; mean difference -118.248, BCa 95% CI [-201.770, -34.726], t(89) = -2.824, p=0.006) than adherent participants.

Non-adherent participants also had higher IPQ Timeline scores than adherent participants (mean difference 6.144, BCa 95% CI [0.528, 11.760], t(89) = 2.194, p=0.033).

Table 4.8: Psychosocial factors scores of adherent and non-adherent patients.

	Adherent (n=65)							Non-adherent (n=14)						
	N	Mean	SD	Min	Max	Skewness	Kurtosis	N	Mean	SD	Min	Max	Skewness	Kurtosis
Beliefs about medicines (BMQ)														
Concern	64	10.12	3.65	5	18	0.23	-1.05	14	11.71	2.70	7	16	-0.08	-1.07
Necessity	64	20.26	3.68	8	25	-1.09	1.29	14	17.36	4.40	9	25	-0.03	-0.53
Necessity/Concern differential	64	10.14	5.08	-7	20	-0.65	1.01	14	5.64	4.27	-3	11	-0.54	-0.35
Self-regulatory Model (Brief IPQ)														
Consequences	63	6.05	3.07	0	10	-0.40	-0.84	14	5.36	3.57	0	10	-0.47	-1.15
Timeline	63	9.56	1.03	5	10	-2.68	7.51	14	9.86	0.54	8	10	-3.74	14.00
Squared Timeline	63	9.61	4.12	5	10	-2.34	5.06	14	9.87	3.10	8	10	-3.74	14.00
Personal Control	62	6.61	2.64	0	10	-1.10	0.69	14	7.43	1.56	5	10	-0.42	-0.47
Squared Personal Control	63	7.11	5.35	0	10	-0.12	-0.67	14	7.58	4.73	5	10	0.01	-0.30
Treatment Control	63	8.81	1.55	3	10	-1.59	2.67	14	9.07	1.21	7	10	-0.76	-1.14
Squared Treatment Control	63	8.94	4.89	3	10	-1.06	0.37	14	9.15	4.58	7	10	-0.69	-1.36
Identity	63	5.25	2.67	0	10	-0.03	-0.84	14	5.43	2.31	0	8	-1.05	1.11
Concerns	63	4.35	3.00	0	10	0.50	-0.87	14	4.14	3.13	0	10	0.09	-0.83
Coherence	63	8.59	1.50	5	10	-0.92	-0.15	14	8.36	1.55	6	10	-0.56	-1.17
Emotional Representations	62	4.10	3.14	0	10	0.21	-1.08	14	3.64	2.59	0	7	-0.32	-1.38
Self-efficacy and Outcome expectations														
Haemophilia-related Self-efficacy	65	105.48	14.01	54	120	-1.37	1.92	14	105.14	9.62	90	118	-0.23	-1.21
Squared Haemophilia-related Self-efficacy	65	106.39	52.04	54	120	-0.12	-1.25	14	105.55	44.80	90	118	-0.12	-1.25
Prophylaxis-related Self-efficacy	65	84.06	18.27	27	100	-1.46	1.53	14	73.94	19.85	31	100	-0.71	0.52
Squared Prophylaxis-related Self-efficacy	65	85.99	52.28	27	100	-0.99	0.04	14	76.38	52.28	31	100	-0.09	-0.70
Positive Outcome expectations	65	37.49	11.45	6	60	-0.30	0.21	14	32.50	10.54	10	53	0.08	1.21
Negative Outcome expectations	64	14.34	9.24	4	40	0.69	-0.30	14	16.93	8.52	5	33	0.46	-0.88
Mood (PANAS)														
Positive affect	63	32.90	9.84	10	50	-0.72	0.20	14	28.73	7.73	12	38	-0.72	-0.05
Negative affect	63	11.72	5.23	7	32	1.64	3.07	14	12.14	4.94	7	21	0.64	-0.92
Log Negative affect	63	10.83	1.47	7	32	0.72	-0.13	14	11.26	1.49	7	21	0.21	-1.33
Social Support														
Frequency	64	18.36	11.21	0	40	0.35	-0.99	14	15.50	8.37	2	30	0.25	-1.08
Satisfaction	59	10.59	7.68	-7	24	-0.11	-0.85	13	8.65	5.89	-1	19	-0.14	-0.62
Frequency*Satisfaction	54	30.74	29.47	-7	120	0.89	0.19	11	27.91	21.58	-3	64	0.71	-0.65

Adherence scores were available for 79 participants. Where transformation has been undertaken the geometric mean and SD are shown. Difference between adherent and non-adherent (*p<0.05, **P<0.001) as measured by independent t-test.

4.4.8 Ability of psychosocial factors to predict adherence

To further test the association between overall adherence (adherence sum scores) and psychosocial factors multiple linear regression analyses were carried out (Table 4.9). It was hypothesized that higher perceptions of necessity of prophylaxis (BMQ Necessity) would be predictive of better adherence and that concerns about prophylaxis (BMQ Concerns) would not be predictive of adherence. In relation to the Self-regulation model of chronic illness, it was anticipated that higher perceptions of chronicity, consequences and treatment control would be predictive of higher adherence.

To start with all psychosocial factors were entered using the fixed enter method, which resulted in a model that accounted for 48.8% of the variation in adherence (df=19, p=.001). In the model better adherence was associated with fewer concerns about treatment, greater belief in the necessity of treatment, greater emotional responses to haemophilia and greater social support. As the majority of factors were not significantly associated with adherence a second model was run in which the factors were entered using the forward stepwise method. In this model (table 4.9), which accounted for 37.5% of variation, greater necessity/concern differential, greater social support, greater emotional responses to haemophilia and more positive outcome expectations were associated with better adherence.

Table 4.9: Linear regression model of predictors of adherence sum

Predicting variables	b	SE B	β	P	ΔR^2
Step 1					.134**
BMQ Necessity/Concern differential	-.744	.216	-.366	.001	
Step 2					.107*
BMQ Necessity/Concern differential	-.785	.204	-.386	.000	
Social support frequency*satisfaction	-.136	.041	-.328	.002	
Step 3					.084*
BMQ Necessity/Concern differential	-.883	.196	-.434	.000	
Social support frequency*satisfaction	-.137	.039	-.331	.001	
IPQ Emotional responses	-1.041	.341	-.294	.003	
Step 4					.049*
BMQ Necessity/Concern differential	-.757	.197	-.372	.000	
Social support frequency*satisfaction	-.125	.038	-.302	.002	
IPQ Emotional responses	-.988	.331	-.279	.004	
Positive outcome expectations	-.213	.089	-.231	.019	

* p<0.05, ** p<0.001

Because the VERITAS-Pro assesses intentional and unintentional adherence separately, and because there were some questions about the validity of the communicating subscale (possibly affecting the adherence sum scores), separate regression analyses were carried out for the remembering and skipping subscales.

Table 4.10 presents the results of linear regression analyses of the skipping sub-scale and psychosocial predictors. As previously, the variables were entered into the model using the forward stepwise method, and accounted for 41.5% of the variance (*p=0.008*). In this model fewer concerns, lower coherence, and better social support were associated with less skipping.

Table 4.10 Linear regression model of predictors of adherence Skipping

Predicting variables	**b**	**SE B**	**β**	**P**	**ΔR^2**
Step 1					0.103*
BMQ Concern	0.031	0.010	0.321	0.003	
Step 2					0.096*
BMQ Concern	0.042	0.010	0.428	0.000	
IPQ Coherence	0.077	0.025	0.327	0.003	
Step 3					0.043*
BMQ Concern	0.042	0.010	0.436	0.000	
IPQ Coherence	0.085	0.025	0.361	0.001	
Social support frequency*satisfaction	-0.003	0.001	-0.209	0.041	

* $p<0.05$

Table 4.11 presents the results of linear regression analyses of the remembering sub-scale and psychosocial predictors. The variables were entered into the model using the forward stepwise method, and accounted for 44.5% of the variance (*p=0.003*). Fewer concerns about treatment, lower perception of treatment control (the extent to which a patient beliefs their treatment can help their condition), and greater satisfaction with social support showing a significant association with better remembering.

Table 4.11: Linear regression model of predictors of adherence Remembering

Predicting variables	b	SE B	β	P	ΔR^2
Step 1					0.1*
BMQ Concern	0.274	0.092	0.316	**0.000**	
Step 2					0.119*
BMQ Concern	0.392	0.093	0.453	0.000	
Square Treatment control	0.050	0.014	0.371	0.001	
Step 3					0.069*
BMQ Concern	0.368	0.090	0.425	0.000	
Square Treatment control	0.056	0.014	0.413	0.000	
Social support satisfaction	-0.117	0.043	-0.270	0.008	
Step 4					0.042*
BMQ Concern	0.339	0.089	0.391	0.000	
Square Treatment control	0.057	0.014	0.426	0.000	
Social support satisfaction	-0.101	0.042	-0.234	0.019	
Positive outcome expectations	-0.058	0.027	-0.212	0.033	

* $p<0.05$, ** $p<0.001$

4.5 Discussion

This study aimed to assess levels of adherence to prophylaxis among young people with haemophilia in the UK, and to identify the key correlates of adherence in this patient group.

4.5.1 Findings

The findings of this study suggest that overall adherence among YPH in the UK is good, and appears to be better than adherence to treatment for other chronic illness. This may be because, due to the relatively few patients, haemophilia teams are able to keep in regular contact with patients, with a particular focus on patients they are concerned about or who need some extra encouragement to keep to their treatment regimen.

The good overall adherence found in this study is in line with some previous studies that looked at adherence to prophylaxis (De Moerloose et al., 2008), but exceeds adherence levels reported by a previous UK study (Llewellyn et al., 2003) and several other studies conducted in Europe and the US (du Treil, Rice, & Leissinger, 2010; Geraghty et al., 2006; Hacker et al., 2001; Lindvall et al., 2006). Differences in adherence levels reported by different studies may be due to the diverse methods used to assess adherence, and variations in the way haemophilia is treated in different countries, or even within countries. Differences within countries are often due to costs, and therefore the way that haemophilia care is funded for individual patients plays an important role (e.g. insurance, state funded, or privately funded). Indeed, several studies from the U.S highlight cost of

treatment as one of the main barriers to adherence (Hacker et al., 2001; P. Petrini, 2007). Because of the unique healthcare system in the UK, which funds all haemophilia treatment for all patients, levels of adherence in the UK are unlikely to be associated with concerns about costs.

Unintentional and intentional non-adherence

When non-adherence was split into intentional (skipping) and unintentional (mostly forgetting) it appeared that non-adherence was more likely to be due to forgetting than skipping. With the busy lifestyles that most YPH live it is quite understandable that they sometimes forget to take treatment. However, this finding may also indicate that patients find it easier to admit to forgetting than skipping, as they are more likely to be 'told off' by the haemophilia team and loved ones if they admit to intentionally skipping treatments whereas they tend to get a more understanding response when they admit to sometimes forgetting.

Differences between adolescents and young adults

It was anticipated that young adults would be worse at remembering treatment (hypothesis 1), and that adolescents would skip treatments more frequently (hypothesis 2). However, there were no significant differences between adolescents and young adults in relation to adherence.

As anticipated (hypothesis 3) there were significant differences in the psychosocial factors that may influence adherence between adolescents and young adults.

The findings suggest that young adults had greater beliefs in the necessity of treatment and greater necessity/concern differential scores, indicating that their belief in the necessity of treatment outweighs their concerns about treatment.

Young adults perceived themselves to have more personal control over their symptoms, and had greater self-efficacy scores in relation to haemophilia in general and prophylaxis specifically. They also had fewer negative outcome expectations, suggesting that they have less negative associations with taking their treatment. In relation to social support young adults reported to receive significantly less social support than adolescents, although their satisfaction with the social support they receive was not significantly different. As a result adolescents and young adults did not have statistically significant different social support total scores (social support frequency*satisfaction).

It is interesting that despite the significant differences in psychosocial factors described above there was no significant difference in adherence between young adults and adolescents. This is likely because the of psychosocial factors that significantly contributed to the variation in adherence in the

regression analyses only the necessity/concern differential showed to be significantly different between the age groups.

Association between adherence and clinical outcomes

It was anticipated that non-adherence to prophylaxis would be related to higher numbers of bleeds and hospital visits (hypothesis 8). However, there was no significant association between adherence as a continuous measure and clinical outcomes (the number of bleeds and hospital visits). However, when the sample was dichotomised into adherers and non-adherers there were significant differences in the number of bleeds and hospital visits. Interestingly, this was not in the anticipated direction, with adherers experiencing more bleeds and visiting the hospital more frequently than non-adherers.

There are several potential explanations for this:

- We collated the number of bleeds and hospital visits that patients had during the last 6 months, whereas we assessed patients' adherence during the last month. Therefore it could be that patients who experienced frequent and/or severe bleeds more than one month ago were motivated to improve their adherence in order to reduce the risk of bleeding, resulting in better adherence scores.
- Adherent patients may be more attentive to bleeding episodes and symptoms of bleeds, whereas less adherent patients may be more relaxed and less likely to interpret symptoms as bleeds. Non-adherent patients may also be less likely to report bleeds to the haemophilia team (through Haemtrack or by contacting the haemophilia centre), resulting in underreporting of their number of bleeds.
- More adherent patients may be more confident in the protection afforded by their prophylaxis, and therefore more likely to engage in physical activity. This in turn may increase their risk of bleeding (due to activity-related injury or increased pressure on joints and muscles), compared to non-adherent people.
- 10-15% of patients with severe haemophilia have a mild bleeding phenotype (Santagostino et al., 2010) which means that they are less likely to suffer bleeds and may therefore 'get away' with suboptimal adherence to prophylaxis.

The findings did not support the expectation that higher perceptions of pain and impact of pain would be associated with better adherence (hypothesis 4). Indeed, pain was not correlated or predictive of adherence and non-adherers did not report more pain or greater impact of pain.

Psychosocial factors of adherence

According to the Necessity-Concerns Framework (Horne et al., 1999) adherence is influenced by implicit judgements that patients make in relation to their personal need for the treatment (necessity beliefs) and their concerns about the potential negative consequences of taking it. Hypothesis 6 was based on the findings of a recent study in a single haemophilia centre in the UK (Llewellyn et al., 2003), which suggest that better adherence to clotting factor is associated with stronger perceptions of necessity of treatment, but not fewer concerns about treatment. However, the findings of the current study indicate that better adherence to prophylaxis among young people with haemophilia is correlated with stronger perceptions of necessity of treatment, as well as fewer concerns about treatment. However, when comparing adherers and non-adherers only beliefs about the necessity of treatment were significantly different (with adherers having greater belief in the necessity of prophylaxis). In the regression analyses only a greater necessity/concern differential (and not greater believe in necessity or fewer concerns in relation to prophylaxis) was predictive of better overall adherence. However, fewer concerns about prophylaxis did predict greater remembering and less skipping.

According to Bandura (Bandura, 2006; Albert Bandura, 1977) better adherence is associated with greater self-efficacy and positive outcome expectations, and fewer negative outcome expectations. This has been supported by findings of studies that have investigated adherence among young people with various chronic illnesses (e.g.Holden, Moncher, Schinke, & Barker, 1990; Iannotti et al., 2006). The findings of the current study suggest that greater positive outcome expectations are correlated with better adherence, and predictive of better overall adherence and better remembering. Although self-efficacy was not significantly correlation to or predictive of adherence, adherers did have greater prophylaxis-related self-efficacy than non-adherers.

In relation to illness perceptions, the findings suggest greater emotional representations (negative feelings such as fear, anxiety or anger about haemophilia) are correlated with and predictive of better overall adherence. This suggests that negative feelings, most likely fear or anxiety about the impact of haemophilia, may act as a motivator to stay on track with treatment. In addition, lower perceptions of treatment control were predictive of better remembering, and lower perceptions of coherence were predictive of less skipping. However, when comparing adherers to non-adherers only illness perceptions in relation to the timeline of haemophilia were significantly different, with non-adherers perceiving their haemophilia to last longer. These findings do not support the anticipation that higher perceptions of chronicity, consequences and treatment control would be predictive of higher adherence (hypothesis 5).

Social support has been highlighted as an important facilitator of adherence among young people with chronic illness (M. R. DiMatteo, 2004; Annette M La Greca & Bearman, 2002; Williams & Bond,

2002). The findings of the current study support this suggestion, with greater social support both correlated to and predictive of better overall adherence, better remembering and less skipping. In addition, adherers reported to have greater social support than non-adherers.

The anticipated association between greater negative mood and lower adherence (hypothesis 7) was not supported by the findings of this study. Indeed, no significant associations were found between mood (neither positive nor negative) and adherence in the sample.

In summary, the findings of this study suggest that psychosocial factors that are widely quoted as important factors in relation to adherence to long-term treatment for a range of chronic illness also appear to play an important role in adherence to prophylaxis among young people with haemophilia. In particular social support, beliefs about the necessity of prophylaxis, emotional responses to haemophilia, and self-efficacy in relation to prophylaxis may play a valuable role in identifying patients who may be least likely to adhere to their prophylactic treatment, any may also form a useful basis for the design of interventions aimed at improving adherence.

4.5.2 Strengths and Limitations

As highlighted in the literature review, the existing literature in this area is very limited in terms of the number as well as the quality of studies published. The strength of this study is that it is a nationwide study (recruiting participants from 13 hospitals across England and Wales, including paediatric, adult and mixed haemophilia centres); has a large sample (nearly 20% of the total population of patients who meet the study criteria in England and Wales); and has a specific focus on young people rather than including patients of all age groups, as there are age specific issues that may influence adherence. Thanks to the large number of participants recruited from different types of haemophilia centres across a wide geographic area the study sample is more likely to be representative of the total population, and the findings less likely to be biased towards individual patients' experiences. Lastly, rather than asking parents or HP to estimate levels of adherence and reasons for non-adherence, this study asked young people to complete the questionnaire themselves.

The main outcome measure of this study, the VERITAS-Pro, is a relatively new scale and no literature exists using this scale in the UK. Therefore the original plan was to triangulate this self-report data with information from treatment logs (self-reported frequency and dosage of treatments taken), and pharmacological data (amount of treatment prescribed and delivered to patients). However, due to technical issues and limited resource haemophilia centres were unable to provide this information. Therefore this study relies solely on the self-report measure of adherence as assessed by the VERITAS-Pro questionnaire, which may be considered a limitation. The results of this study suggest that there may be some issues around validity of the VERITAS-Pro, as the

majority of missing data for this scale was due patients answering ‘not applicable’. This appeared to be particularly the case for questions that assume that patients take treatment according to a pre-agreed schedule that does not allow for flexibility. This reflects the fact that the VERITAS-Pro was constructed and validated in the US, and perhaps does not reflect the more flexible and personalised way in which many YPH in the UK manage their haemophilia treatment. For instance, one of the questions asks patients if they make decisions about their treatment themselves, without calling the Haemophilia Centre. According to the VERITAS-Pro scale this behaviour would be classed as non-adherent. However, patients in the UK are increasingly encouraged to tailor their treatment around their lifestyle based a number of principles that have been pre-agreed with their haemophilia doctor. In reality this means that patients make day-to-day decisions about changes in the dose and/or frequency of their injections without contacting the haemophilia team. Therefore, some patients who would be considered non-adherent according to the VERITAS-Pro communicating sub- scale would not be considered non-adherent by clinicians.

A strength of this study is that it assessed a wide range of psychosocial factors that have been found to be associated with, or predict adherence. However, to keep the questionnaire to an acceptable length illness perceptions, mood and social support were assessed using short form scales. These scales are not as comprehensive as the longer versions, which may have influences the findings to some extent. However during the design of the questionnaire it was decided that the benefit of assessing a wide range of factors would outweigh the downside of using some shorter scales in the questionnaire. Another limitation that should be highlighted is the fact that clinical outcome data (bleeds and hospital visits) were collated by nurses from individual patient medical files. This method is prone to inaccuracies and missing data as medical files are often incomplete and difficult to read. Therefore, the unexpected association between adherence and more frequent bleeds and hospital visits could be due to errors and missing data.

In order to provide a comprehensive analysis of adherence in the sample, the questionnaire assessed a number of psychosocial factors that have been shown to be associated with adherence among young people with other chronic illnesses (including beliefs about medicines, illness perceptions, outcome expectations, haemophilia- and prophylaxis-related self-efficacy, feelings, and social support). To keep the questionnaire to an acceptable length, a number of these factors were assessed using a short-form scale (such as the Brief Illness Perceptions Questionnaire), rather than more comprehensive or full-length scale (such as the Illness Perceptions Questionnaire). Although it is unlikely that the use of these shorter version questionnaires has significantly biased the findings, it may have influenced the size or strength of associations reported.

4.5.3 Implications

Notwithstanding the limitations discussed above, the findings of this study have a number of implications. The findings of this study suggest that adherence to prophylaxis among YPH is generally good, and much better in comparison to adherence in other chronic illnesses.

As described above, the findings of this study suggest that the VERITAS-Pro scale may require some revisions, to improve validity for research in the UK. It appears that the skipping and remembering subscales tap into distinctly different types of (non-)adherence, and it may therefore be useful to carry out analysis on each of these subscales separately in addition to adherence sum scales.

As collating clinical data from medical files is resource-intensive, and likely to result in missing and inaccurate data, it would be advisable to include self-report measures of bleeds and hospital visits in any future studies. This would allow researchers to validate information from medical files against self-report data, and may give some valuable insight into the extent to which self-report information agrees with information from medical files.

4.5.4 Conclusion

It appears that adherence among YPH is relatively good, which indicates that patients are knowledgeable and motivated enough to look after their haemophilia well, and that the haemophilia care and support they receive is generally working well.

The findings of this study suggest that social support, beliefs about the necessity of prophylaxis, emotional responses to haemophilia, and self-efficacy in relation to prophylaxis may play a valuable role in identifying patients who may be least likely to adhere to their prophylactic treatment, any may also form a useful basis for the design of interventions aimed at improving adherence.

Chapter 5: Approach and methodology for three qualitative interview studies

5.1 Introduction

The qualitative research included in this thesis consists of three separate interview studies which all employ the same approach and methodology. The aim of the qualitative studies was to examine participants' personal experiences in relation to prophylaxis, and how they make sense of these experiences. Participants for the first study were young people with haemophilia (YPH) who follow a prophylactic treatment regimen. Participants for the second study were parents of YPH who follow a prophylactic regimen, and participants for the third study were haemophilia healthcare professionals (HP). This Chapter will start with a brief summary of the qualitative approach that was utilised for the studies, after which a description of the methodology will follow.

5.2 Interpretative Phenomenological Analysis (IPA)

IPA was the chosen methodology because it aims to offer insights into how a given person, in a given context, makes sense of a given phenomenon (Jonathan A Smith, 2010). As part of the "double hermeneutic" employed by IPA the researcher tries to make sense of the participant trying to make sense of their experiences (Smith and colleagues, 2003; 2009) . Therefore IPA was found to be the ideal methodology to examine participants' experiences and perceptions in relation to prophylaxis. IPA studies usually draw on the accounts of a small number of people who have certain experiences in common (Reid et al., 2005). Data were collected through face-to-face semi-structured interviews which were audio-recorded. To try and encourage participants to tell their story in their own words and time, the researcher used as few prompts as possible. The interviews were transcribed verbatim, and then analysed following IPA principles and guidelines (Jonathan A. Smith, 2003; J. A. Smith, & Osborn, M. , 2008). The transcription process, seen as the first stage of IPA, is described below, followed by a detailed description of each of the four Hermeneutic Cycles (HCs).

5.3 Rigour, validity and credibility

Various guidelines (Elliott, Fischer, & Rennie, 1999; Snape & Spencer, 2003; Yardley, 2008) have been developed to facilitate the assessment of quality and rigour in qualitative research. Yardley's (2000, 2008) '*Characteristics of good qualitative research'* were used as the guiding principles to ensure that the research would meet standards in relation to rigour, validity and credibility. Key considerations in the research process that will be demonstrated in the following chapters are transparency of data presentation, reflexivity around the researchers own assumptions and consideration of alternative perspectives.

5.4 Data collection

Smith & Osborn (2008) recommend the use of semi-structured interviews to collect data for IPA studies. This facilitates a more informal and free-flow interview, which enables the researcher to follow cues from participants and probe areas of interest that appear particularly relevant to each individual's experiences.

Semi structured interview schedules (Appendix 5.1) were developed based on relevant literature and guidance from Smith & Osborn (2008). These were then circulated to the research supervisory team and a number of patients and haemophilia doctors and nurses for validation. Some revisions were made in response to their comments.

The schedules were used as interview guides only, allowing participants to tell their own story in their own words. Every effort was made to deliver questions in an open-ended and non-directive style, to create an atmosphere in which participants felt comfortable to share their story without being led too much by the interviewer's questions. After each interview the researcher made detailed notes about the interview experience. This included the researchers' thoughts, feelings and impressions as well as anything that might have affected the interview, such as salient points about the interview environment or interruptions that occurred during the interview.

Participants were given a choice about whether they would prefer to be interviewed at home or at the hospital. Eight out of eleven YPH and all four parents were interviewed at the hospital and three patients were interviewed at home. All six HP were interviewed in a private room at their place of work. Interviews lasted between 35 to 95 minutes and were audio recorded and then transcribed and analysed. The transcription and analysis was completed for one study at the time to ensure there was no confusion between the different studies. The patient study was completed before the parent study and the HP study was completed last.

5.5 The transcription process

Transcription was conducted partly by the researcher and partly by a transcription service in three stages:

• First transcription - the ‘everything audible’ version
• Second transcription – the ‘pre-validation, cleaned and confidentialised’ version
• Third transcription – IPA format

5.5.1 First transcription

The recordings of the interviews were firstly transcribed on the basis of ‘everything audible’ meaning that in addition to basic conversation, additional noises and events (such as stuttering, interjections, repetitions, hesitations, part words and background noises and events) were also transcribed. This was to ensure that future transcriptions stemmed from the maximum possible transcribed content. No audible material was overlooked and punctuation was kept to an absolute minimum, as any additions or changes as a result of the transcription process itself may inadvertently alter meanings.

Instead of punctuation, a system of identifying pauses in the conversation of different lengths was used to reflect the natural way in which the conversation flowed. This convention is shown in Table 5.1. As regards other punctuation, commas were used sparingly, and question marks were only used when it was clear that a question was being asked. If a portion of interview was inaudible then: ‘[inaudible]’ was used.

Table 5.1: Convention employed to indicate the flow of conversation in the first transcription

‘ ’ (3 spaces)	are used to indicate a short pause
‘…’ (3 dots)	is used to indicate a definite break
‘[hesitation]’	is used to indicate a break in the flow where a participant hesitates before they answer

5.5.2 Second and third transcription

After the first transcription, a second ‘cleaned and confidentialised’ transcription was made in which:

1. Background noise, stuttering, interjections, repetitions and ‘part words’ were removed. Indication of emphasised words that had been underlined in the first transcript was retained.
2. Punctuation was inserted carefully so that the transcription read as a narrative. However, the author was mindful of the potential for punctuation to subtly alter intended meanings; adding punctuation only at the absolute minimum level. Commas were only used sparingly.
3. Then any names and locations were confidentialised. Great care was taken to ensure that none of the interview participants could be identified by anyone, in particular their haemophilia healthcare team.

As haemophilia is such a rare disorder, it is relatively easy for HP to identify their patients based on very limited information. Therefore in some instances names of cities, towns or villages were changed and references to the number of (un)affected siblings mentioned by participants were removed.

Although the second transcription was ‘cleaned’, no attempt was made to correct grammatical errors, primarily because the transcript was intended to accurately represent the spoken word, not merely a ‘correct’ and ‘easy-to-read’ version of the spoken word. The first eight participants were given the opportunity to review their interview transcript for validation; however none of these participants took up the opportunity to do so. Due to time restrictions, and none of the previous participants taking the opportunity to review their interview transcript it was decided that transcripts of the final 6 participants would not be sent out for validation.

As part of the third transcription each interview transcript was re-read again to ensure that each of the three steps described above had been completed and that the transcripts were ready for analysis. They were then imported into NVivo, the software that was used to complete the first stage of analysis.

5.6 Analysis

5.6.1 The 'IPA-ready' transcripts

IPA is inherently a dynamic process (Smith 1996). Although the principles set down by Smith and colleagues (Jonathan A. Smith, 2003; Jonathan A Smith, 2010; J. A. Smith, & Osborn, M. , 2008) were closely followed throughout, the result of the practical application of those principles was an idiosyncratic data analysis. The initial analysis was carried out using NVivo software, and therefore does not follow the typical IPA format of left-hand and right-hand columns (or left- and right-hermeneutic). Instead each transcript went thought the following process:

- While reading and re-reading the transcript comments and annotations were made (in NVivo). This stage is often referred to as the 'left-heuristic' as these comments are made in the column to the left of the transcript.
- While re-reading the transcript and annotations the text was coded (in Nvivo). This is often referred to as the 'right-heuristic' referring to the column on the right.
- The coded transcript was then reviewed, and the coding was refined where needed (see appendix 5.2 for an example page).This completed the first hermeneutic cycle. To illustrate how the dynamic processes evolved appendix 5.3 shows the full list of themes after the first hermeneutic cycle for study one (YPH).
- The NVivo coded transcript was then exported, creating an Excel spreadsheet containing one line for each code and the following columns:
  - Name of the code (node in NVivo)
  - Number of coding references (frequency it was used to code a section of the transcript)
  - Example of a coded piece of text for each code
  - Notes/reflections on what the coded text indicates about participant experiences and the way they make meaning of this
  - Researcher's reflections (bracketing off personal interpretation that may interfere with analysis)
  - Themes (identifying themes within the codes). This completed the second hermeneutic cycle.
- The themes were then reviewed with the aim of identifying overarching themes, which were reported in an additional column. This completed the third hermeneutic cycle.
- Finally, the overarching themes were refined and presented in a table together with each of their subordinate themes. This completed the fourth and last hermeneutic cycle.

5.6.2 The first hermeneutic cycle (HC)

The 'left-hermeneutic'

Before commencing analysis the author read and reread the example of IPA provided by Smith & Osborn (2003) particularly the chapter covering data analysis (pages 64-79), which suggest that 'left-hermeneutic' is achieved by:

- Summarising and paraphrasing
- Associations that come to mind
- Connections that come to mind
- Preliminary interpretations
- Commenting on the use of language
- Sense of the participants themselves
- Similarities and differences between and within transcripts
- Echoes, amplifications and contradictions

The 'right-hermeneutic'

According to guidelines by Smith & Osborn (2010) the right-hermeneutic is achieved by:

- Concise phrases which aim to capture the essential quality of the left-hand hermeneutic
- Phrases at a slightly higher level of abstraction
- Might use psychological terminology
- Phrases that allow theoretical connections but are firmly grounded in the spoken words of the transcript

The next stage was to read and re-read the transcript to get a feel for the overall nature of the participant's personal story, and to clarify and engage with the narrative before moving on to the *'left-hermeneutic'* process described above. The reflections, comments, notes, questions and reiterations that resulted from this process were added to the transcripts in NVivo using the *Annotations* function.

Particularly at the start of the *'right-hermeneutic'* coding process it was sometimes difficult to find 'concise phrases' that adequately captured the essential quality of the left-hermeneutic, without being too detailed or too abstract. In some cases it was therefore decided to include more than one code. This was usually because:

- The left-hermeneutic being analysed did not fit a single theme
- There wasn't a clear focus within the left-hermeneutic
- There was more than one dimension to the left-hermeneutic (such as a figurative and literal expression being made simultaneously)

The coding was carried out in NVivo using the *Node* function.

During the analysis it was clear that, despite detailed bracketing in the reflective journal, the author was 'seeing' the text in ways that were likely to be influenced by personal interpretations and therefore biased in some way. Therefore a column was added to the analysis sheet that provided a place for the author to record personal interpretations, to try to stay with the participant's individual experience and the way in which they made meaning of their experience.

As recommended by Smith & Osborn (2003), it was decided to firstly conduct IPA on a single interview in its entirety. The remainder of the transcripts were taken through each of the hermeneutic cycles together, producing a list of themes for the entire study at the end of each HC.

5.6.3 The Second HC

At the end of the first HC the coded transcript was exported from NVivo into Excel to allow a more free-flow analysis with the aim to identify overarching themes. This sheet included one line for each code, and columns to record the name of the code, the number of times it had been used in the transcript for each participant, and an example of a piece of text that had been allocated this code.

Columns were then added to record the results of the second cycle of analysis. During this cycle the researcher aimed to identify what each code meant to participants, and identify emerging themes to organise the codes thematically. This involved moving to more interpretative level of abstraction to allow theoretical connections within and across cases, whilst remaining grounded in each participant's individual account. During this process the researcher was mindful of any personal interpretations that may bias the analysis, recording these in a separate column on the sheet (bracketing off).

Appendix 5.4 shows an example of a transcript page at the completion of the second HC. At the end of the second stage any themes not directly relating to adherence were separated out and not taken further to the next stage of analysis. However, these themes were retained as they were useful in setting the scene and developing a deeper understanding of what it is like to be a YPH in the UK.

5.6.4 The Third and Fourth HC

During the third cycle, the themes were refined and re-organised underneath superordinate themes. This was done by re-reading the specific texts related to the emerging themes, but also by re-reading the context of entire coded transcriptions. The emergent themes were listed in order of appearance and attempts were made to look for and make sense of connections between them, creating theme clusters and ultimately superordinate themes. Smith & Osborn (2008) suggest imagining a magnet, "with some themes pulling others in, helping to make sense of them". Throughout this process it was essential to continually return to the transcripts to ensure that the superordinate themes still reflected what participants had actually said. Appendix 5.5 shows an example of a transcript page at the end of the third HC.

During the fourth cycle these main (superordinate) themes were refined and reorganised and presented in a table together with the subordinate themes underneath each main theme.

5.6.5 Writing up the results

The list of superordinate themes and corresponding subordinate themes was translated into a narrative account that expanded the analysis and explained the themes, illustrated with verbatim extracts. During the process the researcher continued to bracket off any personal reflexions or interpretations to stay true to the participants stories.

Chapter six presents the analysis of patients' accounts of adherence to their prophylactic treatment. Chapter seven presents the analysis of parents' accounts of managing their sons' haemophilia, including adherence to his prophylactic treatment. Chapter eight presents the analysis of haemophilia HP accounts in relation to adherence to prophylactic treatment. Although the three studies are similar in that they address the same issue, because they reflect different perspectives they are subtly different. To retain these differences the specific methodology for each of the studies, including recruitment and data collection, will be presented at the start of each chapter. Although the following chapters will each end with a summary of the findings, an overall discussion relating to the results of the three qualitative studies combined will follow in chapter 9.

Chapter 6: Interpretative Phenomenological Analysis of patients' accounts of adherence to their prophylactic treatment

6.1 Introduction

This section presents the results of the Interpretative Phenomenological Analysis (IPA) of participants' accounts of managing their prophylactic treatment regimen. The aim of this study is to examine the complexities surrounding prophylaxis and adherence to this treatment among young people with haemophilia (YPH). This will provide context to the quantitative findings described in chapter 4, and contribute to a better understanding of what drives (non-)adherence in this patient group.

6.2 Methods

6.2.1 Recruitment

Participants were recruited in five haemophilia centres across England and Wales. Eligible patients were approached while they were in the haemophilia centre for a routine check-up appointment. All participants who met the inclusion criteria (aged 12-25, diagnosed with severe haemophilia and following a prophylactic treatment regimen) were invited to take part, and all participants who agreed to take part were interviewed.

6.2.2 Participants

Participants were 11 males with a mean age of 18.82 years (SD=4.99) who follow a prophylactic treatment regimen for their severe haemophilia (see Table 6.1 for details).

Five participants lived with their parents, three lived independently with friends or housemates, and the remaining three lived with a partner or wife.

Table 6.1: Young people with haemophilia interview study participant characteristics

Participant code	Ethnicity	Age	Treatment regimen
1	White British	17	Three times per week
2	White British	24	Activity based
3	White British	21	Twice per week Long-acting
4	White British	12	Three times per week
5	White British	25	Three times per week
6	Asian Pakistani	22	Alternate days
7	White other European	13	Twice per week Long-acting
8	White British	12	Alternate days
9	White British	16	Daily
10	White British	21	Three times per week
11	White British	24	Three times per week

6.2.3 Data collection

Each participant was interviewed face-to-face at their home or in a private room at the haemophilia centre. The interviews were semi-structured using a topic guide (appendix 5.1), although participants were encouraged to tell their own story in their own words with as little interruption from the interviewer as possible. At the start of their interview participants were invited to describe their experiences in relation to their haemophilia, starting with what it was like when they were a child. The main aim of these questions was to ease participants into the interview and gain a sense of how they felt about their haemophilia and the extent to which it influences their life. To gain insight into their experiences and perceptions in relation to prophylaxis, participants were then invited to describe their treatment regimen, their feelings about their treatment and potential barriers and facilitators to their adherence. Lastly participants were asked about the social support they receive in relation to their haemophilia and treatment. The order in which the above subjects were discussed was flexible, and very much driven by participants themselves. In some of the interviews very few prompts were needed, as

participants were very keen to share their story. In other interviews the prompts were used to encourage participants to 'open up' and share their story, or to bring the discussion back to experiences and perceptions in relation to prophylaxis. Interviews were recorded and then transcribed verbatim before being analysed following the IPA methodology.

6.2.4 Analysis

IPA emphasises that the process of discovering themes is based on the researcher being engaged in a double hermeneutic (Smith, Flowers & Larkin, 2009), with the aim to make sense of the participant attempting to make sense of their experiences. These themes, therefore, form one possible account of how YPH experience their prophylactic treatment regimen. This analysis is partial and subjective and may have reached different conclusions and highlighted different aspects in comparison to what other researchers may have found. After examining themes, and convergence and divergence of themes, and after immersion in the data, it was decided to report those that emerged most strongly from the interview data and that were relevant to the research questions. In this chapter these themes will be explored and illustrated with verbatim extracts that were selected from across all participants' transcripts, to ensure they were representative of the sample. In instances where different participants had different opinions or experiences, all views are illustrated. In cases where participant responses were similar, only those quotes that illustrate the theme most clearly have been included. This approach was true to the aims of the study, participants' accounts and the richness of the data.

6.3 Results

6.3.1 Superordinate and subordinate themes

Participants' accounts clustered around four superordinate themes, which are shown in table 6.2 together with their related subordinate themes. The table also shows for which participants each of the subordinate themes was relevant.

Table 6.2: Young people with haemophilia interview study superordinate and subordinate themes for each participant

Superordinate	Subordinate themes	Participants										
		1	2	3	4	5	6	7	8	9	10	11
Difficult balance between good self-management and not letting haemophilia stop you from living the life you want to live.	Haemophilia, bleeds and pain are part of life and who I am.	x		x	x	x	x	x	x	x	x	x
	Patient is haemophilia expert.	x	x	x	x		x	x	x		x	
	Avoiding risk is key.	x	x	x		x			x		x	x
	I tailor my treatment around my lifestyle.	x	x		x	x		x	x	x	x	
Grappling with barriers that make it harder to adhere to prophylaxis.	Barriers to adherence.	x	x				x	x			x	x
	Haemophilia- and treatment related anxiety.	x	x	x	x	x	x	x	x	x	x	x
	Responsibility for treatment is taken on gradually from a young age.	x	x		x	x		x		x	x	x
	Inhibitors have a significant impact on my treatment and health outcomes.						x			x		
I don't like taking treatment but hardly ever miss an injection.	Reported adherence is high.	x	x	x	x	x	x	x	x	x	x	x
	Taking treatment is inconvenient and no fun.		x		x	x	x	x		x	x	x
	Taking treatment is no problem, it's part of my routine.	x	x	x	x	x	x	x	x	x	x	x
	Treatment protects me so I can live a normal life.		x	x		x	x			x	x	x
Support from family, friends and the haemophilia centre keeps me on track.	Support from mum and dad is key.	x	x	x	x				x	x	x	
	Social and peer support.	x		x	x			x	x	x	x	
	Haemophilia care in the UK is second to none.		x		x		x		x			
	The staff at the haemophilia centre is very supportive and they encourage me to keep to my treatment regimen.	x	x	x	x		x	x	x	x	x	

6.3.2 Theme 1: Difficult balance between good self-management and not letting haemophilia stop you from living the life you want to live.

This theme encapsulates the impact haemophilia has on day-to-day life of YPH. Often diagnosed at a very young age, haemophilia is not only a lifelong health condition, it is part of who they are and the way they live their lives. Participants described how they were often in and out of hospital as children, resulting in school absence which for some had a negative effect on academic and professional opportunities. They also described how they had missed out on social occasions and opportunities to make friends because they were often excluded from activities that were deemed too risky. The young people involved in this study vocalised a strong desire to live a 'normal' life, however for most of them managing risk is an important part of their daily routine. This includes taking their prophylactic treatment and taking top up treatments to provide extra protection for physical activities.

Subtheme 1: Haemophilia, bleeds and pain are part of life and who I am

As haemophilia is usually diagnosed in the first few years of life, patients have always lived with the condition and it is therefore part of their identity.

> *It's something obviously I was born with it so I don't know any different. So me for me it's uhm it it's just part of my lifestyle (P.2, 24 years old)*
>
> *I just kind of accept it as a part of who I am and what I've got. (P.1, 17 years old).*

Some of the participants felt that having haemophilia had not only shaped their life, but also their personality. Having haemophilia clearly had a big impact on them when they were growing up, and particularly those with non-affected siblings were aware that they were 'different' and were treated differently by parents, teachers and peers. Missing school regularly affected their qualifications, and consequently their job prospects.

> *It changes who you are because I, never going through it, I probably would have been a completely different person. Of course you would because you will have the additional things going on. Wouldn't have missed so much time off school, like when my brother had a couple of weeks off because he was ill, they had a letter sent because he missed so much time, now I could miss time and it wouldn't, because I've got like a, not so much an excuse, just different circumstances -- It's like when I broke my leg some of my friends …I went into the ambulance that night and then I had to go back into the school to do my GCSEs. I only did a couple because of the amount of time I missed and I didn't see some of them again which didn't bother me because it was just oh they weren't great people (P.8, 12 years old).*

Whereas for others it meant they had more time to focus on academic activities and achievements, particularly in the run up to GCSE and A-level exams.

> *It's easy. Just make notes because that's something that I've gotten used to now after not being able to do much sport, I just sit and learn things. (P.9, 16 years old)*

Striking a balance between living a normal life, while avoiding situations that increase the risk of bleeding is challenging for most young people who were interviewed for this study. However, it seems that there are many different interpretations of what 'avoiding risk' is, and how this influences the way you live your life. Some participants are more or less able to live the life they want, as long as they take their treatment to protect themselves. This included two young adults who live very active lifestyles and take part in sports at a competitive level. Whereas other participants felt that they have to miss out on many things they would like to do, because of their haemophilia.

> *But knowing my limitations is definitely, ah, a very important part of having haemophilia, cos if you go past what you're limited to be able to do, then you are gonna cause more damage. (P.1, 17 years old)*

Participant 1 appeared to have quite ambivalent feelings about the way haemophilia affects him. He felt quite strongly that he would not let his haemophilia hold him back, but avoiding risk appeared to be quite central to his life. This ambivalence was not unique to this participant, although it was not quite as strong in others. The majority of participants mentioned some limitations to what they are able to do, either because they want to avoid risk, or because they have already suffered joint damage as a result of recurring bleeds.

Many people with haemophilia develop target joints (recurrent bleeding in a particular joint) by the time they reach young adulthood. Recurrent bleeding in these target joints can lead to joint damage resulting in mobility issues or disability. Most people interviewed for this study appeared to accept haemophilia-related issues (e.g. bleeds, pain, and joint damage) as part of their life. They tend to take a 'you just have to get on with it' approach, and do not dwell on these issues. Some recognised that their joint problems were probably caused by recurring activity-related bleeds during their childhood. Some voiced regret as they now realise that these recurring bleeds were caused by risky activities, such as playing contact sports or rough play with friends.

> *Whereas before I had all this ankle problem I'd just do what I want really. Ehm, all the things what they'd say they didn't want me to do, I would just go and do it, not to be a pain, but cos I wanted to. But I'm a bit more calmed down now. So I don't need to go do all that stuff (P.3, 21 years old).*

For many patients their joint damage results in significant and frequent pain. However, it appears that pain does not stop them from 'getting on with it' as they are so used to pain and have found a way to cope with it.

> *It's something I --my body's got used to so much that it kind of just ignores it now. If I-- If for example I knock against something you-- you do notice it's there quite heavily--because the pain comes flooding back very quickly. But that settles down, but it's always there. And I've kind of accepted the fact that it's always gonna be there. But it's just easier because my body ignores it now (P.1, 17 years old).*

Subtheme 2: Avoiding risk is key

Many patients are diagnosed when they first start moving around as small children. The small bumps and falls that happen to all us when we learn to crawl or walk can cause severe bruising in children with severe haemophilia. This is often a traumatic experience for parents, as they learn that even low-risk day-to-day activities can cause harm to their child. Almost all participants explained that while they were growing up they were not able to join in with all activities at school, or with friends. For some this meant that they were also excluded from playing outside at break times at school, on advice from the haemophilia team or because school or parents felt it was too risky. Some felt that not being able to join is when they were at school held them back, and made it difficult for them to make friends and develop social skills.

> *As I said I try not to let the Haemophilia hold me back, but the fact that we'd been told that I shouldn't-- to protect me, that I shouldn't go out at break or lunch was what held me back. (P.1, 17 years old)*
>
> *Sometimes at school I do try and do football and things like that but I mean I've been taught to like stay away from it but it's hard. Because I just want to do the same as everyone else and be active and do sports and stuff but like because my illness it kind of stops me a little bit. (P.8, 12 years old)*

It became clear that different families and individuals deal with haemophilia in different ways, and perceive the potential risks associated with activities differently. However, it appears that managing risk is an important part of life for all young people involved in this study. For some this means that they keep to their treatment regimen religiously, so that they feel protected while they get on with the life they want to live.

> *Like If I am doing anything active obviously I would have always had my medication uhm. I don't really leave anything to chance. Uhm so as long as I've had that then there is not a huge panic uhm but obviously if I have broken a bone then you're gonna have to go to hospital either way uhm (P.2, 24 years old)*

For others managing risk has a more central role in their lives, where each activity is risk assessed, and where limitations to what they are able to do are an important consideration in everyday life.

> *But knowing my limitations is definitely, ah, a very important part of having haemophilia, cos if you go past what you're limited to be able to do, then you are gonna cause more damage.(P.1, 17 years old).*

Particularly participants who live an active lifestyle feel their treatment is crucial in reducing the risk of activity-related bleeds and preventing problems. This is clearly also an incentive to adhere to their treatment regimen, and sometimes take additional top-ups to be prepared and ensure they are covered for their activities.

> *Recently I've done a 10k run and I knew that the week before I'm training for it, make sure you've given yourself plenty of factor, maybe increase the dosage a little because you've got a big run coming ahead and if something were to happen or generally you're going to ache after the run anyway so it would be good to have that factor in your system and a good healthy amount in that week before to get you prepared. So if I did miss something, which I didn't, I would have been worried just in case something happens or I get a cut or something or I bang my head or something and you keep on bleeding and bleeding, whereas if you were prepared then you wouldn't bleed as much (P.10, 21 years old).*

It is interesting that patients' perceptions of the advice they receive from their haemophilia centre differs widely, with some suggesting that they feel that they are not allowed to get involved with sports, whereas others feel that their haemophilia centre encourages them to be active and fit. This could be because different haemophilia centres give different advice, but could also be due to different interpretations of the same advice. This may indicate that HP need to consider more carefully how the advice they give is understood and implemented. Particularly as individual circumstances, family dynamics and personalities will influence the way in which patients and their families take on advice.

> *I think there's a couple of haemophilia centres who aren't handing out, just aren't really handing out treatment. They're just saying don't do sport, if you continue to do it we don't give you the treatment. Which is a shame to hear because I know all the centres <in this area> encourage sport and encourage an active lifestyle. And you know I've learned since I was swimming at a high level that's when all my problems stopped. That coupled with the medication. It's been super fit, super healthy, treating the haemophilia with a bit of respect. (P.2, 24 years old)*

As illustrated by the above quote, feedback from several participants in this study suggests that being fit, healthy and strong helps to manage haemophilia and reduces bleeding. Many haemophilia

centres advise their patients to take up swimming, as it is a non-weight bearing activity that can help patients to stay fit and strong without risk of injury. This advice seems to be taken on by many patients, and several participants in this study mentioned that they swim regularly, or are intending to take up swimming in the near future.

> *I've always liked swimming but my mum says that we're going to try and do get into doing more things like swimming, activities that I can do. (P.8, 12 years old)*
>
> *They've opened a new baths by me so hopefully I'm gonna start going there soon. If I could play football like you run around for like ninety minutes, that could affect me like the next day because I could have sore ankles, because swimming's not weight-bearing it's ideal (P.11, 24 years old)*

The theme of reducing risk does not only apply to physical activity, participants also suggested that they do not like to take any chances in relation to other elements of their haemophilia management. For instance, several participants mentioned that they would not trust a digital device to remind them to take their treatment, instead relying on several ways to remind themselves. One participant described how he checks each box individually before signing for a new treatment delivery.

> *I don't think we've ever had the wrong medication delivered--but it-- we have to check just-- Just in case /just to -- for peace of mind-- (P.1, 17 years old).*

Another described how he travelled back from abroad to have his injury treated in his usual NHS haemophilia centre rather than relying on treatment in a foreign hospital.

> *To make sure I was treated in England cos I trust yeah I trust the NHS with my life basically (P.2, 24 years old).*

Subtheme 3: Patient is haemophilia expert

In particular participants aged 18 and older described how they feel that they are experts in haemophilia. They have learned how to recognise the symptoms of a bleed, they know what kind of activities increase the risk of bleeding and they know how to treat themselves if a bleed does occur.

> *I think, I'm also haematologist [laughs] because I had so much experience of these things but obviously I feel I had to teach myself, I've improved myself a lot and I've gained enough confidence too (P.11, 24 years old)*

As haemophilia is a rare condition, several participants described situations in which (non-haemophilia) HP did not know how to deal with their condition, or gave them incorrect advice (e.g. some were prescribed nonsteroidal anti-inflammatory drugs, which can worsen bleeding problems). For some participants these experiences encouraged them to become more self-sufficient, and

potentially increased their reluctance to allow others to do their treatment or even their blood tests. Although in some cases this may also be related to some anxiety around needles and injections.

> *When I've been in hospital in the past I have still done all my own injections. At one time I even had a doctor come and ask me, cos they needed help to mix it up. Yeah, like I don't let anyone do blood tests, I just do it all myself. I don't like people putting needles in me; I'd rather do it myself (P.3, 21 years old)*

Even those participants who did not describe themselves as experts appeared very confident about their abilities to manage their haemophilia, and were mostly quite knowledgeable about the way factor replacement treatment works.

> *Cos there's nothing high-risk about sleeping. The only time I'll take it in the evening is if I've had like 2000 on a Monday and then I am doing something active on the Tuesday evening then I'll maybe have a top-up of a 1000 that evening (P.2, 24 years old)*

Subtheme 4: I tailor my treatment around my lifestyle

In recent years the focus in haemophilia care has been moving towards a more individualised approach, where patients are encouraged to tailor their treatment around their lifestyle. So instead of the standard 3 injections per week (usually on Monday, Wednesday and Friday in the morning), patients may tailor the treatment frequency and dosing around their activities and lifestyle. Many patients also take additional treatments (top-ups) to cover themselves for ad-hoc activities on days that fall outside of their usual prophylactic regimen. The majority of participants in this study tend to tailor their treatment using top-ups. However two participants described more flexible regimens that they tailor on a daily basis around their very active lifestyles.

> *I can have some pretty intense weeks. Where I maybe go over, uhm not my quota because there is not really a quota for it, but kind of if I've taken it every day and I've had couple of days where I've gone 1000 and 2000. If I have a day or a few days where I am not really active then I sort of try and knock it back quite a bit. (P.2, 24 years old)*

This personalised approach to prophylactic treatment raises some interesting questions in relation to adherence, as in some instances behaviour that would have been considered non-adherent just a few years ago (e.g. reducing number of injections during a 'quiet' week), may now be seen as an acceptable adjustment. Equally, the definition of 'over-treating' may also need to be revised, as patients who increase the dose or frequency of their injections to accommodate a more active lifestyle are not necessarily over-treating. This has some important implications for patient education and information; adherence assessment and research; and haemophilia care. Patient education about treatment is likely to become more complicated, as tailored treatment regimens are more difficult to explain and require patients to have a better understanding of how the treatment

works. Assessing adherence will also become more complicated, as standard questionnaires may not accommodate a more flexible treatment approach. This will have implications for adherence research but also for routine care, as HP are likely to find it more difficult to ascertain if their patients are adhering to their treatment.

6.3.3 Theme 2: Grappling with barriers that make it harder to adhere to prophylaxis

This theme encapsulates barriers to adherence to prophylaxis as described by the participants in this study, and may therefore not include all possible barriers to adherence that a young person may experience.

Subtheme 1: Barriers to adherence

Most young people involved in this study have a busy lifestyle, which at times can make it hard to fit treatment in. Many leave home early in the morning to get to school or work, and fit in social and physical activities before they return home in the evening.

Most participants mentioned that they have to get up a little earlier to take their treatment and that when they are particularly busy they do sometimes forget.

> *I was going to be at work so I really didn't find enough time to do it and when I come back I was really tired, I went to sleep (P. 6, 22 years old).*
>
> *In the morning I'm normally in a rush. So that's when I normally tend to have it, so that's why I tend to forget. I struggle to keep track of the days as well. So, I remember I started to just feel a bit - - just a bit funny like in the joints. And a bit achy. And then I realized I've gone four days without it. So that made me realise that's why I was aching. (P.3, 21 years old)*

Next to forgetting, one of the main barriers for the participants in this study is the intravenous injection. It is not very pleasant to have to inject yourself several times each week, and several participants mentioned that they would much prefer to take their treatment through oral tablets, or subcutaneous injections like insulin-dependent diabetics. Although most participants did not describe any issues around needle phobia, it appears quite common for patients to experience some issues around venepuncture or venous access. In particular for younger patients, who perhaps have not had as much practice. Not being able to find or access a vein can be frustrating, painful and sometimes can cause anxiety.

Some patients described how they tend to give up on their injection if it doesn't work the first or second time, and come back to it later in the day or even the following day.

> *…sometimes when you put the needle in, sometimes it can be quite difficult. Cos you can't always you don't always find the eh find the ehm the vein. You don't always find it. But it doesn't --it can -- cos I got used to it you normally find them now. (P.4, 12 years old)*
> *I have, I do have -- I sometimes have trouble with them, the veins. But it is not - - recently it's not been too much of a problem. Like if it's not gone in the first time, then you can just get another needle whatever and just try again. (P.3, 21 years old)*

Once they have found one or two injection sites that work well, most patients tend to stick to those sites for all their injections. This makes it easier and less painful, particularly as the sites become less sensitive due to the scar tissue that results from frequent injections.

> *I could obviously just go into another vein. But that would just be going into tender skin then (P.3, 21 years old).*

Sometimes there are practical reasons why patients struggle to take their treatment. They may not be able to find an appropriate or private place, or may not be able to do the injection themselves because of an injury. For instance, if a right-handed person has an injury to their right arm, it would be very challenging for them to take their treatment themselves.

> *I broke my elbow so I couldn't actually treat myself so I had to direct my sister to do it (P.2, 24 years old).*

In emergencies patients may not always be able to mix up and take treatment themselves. Two participants mentioned that the design of the treatment, and the way it is mixed up in preparation for the injection, makes it quite challenging for inexperienced people to help. This makes emergencies more stressful, and may increase general anxiety about managing life with haemophilia. One participant described an experience during a 'lads holiday' which has made him more anxious and risk averse about going away with friends or attending parties that involve alcohol and young people having fun.

> *"I'm going to have to go back to the room to treat myself, can one of you come and help me?" my mates offered and we went back. It was hard for me to do it because it was bleeding, so I had to describe to my friend how to make the bottle up to get the injection ready. Obviously I don't expect my friend to inject me. But I thought if you make it up for me I could put this extra pressure on and give myself a bit more time to make it stop. So when I come to inject and go like that then the blood will be minimal compared to if I just make it and the blood flow is going*

down. So I was telling him but it was slightly complicated. For me it's second nature, but obviously for him I was just …trying to take it on board what I was giving to him. But if it was just maybe an easier way of making it or less compartments. Sort of readymade so all you have to do is inject then it would be like simpler. I could have just got on with it. (P.10, 21 years old)

One participant also mentioned that changes in the design or packaging of existing treatment, or changing to a different treatment, can be challenging. The frustration of having to buy materials that used to come with the treatment for free (such as antiseptic wipes), became a barrier to adherence for this individual.

> *…it takes long because in that little package, they don't have the dry things for your hand and the wiping and the plaster because we used to have that in the other box. (P.7, 13 years old)*

Because prophylactic treatment involves an intravenous injection, it is important for patients to find a private and clean place to do their treatment. When at home, or in a familiar location this is often not a problem. For instance, several participants described how they are able to take treatment at work or school if they need to. However it can be challenging to find an appropriate place when on holiday, or out and about.

> *I've never had factor on a plane before, and then we get in the airport and it's hustle and bustle, you can't really pull the lads to one side say "I've got to go to the toilet and do it", so ''I'm not really going to have treatment here until I get home''. So it was just the fact that I couldn't have any, that was more the worry. It made me feel a bit not organised, not good about myself (P.10, 21 years old)*

Subtheme 2: Haemophilia- and treatment related anxiety

As described above, anxiety can make the intravenous injections more challenging, particularly for patients who have venous access or venepuncture issues.

> *What makes treatment difficult is if I'm in-- If I'm stressed. If I had a stressful day and I'm doing it in the evening it's difficult to locate veins. Because they tend to shy [laughs] away from you. If I'm in a bad mood they shy away. I--it's always very mood specific. If I'm quite relaxed and n a good mood then I can easily see them on the surface and it's easy to get in there. (P.1, 17 years old)*

Most of the participants were not particularly anxious or stressed about their injections, although two of the younger participants who were not doing their own injections yet appeared a little anxious about the idea of taking over their own injections.

> *I have to one day obviously do it but it's a bit scary, but I do have to eventually (P.8, 12 years old).*

The majority of participants explained that having to do their injections themselves was difficult to start with, but became easier with time and experience. None of the participants developed needle phobia, or anxiety about injections, although there was some indication that some of them may not have been completely at ease with their treatment. Several participants explained that they would never take their treatment in front of someone else, or would only do it in front of people they are familiar with.

> *Generally I'll always do it before I go out or a place or work is okay because you're familiar with work so, I don't like doing it in front of like, I don't mind doing it in front of but, you know, people that don't know about it and don't know what it is, that's, so generally I always make sure I have it in a safe place at home, have it at work, have it at a friend's house… (P.10, 21 years old)*

Not wanting to take treatment in front of others perhaps indicates that there is some anxiety about how others respond to the injection, and possibly some concern about stigma. Some participants described how reactions from work colleagues and potential partners can sometimes be upsetting or cause insecurity.

> *Whereas some girls maybe I've seen in the past they're like "what is it? What is it? You have to inject yourself, you know, I don't understand why" and makes you look a bit like, you know, it shows you up, makes you feel like, you know, I'm not good enough because I've got to inject myself or because it looks bad and as soon, normally generally the girls, I explained to them and said "look this is what it is, this is what I have to do" and they're fine. (P. 10, 21 years old).*

It is clear that even for patients who have supportive families and friends around them, haemophilia can cause anxiety at times. Bleeding episodes can be painful and can cause stress or anxiety for patients and their loved ones. Particularly in cases where the bleeding causes them to miss school, work or social occasions because they cannot move around or have to take rest to recover.

Patients interviewed for this study generally took a 'You have to get on with it' approach to life with haemophilia, indicating a certain level of pragmatism and not wanting to dwell on issues. However, it became clear that for some of them haemophilia-related issues can become overwhelming at times.

> *Like if I have a bleed and I'm resting, I sometimes go on the Xbox and just like play and kind of forget about like the bleed. (P.8, 12 years old)*

Some described how they would 'flee' from their haemophilia for a while by becoming absorbed in a film or computer game, others engaged in more active coping mechanisms like speaking to friends or seeking psychological support to help them deal with issues related to their haemophilia.

> *It's great; it's good to relieve stress that way because she understands me. It's a lot easier if someone else knows all about (P.9, 16 years old)*

> *I do have counselling as well. And it all must stem back to when it all started or whenever. That's just another problem I think. Just for someone to talk to, it is helpful. But I don't like to --- I don't like to talk about a lot of things. I keep a lot to myself, so that's why I go there. So yeah, haemophilia does cause a few problems in that way. Yes, it's all about that, obviously growing up with it (P.3, 21 years old).*

Some participants were able to access psychological support through their haemophilia centre directly, or through a referral from their haemophilia consultant to a psychological support service provided by the hospital or local NHS trust. However, long waiting lists or difficulty in accessing psychological support meant that some participants decided to find a private counsellor or therapist, whom they have to pay themselves. Regardless of how they accessed the support, participants felt it was very helpful to discuss their haemophilia-related issues with someone outside of their family, social circle or HP. Without prompting from the interviewer several participants suggested that it would be helpful if psychological support was easier to access. They felt that in an ideal world psychological support would be available through haemophilia centres, so that patients could receive support without delay and without incurring costs. Support from family, peers, friends and the haemophilia theme will be addressed in more detail below under theme 4 (page 99).

Subtheme 3: Transition of responsibility for treatment

As patients tend to be diagnosed at an early age, their parents or caregivers are usually responsible for their treatment to start with. Initially they come to the haemophilia centre for every treatment, or in some cases a nurse may visit the family at home to help with the injections. Once parents are confident and skilled enough to do the injections themselves, patients move onto home treatment.

This can be a very positive step forward, as it dramatically reduces the number of required hospital visits. However, it can also cause some difficulties, as parents have to inject their son several times per week without support from a HP. This study did not interview parents and children from the same family, so we are not able to check if there are any links between parental anxiety and the way patients take over responsibility for their treatment. However, it is likely that in families with high parental anxiety around haemophilia and prophylaxis, patients may find it more challenging to start doing their own injections.

Although there did not seem to be much anxiety about treatment among the older participants in this study, the younger participants who had not taken over full responsibility for their treatment were clearly anxious about having to start doing the injection themselves. Participants were unable to verbalise how they felt in detail, other than saying that they were worried or found the idea of injecting themselves a bit scary. However, despite feeling apprehensive, they also recognised that they had to take over responsibility eventually, adopting a 'You have to get on with it' approach.

> *It's okay, the only thing I'm really worried about is when I have to inject myself but then I think that everyone with haemophilia has to do it (P.8, 12 years old)*

The age at which patients take over treatment responsibility from their parents appears to vary widely, with some patients being able to inject themselves from age four, while others still rely on help at the age of 20.

> *I think from like 6/7 I've been doing it myself and it's just, you just get used to it, it becomes a part of what you have to do. (P.11, 24 years old)*

> *Yeah. I think about 15, 16 years old I went to the hospital there and they said, you know "you need to learn" and practiced doing it there for a couple of hours and then I walked away thinking "yeah, I know how to do it now" so mixing it, making it and really got myself involved with it, so yeah. (P.10, 21 years old)*

It appears that there is not a set age or time to train patients to do their own injections, although in many haemophilia teams appear keen for young people to become independent by the time they go to secondary school. In reality, the time at which patients start doing their own injections is often dictated by practicalities. For instance, several participants explained that they had to learn to do it themselves because they wanted to go on a school trip. In other families it may be because mum has to look after younger siblings and doesn't have time to help with treatment, or she may need to leave home early for work. However, in most families parents stay involved with their son's treatment in some capacity right up to when he leaves home.

Subtheme 4: Inhibitors have a significant impact on my treatment and health outcomes

Two participants in this study suffered with the added complication of inhibitors, which has made managing their haemophilia significantly more challenging. Inhibitors occur when the immune system starts to create antibodies to block the effects of the clotting factor. The inhibitors can make treatment less effective, making it more difficult to prevent and control bleeding. For one of the participants, who has had inhibitors since he was a small child, it has had quite a negative impact on his quality of life. He is on an intensive treatment regimen that involves daily injections of large volumes of treatment, and relies on a wheelchair and crutches to get around due to the severe joint damage that he has suffered due to frequent bleeding issues. Because of the large treatment volume he uses a Hickman line, which is a central venous catheter. As the risk for infection using a Hickman line is much greater, it is very important that the environment is aseptic. This can make administering the treatment very challenging and time consuming, which at times may negatively impact on adherence.

> *I just wish it was more concentrated because at the moment it's really, there's a lot of syringes and stuff involved with doing it and that's what stopped me having a, not having another Hickman line because it would just be too much to put through a needle every day. (P.9, 16 years old).*

6.3.4 Theme 3: I don't like taking treatment but hardly ever miss an injection

Although needle phobia or venous access did not appear to be an issue for the majority of participants, almost all mentioned that they did not like taking their treatment and would much prefer to take a tablet or subcutaneous injections similar to insulin-dependent diabetics. The key issue for most patients appeared to be the fact that the treatment consists for an intravenous injection that is not very pleasant, and can be time consuming.

Subtheme 1: Reported adherence is high

Despite the treatment being quite unpleasant for patients, self-reported adherence among participants in this study was high. Very few participants admitted to deliberately skipping treatments, and those participants who did would usually only skip a treatment if they were expecting to have a very inactive day. As described above, these circumstances are not necessarily considered as non-adherent for those participants who have agreed a more tailored treatment regimen with their consultant.

> *We do sometimes just not bother with the treatment, if I'm not going to be doing anything that day (P.9, 16 years old)*

None of the participants felt that adherence was an issue for them, and most were very motivated to keep to their treatment regimen. Some participants admitted to sometimes forgetting treatments, due to their busy lifestyle or being distracted by other priorities.

> *over really important stuff it's no I don't miss it. But I've had the odd uhm kind of day where I've gone uhm. Where I've had an active day and I've got halfway through it and bugger it I didn't take my medication. So uhm I'll either go home and take it or if I just be super careful then… Uhm So I think you know maybe we're talking twice a year I make a mistake with it.(P.2, 24 years old).*
>
> *Yeah, I occasionally do forget it… if I have forgotten during the day mum would say have you done it? If not, right, you do it tomorrow morning then ---(P.4,12 years old)*

Most participants take their treatment as soon as they realise they have forgotten it, others wait to the next morning to make up for it. There were two participants who, despite reporting high adherence, described situations where they may miss two, three or even four injections in a row. It was not clear what the actual level of adherence of these participants was, and the language they used indicated that perhaps they were a little confused about this themselves. For instance, participant 1 initially reported a very high level of adherence, and that any missed treatments were due to forgetting rather than skipping. However, the language he used suggested that perhaps he does skip injections occasionally.

> *No I-- I won't deliberately miss two three or four in a row, and if-- if-- the problem is if I forget one--the little dull aches a bit, yeah ok, if I miss two then they get worse, then it-- then that's it. Because you realise, yeah I've missed two, I need to get it done. And even if it's a day when I'm not treating, I'll treat myself for it. Because I can't get these bruises (P.1, 17 years old)*

Some participants described being quite anxious or worried about the risk, when they realise they have forgotten their treatment. They clearly feel that their treatment protects them, and feel vulnerable when they realise they are not covered by treatment. For these participants this anxiety could also act as an extra motivator to adhere, as it appeared that these participants forget very rarely, perhaps less than those who did not voice anxiety about forgetting.

> *But I mean it's such a for me it's a really horrible feeling to be doing something active having not had my medication because then you know you're you're vulnerable. Uhm So I think you know maybe we're talking twice a year I make a mistake with it.(P.2, 24 years old).*

One participant in particular described how forgetting treatment affects his mood, and makes him feel disappointed in himself. He feels happy when he has had his treatment, as he knows he is protected. But when he has forgotten his treatment he feels exposed and anxious.

> *A bit like exposed, feel a bit like, you know, a bit disappointed in myself in a way, sort of a bit like I should have had some before and I feel a bit like anxious to get it done really and I go in a bit of a bad mood or I go a bit, you know, feel a bit uncomfortable and not as happy as usually would be. (P.10, 21 years old)*

Subtheme 2: Taking treatment is inconvenient and no fun

It is very clear that none of the participants enjoy taking their treatment, and would much prefer not to have to take it. Although needle phobia does not seem to be much of an issue for any of the young people that were interviewed for this study, many of them did mention that they do not like having to inject themselves intravenously.

> *No, not at all. For preference, if I'm being really picky I'd like to do it a little bit less. Just because like everyone. I'd like to not do it all. (P.5, 25 years old)*

A number of the interview participants explained that they would much prefer to take a tablet, or subcutaneous injection like insulin-dependent diabetics.

> *maybe just that instead of having treatment, different things like a bit of medicine or something to do with it. Like instead of doing the injection you just gotta take a tablet. I know that you can't do that but … (P.4, 12 years old).*
>
> *The other thing at times, like I wish it could be like a diabetic who gets it in a pen? (P.11, 24 years old)*

Most participants explained that they tend to inject in the same place, as this is much easier for them and less painful (as the injection site becomes scarred and numb to the pain of injections).

> *Um, it's alright, I've got used to it now because I've had so many needles, I've been-- Like my veins are quite scarred so I don't feel it anymore and I just have to live with it (P.8, 12 years old)*

One of the most frequently mentioned issues around the treatment was that it can be quite time consuming. As most patients take their treatment in the morning it can be difficult to fit it in, and some participants admitted to sometimes having to miss breakfast when treatment takes a bit longer than usual, or when they do not have time for both treatment and breakfast.

> *the prophylaxis only really takes about 20 minutes but I don't really have time for breakfast afterwards so it's quite irritating before school but most of the time it's not really too bad (P.9, 16 years old)*

However, most participants appeared to realise how important treatment is for them. They feel that prophylaxis allows them to live the life they want, and reduces the number of bleeds they suffer. Therefore, although they do not like their treatment, they take it as religiously as they can. Being on a home treatment plan means that patients do not need to come to the hospital for treatment, which allows them to get on with their normal day-to-day life.

> *Obviously sometimes it does frustrate you a little bit but it's more better to treat yourself at home and being in a comfort than coming along to the hospital every day (P.6, 22 years old)*

Interestingly, there was one participant who really disliked having to mix the treatment. He was not concerned about the injection itself, but felt mixing up treatment is boring and tedious and resented having to do it before every injection. He explained that his parents would often mix his treatment for him when he was growing up, which made life a little easier for him.

> *and that's something just at times, especially when you're growing up sometimes, like once a week for someone to mix it for you so you ain't got to worry about it, it's just "here you are, I've done it", ain't giving it, it's just mixing it, especially when there was a lot of it, it was really tedious. (P.11, 24 years old)*

Only one participant mentioned that when he gets frustrated with his treatment, he gives up and leaves it to the next day. However, it is important to note that this participant has some specific challenges due to his inhibitors, which requires him to take a much larger volume of treatment on a daily basis.

> *I get frustrated with it pretty easily if I'm doing it myself and if I get too frustrated I just stop doing it altogether and I won't bother for that day. (P.9, 16 years old)*

Subtheme 3: Taking treatment is part of my routine

Although many participants admitted that they dislike their treatment, they also appeared to have accepted it as part of their life and have fitted it in their routine. For most it has become just another thing they need to do before they leave home in the morning.

> *it's become second nature. It's an easy thing to do now. I get up early in the morning and I sit-- sat at the breakfast bar in there and I just sit and do it. I don't even give it a second thought, you put it together and inject (P.1, 17 years old).*
>
> *It's uhm it's just something that's gotta be done. It's like it's like having a shower in the morning. That's pretty much the long and short of it. (P.2, 24 years old)*

Participants described how the prophylactic injections were often difficult and painful when they were younger, particularly when they were learning how to do the injection themselves. But by the time people with haemophilia reach young adulthood they tend to be very skilled, and able to inject themselves without any issues.

> *Yeah, I can do it with my eyes closed I reckon [both laugh] if I had to I think I could. (P.5, 25 years old)*
>
> *Not really no, I really find it quite easy. I don't really need much help with it to be honest. You get used to it. It's quite easy now to sort it out (P.4, 12 years old).*

In recent years factor replacement treatment has improved significantly, which has made it much easier for patients to keep to their regimen. Key improvements include the reduction in volume (making it easier to mix up and requiring much smaller syringes); easier to store and transport (it does not require refrigeration and the boxes are much smaller) and the improved instructions on the packaging (particularly helpful in emergencies when other people may need to mix up the treatment).

None of the participants suggested that these improvements have had a direct positive influence on their adherence, particularly as their adherence was generally already quite high. However, they felt that taking their treatment has become a lot easier and less time-consuming, which in turn may reduce negative associations with treatment and therefore reduce the risk of patients skipping treatments.

> *It's a lot smaller now, so it's a lot easier. You haven't got to take these massive bottles which takes hours to mix up. It's all very easy, you squirt in, you squirt out, and it's all very quick these days (P.5, 25 years old).*
>
> *It used to it had to be kept like fridge cold. But now it's more just under more like room temperature which is fine. Which makes life quite easy (P.2, 24 years old).*

As described above, non-adherence in this patient group tends to be due to forgetting. Many participants described easy and practical solutions that help them to remember to take their treatment, such as visual reminders (e.g. putting the bright yellow sharps bin on the breakfast bar); linking treatment to particular activities (such as having breakfast); and digital reminders (alerts on a mobile phone, tablet or computer).

It appeared that they were keen to find their own solutions, and were therefore not always keen to discuss different strategies with the haemophilia team. Participants appeared to feel that people need to find their own way of managing their treatment, as everyone is different and has their own challenges to overcome. For instance some were keen to use their smartphone for reminders,

whereas another participant explained that he would never trust a digital device alone without a back-up reminder.

> *So it would make a noise or whatever, so you'd know it was that day. But that's just then trusting a device to tell you when to do it without thinking… (P.3, 21 years old).*

Despite the various reminders, and the motivation to keep to their regimen, some participants admitted that they do occasionally forget their treatment. This is often because they live busy lives, and are sometimes distracted by other priorities. However, they tend to have some treatment stored at work or school so that they can take their treatment there in case they have forgotten to do it at home. Having some treatment stored at work or school provides an extra safety net, which seemed particularly important for those participants who do not like to take any risks with their health.

> *but I've also got some at work. You know, just in case I need it. Like in an emergency, which I've had to before. Or just in case I forgot to take some with me, so there's always some there (P.3, 21 years old).*

Subtheme 4: Treatment protects me so I can live a normal life

Many participants explained that they feel their prophylactic treatment protects them, and allows them to live a normal life. For some that means that they feel protected in everyday activities, such as going to school or work. Others feel that prophylaxis supports them in living a very active lifestyle, including competing in top-level sports.

> *It's helping me lead a normal life. (P.2, 24 years old)*
>
> *The treatment works quite well, it stops most bleeds. It's only the serious ones that get through now. We do a big dose before and after the activity … I'll still get a small bleed but nothing like as bad as I would get if we didn't (P.9, 16 years old)*

Many of the young people explained that they top-up to cover themselves for sport and physical activities. Most seemed to recognise that in addition to reducing the risk of bleeds, prophylactic treatment helps to prevent long-term issues such as joint damage.

> *If I don't take my medication I'll start getting internal bleeds that's going to affect me later in life with joint damage and what not. (P.2, 24 years old)*
>
> *You do get a better treatment, you develop more chances to progress yourself with the time. (P.6, 22 years old)*

6.3.5 Theme 4: Support from family, friends and the haemophilia centre keeps me on track.

For the young people involved in this study looking after their health includes a number of self-management behaviours, some of which can be quite challenging. The majority of participants felt that they would not be able to look after themselves without support from their parents and the staff at the haemophilia centre. This theme covers all the forms of support that were described by participants.

Subtheme 1: Support from mum and dad is key

During the course of this research it became clear that parental support is particularly important in relation to adherence. As described above, in the majority of families parents are responsible for their son's treatment for the first decade or so. This means that they have to inject their son several times each week, log each treatment on the log, arrange for treatment to be delivered, arrange regular hospital check-up appointments, and be on stand-by just in case their son experiences a bleed at school.

> *I think they was always worried and mum would come into school every now and then to give me treatment and things if I needed, if I fell over in the playground or, you know, when I was younger they'd come in and they'd say, you know "I'm here, we need to do this, we need to do that". (P.10, 21 years old)*

Parental support appears particularly important in encouraging adherence, as parents tend to remind their son to take his treatment every time it is due. Some parents continue to remind their son to take his injections even after he has left home, this appears to be a habit of a lifetime that is difficult to break. Many parents also continue to do the actual injection every now and then, just to share the burden or make life a little easier for their son.

> *and that's something just at times, especially when you're growing up sometimes, like once a week for someone to mix it for you so you ain't got to worry about it, it's just "here you are, I've done it", ain't giving it, it's just mixing it, especially when there was a lot of it, it was really tedious (P.11, 24 years old)*.

Two participants, both living independently, described how their mother still telephones them most days to remind them when their injection is due. Parents often also stay involved with arranging the deliveries of treatment, and continue to help when bleeds or other health issues occur.

> *now that I am a bit older I am quite self-sufficient with it, but uhm cos I travel a fair bit so my mum looks after, the treatment gets delivered to my mums house rather than mine, cos uhm mum is in a lot more often than I am. She'll keep an eye on my stock I've got. Uhm so, yeah they are still. Yeah everyone supports me really nicely (P.2, 24 years old).*

In addition to caring for their son, some parents become involved with organisations or charities that support people with haemophilia, such as the Haemophilia Society (a nationwide charity that supports patients and families that are affected by bleeding disorders). These organisations are involved in a range of activities, including fundraising, lobbying and peer support, and become an important part of a family's support network.

> *Yeah. She's still doing events and things, you know, she's helped me raise money for the run just gone, she helped me get the shirts for me, sponsor forms so, you know, she's still very much involved in that kind of thing and she likes to raise money just as much as me so—(P.10, 21 years old).*

Subtheme 2: Social and peer support

In addition to support from parents and siblings, many patients described a supportive social network they could rely on for practical and emotional support.

> *And especially with the friends who I've been on holiday with they understand it a lot better because I understand their problems they understand my problem, we know what our limitations are--and we can just stick together make sure each one of us completes it (P.1, 17 years old).*

Whereas some others felt that they did not need any support or help from friends, possibly because they are very keen to be independent, or find it hard to accept help as this could be perceived as a sign of weakness.

> *Not really, to be honest because I feel, I don't normally like to rely on other people, I like to keep it to myself and just do it on my own basis so that behaviour may be just I don't rely on-- I don't normally just ask them, oh can you do this thing for me, do that thing for me, I normally keep it to myself (P.6, 22 years old).*

As described above, some participants felt that they had missed out on social development due to their haemophilia. This appears to be particularly relevant for participant 1, who felt that it took him a

lot longer to develop his social skills, and therefore found it difficult to make friends and form relationships. This participant appeared to have quite ambivalent feelings about the way his haemophilia affects him. He felt quite strongly that he would not let his haemophilia hold him back, but also described how he felt that there are many limitations to what he can do due to his condition.

> *I try not to let the Haemophilia hold me back, but the fact that we'd been told that I shouldn't-- to kind of protect me, that I shouldn't really go out at break or lunch-- that was what held me back (P.1, 17 years old).*

Advice about what activities children with haemophilia should avoid has changed in recent years, and many boys are now allowed to take part in physical education lessons at school as long as they avoid contact sports such as rugby and hockey. Any activities that may cause head injury need to be avoided at all costs, as intracranial bleeding represents one of the biggest risks. However, it is unlikely that young boys who are growing up with haemophilia today are excluded from playing outside at break time at school. Hopefully this means that this new generation is able to take part in most activities at school, and does not miss out socially. This in turn may help them develop social skills and form supportive friendships. This certainly appeared to be the case for the younger participants in this study, who described very supportive friendships.

> *It doesn't really bother me that much now because most of my friends at school help me. It feels alright because most of my friends know about it and they to talk to me about it (P.8, 12 years old).*

> *Sometimes when I'm at school I do talk about it or like if I say I'm in pain they normally help me and take me to a teacher (P.4, 12 years old).*

One form of social support that may be particularly helpful is peer support from other young people who are affected by haemophilia. As it is such a rare disease, patients do not often meet other people who are affected. Participant 3 joked that he always felt that he was the only person with haemophilia, even though he knew from the hospital that there were other boys. Now that he is in his early twenties he receives psychological support from a counsellor to help him talk about his haemophilia and the way it has affected him. It may have been quite helpful for him to meet with other boys like him when he was younger, and may have helped him feel less alone with it all. Some of the hospitals that were involved in this study have peer support groups, and organise social outings to give YPH the opportunity to meet each other. Pressure on budgets and resources make it hard to keep these activities going, and in some of the hospitals they have now stopped.

Interview participants indicated that they had benefitted from opportunities to interact with other YPH outside the hospital setting.

> *It's really good spirited, everyone's in a good mood, they do swimming and things and it's for charity and there's bike rides and things, haemophilia so, I think mum puts her effort in and so do all the other society people, they put their effort in and get kids involved and get their husbands involved and their mums involved so it's fun. I enjoy it, yeah. (P.10, 21 years old)*

Subtheme 3: Haemophilia care in the UK is second to none

People with haemophilia in the UK receive their treatment from the NHS free of charge. Haemophilia can affect patients in many different ways, and different treatments can impact on each other (e.g. dental work can cause severe bleeds, and so needs to be planned in conjunction with the haematology team). For this reason haemophilia care is often centralised through comprehensive care centres (haemophilia centres). These centres are able to deliver different care needs directly, or through collaboration with other local centres (including musculoskeletal care, dentistry, physiotherapy, etc.). The experiences of patients who have come to the UK from other countries illustrates that haemophilia care in the UK is amongst the best in the world.

> *since I came here I was trained myself to give the treatment, coming up, look this is on three months, every three months, getting communication whenever I need them, trust me, it's the best support I can get ever so I think I wouldn't give any more suggestions to getting things from the right places because to me, it's organised..(P.6, 22 years old)*

Although having haemophilia has had a negative impact on many of the participants in this study, several described how they felt lucky to have been born in the UK, as they realised that they would not receive such excellent healthcare in some other countries.

> *I know, I've read, I've seen stories from other countries where there isn't the support there isn't the treatment and it's you know, it's killing kids basically. It's uh they're just leading just horrible lifestyles, it's yeah it makes me feel lucky that we've got the system in place we have. (P.2, 24 years old)*

Participants were particularly positive about the support they receive from the team at the haemophilia centre, recognising that this support helped them keep on track with their treatment and helping them through difficult situations.

Subtheme 4: The staff at the haemophilia centre is very supportive and they encourage me to keep to my treatment regimen

The majority of patients appear to have a good relationship and regular contact with the team at the haemophilia centre. Sometimes this is just informal contact to check how patients are doing, and other times it may be specifically aimed at providing support or solutions for specific issues. Many of the HP I came across have worked in the same haemophilia centre for a number of years, and have seen patients grow up from babies to adolescents and young adults. As a result they know most of their patients well, and appear to have a sixth sense on when particular individuals needs additional support.

> *Yeah, it's nice to know, they ring up and ask and they're concerned and, you can, obviously it was a mistake on my behalf so I said like no, and they told me how to do it properly and generally it was, the nurses are good I think, yeah, they're okay. They help out as much as they can and it was good that they're keeping an eye on me really. (P.10, 21 years old)*

In all of the haemophilia centres that were involved in this research nurses appear to keep a close eye on their patients, particularly those who suffer from regular bleeds. They tend to do this by logging onto the online treatment log (Haemtrack) to check if patients have logged any bleeds and also to monitor prophylactic injections.

Haemophilia centres encourage patients to contact the centre whenever they have a serious bleed, so that they can assess if the patient needs to come to hospital or if they can treat the bleed themselves at home. In many cases where a review of Haemtrack reveals that a patient may not be adhering to their agreed treatment regimen, or has had a serious bleed without contacting the centre, nurses contact the patient to discuss potential issues. This appears to encourage patients to adhere to their prophylaxis, and stay on top of managing any bleeds.

> *Generally the nurse will ring up and say "you've had a lot of factor, we're looking on your Haemtrack, you've had a lot", I think one time they'd mistaken, I had this ankle injury but I kept putting it was a follow-up bleed, because it was the same sort of bleed reoccurring again, but in fact I should have done new bleed every times, so it looked like I'd had this bleed for like nine hundred hours or something. So then they rang up and was like "look, is this bleed this bad or is it because it's, you know, it's reoccurring but is it because it's a new bleed? (P.10, 21 years old)*

It appears that many haemophilia centres use the carrot and stick approach, where they combine regular encouragement and support with a telling off when patients are not adhering to their treatment.

> *I know definitely you do get the same motivation when every time I go for the clinic appointments, trust me, I do get a big lecture! (P.6, 22 years old).*

Regardless of how the different haemophilia centres approach different patients, all participants in this study were very positive about the healthcare and support they receive. It is clear that patients receive more than just medical attention from their haemophilia team, and that nurses, haematologists, psychologists, physiotherapists and other allied health professionals often go out of their way to support their patients.

> *Support from the centre makes me feel less alone (P.3, 21 years old)*
>
> *The nice thing for me is I know they're there if I need them (P.2, 24 years old)*

One example that illustrates the faith and trust that patients have in their NHS haemophilia centre is of a patient who experienced a medical emergency abroad. He was in great pain, but chose to travel back to England to make sure that his injury was treated in the haemophilia centre he has been attending since he was a baby. He believes that the care he receives through the NHS is unrivalled, and trusts the NHS with his life.

> *I phoned the doctor at 1 o'clock in the morning cos I needed surgery and he he was there. And I mean you don't that sort of service is unrivalled I think by anywhere…I had my car and I drove drove back to England to make sure I was treated in England cos I trust yeah I trust the NHS with my life basically. So it was so uh see that's the extent that I yeah trust the NHS. (P.2, 24 years old)*

6.4 Discussion

The findings of this study suggest that haemophilia can have a significant impact on young patients' lives, even for those with few symptoms or haemophilia-related issues. Often diagnosed at a very young age, haemophilia becomes part of who patients are and the way they live their lives. Participants appeared very keen to live a 'normal' life, however for most of them managing risk is an important part of their daily routine. For many participants there appeared to be a tension between their desire to be normal and successful self-management.

Self-reported adherence in the sample appeared to be good, with few participants admitting to intentionally skipping injections. However, due to the increasingly personalised and flexible approach to prophylaxis adherence is not straightforward to define. Several participants appeared

slightly confused when describing their own levels of adherence, particularly when they were asked to distinguish between forgetting and skipping.

The main barriers to adherence suggested by participants were the time and effort needed to take treatment (fitting this in an already busy lifestyle) which at times causes them to forget; dislike of the intravenous injection; venous access issues; anxiety or stress (both related and unrelated to haemophilia); and being out of the normal routine (e.g. on holiday).

The majority of participants described how support from their family, friends and haemophilia team helped them to keep on track with their treatment. In particular parents appear to be very involved with their sons' haemophilia management, even after they leave home. Almost all participants agreed that they have a good relationship with their haemophilia team and that the help and support they receive from them helps them to keep on track with their treatment.

There is significant overlap between the results of the three qualitative studies included in this thesis (investigating experiences and perceptions of patients, their parents and HP respectively). And because the findings also appear to complement each other, it was decided to include one comprehensive discussion chapter (chapter 9) that will describe the findings, implications, strengths, weaknesses and conclusions of all three qualitative studies.

Chapter 7: Interpretative Phenomenological Analysis of parents' accounts of prophylaxis and their sons' adherence to this treatment

7.1 Introduction

This chapter presents the results of the Interpretative Phenomenological Analysis (IPA) of participants' accounts in relation to their son's haemophilia, and his prophylactic treatment. The aim of the study is to examine parents' experiences and perceptions in relation to prophylaxis, and adherence to this treatment, and the way they make sense of these experiences and perceptions. Together with the findings of the IPA studies described in chapter 6 (young people with haemophilia, YPH), and chapter 8 (haemophilia healthcare professionals, HP), this study is anticipated to contribute to a better understanding of facilitators and barriers to adherence to prophylaxis among YPH.

7.2 Methods

7.2.1 Recruitment

Participants were recruited in five haemophilia centres across England and Wales. Potential participants were approached while they accompanied their son while he attended a routine check-up appointment in the haemophilia centre. All participants who met the inclusion criteria (parent of a young person aged 12-25 inclusive, who has been diagnosed with severe haemophilia and follows a prophylactic treatment regimen) were approached by a nurse or doctor to invite them to participate in the study. All participants who agreed to take part were interviewed.

7.2.2 Participants

Participants were two males and two females who were all parents to a young male with haemophilia (see Table 7.1 for details). To protect confidentiality and anonymity, the parents interviewed were not related to participants interviewed for the study described in the previous chapter.

Table 7.1: Parent interview study participant characteristics

Participant code	Ethnicity	Sex	Age of son with haemophilia	Other children	Other children affected	Living arrangements
Parent 1	White British	Male	24	Yes	No	Son lives with his wife/partner and child(ren)
Parent 2	White British	Female	24	No	-	Son lives with his wife/partner and child(ren)
Parent 3	White British	Female	14	Yes	No	Son lives with parent
Parent 4	Black African	Male	15	Yes	No	Son lives with parent

7.2.3 Data collection

Each participant was interviewed face-to-face in a private room at the haemophilia centre. The interviews were semi-structured using a topic guide (appendix 5.1), however participants were encouraged to tell their own story in their own words and time with few interruptions from the interviewer. At the start of their interview participants were invited to describe their experiences in relation to their son's haemophilia, starting with what it was like when he was born and diagnosed. The main aim of these introductory questions was to build a report with participants and to gain a sense of how they felt about their son's haemophilia. To gain a good insight into their experiences and perceptions in relation to their son's prophylaxis, they were then invited to describe their son's treatment regimen, their feelings about prophylaxis, and potential barriers and facilitators to their son's adherence. Lastly participants were asked about the social support they receive in relation their son's haemophilia, and what support they offer to their son in relation to his haemophilia and treatment. The order in which the above subjects were discussed was flexible and driven by the way in which the conversation with participants developed. Several of the participants explained that they had not been asked to share their experiences in relation to haemophilia before. These individuals were grateful for the opportunity to share their experiences and keen to share their story about their entire haemophilia journey. In these circumstance prompts were used to bring the discussion back to experiences and perceptions in relation to prophylaxis.

Interviews were recorded and then transcribed verbatim before being analysed following the IPA.

7.2.4 Analysis

As described in chapter five, IPA emphasises that through the process of discovering themes the researcher aims to make sense of the participant attempting to make sense of their experiences. Therefore these themes form only one possible account, and the researcher may have reached different conclusions and highlighted different aspects in comparison to what other researchers may have found if they had analysed the same data.

After immersion in the data, and examining themes and the convergence and divergence of themes, it was decided to report those themes that emerged most strongly from the interview data and that were relevant to the research questions. In this chapter these themes will be explored and illustrated with verbatim extracts that were selected from across all participants' transcripts. In instances where different participants had different opinions or experiences, all views are illustrated. In cases where participant responses were similar, only those quotes that illustrate the theme most clearly have been included. This approach was true to the aims of the study, participants' accounts and the richness of the data.

7.3 Results

7.3.1 Superordinate and subordinate themes

At the start of their interview parents were invited to describe their experiences in relation to their son's haemophilia, starting with what it was like when he was a child. They were then asked about their perceptions in relation to their son's prophylactic treatment and barriers and facilitators to his adherence. Participants' accounts clustered around four superordinate themes, which are shown in in table 7.2 together with their related subordinate themes. The table also shows for which participants each of the subordinate themes were relevant.

After examining themes and the way in which they were embedded and linked, and after immersion in the data, it was decided to report the master themes which emerged from the transcripts and that were relevant to the research questions. In this chapter these themes will be explored and illustrated with verbatim extracts from the interview transcripts. The illustrated quotes were taken from across the transcripts of all the participants, to ensure they were representative of the sample.

Table 7.2: Parent interview study superordinate and subordinate themes for each participant

Superordinate themes	Subordinate themes	Participants			
		Parent 1	Parent 2	Parent 3	Parent 4
Self-management	Logging treatment on Haemtrack	x			x
	Avoiding risk	x	x	x	x
	Treating bleeds	x		x	
Drivers of adherence	Barriers	x	x	x	x
	Facilitators	x	x	x	x
	Skipping or Forgetting?		x	x	x
Impact of haemophilia	Social impact	x	x	x	
	Impact on academic and career prospects	x	x	x	x
	Impact on parents and siblings	x	x	x	
Haemophilia care	Support from haemophilia centre	x	x	x	x
	His haemophilia has become part of our lives	x	x	x	x
	Haemophilia awareness needs to improve		x	x	

7.3.2 Theme 1: Self-management

In addition to adhering to their agreed treatment regimen, YPH are expected to engage in a number of other self-management behaviours. This theme encompasses all of the behaviours that were described by parents that were interviewed for this study, including logging treatment, avoiding risk and treating bleeds.

Subtheme 1: Logging treatment on Haemtrack

Patients who receive home delivery of their prophylactic treatment are required to log each treatment they take. Treatment logs enable the clinical team to monitor their patients, check if they adhere to their treatment, treat bleeds appropriately, and do not waste treatment. Treatment logs can also be useful starting points for discussions between clinicians and patients about treatment, and help decide if a patient is on the right regimen. Haemtrack is a UKHCDO (United Kingdom Haemophilia Centre Doctors' Organisation) system that allows patients to log their treatment online or via a smartphone app. It works like a diary, where patients can add their treatment and other details including date and time, the product used and the reason for treatment. Haemtrack data is

saved in the National Haemophilia Database and helps the UKHCDO to plan haemophilia services, inform purchasing decisions and to learn more about the treatment and complications of bleeding conditions. Haemtrack is now part of standard care, and most haemophilia centres require their patients to use it. However, in some cases patients continue to complete paper treatment logs, which are then transferred to Haemtrack by the haemophilia centre.

Most patients, parents and clinicians who were involved in this study recognised Haemtrack as a useful tool. However not all patients appear to complete Haemtrack as required. Parents appeared to be keen for their son to log each treatment on Haemtrack directly after taking it, but recognised that this was probably not realistic. Completing Haemtrack is just another thing to do, which competes with the many other activities that keep young people busy.

> *In terms of keeping the records up to date, that is still a work in progress. Because if he has an injection in the morning with a view to entering it on the system later in the day, the likelihood that it will get forgotten is fairly high. I'll probably search the App Store and see if there's anything on Haemtrack that will be more convenient for him because he's always on the phone anyway [laughs] so as soon as he's had his injection that would be quite easy to upload details on the phone. (Parent 4)*

Interestingly, there does not necessarily seem to be a relationship between adherence to treatment and adherence to completing Haemtrack logs. It appears that even young people who take their treatment religiously do not always complete their logs.

> *I think it probably would if, um, especially in terms of recording [laughs] his details on the, on the Haemtrack because that's the one area that is still hit and miss because he will have his, um, treatment but may not record it on Haemtrack so-- (Parent 4)*

Subtheme 2: Avoiding risk

Parents of children with haemophilia learn early on that even low-risk day-to-day activities can cause harm to their child. Diagnosis is often preceded by severe unexplained bruising, caused by small bumps and falls as babies learn to crawl and walk. As children grow up and become more physically active there are often frequent visits to the hospital to receive treatment for activity-related bleeds, and a significant percentage of patients develop joint damage caused by repeated bleeding. All the parents who were interviewed for this study explained that they worried about the potential risks of physical activity, and that they were always conscious of ways in which they could reduce or manage the risk for their son.

Parents described how they had limited the physical activities that their son could take part in, usually on advice of the haemophilia team. For most this meant that their son was able to take part in Physical Education (PE) at school, but only in sessions that did not involve high risk sports (such as rugby and hockey). However, two parents described how their son was not able to participate in PE lessons at all. In both cases this was because the combination of haemophilia with other medical issues, such as loose ligaments, significantly increased the risk of bleeding.

> *No, he hasn't been able to do PE for a couple of years now, because he got to the risk, the risk factor was there. Like, if he joined in, because his ligaments were so loose, he'd go over, then there'd be a bleed, so it was a case of, you know, what can, what can he do that wouldn't cause bleeds. (Parent 3)*

Reducing risk can also have negative consequences. Being involved in sports and other physical activities has been shown to positively influence physical and mental health, which some YPH may miss out on. One of the parents expressed concern about his son limiting his participation too much for fear of injury, and was worried that he would miss out on things that he loves doing as a result.

> *but I sort of worry as well as to whether he's maybe sort of limiting his activities in fear of whether or not he's going to have a bleed because he does play football, he does participate in school activities but as you say he is a teenager now and sometimes it's not very easy to know exactly what he's doing or why he's doing it. He says he plays football in school, he plays basketball in school but I sometimes worry whether he's sort of limited his participation in those for fear of either injuring himself or aggravating an injury. (Parent 4)*

All parents recognised that it was important for their son to be physically active, and it appears that most would organise alternative activities, such as swimming, to ensure that their son would get sufficient exercise.

> *so he's had his legs in splints and all sorts, so we just came to the decision that, you know, no PE, but what we've had to do with him is like do a lot of taking him swimming, like after school, and things that aren't so harsh on his body, just to keep him sort of with some exercise. (Parent 3)*

The interviews with parents supported the findings of the patient interviews, highlighting that managing risk is an important consideration in daily life. In addition to taking treatment and reducing risky activities, this also includes avoiding potentially dangerous situations. This influences academic and professional choices, as certain career choices would not be appropriate for

someone with haemophilia. It also impacts on social life, particularly for young people who want to enjoy the nightlife with friends. This is not just because consuming alcohol increases the risk of accidents, such as falling or bumping into things. It is also because people in groups sometimes get involved in physical confrontation, whether that is 'play fighting' or brawling.

For parents this means additional worry when their son wants to go out independently with friends, and often means they are 'on-call' to pick him up at any time during the night.

> *If they're going off and they're getting into trouble, just ring me and I'll come and get you, it doesn't matter if it's two, three, four o'clock in the morning," and very often I'd have a phone call, "Oh mam, the boys are messing about, can you come and get me," so yeah fine (Parent 2)*

Although parents described how they would worry about their son going out with friends, they also recognised that that he was probably more sensible and responsible that any of his friends. Several of the parents felt that their son was probably more sensible because of this haemophilia.

> *because he's haemophiliac he don't back down, he knows he's got to be careful, it's like if he sees a gang of lads, a confrontation, he'll say no, I can't get involved and walk away. (Parent 1)*

Subtheme 3: Treating bleeds

Very few patients do not experience any bleeds, even those who regligiously adhere to their prophylactic treatment may experience occasional bleeds. For some patients this may only be once a year, whereas others suffer from more regular bleeds that have a significant impact on their lives. Treating bleeds quickly and appropriately is very important to prevent longer term problems. Most haemophilia centres encourage patients to contact the centre when they are experiencing a bleed, so that they can assess (over the telephone) if the patient can treat the bleed themselves or if they need to come to the hospital.

> *That was good like that, you could phone the hospital at any time of day, I mean even if it was out-of-hours, the doctor would come on the phone or phone you back. They'd say, give him 2000 units or whatever they wanted you to give him, if there's no improvement tomorrow bring him over or they'd say, bring him over and they'd give him treatment there at the hospital and then they'd say, treat him every day with so many units and if by Friday he's no better, I mean I phoned back every day (Parent 1)*

Parents appeared to be aware of the importance of treating bleeds appropirately, and felt this was just as important for their son as him adhering to his prophylactic regimen. In particular one of the parents voiced concern about bleeds, as he feels that perhaps his son does not take them seriously enough.

> *That's what I keep saying to him, all of them are the same because to them it's just life, it's a bleed, you know what I mean, they don't think. 'Oh well, Dad I'm used to it, I've grown up with it'. Yeah, but you still need to put it on your computer, I've had a bleed in the left leg, right leg, arm, just so they know, I say so they know what's going on with you and they're all the same because they've grown up with it, some of the kids, they don't put it down and it's just another day in their life. (Parent 1)*

It became clear that each of the parents interviewed are very involved with their son's treatment, even parents of young adults who no longer live at home. In particular at times when their son is suffering with a bleed they tend to be there to offer practical help (such as driving him to the hospital), but also to support him in treating the bleed and deal with the hospital if needed.

7.3.3 Theme 2: Drivers of adherence

This theme encapsulates all barriers and facilitators that influence adherence among YPH, as perceived by their parents. As discussed in the previous chapter, each individual is different and is therefore likely to have different experiences in relation to their haemophilia and prophylactic treatment. However, during the interviews it became clear that there were commonalities in relation to the barriers and facilitators to adherence that different participants described, and reasons why they believe their son may forget or skip some of his treatments.

Subtheme 1: Barriers

Lifestyle

One of the main barriers mentioned by parents was that their son's busy lifestyle sometimes interferes with treatment. Patients who have to get up early to go to school or work may find it difficult to take their treatment in the morning. Particularly when they get up too late, or have other important things to do.

Others may be preoccupied with other things they have to do, which can lead to them procrastinating their treatment.

> *But when he was younger, me and his mum, we made sure we done it, he got it done but when he left home, I think it was just the hustle and bustle of daily life, I'll do it in a minute, that's younguns for ya, everything's in a minute and in a minute never seems to come (Parent 1)*

Routine

Being out of your normal routine can also make it difficult to take treatment. For instance, when you are on holiday you may forget what day it is, or be distracted by holiday activities. It is also likely that a different sleep pattern on holiday influences the time treatment is taken. Most parents explained that forgetting one treatment usually is not an issue, as they just compensate for it by moving the treatment days for the rest of the week. However, these ad-hoc changes to the regimen can lead to confusion and more missed treatments

> *I think there was when I was on holiday, because I forgot my days, because when you're relaxing, you've gone two weeks, but it was only a case of, I'll just give him the treatment today and then move it on another couple of days. So you just have to remember they've still got to have it, but just move your next lot on another couple of days and then your week just sort of sorts itself out (Parent 3)*

Not wanting to be 'different'

During the interviews it became clear that parents felt that not all missed treatments are due to forgetting. All parents described periods, mainly during adolescence, during which their son was reluctant to take his treatment or would miss treatments because he did not feel like taking it.

> *I think between the ages of 13 and 15 there's a time there when things were not really working properly and you check whether or not he's had his treatment and sometimes he wouldn't have had or he would say he had his treatment but when you try to harmonise the quantities available as compared to what he said he had used then they were not actually matching up but I mean we sat down, we had a discussion with him about the importance of continuing with the treatment, of course with the nurse upstairs, just to totally emphasise that (Parent 4)*

Parents felt that this was probably because their son did not want to be different to his peers, and resented having to inject himself with treatment so frequently.

> *Oh what's the point, you know, oh why?" he's gone through moments like that and like when he was younger growing up he refused to have his treatment, "I don't want my treatment, I want to be normal, I want to be like everybody else, I don't see why I should have to have these all the time," (Parent 2)*

Venous access and needle phobia

Other reasons why young people may not want to take their treatment are issues around venous access and needle phobia. Patients who have difficulty in accessing their veins often require help with their injections, and may come to the hospital to receive treatment. However, this is not feasible for patients who are on regular prophylaxis because of the number of injections they require. In many cases this means that a parent or other caregiver continues to do the treatment until the patient is able to inject himself.

> *Yes, sometimes his veins are really bad and that's when his wife will ring me, "Oh can you come up?" 'cos sometimes we've been down here and depending sometimes on who does it, if he's having a bad day and I'm down here and they've tried a couple of times I'll do it, and but yeah sometimes his veins are absolutely horrendous, especially if he's not well as well, if he's got something else going on, you know, like if he's got a cold or tonsillitis or something, then his veins are (Parent 2)*

During the interviews it was not always easy to distinguish between venous access issues and needle phobia, as the two can be related. It appeared that for patients who have difficulty in finding good veins taking treatment can cause anxiety, which in turn can lead to needle phobia. Resolving needle phobia can be a complex situation, which not only requires a patient to overcome their anxiety and fear, but also requires their parent to let go and allow their son to become independent. One of the parents explained that for the time being it was just easier to continue doing the treatment for their son, not only because he has some issues around venous access, but also because he appears to suffer from needle phobia.

> *I still do it for him because he can't do it himself. Just the idea of sticking it into himself, he's all caggy hands, because he's only got one arm which is good with the veins, and you can guarantee, usually that's the arm he's hurt [laughs]. So it's not, I keep asking him to do it. And probably, if he stays on it in adult life, that maybe he'll start doing it himself then*
>
> *(Parent 3).*

Other psychological issues

In contrast to needle phobia, some of the other psychological issues that were reported by parents are not necessarily as clearly associated with prophylactic treatment. However, parents felt quite strongly that their son's issues (such as OCD, and general anxiety and stress) were directly related to haemophilia and the treatment.

> *My son's got OCD and I'm convinced it's from, I don't know whether it's from spending so much time in the hospitals, and with the haemophilia and having to do everything a certain way but he's got terribly OCD (Parent 2).*

Although it would be difficult to confirm whether haemophilia directly causes psychological issues such as anxiety, it is clear that parents felt that haemophilia plays an important role. They also felt that anxiety or external stresses (such as bereavement) interfere with haemophilia treatment and sometimes directly cause physical symptoms such as bleeds.

> *Since we found out about my mum having cancer, they told us the end of January that there was nothing they could do for her, and she went in the hospice for some respite, on then they told us that she only had a couple of days to a week and… obviously then we told him and since then he had a bleed then a couple of days later, so I do think stress plays a part in it (Parent 2).*

Although it would be hard to prove a direct causal relationship between haemophilia and the psychological issues that parents described, it is clear that those patients who suffer from stress or anxiety find it harder to manage their haemophilia, and may suffer physical symptoms such as bleeds as a result of their missed injections. In turn, these physical symptoms are likely to cause more anxiety or stress. Equally, it is likely that patients who have experienced frequent and/or severe bleeds are more likely to suffer from psychological issues due to the pain, stress and lifestyle-limiting physical symptoms caused by bleeds. It became clear from the parent interviews that young people who suffer with treatment-related issues (such as venous access or needle phobia) also suffer from other anxiety or stress-related issues (such as stress-related migraines).

> *he said his head feels like it's exploding, like they're sitting him down and they're asking him questions and everything, and yet the neurologist has said, "He knows how to try and de-stress himself", take yourself away, quiet room, you know, and everything (Parent 3).*

Subtheme 2: Facilitators

Routine

As time passes many patients and their families find their own solutions to make remembering and taking treatment easier. These solutions tend to be very specific to each family, depending on their individual circumstances. However, one key thing that they all agreed on was that it is important to establish a good routine, which helps you to remember when treatment is due. The regular time also allows patients to set reminders or alarms for themselves, or for others to send them reminder messages.

> *Well obviously doing it at a regular time, that's got to be most important because they-- generally with the prophylaxis it's normally say like a Monday Wednesday and a Friday anyway, or Tuesday, Thursday, Saturday. So I think that would be quite easy generally to implement. Just send reminder texts or emails, but yeah I think a reminder text would probably be the easiest. (Parent 2)*

Building the treatment into the routine also means that the extra time that is needed to take treatment is planned for. So in most families this means getting up a bit earlier, getting breakfast ready the evening before, or finding a quicker way to get to work or school to compensate for the time spent on treatment.

Maturity and independence

In addition to establishing a good routine, parents felt that it is important to talk to your son about his haemophilia and treatment. This may help them understand why taking treatment is so important, and help them develop the maturity and self-management behaviours that are required.

> *I think we had that discussion just explaining the importance of continuing to take the treatment in order to prevent something from happening rather than trying to address it once it had happened. I think as you imply sort of it's part of the maturing process. I think he can see that correlation quite clearly now and he appreciates that it's no good lying in hospital while you could be out doing other things. If just by complying with his treatment he can prevent himself from having to, to come into hospital and all that then everything works out alright (Parent 4).*

However, most parents also agreed that it is important to give young people some leeway and give them the room to find out for themselves why their treatment is so important. For instance, if they miss out on activities or opportunities to have fun because of a bleed, they may come to accept that they need to take their treatment in order to prevent bleeds.

> *Um, I remember a few years ago when there was, um, the tall ships thing and we had all planned to, [laughs] to go and attend and see but he couldn't because he was in hospital, I think he didn't really like that (Parent 4).*

Parents agreed that it is likely to be much more powerful if young people find out for themselves why their treatment is so crucial, and that nagging them to take their treatment all the time can have a negative impact.

> *You can't make them. And it doesn't matter how much you tell them they need it. Whether he's got a bleed at the time it doesn't matter, because if they dig their heels in there's no point. So it's, fine, whatever, just go and do what you want to do. Go on your computer for an hour, go chill out, go de-stress and I'll come up and we'll have a chat in a little bit and that's the only way you can do it and that's the way that I've learnt over the years to counteract, you know, he's saying no I don't want my treatment, I want to be normal and that's the only thing you can do. It's just patience really, just learning as well about your child because you know, with him, that you leave him be for a little bit instead of-- you know, just calm down and get over his rant then he's fine, and that's all you can do, yeah. (Parent 2)*

Social support

For the majority of parents interviewed their son was the first person diagnosed with haemophilia in the family. However one of the parents explained that she and her sisters all have sons who are affected by haemophilia. Although this has caused much upset and difficulty for the family, it has also meant they were able to support each other much better as they all understood the specific issues associated with haemophilia.

> *Yeah, it probably has because there is quite a few boys, so it's almost like haemophilia's normal, I think (Parent 3).*

In addition to social support from family, parents felt that support from the Haemophilia Society had been important. They described a range of different ways in which the society had supported them, including help with accessing financial support, giving advice, and providing a support network. The

haemophilia society organises peer support groups and activity breaks for YPH, which allow them to socialise with other young people affected by haemophilia. Parents felt that their son had benefited from attending these activity breaks, as they had provided informal opportunities for him to learn and talk about haemophilia outside of the hospital or home environment. They also felt that it had probably helped them to step back and allow their son to become more independent.

> *When he was a kid, he's gone on holiday with them because they have a nurse with them and it's made a difference. The first time he went away his mum was worried. He only went for seven days. I said don't worry. Phone him every day, because there's a nurse there. And he had a fabulous time. So some things he might have missed out on, but he made up in other ways (Parent 1).*

Some haemophilia centres provide peer support groups for YPH, or even organise social outings. It appears that some hospitals have stopped or reduced these activities, mainly due to pressures on funding. However, parents were keen for the hospitals to continue to provide these activities locally, and would encourage their son to attend.

> *He quite enjoyed that but there hasn't been anything like that as far as we're aware since. But activities like that when they're available I think would be useful in sort of getting them together, exchanging ideas with other children with haemophili. I know there's the Haemophilia Society but the activities here at the hospital probably something that we need to encourage him to participate a bit more, yeah (Parent 4).*

One parent also suggested that it would be a good idea to put parents of children with haemophilia in touch with each other, to encourage informal support between parents.

> *You've got the option to say, "Oh hi, I'm such and such, I come down to the Haemophilia Centre as well and I understand you've get a little boy who goes there," and yeah it would help. Be nice to have a chat and go for a coffee, or even just have somebody at the end of either the telephone. You could say, "Oh hi, how's your day been, how's your little one, have you been down the centre lately, has he had any bleeds? "Ooh mine-- we've had three bleeds in the last month, how's your little one doing?" Just something like that (Parent 2).*

Psychological support

In addition to clinical care, some haemophilia centres also provide psychological services to their patients. Some centres have their own team of psychologists embedded in the haemophilia centre, whereas others have close links with psychologists who are attached to the hospital or are able to refer patients to a local psychological support service. Only one of the centres involved in this study has direct access to a psychologist, who sits in on many of the routine check-up consultations. The psychologist is therefore known to most patients, and the barrier to access psychological support is therefore low.

Interestingly, the parent who was interviewed at this particular centre was very positive about the psychological support that her son receives, whereas the parents in the other centres were perhaps not aware that these services may be available to their sons, or that their sons may benefit from this kind of support.

> *I think it would save a lot of problems for a lot of boys with haemophilia when they get to their teens, I do, to have somebody to talk to as they're growing up and the way that haemophilia impacts on their life, their everyday life in school, yeah, definitely (Parent 2).*

Of course not all individuals will need psychological support, as experiences in relation to haemophilia, and life generally, differ widely between individuals.

> *So, I suppose, everyone's different. I mean, I have seen the kids here where they're literally crying and screaming and I suppose that's when you feel really guilty trying to stab them with a needle. So, I suppose, every family, you know, depends on the child that's having it and the parents giving it and whatever, so I've been lucky, he just gives me his hand and that's it [laughs]. (Parent 3)*

However, as described in the next chapter, many haemophilia HP feel that many of their patients would benefit from psychological support at least at some point in their life.

Subtheme 3: Skipping or forgetting?

This sub-theme describes parents' experiences and perceptions in relation to non-adherence. When describing non-adherence, it is important to distinguish between intentional (skipping) and unintentional (forgetting) non-adherence.

From the interviews it became clear that parents felt that all YPH skip their treatment once in a while. Most parents described situations where they have to remind (or nag) their son to take his treatment.

> *Sometimes you've got to nag, yeah, sometimes you've got to give a bit of a nag and say, "Right, come on, have you done your treatment?" "No, not yet," "Right, come on then, treatment now," (Parent 2)*

However, most also felt that it is quite understandable that their son wants to skip his treatment every once in a while and try to give him some leeway.

> *We sort of try to give him a bit of the leeway, you don't want to be on his case all the time (Parent 4).*

All parents agreed that the key thing is that he takes his treatment before he does anything active, and there are no long gaps between injections. They appeared to understand how treatment works, and had worked out a way of compensating for any missed injections.

> *As long as he has it when he's doing something active, then it does all sort of fit into place. So, if I miss it on the-- because it's a big gap, I can't really miss it, can I? I mean, when it's three times a week, we have more chance of missing it, especially if you've done a needle wrong and you were dreading that Wednesday. And you're thinking, oh, I'll do it tomorrow. But that's probably when you could mess up more, than being on twice a week. You've got more days to play with. Yeah, it's fine (Parent 3).*

Although all of the parents agreed that their son sometimes skips an injection deliberately, they also felt that the majority of missed injections are due to forgetting.

> *usually he'll be having his injections on the morning and sometimes you find he's ready to leave for school and ask him. Hey, I haven't seen you have your injection this morning. And he realises he's probably forgotten that it was Thursday. But I think-- Well without being paranoid keep an eye on Mondays and Thursdays if he does forget either his mum or myself surely would remind him (Parent 4).*

As explained previously, establishing a good routine can help patients to keep to their regimen. If they are out of their normal routine (e.g. on holiday) they are more likely to forget.

> *The only time is when he's on holiday (Parent 3).*

Parents understood the clear distinction between skipping and forgetting, however it was not always clear which one they were referring to when they described their son's non-adherence. Perhaps they are not entirely sure why their son misses his treatment every now and then, or it could be that they feel it is easier to justify forgetting an injection, rather than deliberately skipping one.

7.3.4 Theme 3: Impact of haemophilia

This theme describes the ways in which parents feel that haemophilia has impacted their son's life and the rest of the family. Although this does not relate directly to adherence, it is important to report as indirectly many of these factors are associated to adherence.

Subtheme 1: Social impact

Three different parents described how they felt that their son's social life and emotional health had been negatively impacted by haemophilia. Sometimes in quite emotional language, they remembered their son being upset about being different, or not being able to take part in certain activities.

> *"I feel different, I don't feel normal, I don't feel normal, I know I'm different, I can't do the same as my friend," you know, "he's going on his skateboard up the skate park and my mother doesn't want me to do it because she thinks that I'm going to fall and bang my head, and I can have a bleed," (Parent 2)*

This can have a positive influence on adherence for patients who believe that the protection afforded by prophylaxis makes them almost the same as others, and allows them to take part in many activities. However, it can also have a negative impact on adherence as young people may feel anxious or upset about having to inject themselves, and feel that it sets them apart from their peers.

> *if he's really down he just says, "Oh what's the point?" when he was younger growing up he refused to have his treatment, "I don't want my treatment, I want to be normal, I want to be like everybody else, I don't see why I should have to have these all the time" (Parent 2).*

Some YPH may feel inadequate and worry about the way their haemophilia could impact their relationship with a (potential) partner. One mother described how her son worries that he may lose his wife because of haemophilia-related stress and complications. This particular individual is wheelchair-bound and suffers with chronic pain and disability which appears to have been caused by haemophilia-related complications.

> *He's worrying because he thinks that because he can't do all the things and he's on bed rest he's stressing 'cos he's convinced that his wife's going to leave him because he can't do anything, and he just thinks that she's just going to get up and say, "Oh, you know, I can't do the stress anymore," (Parent 2)*

Another parent explained that her son attends a school where there is a lot boisterous behaviour between the boys, such as play fighting and thumping each other. In this context being different can also mean that a boy may get singled out or bullied. This could be because he cannot take part in this behaviour, or is disproportionately affected by it (e.g. more severe bruising or bleeding). It appears that this boy is able to stand up for himself, and does not appear to be worried about it. However, boisterous behaviour and potential physical bullying at school represents an extra risk for YPH.

> *He said to me a couple of weeks ago that someone came up to him and said, "Oh, you bleed. If I hit you, you're going to bleed" and he went, "No", you can hit me and I won't bleed. But I'll hit you hard twice back" and he will [laughs]. So he was just like, "Oh, okay mate, it's alright". I mean, he's got a big bruise on his arm at the moment from school, it's been there for about two weeks. It's a big yellow one on his muscle. Obviously takes longer to clear up, doesn't it, but it wasn't a bleed, it was a bruise. And he's not bothered, he's like, well, you should see his arm [laughs]. So, he's been fine (Parent 3).*

YPH are likely to miss school quite regularly, because of bleeding-related issues or regular hospital check-ups. This means that they miss out socially, as they are sometimes unable to take part in activities, attend birthday parties or take advantage or other opportunities to build friendships.

> *And it probably has affected his social circle, because he's had to have a lot of time off school and he's had to have a home tutor and that kind of thing, so he's missed a big gap in his grow-- between twelve and fifteen. Where his friends that he had had gone on and made their groups of friends and they do the skateboarding and all that kind of thing, so he's sort of missed out on that (Parent 3)*

Instead of socialising with friends, YPH have to find other ways to occupy themselves while they are on bedrest, or admitted into the hospital. This can shape the way they look at life or even their personality. This is not necessarily a bad thing, as one of the parents explained when he described his son's ability to concentrate and entertain himself.

> *has been a loner as well, I actually do think it's because of his haemophilia, he's always liked his own company, he can-- The thing with him he can, he can sit down and do summit, me other son, he ain't got the concentration like he does and I think that is through his haemophilia, not on his own, he's like, he'll be on his own but like not other kids round him because he's been in hospital, confined to bedroom, a bed, complete bed rest, been at home, bed rest, he's had his telly, he's had his game and that as much as you can give him like but they have to have rest, I mean he's hurt his thumb and a young lad who's hurt his thumb and he's got his PlayStation to play, oh my Lord! (Parent 1)*

Subtheme 2: Impact on academic and career prospects

In addition to missing out socially, parents felt that their son had missed out on academic or career opportunities because of regular school absence and haemophilia-related issues. Three parents described how the situation was quite good when their son was in primary school, but that things got a lot worse when he moved to secondary school. One major issue that they described was that schools were not adapted and did not have a lift, which meant that children using crutches or a wheelchair could not attend all their classes.

> *it's always one thing that's bugged me, he missed a lot of school. When he went to high school that was terrible, every time he got a bleed they'd send him home, wouldn't have him in school, if he was in his wheelchair 'health and safety', which I think is rubbish! I mean, through his life at high school he was never there for his illness and he spent a lot of time in hospital, they used to have teacher in the hospital but it weren't the same and I had to try and explain to my other son, he missed out on a lot of stuff, not like, definitely he got stuff the same as other teens at Christmas and that but I think it's the lifestyle. (Parent 1)*

Most of the parents interviewed also felt that teachers and managers at school had been rather unhelpful, and far too focused on academic and attendance targets, which their son was unlikely to meet due to his haemophilia. One parent described the struggles with her son's school, and felt that school set him up to fail.

> *They weren't helpful at all, in the end I had to get him statemented so that we could get the help that he needed and they basically brushed him off and they said -- this is form one we*

went in and parents' evening -- "Oh judging by the results of his exams now, when he gets to form five--" I think it's year ten now, they said, "oh that his predicted grades are going to be like basically all fail," I said, "Well how can you predict that, that's four years away?" and so because of that they like basically weren't interested. And I had him statemented then and he came out of school, he sat his English GCSE a year early, they fast-tracked him, a B in maths, a B in his chemistry, biology, all his sciences, he came out with mostly Bs (Parent 2)

Two other parents described how they felt that their son had been labelled a 'problem child' because he missed school regularly (affecting the school's attendance statistics), or was unable to take part in PE lessons or classes in upstairs classrooms.

I think it still comes down to school targets. I don't really think it's actually the child that they're that worried about, I think it's their targets, and that's a pressure, obviously, they're getting from the government and whatever. That's the biggest struggle, and most parents would say school (Parent 3).

Or, and the one school, when he went to one, they used to put him, the one room they used to put him which was one for kids who played up and he used to go, why should I go in there because I'm a haemophiliac, I ain't played up but I'm in the same room as them (Parent 1).

However, it is important to highlight that not all YPH have negative experiences at school. Perhaps the situation has improved over the last decade, as parents of younger patients appeared to have more positive experiences in relation to school. This is probably also because their sons did not suffer many bleeds, and therefore did not have significant mobility-related issues. They did however also appear concerned about their son missing school because of frequent hospital visits.

so about an hour here, an hour for the appointment and an hour back so he misses a couple of hours of school but he's able to go back and continue with his studies so if that's happening just once in three months it's not too much of a concern but when it used to be every six weeks, with the schools having their targets as well on absence, whether or not it's authorised absence, it was a bit of a concern but not anymore (Parent 4).

Even young people who successfully pass their GCSE and A-level exams can find it difficult to progress their education or career. One of the parents explained that her son was not able to take up the university place he was offered, because he would not be able to get to lectures in his wheelchair.

He had a massive bleed in his leg, he was cast. And at the University it's all on a hill, not suitable for wheelchairs. And then he wasn't allowed to go in the lecture rooms and labs on crutches. And I said, "Well I can't see that, I thought you were supposed to accommodate people," "Oh yeah, but there's certain ones," and so he couldn't do it and he hasn't gone back, (Parent 2).

Another parent's story illustrates that even young people who obtain a qualification may struggle to find work, as potential employers worry about the impact that haemophilia may have on performance or attendance.

Because he's a haemophiliac no-one would give him a chance to work because of insurance… I know you're well aware but with haemophilia some people won't give him a chance plus him being severe haemophilia you can have a spontaneous bleed (Parent 1).

From the interviews it became clear that all parents felt that haemophilia had in some way affected their son's schooling. This ranged from missing school occasionally to attend hospital check-ups, to missing significant periods of school which in turn had a negative impact on academic achievement. Three of the four interviewees felt that the lack of support and understanding from school was a key issue, as it often lead to a battle between parents and school management.

Subtheme 3: Impact on parents and siblings

Haemophilia usually has a clear impact on parents, siblings and sometimes other family members. One mother explained that she felt very guilty after her son's diagnosis. This was not helped by the haematologist encouraging her to get sterilised within a year of her son's birth, as they felt that she should not risk having another child with haemophilia. This had a huge fall-out for the family, and caused friction between the parents. This mother's experience may not be representative of all mothers, but it did highlight that haemophilia, and the way HP approach parents, can have a devastating impact on emotional well-being and family dynamics.

I felt guilty because when he was first diagnosed, even though I knew it was in the family I used to think well perhaps if I'd ate this or perhaps if I'd done that, would it have been different. And my husband when my son got older and we've sat talking and I said something about getting sterilised and he said to me, "Well I'm not getting sterilised, you're the one with the problem, I can have normal kids." So he said, "If I have more kids, they'll be fine, so I'm not doing it, I'm not the one with the problem, it's you." And we split up not long after that mind we did, but yeah so there was always guilt and even now I still feel guilty (Parent 2).

Another parent became quite emotional when he described the period before his son was diagnosed, as he and his wife were accused of abusing their son, because he had such severe bruising. He described how frightening it was when his son was finally diagnosed, as the family did not know anything about haemophilia. However, his story was also quite positive, as he described how the whole family learned about the condition and how to manage it. Many parents were quite philosophical about life as a parent of a child with haemophilia; the first few years are hard but haemophilia becomes part of your life and then you just get on with it.

> *Social Services was called because they thought we was hitting him and I think everybody who has haemophilia, they've all gone through that. They saw us when he'd been in hospital for five days and they couldn't diagnose him. They moved us to the haemophilia centre and they diagnosed him, severe haemophilia. It was frightening because we'd never heard of it but now because I've grown with it, he's grown up with it. It was frightening at the time, me mum used to try and wrap him in cotton wool. But you've got to let them get on with it; you've got to let them enjoy life (Parent 1).*

Situations such as the two described above are perhaps less likely to happen today, as haemophilia teams are very active in raising awareness and knowledge of haemophilia in patients' direct social environment (such as family), as well as the wider environment (such as childcare settings, school, sports clubs, GPs, etc.). The assumption is that this better knowledge and awareness of haemophilia will prevent issues and support parents in managing their child's haemophilia.

The advances in medical treatment also mean that today many YPH can live a fairly normal live, with relatively few bleeds. However, particularly for patients affected by the consequences of regular bleeding episodes (ie mobility issues or disability), haemophilia can still have a significant impact on day to day life. This in turn can also affect their relationships with their partner and family, as haemophilia is likely to impact all of them.

> *It just causes so many problems with just everything, everyday life. Even with the school holidays, we know that to take my granddaughter out we've got to think about where we're going. We've got to make sure that you've got enough pain relief for him. We can't really go too far because he will sit in the car, it's painful for him and so it's not just an impact on his life, it's everybody's. I worry because he's married, that him and-- I don't want to interfere, but then sometimes I-- like sometimes he'll come and stay down with us to give his wife a break (Parent 2)*

Two of the interviewed parents appeared to worry about their son constantly, even now that they are becoming older and independent. It is difficult to confirm the extent to which haemophilia contributed to this based on the interviews, but it is likely that it played a role.

> *I find it hard like when he was younger and he was in the hospital I was there constantly with him, didn't go home, just stayed in hospital constantly, but of course now obviously now he's grown up, I can't do it, even though I want to, but you can't. But it is hard and when he was younger the support chain wasn't as good as it is now, when you listen and you talk to him and obviously they talk to other parents, that I think the support network is different now than what it was like 25. I mean as long as it was in the day the support network was there, but it's the out-of-hours one was always the issue. (Parent 2)*

In addition to the emotional impact of haemophilia, there are also many practical implications in day-to-day life. Something that many people would not think about twice, such as going on holiday, can be tricky and expensive to organise. For instance, popular holiday destinations such as Turkey are ruled out because adequate haemophilia care is not available. One mother explained that she has had to cancel several holidays because her son could not travel due to a bleeding episode, so now she books holidays at the last minute.

> *But, yeah, it'd be nice, I suppose, to book a holiday a year before like some people do and then you've got something to look forward to the whole year. But I think, it just becomes part of your life so you just don't, you never think about it. (Parent 3)*

Several of the parents explained that they try hard to find activities that the whole family can do together, to encourage their son to get exercise without risk of bleeding. This means that family outings and activities have to be tailored to the child with haemophilia, which does not always go down well with other sibling and can be expensive and time consuming to organise.

> *So we just came to the decision: no PE. But what we've had to do with him is like do a lot of taking him swimming, like after school. And things that aren't so harsh on his body, just to keep him sort of with some exercise. So I suppose that's the way it has affected, like our lives. That's what I say, we do more to help with the other things that he needs that he can't get from school. So, as I say, he's missed a lot of time off school, ever since he started school, you know, with nose bleeds and legs and head bumps and arms and fingers and [laughs] (Parent 3).*

It became clear that in many families the main focus is on the son with haemophilia, which can also lead to tension between siblings. One father explained that his other (unaffected) son told him that he wanted to have haemophilia too, so that he would get as much attention and would not have to go to school every day.

> *him and his brother they fight like cat and dog when they was little and I've even had because like he was in hospital, the littlun said to me, ''I wish I'd got haemophilia''. ''What did you say that for?'' ''Because he has stuff'' (Parent 1)*

Another important consideration is the impact on parents' work or career. Two of the parents that I interviewed gave up work, as they found it impossible to combine their work with looking after a child with haemophilia. A third parent found alternative employment working in the family business, which allowed her the flexibility she needed to look after her son.

> *So I think now with all this new rules and regulations they have to be more flexible with you, whereas when he was born they weren't, you know, it was like well basically tough like, you know, whereas again it's time isn't it and again it's understanding isn't it with employers, and you know, and I-- you know, with all the disability rights and everything, you know, I think that, I think that's made a lot of difference because people are-- they're more flexible, you know, they have to be. (Parent 2)*

But of course haemophilia can also have a positive influence in different ways. Some parents described a very close relationship with their son, and others explained that looking after their son and overcoming their apprehension to do the injections, had given them confidence in their own abilities.

One mother explained how she had suffered with needle phobia initially, but eventually became a phlebotomist after her son left home.

> *when he moved out and I thought what do I do now and then I thought well, I'll go back to work. I said, oh what do I do, so I thought oh I'll apply for a job as phlebotomist and anyway that's why I thought well I'd basically been doing it for the last like 20 odd years so-- and so I applied for it. (Parent 2)*

7.3.5 Theme 4: Haemophilia care

This theme encapsulates how parents experience and feel about the haemophilia care that their son (and their family) receives through the NHS. This includes parents' descriptions of support from the Haemophilia centre, treatment, and haemophilia awareness among the wider healthcare community.

Subtheme 1: Support from haemophilia centre

All parents felt that the support from the haemophilia centre is great.

> *The support off the hospitals is big, couldn't knock it, they've been golden, so the hospital side of it has been good (Parent 1).*

It appears that staff turnover is low in most haemophilia centres, which means that families tend to deal with the same consultants and nurses for years. This allows the haemophilia team get to know the patients and their families, and vice versa. This also means that the team are able to identify potential issues, such as non-adherence, early and work with families to address these.

> *Oh, it's excellent. I definitely do not have any complaints. The consultant who's seen him today, she's been seeing him for quite some time, um, started with Dr A and Dr B were here, I haven't seen them much of late, I don't know whether [laughs] they're still on there but she has been seeing him regularly so, um, I think they're quite familiar with [laughs] his case, yeah. (Parent 4)*

Parents feel that if they have any issues they can always call the haemophilia centre for advice, or in some instances just a bit of moral support.

> *Probably got good support from here when he was a baby, we was always here. And then as soon as I could do the treatment at home, that was all set up. And if I've got any problems, I'll give the unit a ring. When there's tablets he's been given but I'm not sure about, then I'll call and check. (Parent 3)*

> *It was good 'cos then if there was any issue then we used to come down and sit and have a chat and they-- it does make a difference. If you've got somebody that you can ring up and say, "I'm feeling a bit stressed," and I think it goes a long way to help, to helping you. (Parent 2)*

In addition to the excellent medical care, parents also felt supported by the haemophilia team in other ways. For instance, when a child with haemophilia starts at a new school a nurse will visit the school to give information, and check what facilities are available in case of emergencies. Some centres also have a social worker or welfare officer, who is able to support families in many different ways. However, in some centres these functions have disappeared due to reductions in funding.

> *I think so, yeah, because when we first were down the Hospital we got a welfare officer who used to look after us, he was brilliant and they helped us sort out when he was old enough to have mobility, sort that side out but then he disappeared, like his job role must have gone and it was hard then to get help with everybody else, they'd try and help you out, the nurse and that, they'd give you letters who you could get in touch with and you'd/ (Parent 1)*

Subtheme 2: His treatment has become part of our lives

Parents agreed that prophylaxis has made life better, and reduces the risk of bleeds and associated issues.

> *Prophylaxis, it has made life easier. Don't get me wrong he still has to go to the hospital and there's still times he needs to come over the hospital. But if he has a bump, he knows himself. He'll go. ''I need to treat that now''. The next day he'll phone me to say ''Dad, I need to go over the hospital'. He'll phone the nurses, he'll ask their advice and they'll say 'have this treatment, no problem'. Or 'No, better come in'. The nurses have been brilliant. So it does, it has made life a lot, a lot easier. (Parent 1)*

In particular in families where previous generations were affected by haemophilia they appreciate the positive changes prophylaxis has made.

> *Whereas in my dad's day, he'd by lying in bed for six months, you know, constantly bleeding and everything. So it's sort of, yeah, it's not too bad, it's manageable. (Parent 3)*

As described in previous chapters, many YPH and their families suggest that treatment becomes part of life. It is just another thing you have to do, which becomes part of your routine.

> *It's sort of now been built into the routine, during the earlier days it was quite hectic but at the moment we've sort of settled into a routine and know what to expect when so it's just one of the things you get on with really. (Parent 4)*

In the early days after diagnosis it is often difficult and stressful for parents to manage their son's haemophilia. Parents described how slowly and gradually haemophilia became part of their lives, and that stress and constant worry reduced. However, all the interviewed parents appear to worry about their son considerably and continue to be involved in managing their haemophilia, even after they have left home.

> *Cos it's a learning experience, you don't know whether that little tiny bruise was a bleed and so it was just worry, just all the time. But as he gets bigger you learn, you adapt, you know what to worry about and what not to worry about, but he's left home now and I still worry, just all the time. I still ring him every night, check how he's doing and, to say about anything you need, how are you doing, have you had your treatment and that, so yeah, it's just worry [laughs]. (Parent 2)*

While recognising the impact that haemophilia has had on their son and the rest of the family, three out of four parents were quite positive about the future and felt well-equipped to help their son manage his haemophilia. They agreed that as long he takes his treatment he should be ok, and be able to enjoy his life.

> *Yeah, it has, but it sort of becomes part of your life. I think, probably, say you were somebody just coming into it and you explained to them, they'd probably think really has messed his life up and stuff, but he's not really ever complained about, he looks to the future. He's had his needles, he actually just thinks, he just gets on with it, like I say, it is part of his life. (Parent 3)*

Subtheme 3: Haemophilia awareness needs to improve

Although they agreed that haemophilia care in this country is very good, several parents described situations in which they felt HP were not aware or knowledgeable enough about haemophilia. This included situations where they prescribed medication that is contraindicated for people with haemophilia, or where they would withhold treatment because they were not confident in treating a patient with haemophilia.

> *And in that time this joint is weaker anyway, you're protecting it a lot, and you want to know what's going on with it. And when you do get to see the consultant a hundred percent of the time he'll say, "Well, not really much we can do because of the haemophilia" and it drives me crazy because I'm thinking, "Well, why have--?". They can whatever needs to be doing, do it. Because the treatment's there, but they're scared, I think, a lot of the time, to do anything. (Parent 3)*

This seems to be a particular issue in situations where a person requires emergency (non-haemophilia related) treatment following an accident, or dental treatment.

> *They'd rather leave a child with haemophilia alone. Even simple things like their teeth. I can see the difference because I've got a child without and a child with. Now, with my daughter if she needs a tooth out, it's a tooth out. If my son needs a tooth out, it's a big process. You're at the dental hospital, you've got to-- can't get through to the dental hospital, they don't answer the phones, you leave messages, it takes months to deal with the fuss. (Parent 3)*

The parents interviewed for this study did not appear to have much confidence in out-of-hours care, and try to avoid it if they can.

> *I dodge out of hours. So occasionally if he's done something on a Saturday, I'll treat him. And if it's okay on the Sunday, I'll leave it and then bring him on the Monday. As for night times, say he's come home from school and he's hurt himself or if he hurt himself after school, say it's five o'clock, then I'll treat him and bring him the next day. So I'm actually dodging out of hours [laughs]. (Parent 3)*
>
> *He will try not to come down out-of-hours or on a weekend because you tend to see the haematologists rather than the doctors from the Haemophilia Centre, it tends to be the on-call haematologists and I think sometimes you're lucky, you get one of the doctors who know you, but generally on a weekend it's hit and miss so (Parent 2)*

Haemophilia care is centralised through regional haemophilia centres. This means that not all hospitals offer haemophilia treatment, and that in some hospitals emergency doctors or nurses are unable (or unwilling) to treat people with haemophilia because they lack knowledge and experience in this area. This can cause issues when a patient is brought in by ambulance after an accident. One parent explained how he had to pick up treatment at home when his son was driven to the wrong hospital by ambulance, and then had to help his son to administer the treatment himself because the hospital did not have factor replacement treatment in stock and staff could not administer treatment that was brought in by patients themselves.

> *they seem to want to take you to another hospital where they can't treat him so the last time I took him there he's sixteen, of a night, I had to fetch his treatment from home, I had to mix his treatment, I had to phone the haemophilia centre, they told me how much treatment to give him there and then, I mixed it up meself, went to give it him, they wouldn't let me because they don't know it was mixed up so I had to make him sit up and give it him to give himself because they couldn't stop him. (Parent 1)*

It is difficult to ascertain if the issues described above are still relevant today, as some of the situations occurred years ago and healthcare provisions may have changed since. However, it appears that due to its rarity many doctors and nurses in other specialties are not knowledgeable enough about haemophilia. Many parents appear to deal with this by becoming 'experts' themselves and seeking advice from the haemophilia centre to provide guidance to other HP.

7.4 Discussion

From the interviews it became clear that parents felt that most YPH skip their treatment occasionally. They agreed that the key thing is that he takes his treatment before he does anything active, and that the gaps between injections are not too long. They appeared to understand how treatment works, and had worked out a way of compensating for any missed injections. All parents appeared concerned about the potential risks associated with physical activity and going out with friends (particularly going out to enjoy the nightlife, including consuming alcohol).

Parents understood the distinction between skipping and forgetting, however it was not always clear which one they were referring to when they described their son's non-adherence. Perhaps they are not entirely sure why their son misses injections, or perhaps they find it is easier to justify forgetting an injection, rather than deliberately skipping one.

The most important barriers to adherence described by parents include lifestyle (fitting treatment in with other priorities such as school); being out of the normal routine (e.g. on holiday); not wanting to be 'different'; issues around venous access and needle phobia; and psychological issues (such as stress and anxiety). The most important facilitators described by parents include establishing a good routine which includes treatment; setting reminders or alarms; parental and peer support; psychological support; helping patients to develop the maturity and self-management that are required to manage haemophilia; and giving young people some leeway and give them the room to find out for themselves why prophylaxis is so important.

Parents appeared to be aware of the importance of treating bleeds appropriately, and felt this was just as important for their son as him adhering to his prophylaxis. It became clear that parents are very involved with their son's treatment, even parents of young adults who no longer live at home. All parents felt that the support from the haemophilia centre is great. It appears that staff turnover is low in most haemophilia centres, which means that families tend to deal with the same consultants and nurses for years. This allows the haemophilia team get to know the patients and their families, and vice versa. This also means that the team are able to identify potential issues, such as non-adherence, early and work with families to address these. Parents felt that if they have any issues they can always call the haemophilia centre for advice, or in some instances just a bit of moral support.

As explained in the last chapter, a comprehensive discussion of all the qualitative studies will be provided in chapter nine.

Chapter 8: Interpretative Phenomenological Analysis of haemophilia healthcare professionals' accounts of adherence to prophylactic treatment

8.1 Introduction

This chapter presents the results of the Interpretative Phenomenological Analysis (IPA) of healthcare professionals' (HP) accounts in relation to prophylaxis and adherence to this treatment among young people with haemophilia (YPH). The aim of this study is to examine participants' perceptions and experiences and the way they make sense of these. Together with the findings of the qualitative studies described in the previous two chapters (which represent the views of YPH and their parents) the findings of this study are anticipated to contribute towards a better understanding of the complexities around prophylaxis and adherence to this treatment among YPH.

8.2 Methods

8.2.1 Recruitment

Participants were recruited in five haemophilia centres across England and Wales. All HP involved in the care for YPH were eligible to take part. To ensure that the findings would represent the views of different members of haemophilia teams, nurses and doctors with different levels of experience and seniority were approached to take part. All potential participants who agreed to take part were interviewed.

8.2.2 Participants

Participants were two haematologists (one Registrar and one Consultant) and four nurses with different levels of seniority (see Table 8.1 for details). To protect anonymity and confidentiality details of which hospital participants work in are not included.

Table 8.1: Healthcare professional interview study participant characteristics

Participant code	Role	Sex
HP 1	Nurse	Female
HP 2	Nurse	Female
HP3	Nurse	male
HP4	Haematologist	Female
HP5	Haematologist	male
HP6	Nurse	Female

8.2.3 Data collection

Each participant was interviewed face-to-face in a private room (or their office) at the haemophilia centre. The interviews were semi-structured using a topic guide (appendix 5.1), although participants were encouraged to tell their own story in their own words with little interruption from the interviewer. At the start of the interview participants were invited to describe an 'average day' in the haemophilia centre to get a sense of what it is like to work in a haemophilia centre. Participants were invited to highlight any changes in haemophilia care that occurred during the last decade, and potential improvements to haemophilia care that they would like to see introduced. They were also invited to describe their experiences and perceptions in relation to prophylaxis, and potential barriers and facilitators to adherence to prophylaxis among YPH. As described in the previous chapters, the order in which the different subjects were discussed was flexible. This allowed participants to tell their own story, and highlight those topics they felt were most relevant. Interviews were recorded and then transcribed verbatim before being analysed following the IPA methodology

8.2.4 Analysis

As described in chapter five, IPA emphasises that the process of discovering themes involves the researcher being engaged in a double hermeneutic (Smith, Flowers & Larkin, 2009), with the aim to make sense of the participant attempting to make sense of their experiences. Therefore this analysis is partial and subjective and may have reached different conclusions than other researchers may have done if they had carried out this analysis. This chapter will explore those themes that emerged most strongly from the interview data and that were most relevant to the research questions. These themes will be illustrated with verbatim extracts that were selected from across all participants' transcripts, to ensure they were representative of the sample. In some instances, where different participants had different opinions or experiences, all views are illustrated. Where participant responses were similar, only those quotes that illustrate the theme most clearly have been included. This approach was true to the aims of the study, participants' accounts and the richness of the data.

8.3 Results

8.3.1 Superordinate and subordinate themes

At the start of their interview HP were invited to describe their day-to-day responsibilities and experiences in relation to haemophilia patients. They were then asked about their perceptions and experiences in relation to prophylactic treatment and barriers and facilitators to adherence to this treatment among their patients. Participants' accounts clustered around four superordinate themes, which are shown in table 8.2 together with their related subordinate themes. The table also shows

for which participants each of the subordinate themes was relevant. These themes were identified, analysed and reported following the same process that was described in previous chapters, ensuring that themes emerged from the data and were relevant to the research questions. The approach used was true to the aims of the study, the experiences described by participants and the richness of the accounts in the data.

Table 8.2: Healthcare professional interview study superordinate and subordinate themes for each participant

Superordinate themes	**Subordinate themes**	**Participants**					
		1	**2**	**3**	**4**	**5**	**6**
Healthcare professionals' estimates of adherence	Adherence fluctuates	x		x	x	x	x
	Timing of injections	x		x	x	x	x
	Variability of symptoms (bleeds)	x		x	x	x	x
	Haemtrack and adherence	x		x	x	x	x
Drivers of non-adherence?	Lifestyle/time management	x	x	x	x	x	x
	Venepuncture issues		x	x	x		x
	Not wanting to be different	x	x		x	x	x
	Absence of symptoms			x	x	x	x
	Family and social issues		x		x	x	x
Improving adherence	Education	x	x	x	x	x	x
	Psychological support	x	x	x	x	x	x
	Peer support	x	x	x	x	x	x
	Support for parents			x		x	x
How can healthcare professionals help to improve adherence?	Being sensitive to individual needs	x	x	x	x	x	x
	Regular contact and continuity of staff	x		x	x	x	x
	Collaboration with schools and community	x		x		x	x

8.3.2 Theme 1: Healthcare professionals' estimates of adherence

During the interviews HP were invited to comment on levels of adherence among their patients, and reasons why they feel YPH do not keep to their treatment regimen. They were encouraged to comment in any way that reflected their own personal experiences and perceptions.

Subtheme 1: Adherence fluctuates

HP found it difficult to estimate adherence levels in terms of percentages, but agreed that adherence is generally good. Four participants estimated that at least 90% of patients adhere to their treatment, one participant estimated that at least 75% adhere, and one participant was not sure.

> *Gosh, quite hard to think of [laughs] I don't know if I could put a percentage. But I would say that the vast majority [pause] are actually quite adherent. I'd say the vast -- I don't know, it's kind of [pause] 75%. I don't know, it's kind of a random number, but I'd say -- or even maybe more. I think, the bulk are more or less [hesitantly] fairly adherent. (HP1)*

> *About 5-10% are people who might not take their treatment as prescribed. (HP4)*

However, participants also felt that adherence levels are likely to fluctuate. They explained that even patients who tend to be very adherent can go through short periods of non-adherence, often caused by circumstances.

> *So some people are really good for a while and they have blips as well but they don't adhere all the time it's just circumstance. (HP1)*

Participants also explained that it is not always straightforward to ascertain if someone is adherent or not. In recent years haemophilia centres have increasingly encouraged patients to tailor their treatment around their lifestyle. Particularly patients who live an active lifestyle may change the dosage and frequency around their activities. Therefore in some cases you may argue that someone who follows a rigid three times per week regimen is non-adherent because they do not top-up in advance of activities.

> *Hmm, so even though they are adhering to their regimen, actually they are sort of non-adherent because they are not managing around their activity. Or treating at the wrong time (HP3.)*

It is also important to consider all the other self-care behaviours that patients are expected to follow in addition to taking their treatment.

> *I suppose my perception would be that adherence is quite good in terms of prophylaxis. It's the other things, so if they're attending clinic, treating their bleeds appropriately, taking it at the right time. I suppose we're expecting quite a high standard on a lot of things. Completing treatment records, they're the things that are really poor adherence rather than the actual sticking to prophylaxis (HP6)*

Subtheme 2: Timing of injections

HP agreed that the majority of non-adherence is about timing of treatment. Indeed three participants estimated that although nearly all (90 to 100%) of their patients take their prophylaxis, significantly fewer patients (50%; 70% and 80% respectively) take it at the agreed time.

> *Well 'as directed' would probably mean before they go to school, and I would think roughly about 70, 80% of them will do that and they will find it easier to do as well because parents have got to go to work as well so everyone comes home at different times. There are some families that just can't do in the morning, they might have three or four children and it's just impossible. That's something that you have to accept and they will do it when the boy gets home from school (HP5)*

The haemophilia professionals interviewed for this study appear to take quite a pragmatic approach, and accept that not all patients will be able to follow their recommended regimen. In most cases they work with the patient and/or family to find a compromise with a focus on reducing the treatment burden while still making sure that the patient is protected, particularly during times that they are at higher risk of bleeding.

> *So although there's lots of positives of daily treatment and that would be ideal in terms of levels. The practicality of that for some families is that it's not going to work. I suppose the compromise then is alternate days or we say "Monday, Wednesday and Friday and once at the weekend". If that's what's prescribed, I would say 90 to 100% of people are doing that. I would say particularly in children that less than 50% of them would be doing it in the morning. I think it's after school, in the evening. I suppose it should be like brushing your teeth that you shouldn't do something without it, but that's not how it works for the families. (HP6)*

In some cases a compromise between the ideal regimen clinically, and a regimen that accommodates patients' lifestyles can ensure that the patient is at least able to take some treatment, rather than none at all.

> *"Okay, well why are you missing it? Is there things we can do to help, is it the time of day?" Cos some patients will do things like, they'll get in their head it has to be done at this time of day. And then things change in their life, or something happens and they can't do it easily at that time of day. But they don't necessarily think, actually you could just do a different day [both laugh] so that helps. (HP4)*

However, it can be challenging to strike the balance between accommodating patients' lifestyles and ensuring treatment efficacy is not affected.

> *We had one who was treating at night, because they had to wake up early to go to work and they didn't want to take the treatment at work, because of what people would say. So the only time he would treat would be when he comes back home. After which - - after he comes home he's gonna go to sleep, so all that factor is just being wasted. (HP1)*

Participants explained that it is important to take personal circumstances and clinical variables into consideration when agreeing a treatment plan. An important variable is the bleeding phenotype, which indicates an individual's tendency to bleed. The variability in bleeding phenotype between patients means that non-adherence does not have the same repercussions for all.

> *Some of our boys do get away with that. A boy who's 17 has always struggled to do prophylaxis, dad's always done it a bit and dad will be away with work so sometimes he wouldn't have it. A really sporty boy, as a family they go off on skiing holidays, never had any problems. What we would prescribe as prophylaxis would not be what they can manage, so when they come to clinic they openly say "We don't do that, we might manage twice a week" but that's okay he doesn't bleed in between, he comes to clinic, his joints are checked and he's managing that because his bleeding phenotype is very different. (HP6)*

Subtheme 3: Variability of symptoms (bleeds)

During the interviews participants were asked whether they felt that bleeds are the best indicator of non-adherence, and the responses were mixed. Some felt that patients who suffer frequent bleeds and those who stop attending clinic appointments are more likely to be non-adherent.

> *Yes I think so, probably bleeds. Well bleeds and not attending clinic, I think when they're not turning up that's a clue of this is all going a bit wrong, but we tend to chase those so yes bleeds… (HP4)*

However, others pointed out that there are patients who keep to their regimen religiously but still suffer frequent bleeds. This could be because the dosage or frequency of their treatment is not sufficient, due to existing joint damage, or other clinical factors that may cause bleeding.

> *I know one guy who kind of adheres, but he's always getting bleeds. So you keep on adjusting their treatment as soon as they recover. Some of which you can put down to having joints which were already knackered from before. But you adjust the treatment. (HP3)*

Of course treatment cannot prevent bleeds that are caused by trauma (a fall, cut, sports injury, etc.). However, prophylaxis is likely to make trauma bleeds less severe and helps patients to heal more quickly.

> *All children are going to get bleeds, there's no such thing as a haemophiliac who doesn't get bleeds, what they're not getting is breakthrough bleeds on prophylaxis, but they will get trauma related things and that's on occasion going to make them miss school, less so than if they're not on prophylaxis because I think being on prophylaxis itself ameliorates the bleed if you like. (HP5)*

Some patients are encouraged to contact the haemophilia centre when they have a bleed, so that they can assess whether the bleed can be treated at home or requires hospital treatment. Most patients are required to log bleeds on Haemtrack (including additional treatment they have taken to treat the bleed). However, it appears that not all patients treat bleeds appropriately. Some do take extra treatment, but do not log it on Haemtrack. Others keep to their normal treatment regimen without taking additional treatment, which often causes the bleed to last longer and cause more damage.

All of a sudden they find themselves with a bleed, some will then just try 'Ok, I've got my treatment tomorrow anyway, so do I wait and do a treatment tomorrow? Whereas they are supposed to treat there and then. But you find someone waiting until tomorrow, cos it wasn't their treatment day. When they call it hasn't resolved. Usually we do regular checks on Haemtrack. If you see several bleeds you give them a call and find out 'are you ok' I see you recorded this' and they will start telling us 'oh, this is the case' so the log is really good. Cos you can see how the bleeding pattern of some people, then you are able to give them advice (HP3).

One of the participants suggested that patients who present late with bleeds are often also those who struggle to keep to their normal treatment regimen, or those who do not attend clinic appointments. So in some cases recurrent bleeding can be an indication that someone is disengaged with their treatment, or is struggling with it.

Some are obvious because they stop coming to clinic, that happens quite a lot, or they miss a lot of appointments and they will show up for one and they're a bit sporadic, so they're just not very engaged with it, things like they'll present late with a bleed, you can also notice they're not picking up their treatment and that kind of thing, and that kind of thing can happen. (HP4)

Subtheme 4: Haemtrack and adherence

As described in previous chapters, the majority of patients who follow a prophylactic treatment regimen are required to log their treatments on Haemtrack, an online treatment log. Haemtrack allows haemophilia centres to monitor patients remotely, to check whether they are taking their treatment as agreed and whether they are experiencing any bleeds. HP were generally very positive about Haemtrack, because they felt that in addition to helping to monitor patients it also helps to engage patients and give them some autonomy.

And I think anything where things like Haemtrack where the patient's much more involved and much more in control, I think that's a really good thing and I think we're trying to go there, or trying to increase the autonomy is really good. (HP4)

Information logged on Haemtrack can be a good conversation starter with patients, and can help to illustrate the link between missed treatments and bleeds. Nurses tend to regularly use Haemtrack to check how patients are doing. They then telephone patients who have logged a bleed, or patients who have not logged treatments for a while. Haemtrack data can help to start a conversation about

adherence, and how the centre may be able to support the patient to keep to his treatment. Haemtrack data are automatically uploaded onto the UKHCDO database, analysed and then presented annually in a summary report. The data are also shared with Specialist Health Commissioners to help justify the significant cost of prophylactic treatment.

> *We have had to write letters and say "We get this amount of money; if you don't give back treatment returns we get less money, so less treatment available and so more people will bleed. If you reduce it to that level, I think most people will accept that and understand there is a responsibility and contract of care (HP5).*

However, it is important to note that Haemtrack is 100% reliant on the accuracy of information entered by patients. One participant felt that some patients may log trauma bleeds as breakthrough (spontaneous) bleeds, as they do not want to admit that the bleed was caused by an activity they should not have been doing. They felt that Haemtrack could potentially be used by commissioners to prove that prophylaxis (one of the most expensive treatments available through the NHS) does not work, as patients should not be having spontaneous bleeds while on prophylaxis. In a time of austerity this is a real concern for haemophilia treaters.

> *But if a boy's been playing football and you've told him the week before he shouldn't be playing football and he gets a bleed, he's not going to put down on Haemtrack that he's had a bleed whilst playing football. He's going to say he had a breakthrough bleed and that's where Haemtrack is very poor. Haemtrack is okay but it's very reliant on what the parent or the boy fills in. So Haemtrack is going to provide a lot of data for the UKHCDO, but it's also going to prove that prophylaxis doesn't work. That's going to be the bottom line and that's so utterly stupid because all commissioners will do is watch the results on Haemtrack,'Goodness me, look at all those breakthrough [spontaneous] bleeds that these people are having on prophylaxis, prophylaxis doesn't work'. Not going to give you this money. It is so badly thought out (HP5).*

HP were unable to estimate how many patients complete Haemtrack as directed, but it became clear that they put a lot of effort in to encourage patients to complete Haemtrack.

> *You get times, months where people are just too lazy to bring their treatment logs. And we have to chase them up. So at times they are really good, you're not chasing anyone up. Then there are times where you are chasing up about a quarter of them. If they don't return for more than 3 months we tell them that they have to come and collect their treatment from*

the centre, rather than having home delivery. But as soon as you tell them that, they start filling it in. (HP3)

Participants explained that many of their patients appear to complete Haemtrack periodically rather than after each treatment as prescribed. This means that Haemtrack may not be as useful to monitor patients' bleeds.

We try to go through it thoroughly monthly to update our own spreadsheet as to who's compliant with returns. So there are those who put it in right away and there are those who leave it months [laughs]. Or there are those who just default random things in I think [laugh]. So when you go through it you can see who's treating. Some are really easy; it's all exactly what you expect. No bleeds, no qualms. Others, there's a random odd bleed. Sometimes they give you insufficient information. And if there is any issues then I phone them and say, 'look I noticed you have such and such' (HP1).

Haemtrack completion rates, and the data entered on Haemtrack are not necessarily indicative of how well patients adhere to their treatment, as even patients who generally adhere to their treatment do not always log their treatment as directed. However, it is probably fair to assume that those patients who complete Haemtrack religiously are likely to be adherent, whereas those who are not engaged with Haemtrack are probably also less engaged with their treatment and haemophilia generally.

I think it's self-selecting thing, I think the people that engage and do it generally are more engaged in their treatment and the condition. (HP4)

8.3.3 Theme 2: Drivers of non-adherence

This theme describes all the factors that HP highlighted as drivers of non-adherence. It is possible that not all potential drivers of adherence that a patient may experience are included in this theme, as only the factors that were described by the HP who were interviewed are included.

Subtheme 1: Lifestyle and time management

When discussing reasons why patients do not adhere to their treatment HP suggested that for many patients it is a question of time and lifestyle. During a busy time, or during a significant life event or change it is much more likely that someone forgets to take their treatment or finds it harder to fit in.

I think the occasional ones, I think some will have a busy period and will genuinely forget and I think that's fine and, that's human error [laughs] and I think -- I don't really see that as a problem. (HP3)

It's usually been a change of circumstance. So a new job, a pregnancy or they've got married. Something that's completely changed their lifestyle. Especially because it's something that tends to be tied to a particular day and a particular time. Anything that alters that and it takes a while for it to settle down again into a new pattern. (HP4)

HP agreed that one of the most challenging aspects of prophylaxis is the timing of the injections. For many patients it would be best to take treatment in the morning, before leaving home. However, HP agreed that this is simply not achievable for all their patients.

You say to somebody to have prophylaxis in the morning before school, as it's wasted in the evening. The prophylaxis then gets done in the evening because life is too busy in the morning. I think that that's also why it's really important that we visit families at home because that gives you a much better reality of what family life is like for them. Families maybe where there's single parents, there's multiple children, that in the mornings before school is a rubbish time. As the health professional and the expert we're saying "This is what you should be doing" but the reality of that happening is really, really difficult in terms of practical. (HP6)

Although non-adherence appears to occur across the board, HP suggested that many YPH go through a period during which adherence is significantly reduced. This often coincides with them becoming more independent, and taking over responsibility for their own treatment from their parents. For some this may be when they leave home, and are forced to look after themselves.

If they're at home they've got the parents there making sure they do the treatment. When you get more to later teens and early 20's that's where I think it probably falls apart more. Once they gain more independence, and they haven't got the parent breathing over them saying "You must take this treatment and do such and such". I think that is where it tends to sort of fall off easier. (HP1)

Gaining more independence does not only affect treatment adherence, it is also likely to impact on other self-care behaviours, such as avoiding risk and managing delivery of treatment.

> *A lot of these boys are starting to go to university and are leaving their family, and if they've not been properly prepared for that. All of a sudden they've not only got to deal with doing prophylaxis and looking after themselves, like any other boy leaving home. But with the added complication of going out and getting completely trollied [drunk] on a Friday, Saturday and whatever other nights. But making sure they're safe to do that, because they haven't got mum sitting there going "oh if you're going out you need to go and do such and such." They've also got home therapy, making sure that it's recorded somewhere, and then also making sure they've enough treatment to see them through to the next delivery (HP2).*

In some cases lifestyle is such an important consideration that patients decide to stop prophylaxis, because they feel treatment is too much of a burden, or stops them from living the life they want to live.

> *There's one gentleman I spoke to and he had-- he just said, "Well I know what you're saying and I can see why you're saying it and you're right, but actually what would be worse for me right now is having to take prophylaxis, so I'd rather live with the fact that I might have a bit of arthritis in one joint in the future than actually spend my 20s doing this," right, okay [laughs], I thought well you can't really argue with it. So I have seen it for that reason as well, where they've made a definite decision (HP4).*

Subtheme 2: Venepuncture issues

Needle phobia or issues in relation to venous access can have a dramatic impact on adherence. HP suggested that needle phobia only affects a small number of patients, but that it is an issue that can consume a lot of time. This is because patients require a lot of support, and in some cases come to the centre for all of their injections.

Children are often taught about their treatment slowly and gradually, starting out with helping to mix treatment, leading to helping with the injection and finally doing it themselves. During this process the haemophilia team have a range of tools available to help, including anaesthetic creams, distraction techniques, and help from play therapists. As a result most children learn to do their injections without developing needle phobia. However, if parents struggle with needles it is more likely that their children will struggle too.

Sometimes I think it's affected by how the parents react to it and how they're feeling about it. We do have play specialists, distraction and we have local anaesthetic creams. If all of those things are in place in the beginning, what you see then in the centre is that we have boys that are three or four that will come in and accept it and it all happens really smoothly. Now that didn't happen without some other things happening before it. But I think it's more perhaps the parents struggle with a bit of needle phobia. And is that needle phobia or the thought of doing something so invasive to your child? (HP6)

One HP noted that issues related to contaminated blood may also cause anxiety or phobia in relation to injections, particularly for patients with family members who were infected with HIV or Hepatitis C during the 1970s and 1980s.

Most probably their family got affected either with HIV or Hep C, or both. So, it's really hard to break through those barriers. That's where I am not so sure whether after that period how much information was given to them about the recombinant factor but we try our best just to tell them 'there's no, it's not from any human'. No matter how you try and explain, it's a bit hard. (HP3)

Several HP highlighted that venous access is an issue that can also affect adherence. For some patients it is very hard to find a vein to inject into, and in some cases it can even be challenging for doctors and nurses to inject these patients.

I think also whether they've got decent veins or not. Again if they're left-handed and all their veins are in their left arm it can be quite tricky. It might not cause a problem, they might adapt quite well to using their right arm but, or right hand but it doesn't always follow. (HP2)

If a patient has an injury in one arm or hand, this can also make it difficult or painful for them to inject themselves. Participants explained that for some patients issues in relation to venous access can make treatment very stressful, and cause anxiety that in turn can lead to needle phobia.

Venous access can often be a massive battle and for some of our families, perhaps where they're not doing so much or children are overweight then it's a real battle with trying to find veins to be able to treat. And that puts stress on the families and on the child; it can lead into some needle phobia. (HP6)

Three participants explained that patients are taught to rotate their injection sites, to prevent any scarring or damage to veins. However, they suggested that many patients use only one or two sites because the skin scars after some time, numbing the skin making the injections less painful.

> *So the people who use the same injection site/ it's just numb. When you train them you try and get- - if they've got multiple veins, to rotate round so that each one can heal and not scar. But some of the guys who have quite bad scarring if they're just using the same injection site do that because it becomes less sensitive and easier for them to do (HP1).*

Subtheme 3: Not wanting to be different

Most interviewees agreed with the suggestion in the existing literature that adherence may be a particular issue during adolescence because of the developmental issues that characterise this period. The main focus for many adolescents is on their social life and asserting independence from parents. They tend to live in the here and now and find it

difficult to understand that not taking their treatment may have repercussions for their future health. They also struggle with the idea that their haemophilia makes them different from their peers.

> *For any adolescent the emphasis to be the same and liked and popular and to be all these things is quite strong isn't it? And they want to do what everybody else is doing and for some I imagine that haemophilia and having to treat themselves may be something that's setting them apart (HP2).*

> *Don't like to be different, don't like to be seen different. Don't want to do it, had enough of it, don't want to stick needles in themselves, no one else to stick needles in them, feel well in themselves, a desire to conform with peers (HP5).*

All participants agreed that most adolescent patients go through a stage of suboptimal adherence, ranging from occasional skipping to complete disengagement with treatment. This period appears to occur mostly between the ages of 12 and 15, and is characterised by patients becoming more independent and assertive.

> *Hmm. 12 to 15 year olds [laughs] just everything's an issue for that age group I think. I used to work in schools with some of that age group and they're just challenging most of the time. I'm going to do the opposite" kind of thing (HP1).*

During this period it can be challenging for the haemophilia team to engage with patients, as patients rebel against the haemophilia team as well as their parents. During the interviews it became clear that particularly nurses spend a lot of time working with each patient, and tend to be very sensitive to each individual's needs.

> *And with some patients 'I don't really want to come to the unit, I don't want to be having treatment, I don't want all this fuss, I don't want all these appointments', and that's a bit more difficult. I can think of a patient that comes and he has a bleed and you've to judge the timing because if you push too much for him to get to clinic and getting prophylaxis they completely back off, because they obviously have a reason that they're choosing not to and it is their body and if they feel like you're really pushing them then they're just going to turn up even later after the next bleed. So sometimes I'll bring it up and other times I won't and I try and do it in little bits, and try and encourage them back. (HP4)*

Subtheme 4: Absence of symptoms

The introduction of prophylactic treatment has revolutionised haemophilia care, and improved patients' quality of life significantly. Some patients even manage to get to adolescence without having experienced any severe bleeds. Some of these patients stop taking their treatment because they find it difficult to understand why they need it, as they have no idea what it is like to suffer a bleed.

> *Because they've had a little bleed and they've never experienced pain like it. People forget that haemothrosis is exquisitely painful. Some boys won't and they'll just say "Okay, I'll accept that and I'll just give treatment when I bleed. But most of them if they do experience a bleed will want to stay on prophylaxis. It's quite difficult to argue if they've not experienced it and it's sort of a predictable outcome of prophylaxis that some boys will forget they've got haemophilia, and can't rationalise why they shouldn't do things like skateboarding, like signing up for soccer clubs. And that's when it becomes difficult because they've lived their life really with prophylaxis and kids have been on regular prophylaxis since the 90's. So they've got no experience of acute bleeds, unless they do something really daft. (HP5)*

Once they experience their first serious bleed due to skipping prophylaxis, many non-adherent patients start taking their treatment again. However, once they have had a period without bleeds they sometimes stop taking their treatment again with more bleeds as a result. This can become a vicious circle for some.

We try and encourage them, I mean - - we have managed to encourage them to a certain extent that they'll go on the prophylaxis. When they know that they are not getting any bleeds they fall back again. And say 'no, no, I don't need it'. But when they got a really bad bleed, that's when reality hits them and says ' no I need to be on prophylaxis'. (HP3)

A minority of patients decide to stop their prophylaxis completely. Interviewees explained that they do what they can to re-engage these patients, but have to accept that this is not possible in all cases. Some patients make the conscious decision to stop their treatment because they feel that reducing the long-term risks to their health does not weigh up against having to take regular prophylaxis.

he just said, "Well I know what you're saying and I can see why you're saying it and you're right, but actually what would be worse for me right now is having to take prophylaxis, so I'd rather live with the fact that I might have a bit of arthritis in one joint in the future than actually spend my 20s doing this," right, okay [laughs], I thought well you can't really argue with it (HP4).

Some HP use case studies of patients who have bleeding-related joint damage to show younger non-adherent patients why taking prophylaxis is so important. Sometimes this 'shocks' a young person into adhering to their treatment regimen again.

You see the older patients that haven't had it and the difference in their joints and their general health. It's like having two cohorts of patients it's really stark. I guess as the older cohort get smaller it's going to be harder and harder to convince the younger one that actually this is a really good plan [laughs] (HP4).

Subtheme 5: Family and social issues

Each family is different and has its own challenges. The impact that haemophilia has on the patient and his family seems to range widely between families, and the interview data does not clarify the exact reasons why some families appear to cope better than others. However, it does suggest that the family set-up and relationship between patients and their parents and siblings appears to be one key factor.

I think all parents try and do their best and they live in a huge spectrum of social environments. I think it's a huge spectrum where people are coming from and people that live in the most poor circumstances and the most chaotic circumstances have done fantastically well persuading their children to take home treatment. And some parents are just pretty rubbish parents. And that's when I think life becomes difficult because there are other priorities in your life because it has to be said that coming in for their treatment overrides lots of other things and sometimes that is quite a negative thing but other times it's a low priority for parents. Luckily we don't have very many families like that (HP5)

Haemophilia teams appear to spend a significant proportion of their time and resource on helping patients who struggle with their treatment due to social issues or chaotic lifestyle.

And we've got another family where we have to do supervised prophylaxis for different reasons 'cos their lives are crazy chaotic and they have huge dogs, like really big dogs in the house and there's nowhere safe to actually…These dogs are quite aggressive so there's no way you'd want anyone using a needle near a child with all this going on. So they come to the unit and get to the prophylaxis and I have to say they do come and they are engaged and things. The first family I was talking about it's quite interesting how it's changed… as the children are getting older it's just adding to the complexity because they're refusing to do it to make their parents look bad with social services and it's very complicated. (HP4)

HP appear to be sensitive to individual circumstances, and appreciate that looking after a child with haemophilia can be stressful. However, it can also be challenging for HP themselves to work with these families. It is not always clear whether haemophilia itself is the cause of stress or anxiety, or whether stress or anxiety caused by outside factors make it harder to manage haemophilia.

I don't think it's a particular type of person but I think it's. Would some of the families be like they were if haemophilia was there or it wasn't there, is it that haemophilia has created some of these stresses or is it actually just as a family and as a unit they would have functioned like this, say throwing haemophilia in just kind of makes that even worse, it kind of exacerbates that (HP6)

8.3.4 Theme 3: Improving adherence

This theme describes all the suggestions that were made by the HP of ways in which adherence may be improved. This includes education of parents and patients, psychological support, peer support and support for parents.

Subtheme 1: Education

HP agreed that knowledge and understanding about haemophilia and how prophylaxis works are crucial, and that education may help to improve adherence.

> *You hope that by promoting and improving their knowledge that that's going to improve their adherence. (HP6)*

When a child is first diagnosed parents are educated about haemophilia and then trained to administer treatment when prophylaxis is initiated. Several interviewees emphasized that it is important to involve patients from an early age, so that they can learn to do their treatment themselves gradually before they start secondary school. Several participants suggested that the key reason to start educating and training patients early is that younger children tend to be easier to engage, and curious to learn.

> *The norm would be persuasion I think and gradual involvement of the child and we do make it quite clear to the boys when they start on prophylaxis, when they're going through prophylaxis in primary school, that the aim is that by the time they go to secondary school they'll be giving their own treatment under pain of death if they don't! And most of them will accept that so then it's a question of really reinforcing when they do come up or if we're seeing them in clinic, particularly the multidisciplinary clinics, to emphasise that and to try and make it more firm so that we encourage boys to start helping the parents at home, mixing up treatment, cleaning the skin, take needles out after finishing treatment, you know doing everything other than venipuncture. And then school holidays we try and get them to come to the unit so I guess depending on how they're doing but certainly from the age of nine they'd be coming to the unit to try and learn some venipuncture (HP5)*

Participants agreed that starting early also ensures that patients are used to doing their own treatment before they hit adolescence, which is a period during which it is generally harder to engage patients.

> *They need to learn before secondary school because if they don't, they're not interested, they go to secondary school and mum's doing it, it's easier, it's always been that way. Whereas if around seven or eight, although they might not be able to take it on completely independently, they're interested, they want to do it, you can reward them, they're young enough that they can have incentives to want to do it. And I think if we get them then that then, we've got two boys that are eight and they're doing it completely independently. They say it's like eating their dinner, it's just part of what life has become for them. (HP6)*

It is important to consider that haemophilia HP are not necessarily trained to be educators and do not always have sufficient time or resources to work with families who are struggling. Several participants suggested that in some cases it can be challenging to ascertain what the exact issues are, and what the haemophilia team can do to help improve adherence.

> *I mean there's an element to kind of their family, their understanding so a lack of knowledge does go a long way to not helping with any kind of compliance. But that, whether that's because they're not interested in learning or they don't have the capabilities to understand it or they just don't, don't want it to be part of their life and they'd rather forget about it, I think that has a big influence in whether or not they are compliant. (HP2)*

Subtheme 2: Psychological support

HP suggested that support from a psychologist, play therapist or social worker can be helpful when working with a patient or family who are struggling with prophylaxis. However, the way in which support from these specialists is accessed differs from centre to centre. In two of the centres that were involved in this study the haemophilia team includes at least one psychologist and/or social worker, who can identify psychosocial issues as they arise and work with patients before problems escalate. In the other centres patients have to be referred to psychological services that are provided by a separate team within the hospital, an associated hospital or in the community. It appears that in many cases it is very difficult to access external support services for patients, due to a lack of funding and resources.

> *You would try and refer for psychological support but we don't actually have anything within the unit and we don't have anything to access. We've had a real difficulty with a gentleman who really does need some long-term therapy, and we don't have that. We have it for patients with HIV or hepatitis and trying to get that in the community is very difficult and very challenging, they don't have the resources and it's so frustrating 'cos you can see that he needs it and he wants it [laughs]. (HP4)*

In contrast, in the centres where psychosocial services are embedded the multidisciplinary team appear to work together to try and meet as many of their patients' needs without the need for referral.

> *I think it helps me sometimes because they're looking from the outside, I'm involved in the moment, they're just kind of observing what's happening and then they can offer some different advice. We've done lots since we had psychology embedded in our service, so there's families with children that are new to haemophilia so a new diagnosis, we do some joint work (HP6)*

Most of the HP who were interviewed felt that a multidisciplinary team that includes a psychologist is the ideal set-up, as patients would see the psychologist as part of the team and the threshold to access support would be low.

> *But it would make it more acceptable if it was part of a team, 'cos I'm sure the reason our social worker works for us as a social worker is there is an element of, "Oh I'm not really seeing a social worker, I'm just seeing…" and so that works [laughs], definitely (HP4)*

Interviewees agreed that, rather than having to see a psychologist separately once potential issues arise, an in-house psychologist may be able to identify issues early and support patients and their families through challenging periods without the need for significant psychological interventions.

> *Whereas I think if we had access to someone most of the time or a lot of the time so this person's not a complete alien to these patients, you or they see things different to the way we would see things. They will ask questions differently to the way that we, we would and, you know, you might, I can't help but think that some of the problems that you do see these patients going through could be nipped in the bud. You wouldn't get so bad that you're having to refer them to a counsellor, it's something that might have been able to have been dealt with before it became a big problem. (HP2)*

Several HP described how they sometimes feel unsure about how to deal with mental health issues that are interfering with adherence. In particular nurses described how they try and support patients as best as they can with psychological or social issues, but feel ill-equipped to do so.

> *if they were in-house it maybe they would be able to build it as part of the relationship with the centre in a more holistic sort of way --- but I think there is a lot of psychosocial bits that as nurses we try to do our best but it would be nice if we had somebody who was a professional who knew how to deal, especially with, because some of them have some pretty major issues that, that, you know, sometimes I think we feel a bit lost with how to really deal with properly and support, because then you end up getting involved in all these sorts of things like I say, that aren't really the haemophilia nursing side of things, you're dealing with a lot of other, sorting out other issues and trying to help. (HP1)*

During the interviews it also became clear that HP felt that play specialists are very helpful when working with younger patients and their parents. They can play with a child to distract them while a doctor or nurse examines or treat them, they help prepare children for surgery, and work with them

pro-actively to ensure that children do not develop a negative association with the haemophilia centre.

> *She'll do play therapy with some of our little ones, so they'll come to the centre when we're not really doing anything but they're just going to have a nice time with her. I think that's also really important that it's not that every time they come here there's a massive traumatic event. So they'll be doing things with her, she'll have them in regularly then she'll also do some things around distraction when we're doing something. If she's been working with a child I think then it's really important. There's been a little boy she's been working with here before he was going to theatre [for surgery] so the little boy didn't have regular treatment so then she came and went with him to theatre to keep that continuity to play some of the things that she'd been doing with him and I think that that helps, I think that's why we're fortunate that we have our own, if we had to tap into somebody else's service all the time then you don't get that same continuity. (HP6)*

Subtheme 3: Peer support

Health professionals suggested that some YPH can feel quite alone with it, as they have never come across another boy with haemophilia due to the rarity of the condition.

> *When you've got spontaneous mutations or split-up families that haven't necessarily kept in contact. I had one little one in clinic, he was convinced he was the only boy with haemophilia. I don't think that's uncommon these days. They go to big clinics, there's lots of people, they're not all necessarily coming to a haemophilia clinic. So a lot of them don't see other boys with haemophilia. Being able to compare themselves with like-for-like is quite difficult for them (HP2).*

Most participants felt that bringing YPH together at peer support groups, or through activities and trips, can be beneficial in many different ways. It gives young people the opportunity to socialise with others who are like them, and compare notes on how they deal with certain issues. Meeting others that are affected by the same condition may make them feel less alone or isolated.

> *We used to do residential trips which were fantastic and we haven't done in a while. But I think that's good if you've got a group of boys together, they're all giving themselves treatment, it's fairly normal, that's the way it goes. I think it really helps, especially if you've got someone that doesn't know other patients. If you can actually get them together that's really good. And then do activities, not limit them that way, that helps. I think that would be a good idea. (HP4)*

In some centres nurses facilitate peer support meetings between young patients to try and address specific issues. For instance, two HP explained that they occasionally bring together non-adherent patients with patients who do keep to their treatment to try and encourage non-adherent patients to get back on track with their treatment.

> *And we got the two boys together and I think it went very well because the one who didn't treat was able to see someone of the same age, and see how he managed to do it himself. And he showed him -- and the other boy who didn't treat himself was able to actually do it himself and it's given him confidence because he didn't seem like the most -- one child was quite a confident child and the other one was not such a confident personality and I think it was good for them and I believe they even exchanged numbers. It just gives them a chance to meet someone else with the same condition. (HP3)*

Peer support groups or activities can also help to educate patients. For instance, the Haemophilia Society used the London Olympics as an opportunity to engage young people and illustrate that despite having haemophilia some are able to participate in sport at a high level.

> *In the Olympic team we've got a few haemophiliacs so they organized some swimming team where they invited the haemophiliacs to see what kind of sports you could do which are with minimal contact. Which may be advantageous (HP1).*

However, participants explained that the current pressures on budgets and resources have made it harder and sometimes impossible to organise regular groups or activities locally. As a result patients have to travel to other parts of the country to attend national or even international events organised by the haemophilia society. In addition to the challenges associated with travel to attend these events, staying in contact with other attendees after the event can be difficult as they may live on the other side of the country.

> *Particularly when we had Social Workers and Psychologists attached to the unit, we had groups for teenage boys. So they had days out bowling and just group activities and a chance to meet others to chat. And I suppose it was easier to do when we did have the resource of having a Social Worker attached to the unit, Psychologists attached to the unit and those resources have long dried up. (HP5)*

Subtheme 4: Support for parents

In many cases parents needs support to help them look after their child. During the interviews it became clear that haemophilia centres are the driving force in educating and training parents, but also in addressing issues that may interfere with haemophilia management (e.g. parents with needle phobia).

It was clear that in centres where psychosocial services are embedded this is often easier. This is because multidisciplinary teams are more likely to have all skills and expertise required to support families, and are able to work pro-actively with families to identify potential issues before they escalate.

> *I had some clinics with the Psychologist and both of us worked with families to reflect on what had happened in the year just gone that was good, what are the challenges of the year ahead? What do we need to be working on together to try and do some proactive things and I think that will be the difference for the new families against the old. I think some of our older families even with children of 10 that have maybe had a really rough ride with haemophilia to get them to accept psychology is a huge challenge. Because almost to just accept it is admitting there's a problem and that makes people feel vulnerable. I think it's how we change that or, as nurses that's, frustrating is the wrong word I think but quite, you kind of feel quite disempowered, you feel that these are your families you work with, you want to help them, you can see something that would be good for them and when they won't accept it, it's quite frustrating I suppose. (HP6)*

In many centres the teams use a range of ways to improve the communication with families, with the ultimate aim is to build better relationships, provide better support and address practical issues. It is assumed that a better informed patient, who has a good relationship with the team, will have better health outcomes as they are more likely to adhere to treatment and contact the centre pro-actively to resolve potential issues.

> *And we're going to try and develop Skype as a means of enhancing that message, that communication, so if there's any doubt about whether treatment or not than maybe for us to use Skype and actually have a look at a child who got a bleed, that might help reinforce or sort out that ambivalence maybe. But I don't know, we're just having a think about it. (HP5)*

8.3.5 Theme 4: How can healthcare professionals help to improve adherence?

HP described a range of ways in which they felt they could help patients to improve their adherence. They all felt that it is important to be sensitive to individual patients' needs in everything they do.

Subtheme 1: Being sensitive to individual needs

Personalising, or individualising, haemophilia care appears to be a key focus that is reflected in many different ways, from designing treatment regimens around patients' lifestyles to adjusting communication to individual needs and being sensitive to patients' circumstances.

> *So I suppose what we try to do as well is to look at our, look at people in the context of their situation because it can't be the same for everybody, it's not, it's doesn't work the same for everybody. (HP6)*

In the past patients would follow a standard treatment regimen on set days (Monday, Wednesday, and Friday). However, in recent years regimens have become increasingly personalised and take individual differences and lifestyles into account.

> *Well it would be true to say that it's not prescriptive or didactic and that people's prophylactic regimens may differ from patient to patient and that depends on the patient, it depends on their bleeding phenotype and it depends on the parents, it depends on the geography, etc. (HP5)*

All interviewees emphasized that personalising care is not just about treatment, but also about the way you approach a patient and communicate with them. This can be about providing telephone appointments to accommodate people who work long hours or considering patient's contact preferences (e.g. email, text or telephone), but also about the tone and language one uses and being mindful of any personal issues.

> *I just think it's very different for different people but, you know, you've kind of got to get to know them and try and build your strategy around that if you can. (HP2)*

Haemtrack can be a useful tool to start a conversation with a patient about how and when they are taking their treatment, and in some cases it can help highlight issues that patients may not discuss with the team without being prompted. In that sense it contributes to the individualised approach, as the team log into Haemtrack during a consultation so that they can look at it with the patient, and work on a solution together.

> *Haemtrack is really good because for some reason people will happily lie to my face [both laugh], then when I get up Haemtrack and they'll say, "Oh, actually I am missing the odd one". It's really odd because they've been really honest and then we look at it. I think sometimes they find it difficult to say to the doctor, actually I'm not doing it all the time or I have missed the odd one. I think Haemtrack is quite good because it's quite nice, not to check up on people but because it starts the conversation and it makes them actually talk about it and you can say, "Okay, well why are you missing it, is there things we can do to help?". Cos some patients will do things like they'll get in their head it has to be done at this time of day, and then things change in their life or something happens and that they can't do it easily at that time of day but they don't necessarily think actually you could just do a different day [both laugh] so that helps. (HP4)*

Although prophylaxis is the treatment of choice, HP appreciate that for some patients it is simply not possible to follow a prophylactic regimen. During the interviews they explained that they often try a range of different strategies that take the individual patient's circumstances into account, but that in some cases they have to accept that a patient does not want to take prophylaxis. In those cases the focus shifts to making sure that the patient does not disengage completely, and adheres to an on-demand regimen to treat bleeds if and when they occur.

> *Other times they've deliberately chosen that actually I don't want to be doing this now and with some patients that I don't really want to come to the unit, I don't want to be having treatment, I don't want all this fuss and all these appointments. And that's a bit more difficult. And you try and I can think of a patient that comes and he has a bleed and you've to judge the timing because if you push too much for him to get to clinic and getting prophylaxis they completely back off, because they obviously have a reason that they're choosing not to and it is their body and if they feel like you're really pushing them they're just going to turn up even later after the next bleed. So sometimes I'll bring it up and other times I won't and I try and do it in little bits, and try and encourage them back. (HP4)*

In other cases haemophilia teams reach a compromise with a patient or family that reduces the treatment burden while still providing some prophylactic cover for the patient.

> *No, I think it's persuasion and education and if they understand why you're saying what you're saying and most of them will go along with that, it makes life harder for families who are rushing around first thing in the morning and that in itself can influence when you're teaching the boys prophylaxis because it's much easier for a parent to spend five minutes to do treatment than to go through this whole thing of letting the boy do everything on a weekday but it's reasonable to start thinking about changing the days and doing prophylaxis at the weekend because then that gives them a bit more time and flexibility. (HP5)*

From the interviews it became clear that HP are passionate about supporting their patients, and believe that a good relationship between patients and the haemophilia team can be crucial in keeping patients on track.

> *There's a lot of things that contribute to compliance and I think not least how well we support them from here and how early that starts I think is fairly fundamental. If we're supportive from the outset and we're available and if they find that the information that's coming back from here is useful. I think ringing in out-of-hours and having a doctor that doesn't really know anything, is probably not very helpful. And it would then "oh what the hell, I'm not going to bother, I'll wait till Monday", potentially that's three days gone if they've done something Friday evening. And it starts quite early I think, and if they've got rubbish veins, if we're crap, excuse the language, but at getting their veins then again if we can't get it how do we teach them how to do it? And it doesn't reflect very well on us and it doesn't build them any confidence in us either so they're not necessarily going to engage particularly well. And, as much as I hate to say it, sometimes I think you really do have to give the extra mile in order to actually get it back from them but you've got to be willing before they're going to be. [Laughs] (HP2)*

Maintaining a good relationship with patients used to be more straightforward, as patients had to come to the haemophilia centre frequently to receive treatment, or to pick up their home treatment. These visits offered an opportunity to catch patients for an informal chat, and enabled the team to quickly identify potential issues. Several participants felt that, now that many patients get their treatment delivered to their home, contact has become less frequent with some patients only coming to the centre once or twice a year.

No, I think the main reasons for that lack of contact are not necessarily home treatment because people have been on home treatment for a long time, home delivery I think because when treatment was picked up from the hospital that was always an opportunity to have a chat to the parents, I think the parents found it very helpful that they could come in and have a cup of coffee and talk about what had been happening. Whereas now it's quite a lot different, so the treatment will get delivered, if prophylaxis is going very well then there's no contact at all with the hospital. (HP5)

Subtheme 2: Regular contact and continuity of staff

HP identified the lack of regular contact with some of their patients as a potential issue that may be associated with low adherence. Participants explained that when contact with a patient breaks down (i.e. when they do not attend clinic appointments, or do not answer telephone calls or letters from the hospital) it can be an indication that the patient is not keeping to their treatment regimen and not treating bleeds appropriately. These patients tend to be aware that they are not looking after their haemophilia adequately, but do not want to engage with the haemophilia team.

The severes [patients with severe haemophilia] are meant to be seen at least six-monthly minimum. But there's been a recent case that people have fallen through the loop --- Weather they've DNA'ed [did not attend], and then they got discharged somehow. Or a patient can walk out without making their appointment. And therefore then they don't have one. You really need to get them in, but getting in contact with them can be difficult. And getting them to come… (HP1)

It can be very challenging to re-engage these patients, and convince them to attend a clinic appointment.

People are less inclined to come because they think they're going to get told off so they think actually I didn't manage this right and it's how we get that quite right as well (HP6).

Interviewees explained that they tend to spend a lot of time and effort trying to contact and chase patients that they are concerned about. They agreed that this tends to be a small group of patients who take up a disproportionate amount of time.

A fairly small group of patients who take up a significant amount of time and worry if you like because they don't adhere (HP4).

During interviews it became clear that HP care about their patients very much and are genuinely worried when a patient goes 'off radar'. In particular nurses felt that they support patients in many more ways than described in their job description. They appear to go above and beyond to help patients, usually with the ultimate aim to get them back on track with their haemophilia treatment.

> *We kind of joke with each other that you're the Nurse, you're the Social Worker, you're the Psychologist, you're the Teacher, you're kind of everything because you're involved in somebody's life often at a really kind of tricky or sticky time. And that kind of happens throughout with our families. We don't have a huge number of children in our centre but what tends to happen is that for each of our families at some point there's a little kind of blip and the intensity of what they need goes up and then fortunately somebody else, they kind of need a little bit less and it's kind of like that's a kind of up and down for all of the families. (HP6)*

Staff turnover appears to be very low in many haemophilia centres, with many staff members working in the centre for many years. As a result HP and patients get to know each other well, and often develop a close relationship.

> *Well there's been a paediatric nurse and she's been here for, has she been doing it? Ten year or maybe, eight years, eight years maybe but you know, you think of younger children so she will have seen them from quite young/ yeah, you do sort of get to know and you get to know more about their wider circumstances over time as well, you know. (HP1)*

Visiting families at home can help with establishing a good relationship, and identifying potential issues that would be difficult to ascertain in clinic.

> *But I think once you start actually going and seeing them outside the hospital it gives you a completely different dynamic on things and them you, and sometimes it becomes a lot more personal and you are more involved in their lives, you're more involved because you're watching them grow-up and they know you, which is nice and it helps to some extent because they've got a better trust and a better bond with you and they'll let you do, you know, that sounds awful but, you know, with their treatment, they've got used to mum and dad doing it, for a lot of them they will let me do it but not necessarily other nurses that, you know, are just as capable but because they don't know them and it's never been done on them and they've not seen them do it, they're not going to do it (HP2).*

Although the close relationship between the haemophilia team and their patients was generally seen as positive by interviewees, it was also recognised that it can lead to over-dependency on a specific nurse or doctor. One nurse explained that she regularly gets contacted on her personal mobile phone by patients, another joked that nurses do not need to say their name when they answer the phone as patients tend to recognise their voices.

> *when I go and see them at home everything, all the contact then once I leave the hospital is on my mobile so they automatically get my mobile number so out-of-hours on occasions I'll get calls and things that are happening over the weekend. I had this argument with my husband the other day actually because I kept getting a few texts from one of them this weekend and it's like "you're not at work, why are you, you know, why are they still bothering you?" I was like "well their treatment doesn't stop just because it's not 9 to 5 Monday to Friday, you know, they're still treating at the weekend and if they're worried about something", you know, (HP2)*

Subtheme 3: Collaboration with schools and community

In addition to working with patients and their families directly, haemophilia teams try to engage and collaborate with schools and community teams as much as possible.

> *I also do go in to see them at home and go to schools, to visit schools for education particularly, often for our boys when they're changing from junior school up to secondary school, that's quite a change, in terms of dependence and the number of staff that are going to be involved with them, it's very different from what it's like in a primary school setting. Sometimes because of our geographical location do quite a bit of supporting other community teams so the thing that sometimes we struggle with, kind of outsourcing it is, is that as a Paediatric Nurse the skill of venepuncture is not something that Paediatric Nurses take on often in a hospital setting, it's the doctors that are doing it. So in the community we have a few teams that have got involved in doing it with some of our children and then if we have other children in that area that really helps but then we have other teams that we're trying to find something more local for our families and we can't find things and that's quite challenging (HP6).*

Collaboration with schools is an important priority for haemophilia teams, as young patients spend a significant amount of time at school and may take part in potentially risky activities, such as PE lessons and playing outside at break time. Interviewees explained that they also try to educate

schools about what haemophilia is, and what it means for the patient and their family, to encourage schools to focus on supporting the patient rather than just managing risk.

> *Schools, um, the Haemophilia Nurses will visit all schools anyway when a child with a bleeding disorder starts, just really to talk generally about the haemophilia and what to do in terms of what happens if they bump their head or they fall over and get a graze on their knee, it's really just to educate and sort of calm people down a bit about you know, this child is not going to bleed to death in the playground and really just to get a sense of perspective about it as well. But they won't be teaching the School Nurses how to give treatments, absolutely not. (HP5)*

Haemophilia Comprehensive Care Centres tend to cover a wide geographic area, which means that patients may live quite some distance from the centre. To make life easier for those patients who are not able to come to the centre because of the distance, the haemophilia teams often engage community teams to provide additional support.

> *Yeah, but they're taking on, so they're doing some of his treatment for the older boy because mum hasn't been able to take that on and they'll be doing that for the younger boy as well and I think the bonus for this family is that the same team of nurses work across the school and the community whereas if they were somewhere else that wouldn't happen, you'd have two or three teams of nurses so that would kind of make it a bit more complex but they've got masses of support. (HP6)*

There is also a significant amount of collaboration with HP in other specialties. This can be challenging, as haemophilia is not necessarily well understood by all due to its rarity. One interviewee felt quite strongly that patients need help and support to ensure they receive adequate treatment for non-haemophilia related health issues.

> *I think we struggle with some of the other specialities and their poor knowledge, not understanding, not wanting to actually get involved in something that's not their thing, which is kind of fair enough but at the same time well if we didn't act the same, if we acted the same way god knows what would happen to some of these people. [Laughs] But, you know, someone's got to advocate for them haven't they? And I think that's where we come in, whatever it is and obviously you draw a line somewhere but at that point you need to find the right person to fill in where you can't. I think that's what it is all about isn't it? It's arming them with the right tools to get from A to B safely and happily so that they're prepared to do what they need to do with those tools in order to get there I think. (HP2)*

8.4 Discussion

HP interviewed for this study felt that adherence among YPH is generally good, although they explained that levels of adherence are likely to fluctuate with even very adherent patients experiencing short periods of non-adherence. As prophylactic regimens are increasingly personalised and flexible it is much harder to ascertain if a patient is adherent. In many cases haemophilia teams only intervene if a patient is presenting with bleeds or not attending check-up appointments, as they are often an indication that someone is not engaged with their treatment, and may be struggling with managing their haemophilia.

Interviewees expressed concern about patients who do not treat bleeds appropriately, as these bleeds often last longer and cause more damage. It was suggested that patients who present late with bleeds, or do not treat bleeds adequately are often also those who struggle to keep to their normal treatment regimen.

Time management and lifestyle-related issues were suggested to be key reasons why their patients do not adhere to their treatment. During a busy time, or during a significant life event or change, someone is much more likely to forget their treatment or find it harder to fit treatment in. Most interviewees agreed with the existing literature that adherence may be a particular issue during adolescence, as a result of the specific developmental issues that characterise this period. It can be challenging for haemophilia teams to engage with adolescent patients, particularly if they rebel against the haemophilia team and parents. Other reasons for non-adherence that were mentioned were issues related to venous access (difficulty in accessing veins or injection-related anxiety); absence of symptoms (patients who have not experienced any serious bleeds thanks to prophylaxis can find it difficult to understand why they need it); family dynamics (relationship with and support from parents and siblings); psychosocial issues (stress and anxiety, chaotic lifestyle, social issues); and a lack of knowledge about haemophilia and treatment.

HP felt that a multidisciplinary team that includes a psychologist, play specialist and social worker would be the ideal set-up to support patients (and families) who are struggling with prophylaxis. However, in most haemophilia centres psychological or social support have to be accessed via referral which is often difficult due to a lack of funding and resources. Participants also felt that YPH together through peer support groups or activities is beneficial, as it gives them the opportunity to socialise and compare notes with others who are in the same position, and may make them feel less alone or isolated. However, they explained that the current pressures on budgets and resources have made it harder and sometimes impossible to organise support groups or activities locally.

From the interviews it became clear that HP are passionate about supporting their patients, and believe that a good relationship between patients and the haemophilia team can be crucial in

keeping patients on track. They explained that they tend to spend a lot of time and effort trying to contact and chase patients that they are concerned about, and agreed that this tends to be a small group of patients who take up a disproportionate amount of time.

As young patients spend a significant amount of time at school and may take part in potentially risky activities, (such as PE lessons) increasing knowledge and awareness of haemophilia at schools attended by patients appears to be an important priority for haemophilia teams. They explained that they also prioritise collaboration with HP in other specialties who are treating one of their patients for a health issue that is not related to haemophilia. This is key because haemophilia is not necessarily well understood by all due to its rarity.

The interviews conducted with HP made it clear that they are passionate about supporting patients in as many ways they can. The underlying motivation appears to be to keep patients on track with their treatment, to ensure optimal health outcomes. Their work is made challenging by pressures on resources, patients' social and psychological issues, and limited understanding of haemophilia within and outside of the medical profession. However, it appears that they manage to maintain their motivation to do their best, which is so very clearly appreciated by patients and their families.

The next chapter will provide a discussion of the findings, implications and conclusions of all three qualitative studies described above.

Chapter 9 - Discussion of qualitative interview studies

The aim of the qualitative studies was to gain a comprehensive view of experiences and perceptions in relation to prophylactic treatment among young people with haemophilia (YPH), their parents and healthcare professionals (HP) in order to better understand what drives (non-)adherence among adolescents and young adults with haemophilia.

9.1 Findings

Table 9.1 presents the superordinate themes of the three studies, and a short discussion of commonalities and differences between the three studies.

There were many commonalities between the barriers and facilitators/motivators of adherence that were described by patients, parents and healthcare professionals (HP). However, there were some differences in the emphasis that was put on different factors. Patients felt that non-adherence was mainly due to treatment being inconvenient, time-consuming and unpleasant. They recognised an association between their mental state and adherence, where stress and anxiety can have a negative impact on adherence, but also in the other direction where treatment can cause some anxiety and stress. Parents felt that psychosocial factors (such as not wanting to be different from peers and prioritising social life) are key barriers to adherence. HP agreed with the barriers that were suggested by patients and parents, but also mentioned social and family issues (such as chaotic lifestyle and lack of parental support).

The analysis suggests that barriers and facilitators/motivators of adherence can be roughly grouped in four areas; the patient themselves, the treatment, the social environment and the haemophilia team. Barriers are mostly related to the patient's lifestyle, negative experiences and perceptions in relation haemophilia and treatment, psychological issues (such as anxiety), and prophylactic treatment itself (venous access, treatment being unpleasant, needle phobia, etc.). Facilitators and/or motivators to adherence are mostly related to the social environment (e.g. support from parents and friends) and care and support received from the haemophilia team.

Table 9.1: Discussion of superordinate themes of patient, parent and healthcare professional interviews

Superordinate themes	**Discussion of commonalities and differences between patients, parents and healthcare professionals**
Patient interviews	
Difficult balance between avoiding risk, managing haemophilia and living a normal life	Patients explained that haemophilia, bleeds and in some cases pain are part of their life and identity. By young adulthood patients feel that they are experts in haemophilia, and have found a way to tailor their treatment around their lifestyle.
I don't like taking treatment but hardly ever miss an injection	Most patients dislike taking treatment because it is inconvenient and at times painful. However, they realise prophylaxis will protect them against bleeds and allow them to live a normal life, which encourages them to keep to their regimen. Most patients have found a way to incorporate prophylaxis into their routine, which helps them to remember it.
Support from parents and the haemophilia centre keeps me on track	Patients tend to be very happy with the support they receive from their parents and the haemophilia team. This support appears to be a key facilitator to their adherence. Many patients also receive support from friends/peers and siblings.
Parent interviews	
Self-management	Parents felt that their son's adherence was generally good in relation to taking his treatment, but that he tends to be less adherent in relation to completing his treatment log, avoiding risky activities and treating bleeds in a timely and appropriate manner.
Drivers of adherence	Parents described similar barriers as patients, but emphasised the psychosocial impact of haemophilia. Parents agreed that social support is a key facilitator and that better access to psychological support would help improve adherence. Parents understood the distinction between skipping and forgetting, but when describing their son's non-adherence it was not always clear which one they were referring to.
Impact of haemophilia	Patients were keen to emphasize that they do not let haemophilia impact their life. However, parents spoke extensively about the negative impact on family life and school, which in turn had a negative impact on their son's academic and career prospects.
Haemophilia care	As patients, parents felt that after the initial period of adjustment haemophilia had become part of their reality and routine. They were very positive about the care/support their son (and family) received from the haemophilia team. Parents felt that awareness among the wider medical profession needs to improve.
Healthcare professionals interviews	
Healthcare professionals' estimates of adherence	Healthcare professionals agreed with parents that overall adherence is generally good, and suggested that non-adherence is mostly about timing of treatment. They also agreed that it is challening to persuade young people to complete their treatment logs, and treat bleeds immediately and appropriately.
What drives non-adherence?	Healthcare professionals described similar barriers to those mentioned by patients and parents. However, they felt that social and/or family issues, and absence of significant symptoms (ie bleeds) are also common causes of non-adherence.
Ways in which adherence can be improved	Healthcare professionals agreed with patients and parents that social support (for patients and parents) is the most important facilitator to adherence, and that psychological support can be hugely helpful and is likely to facilitate better adherence.
What do healthcare professionals think they can do themselves to improve adherence?	Haemophilia healthcare professionals appear motivated and dedicated to support patients and their families. They are often sensitive to individual needs, and go above and beyond to support patients. This includes staying in regular contact with patients who are struggling, and visiting schools and sport clubs to raise awareness and educate care givers in how to look after a boy with haemophilia.

The patient

The findings of the three interview studies suggest that haemophilia can have a significant impact on young patients and their families. Patients are keen to live a 'normal' life, and parents and HPs do what they can to support this. Managing risk appears to be an important part of daily life, and many patients experience a tension between their desire to be normal on the one hand and managing their haemophilia successfully on the other.

Patients, parents and HPs described that it can be challenging to fit treatment in with other priorities such as school, work and social life. This is particularly because treatment often has to be taken before a patient leaves the house in the morning, which means that they have to get up earlier to allow enough time to take treatment. Most patients and parents described how prophylaxis has become part of their routine, and that they find it challenging to remember treatment when they are out of the normal routine (e.g. on holiday, or away from home).

Parents and HPs felt that adherence is a particular issue during adolescence, as a result of the specific developmental issues that characterise this period. They explained that it can be challenging to engage with adolescent patients, particularly if they rebel against the haemophilia team and their parents. During this stage young people often strongly identify with their friends and resent being different due to their haemophilia. In some cases this leads to non-adherence and disengagement with haemophilia and treatment more generally.

Several patients and parents described psychological issues (such as stress and anxiety) that they felt had had a negative impact on adherence. But also that treatment can cause anxiety and stress in situations where there are issues in relation to venous access or needle phobia. This in turn can lead to worse adherence.

HPs mentioned that a lack of knowledge about haemophilia and treatment and in particular an absence of symptoms can lead to non-adherence. This is because patients who have not experienced any serious bleeds thanks to prophylaxis can find it difficult to make the connection (between prophylaxis and absence of bleeds) and to understand why they need to take prophylaxis.

Social environment

Patients explained that support from parents, friends, and the haemophilia team is the most important thing that helps them keep on track with their treatment. In particular parents tend to be very involved with their sons' haemophilia management, and often continue to support with treatment after he leaves home.

HPs agreed that social support is an important facilitator to adherence, but also felt that issues in relation to a patient's social environment can be a barrier to adherence. Examples of situations that

can have a negative impact on adherence that they described include a lack of family support, a chaotic lifestyle, and issues related to relationships within and outside of the family.

The treatment

YPH, parents and HPs agreed that adherence tends to be good. However, due to the increasingly personalised and flexible approach to prophylaxis, adherence is not straightforward to define and assess. Some patients and parents appeared slightly confused when describing adherence, particularly when they were trying to distinguish between forgetting and skipping. This could be due to confusion, or because they find it is easier to justify forgetting an injection rather than deliberately skipping one.

Both patients and parents felt that it is ok to miss occasional injections, as long as the gaps between injections are not too long. They also felt that it is important that treatment is always taken in advance of physical activities, to reduce the risk of activity-related bleeding. HP agreed with this to a certain extent, particularly because they conceded that it is very difficult to convince a patient who does not bleed to improve their adherence. They also explained that at times they find it challenging to ascertain whether their patients are adherent or not. In practice they therefore tend to direct their focus towards patients who are presenting with bleeds or those who have clearly become disengaged with their treatment (e.g. not attending clinical appointments, not responding to letter or telephone messages, not completing treatment logs, etc.).

One key barrier to adherence is the fact that treatment can be time-consuming and unpleasant; particularly if there are issues in relation to venous access or needle phobia.

Facilitators mentioned by both patients and parents included establishing a good routine; setting reminders or alarms;; and psychological support (from psychologists, counsellors, social workers, or other support workers). In addition, parents felt that it is important to give young people some leeway, and allow them the space to develop the maturity and self-management skills that are required to manage haemophilia, and find out for themselves why prophylaxis is so important.

Parents appeared to be aware of the importance of treating bleeds appropriately, and felt this was just as important for their son as him adhering to his prophylactic regimen. HP expressed concern about patients who do not treat bleeds appropriately and suggested that these patients are often also those who struggle to keep to their prophylactic regimen.

The haemophilia team

Both parents and patients felt that the support from the haemophilia centre is excellent. They felt that they can always call the haemophilia centre for advice, or in some instances just a bit of moral support. In particular nurses, who have often worked in the centre for a number of years, appear to play an important role in supporting patients and their families. Because of their often pro-active approach they are able to identify potential issues (such as non-adherence) early, and then work with patients to try and find a solution. It appears that nurses often become involved with a range of issues that may affect patients, which are not necessarily always limited to medical problems.

HPs felt that a multidisciplinary team that includes a psychologist, play specialist and social worker would be the ideal set-up to support patients (and families), particularly those who are struggling with prophylaxis. They also felt that bringing YPH together through peer support groups or activities is beneficial, as it gives them the opportunity to socialise and compare notes with others who are in the same position. HPs described how patients who are managing their haemophilia successfully (and adhere to their prophylaxis) can become role models for patients who are struggling with their treatment. They described examples of situations in their own haemophilia centre where these peer support relationships had resulted in improved adherence among young people who had previously struggled.

Increasing knowledge and awareness of haemophilia at schools attended by patients appears to be an important priority for haemophilia teams. Another important part of their role is collaboration with HP in other specialties, particularly those who are treating one of their patients for a health issue that is not related to haemophilia. This is key because haemophilia is not necessarily well understood by all due to its rarity.

9.2 Strengths and Limitations

As highlighted in the literature review, the existing literature in this area is very limited in terms of the number as well as the quality of studies published. The strength of these qualitative studies is that they are nationwide (recruiting participants from five haemophilia comprehensive care centres across England and Wales, including paediatric, adult and mixed centres). Additionally, the focus in the studies is specifically on young people, rather than including patients of all age groups. This is particularly important because there are age specific issues that may influence adherence. Participants include YPH, parents of YPH, and HP, who were recruited from five very different centres (in terms of their geographic location as well as their organizational structure). As a result the findings represent views of a range of individuals, who are likely to have different experiences and perceptions in relation to haemophilia and prophylaxis. Another key strength is that these studies are part of a larger mixed method research project, in which quantitative and qualitative

findings complement each other to present a comprehensive study of adherence to prophylaxis among young people in the UK.

The most important limitation that needs to be highlighted is the fact that all the interviews were conducted by a PhD student with limited previous experience in qualitative research. This potentially may have influenced or biased the discussions with participants, particularly during the first few interviews. The interview data represent the lived experience of individual participants, which are not necessarily representative of the whole population. It is possible that those YPH who agreed to be interviewed are more motivated and engaged in relation to their treatment, and that YPH who are non-adherent or disengaged with their treatment would have been less likely to take part in research about adherence. Particularly because disengaged patients often do not attend their clinical appointments, and would therefore not have been approached to take part. It is impossible to know whether the lived experiences represented in the interview data are still true today, as individual circumstances, experiences and perceptions may have changed since the interviews took place, or indeed may fluctuate over time. However, as the findings from the YPH, parent and HP studies were broadly in line it is reasonable to assume that the findings are representative of the wider haemophilia community. Another potential limitation is that the majority of interviews took place within hospitals. The interviews were always conducted in a private room, and participants were reassured that everything they said would be confidential. However, patients' responses during the interview may have been biased or influences by their previous (potentially stressful or traumatic) experiences in the hospital.

9.3 Implications

Notwithstanding the limitations discussed above, the findings of this study have a number of implications. The findings from interviews with patients, parents and HP indicate that adherence is generally good among YPH. Support from parents and the haemophilia team appear to be the most important facilitators to their adherence. Haemophilia teams tend to have good relationships with many of their patients. These relationships are often maintained by regular contact, particularly with those patients who are struggling. In the current economic climate, and context of reorganisation and rationalisation of the NHS, this model of care may come under increased scrutiny and may not be able continue if resources are cut. However, the findings from this study provide evidence for the benefits of the current approach in managing patients with severe haemophilia, and may therefore help haemophilia centres to build a case to retain their current level of resource.

Many patients require, and indeed access, additional support from a psychologist to help them with the psychological and social impact of haemophilia. YPH, parents and HP agreed that psychological support is an important element of the comprehensive care that many haemophilia patients require.

They felt that this support should ideally be provided within the haemophilia centre setting, so that the threshold to access this support is low and psychologists are able to work with patients pro-actively to address issues before they escalate. HP felt strongly that regular psychological input would contribute towards better patient outcomes, particularly for patients who struggle or are disengaged with their treatment. However, several of the centres involved in this research no longer have (or never had) a psychologist embedded in their team. The findings of this research may help centres to put forward an argument to improve access to psychological support, or indeed appoint a psychologist in their centre.

The findings also indicate that, due to the increasingly flexible approach to haemophilia treatment in the UK, adherence to prophylaxis is difficult to define and assess. HP agreed that they often prioritise working with patients who are clearly struggling, as indicated by bleeding episodes or other haemophilia-related issues they present with. This is partially because they have to prioritise due to limited resource and time, but also because patients who are not bleeding are often assumed to be doing well, even if they are not adhering to their treatment.

Patients' tendency to bleed is not only determined by the severity of their haemophilia and extent to which they adhere to their treatment. But also by their bleeding phenotype, which can be relatively mild even for patients with severe haemophilia. Therefore it could be that a patient with severe haemophilia 'gets away' with non-adherence to a certain extent, and may not necessarily need to improve their adherence. The findings of this research suggest that it may be useful to shift the focus of future research away from looking for ways to improve adherence generally, but rather to focus on improving adherence among those patients who are likely to have worse outcomes due to sub-optimal adherence. It would be useful for the haemophilia HP community to discuss adherence in this wider perspective, to come to a nationwide agreement of what good adherence looks like in the context of improving outcomes in this patients group.

9.4 Conclusion

Adherence to prophylaxis among YPH tends to be good, and support from parents and the haemophilia team appear to be crucial to maintain good levels of adherence. The findings from the qualitative studies indicate that there is a need for the haemophilia healthcare community to consider ways in which to assess adherence that reflect the increasingly flexible and personalised approach to prophylaxis. With increased pressure on resources haemophilia teams may not be able to maintain regular contact with all patients. They may therefore need to focus their attention on those patients who are struggling (e.g. presenting with bleeds), or are clearly disengaged with their treatment (e.g. not attending regular check-ups, difficult to contact or not completing treatment logs).

Chapter 10 - General discussion

The aims of this mixed methods research project were to assess levels of adherence among adolescents and young adults with haemophilia, and learn what drives their adherence.

10.1 Findings

The quantitative findings of this study suggest that overall adherence among young people with haemophilia (YPH) is generally good. The qualitative findings confirm this, and suggest the support provided by haemophilia centres is likely to contribute to these high levels of adherence. The good relationship and regular contact between the clinical team and their patients appears to enable healthcare professionals to identify and address potential issues (such as non-adherence) early.

Unintentional and intentional non-adherence

The quantitative study found that non-adherence was more likely to be due to forgetting than skipping. It is likely that young peoples' busy lifestyles are partially responsible for this. However, findings from the qualitative studies also indicate that patients may find it easier to admit to forgetting than skipping. This may be because they are more likely to be 'told off' if they admit to intentionally skipping injections, whereas they get a more understanding response when they admit to sometimes forgetting injections. The increasingly flexible approach to prophylaxis can at times make it confusing for patients to work out when their next injection is due, leading to unintentional non-adherence. It can also make it more challenging for the haemophilia team to ascertain the extent to which individual patients adhere to their treatment regimen, and identify the reason why they miss injections.

Differences between adolescents and young adults

Interestingly, the quantitative findings suggest that despite the fact that there were some significant differences between adolescents and young adults in terms of psychosocial factors that may be associated with adherence, there was no significant difference in their level of adherence. This is most likely because the psychosocial factors that were significantly different may not significantly contribute to the variation in overall adherence.

However, that does not necessarily mean that it has no merit to assess differences in psychosocial factors between age groups, as they may provide further insight and help identify potential areas for intervention or improvement. For instance, young adults had greater beliefs in the necessity of treatment and greater necessity/concern differential scores, indicating that their belief in the

necessity of prophylaxis outweighs their concerns about this treatment. This suggests that potential interventions to change patients' beliefs in relation to necessity of and concerns about prophylaxis may be better targeted towards younger patients.

In relation to social support the findings suggest that although young adults receive less support, they are not less satisfied with the support they receive. This indicates that adolescents are likely to require more/more frequent support with their treatment. The interview findings confirm this, and suggest quite strongly that support by parents and the haemophilia team are key facilitators that help in particular young patients keep on track with their treatment.

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Association between adherence and clinical outcomes

In the quantitative analyses there was no significant association between adherence as a continuous measure and clinical outcomes (the number of bleeds and hospital visits). However, when the sample was dichotomised into adherers and non-adherers there were significant differences in the number of bleeds and hospital visits. Both of these findings are in line with a recent single centre study in the US (Duncan, Kronenberger, Krishnan, & Shapiro, 2014). However, the direction of the relationship between adherence and bleeds was not in the direction suggested by Duncan and colleagues (2014). Interestingly, the findings of our study suggest that adherers experience more bleeds and visit the hospital more frequently than non-adherers. As described in chapter five, there are several possible explanations for this:

- Clinical data were collated retrospectively for a six month period (i.e. the number of bleeds and hospital visits that patients had during the last six months), whereas patients were asked to report their adherence during the last month. It could therefore be that patients who experienced frequent and/or severe bleeds more than one month ago were motivated to improve their adherence during the last month in order to prevent further bleeds.
- It may be that more adherent patients are more attentive to bleeding episodes and symptoms of bleeds (and more likely to report bleeds through Haemtrack or by calling the haemophilia centre), whereas less adherent patients may be more relaxed or less likely to interpret symptoms as bleeds (and less likely to report bleeds). It may therefore be that the number of bleeds for non-adherent patients are under-reported in their clinical notes.
- Patients with good adherence may be more confident in the protection afforded by their prophylaxis, and therefore more likely to engage in physical activity compared to non-adherent patients. This in turn may increase their risk of bleeding (due to activity-related injury or increased pressure on joints and muscles).
- Patients with a mild bleeding phenotype are less likely to suffer bleeds and may therefore 'get away' with suboptimal adherence to prophylaxis.

The current literature suggests that indications for and the efficacy of prophylaxis in adults with haemophilia remain controversial. It appears uncertain whether prophylaxis should stop or continue once adulthood is reached (Hay, 2007). Currently, many patients (particularly those with an active lifestyle) with severe haemophilia in the UK continue their prophylactic treatment into adulthood. However, there are also patients who choose to follow a less intensive regimen (usually by reducing the frequency of injections), or even switch to on-demand treatment without any prophylactic injections. The current more flexible approach to prophylaxis allows haemophilia teams to work with each individual patient to find a regimen that works for them in terms of lifestyle but also affords them the protection required to minimise bleeds

In future research studies it would be useful to validate clinical outcome data collated from medical files against self-reported data, so that the analysis can provide more insight into the association between adherence and clinical outcomes. The addition of a haemophilia-related quality of life measure would allow for analysis of the wider implication of non-adherence, rather than just focussing on clinical outcomes such as bleeding episodes.

Psychosocial factors of adherence

Social support has been widely reported as an important facilitator of adherence (DiMatteo, 2004; La Greca & Bearman, 2002; Williams & Bond, 2002). The quantitative findings provide further evidence for this suggestion, with greater social support both correlated with and predictive of better overall adherence and better remembering and less skipping. The qualitative findings indicate that patients, parents and HP all feel that social support (from parents, family and friends) is a key motivator that helps patients to keep on track with their prophylaxis. The close relationship with the haemophilia team, and the support that patients and their families receive from them, were also highlighted as important facilitators to adherence. HPs explained that they do what they can to support patients and their families, as they feel this directly contributes to patients' adherence.

Findings from a previous UK study which recruited participants aged 12 years and older in a single centre in London (Llewellyn et al., 2003) suggest that better adherence to clotting factor is associated with greater perceptions of symptomatology (Illness identity) consequences of haemophilia, and necessity of prophylaxis, but not fewer concerns about this treatment. However, the findings of the current study indicate that both greater perception of necessity of prophylaxis and fewer concerns about this treatment (and therefore the necessity/concern differential) are associated with better adherence. Only a greater differential (and not greater belief in necessity of prophylaxis or fewer concerns about this treatment) was predictive of better overall adherence. However, fewer concerns were predictive of both better remembering and less skipping. The

interview findings also highlight that patients feel that the reason they keep to their regimen is that they believe they need prophylaxis to prevent bleeds, and live a 'normal' life.

In relation to illness perceptions only perception of greater emotional responses (negative feelings such as fear, anxiety and anger) was associated with better adherence. This suggests that these negative feelings, most likely anxiety or fear about haemophilia, may act as a motivator to stay on track with treatment. However, when comparing adherers and non-adherers only illness perceptions in relation to the timeline of haemophilia were significantly different, with non-adherers perceiving their haemophilia to last longer. It is interesting that only negative feelings in relation to haemophilia, and not negative mood in general, was associated with adherence. Indeed, there was no association between positive or negative mood and adherence.

The findings suggest that greater positive outcome expectations (perception that taking treatment will have positive outcome) are correlated with better overall adherence, and also predictive of overall adherence and better remembering. Although self-efficacy was not significantly correlated to or predictive of adherence, adherers did have greater self-efficacy scores in relation to taking their prophylaxis. This suggests that talking to patients about the efficacy of prophylaxis (providing protections against bleeds), and helping them to develop the skills and confidence to take their treatment, may help patients keep to their regimen.

In summary, it appears that better social support, greater belief in the necessity and efficacy of prophylaxis, fewer concerns about this treatment and more negative feelings about haemophilia are the most important factors associated with better adherence among young people with haemophilia.

Facilitators and barriers of adherence

There were many commonalities between the barriers and facilitators/motivators of adherence that were described in interviews with patients, parents and healthcare professionals (HP). However, there were some differences in the relation to the order of importance that participants put on different barriers. Patients felt that non-adherence was mainly due to treatment being inconvenient, time-consuming and unpleasant. They recognised an association between their mental state and adherence, where stress and anxiety can have a negative impact on adherence, but also in the other direction where treatment can cause some anxiety and stress. Parents felt that psychosocial factors (such as not wanting to be different from peers and prioritising social life) are key barriers to adherence. HP agreed with the barriers that were suggested by patients and parents, but also mentioned social and family issues (such as chaotic lifestyle and lack of parental support). The qualitative analysis suggests that barriers and facilitators/motivators of adherence can be roughly grouped in four areas; the patient themselves, the treatment, the social environment and the haemophilia team. Barriers are mostly related to the patient's lifestyle, negative experiences and

perceptions in relation haemophilia and treatment, psychological issues (such as anxiety), and prophylactic treatment itself (venous access, treatment being unpleasant, needle phobia, etc.). Facilitators and/or motivators to adherence are mostly related to the social environment (e.g. support from parents and friends) , care and support received from the haemophilia team, and positive treatment beliefs.

Combining the qualitative and quantitative findings suggests that key facilitators to adherence are: greater belief in the necessity of prophylaxis, fewer concerns about prophylaxis, greater positive outcome expectations, greater negative emotions (such as fear and anxiety) in relation to haemophilia, more frequent social support and greater satisfaction with this support, positive experiences and perceptions in relation to treatment, and the support and guidance received from the haemophilia team,

In relation to barriers, the quantitative and qualitative findings suggest key factors relate to the patient's lifestyle (e.g. chaotic lifestyle, or finding it hard to fit treatment into a busy schedule), negative experiences and perceptions in relation haemophilia and treatment (including concerns about treatment), not believing in the necessity of treatment, psychological issues (such as anxiety or mental health issues), lack of social support, and prophylactic treatment itself (e.g. venous access, treatment being unpleasant, and needle phobia).

A recent systematic review in relation to adherence to prophylactic treatment (Schrijvers et al., 2013) suggests that key motivators of adherence include experience of symptoms, a positive belief of necessity of treatment and a good relationship with the healthcare provider. And that the key barriers to adherence are infrequent or absence of symptoms and increasing age. The same review suggests that the key determinants of adherence to prophylaxis are age, symptoms, beliefs, and the relationship with the health care provider. The findings of the current study confirm that beliefs in relation to prophylaxis and the relationship with the haemophilia team are key determinants. However, the findings suggest that in addition, social support, lifestyle, more positive (and fewer negative) experiences and perceptions in relation to treatment and its efficacy, and negative emotions about haemophilia also play an important role.

10.2 Strengths and Limitations

The existing literature is limited, as very few studies have been published in relation to adherence in this patient group. As yet no studies have been published that have applied a mixed methods approach. Other limitations of the current literature are that most of the studies were conducted outside of the UK in countries where haemophilia healthcare is organised in a different way. The increasing flexibility and personalisation of prophylactic regimen in this country have thus far not received much attention in the literature.

The strength of this study is that it is a nationwide mixed method study with a large sample. It has a specific focus on YPH, who are likely to have had a very different experience in relation to their treatment in comparison to older patients (who most probably did not have prophylaxis available to them when they were young). The advantage of the mixed methods approach adopted in this research is that it allowed rigorous assessment of adherence and its correlates, and in-depth analysis of experiences and perceptions of YPH, parents and HP. In combination these quantitative and qualitative findings contribute to a deeper and more comprehensive understanding of adherence to prophylaxis among YPH, and the key drivers (barriers and facilitators) of adherence in this patient group.

Detailed descriptions of the strengths and limitations of the individual studies included in this research are reported in each individual study chapter. However a short summary of the key limitations follows below.

A key limitation of the quantitative study is its cross-sectional design, which means that the findings are based on a 'snapshot' of the outcome and the characteristics associated with it at a specific point in time. As a result the findings may have been different if the data were collected at a different point in time. Cross-sectional data also makes it difficult to make causal inference.

The main outcome (self-reported adherence) was assessed by a relatively new scale, the VERITAS-Pro, which has not been validated for use in the UK. The findings suggest that the VERITAS-Pro may lack some content validity, as the majority of missing data was due to participants indicating that certain questions were not applicable. This reflects the fact that the scale was constructed and validated in the US, and does not consider the increasingly flexible and personalised approach to prophylaxis in the UK. Another limitation relates to the clinical data, which was collated from individual medical files. Because this process is resource intensive haemophilia centres were unable to provide clinical information for all participants. In addition to missing data it appears that the clinical data also included some inaccuracies, possibly because it can be challenging to ‘decipher’ information in medical files. Lastly, to keep the questionnaire to an acceptable length some of the psychosocial factors were assessed using short form scales. These scales are not as comprehensive as the longer versions, which may have influenced the findings to some extent.

The most important limitation of the qualitative studies that needs to be highlighted is the fact that all the interviews were conducted and analysed by a PhD student with limited previous experience in qualitative research. This potentially may have influenced or biased the discussions with participants (particularly during the first few interviews) and analyses and conclusions drawn from this analysis. To reduce the risk of bias the qualitative analysis was supervised by an experienced qualitative research supervisor, who validated the themes identified by the researcher.

The interview data represent the lived experience of individual participants, which are not necessarily representative of the whole population. It is possible that those YPH who agreed to be interviewed are more motivated and engaged in relation to their treatment, and that YPH who are non-adherent or disengaged with their treatment would have been less likely to take part in research about adherence. Particularly because disengaged patients often do not attend their clinical appointments, and would therefore not have been approached to take part. It is impossible to know whether the lived experiences represented in the interview data are still true today, as individual circumstances, experiences and perceptions may have changed since the interviews took place, or indeed may fluctuate over time. However, as the findings from the YPH, parent and HP studies were broadly in line it is reasonable to assume that the findings are representative of the wider haemophilia community.

10.3 Implications

Notwithstanding the limitations discussed above, the findings of this study have a number of implications. The qualitative and quantitative findings were broadly in line in terms of estimated levels of adherence, and the key facilitators and barriers of adherence.

Framework to understand Adherence

One key finding of the current study indicates that in the context of the increasingly flexible and personalised approach to haemophilia treatment, a focus on improving adherence to prophylaxis alone may not improve outcomes for all patients. Patients, parents and healthcare professionals all suggested that the increasingly flexible approach means that adherence is more difficult to define and assess, and that what was historically seen as 'good adherence' is no longer relevant. For instance, many patients now have an agreement with the haemophilia team that allows them to tailor their treatment on a day-to-day and week-by-week basis, to ensure that they are adequately protected against bleeds when they need to be, and that they do not need to 'waste' treatment on days that they do not require such comprehensive protection. This means that they would not be seen as non-adherent if they skip a treatment, as long as it is within the boundaries agreed with the haemophilia team. Clinicians appear to focus their efforts more and more on patients who experience bleeds or those who are clearly disengaged with their treatment and health situation. Patients who are not presenting with bleeds or other issues (e.g. pain, reduced mobility, concerns or anxiety about haemophilia and treatment), are usually only seen at their regular six-monthly check-up and not contacted unless the haemophilia team have a specific reason to speak to them.

Therefore it appears that the way in which adherence to prophylaxis among people with haemophilia is looked at requires updating to reflect the more flexible approach described above. The below framework proposes that adherence should be considered in relation to the key clinical

outcome (bleeds), and health-related quality of life (which includes physical, mental, emotional, and social functioning). Together bleeds (often reported as Annualised Bleeding Rate, ABR) and quality of life (QoL) provide a good indication of both physical and mental wellbeing. If one would focus solely on ABR, it would be difficult to ascertain how well a patient is doing generally, as the number of bleeds a patient suffers may not be directly related to their QoL. Equally, if one would solely focus on QoL there would be a risk that one would not consider (preventable) bleeds of patients who have a good QoL score.

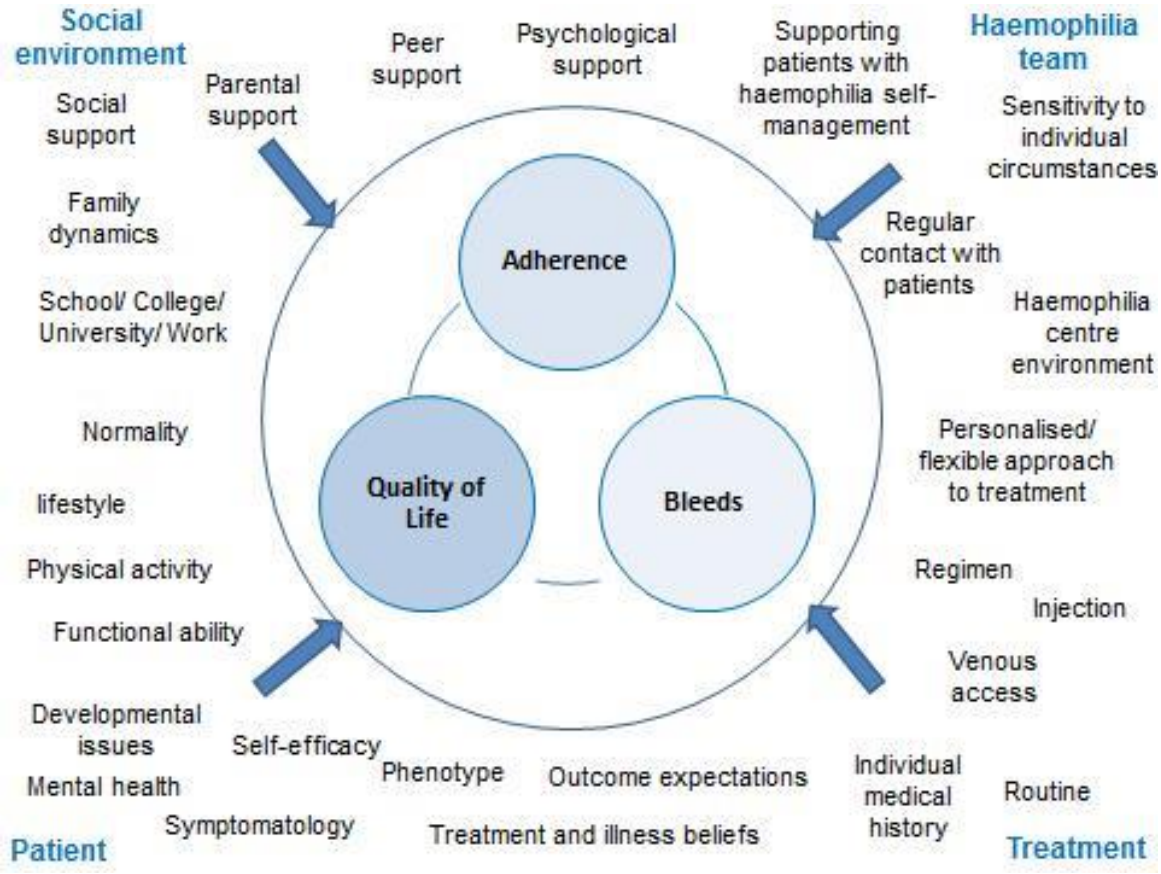

Figure 10.1: Framework for understanding adherence among young people with haemophilia

The framework suggests that both bleeds and QoL have a bidirectional relationship with adherence. For instance, in many cases non-adherence may cause a bleeding episode which in turn is likely to have a negative impact on a patient's QoL. Particularly if the bleeding becomes recurrent and leads to long-term damage and potentially disability. In reverse the absence of bleeds is likely to improve quality of life for many patients. However, according to the existing literature and findings from the

healthcare professional interviews absence of bleeds can also decrease adherence (as patients do not consider treatment necessary), which in turn can then lead to bleeding.

It is important to emphasize that not all bleeding episodes are caused by non-adherence. In some instances an injury caused by physical activity or an accident may cause a bleed. In other circumstances physical activity without apparent injury may still cause a bleed due to the pressure that exercise may put on joints or muscles.

In particular the qualitative findings of this study suggest that some of the factors that are associated with adherence are also associated directly with bleeds and QoL For instance a treatment approach that is sensitive to an individual patient's circumstances is likely to improve adherence, but is also likely to improve several dimensions of QoL, such as mental well-being (being less anxious about treatment and feeling understood and supported) and physical activity (a personalised or tailored prophylactic regimen allows patients sufficient protection for physical activity). However, it may also reduce bleeds directly (e.g. a regimen that is tailored around a patient's lifestyle is likely to prevent activity-related bleeds). Considering adherence together with QoL and bleeds is likely to improve HP and researchers' understanding of this patient group, and enable them to put in place interventions aimed at improving patient outcomes that go beyond solely improving adherence or clinical outcomes.

Based on the qualitative and quantitative findings presented in this thesis, the framework proposes that factors that influence adherence, QoL, and bleeds can be broadly categorised in four groups: the patient themselves; their social environment; their treatment; and the haemophilia team. However, the framework is not prescriptive about where each factor sits exactly in terms of which category they belong to and which of the three outcomes they are associated with. This flexibility in the framework recognises that key drivers of adherence are likely to vary between individual patients and circumstances, depending on patients' symptomatology, treatment-related experiences, social circumstances and clinical variables (such as bleeding phenotype and joint health). As haemophilia teams care for patients in an increasingly personalised manner, it follows that any approach aimed at improving outcomes or QoL should follow the same personalised approach. This is something that many haemophilia HP already recognise, and in many cases have implemented in their daily practice. Good examples of this are the way in which many nurses approach patients who are struggling with their treatment, or who have disengaged with treatment and/or the haemophilia team. Nurses in particular appear very sensitive to individual needs in considering the best way to approach and work with each individual patient.

In their systematic review Schrijvers and colleagues (Schrijvers et al., 2013) present a model of the factors that influence adherence among patients with haemophilia who use prophylaxis. Their review includes studies of haemophilia patients of all ages, so it does not look specifically at young people. Motivators included in their model are: a good relationship with the health care provider,

experience of symptoms. Barriers included in the model are: Absence of or infrequent symptoms, and increasing age.

Figure 10.2 below is an updated version of this model, which presents the barriers and facilitators to prophylaxis among young people with haemophilia specifically, which were identified by the quantitative and qualitative studies. Motivators to adherence among YPH are highlighted in green whereas barriers are highlighted in red. The centre of the model includes Quality of Life, Bleeds and Adherence, rather than just adherence. This reflects the finding that, due to the increasingly flexible and personalised approach to prophylaxis in the UK, it is no longer relevant to look at just adherence as described above.

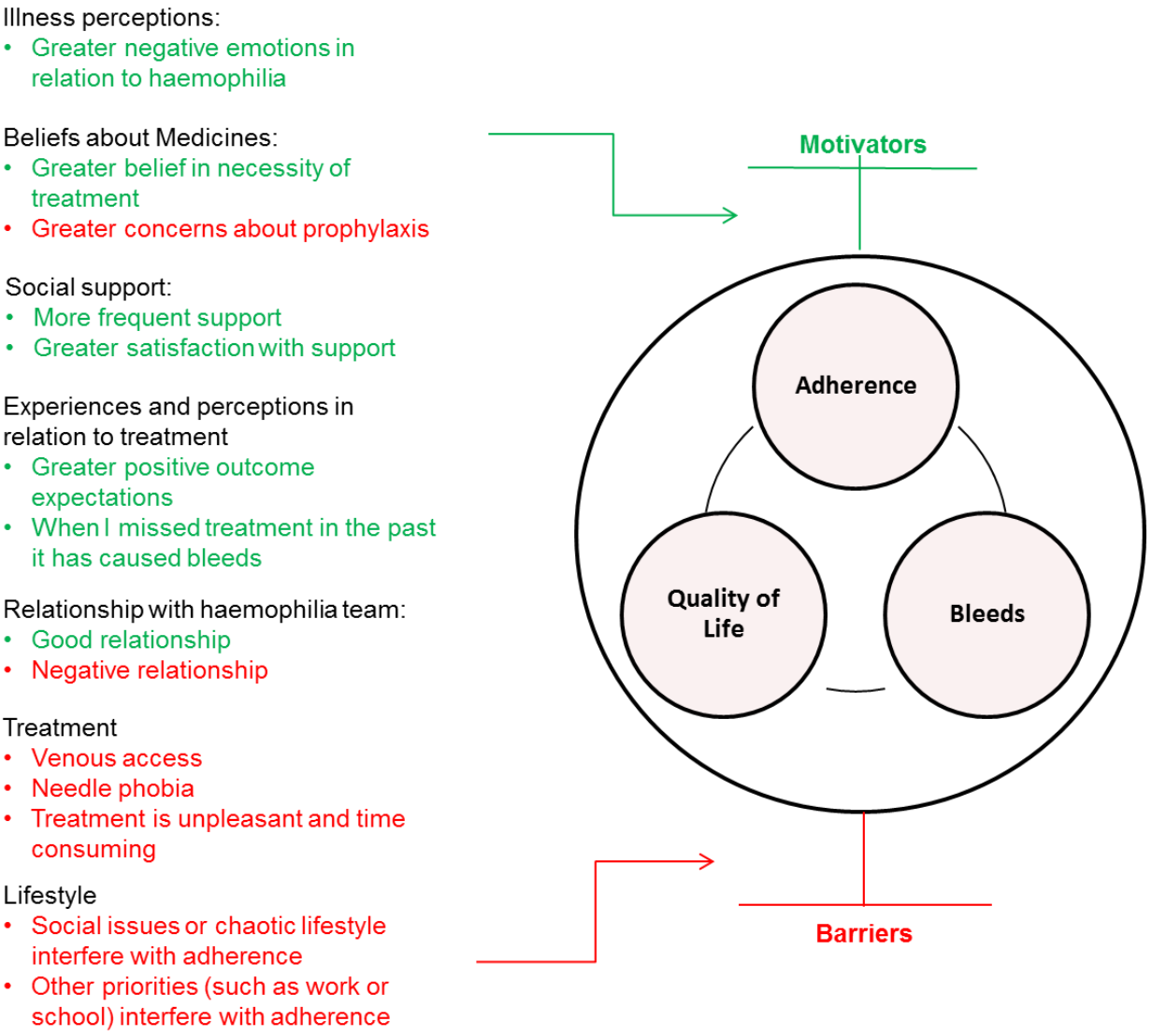

Figure 10.2: Factors influencing adherence to prophylaxis among young people with haemophilia

Assessing adherence, clinical outcomes

Adherence was assessed using the VERITAS-Pro scale (N. Duncan et al., 2010), which measures self-reported adherence to prophylaxis. The findings from the study suggest that it appears a reasonable measure of adherence in this patient group. But that its validity could potentially be improved with some revisions to reflect the increasingly flexible and personalised approach to prophylaxis in this country. Ideally triangulation of data collected (using a revised version of the VERITAS-Pro, Haemtrack treatment logs and pharmacy data) should be carried out to test the validity of the revised scale, as the research included in this thesis had originally intended to do.

Any future studies should address the issues that prevented the current study to collate Haemtrack and pharmacy data, to ensure that triangulation of data can be carried out. In terms of clinical outcomes (number of bleeds and hospital visits), it would be useful to include self-report measures in future studies to validate clinical information collated from medical files. It would also be useful to assess participants' physical activity as during this study it became clear that physical activity is likely to increase patients' risk of bleeding.

Potential interventions

As knowledge and believe in the efficacy of prophylaxis (positive outcome expectations) was found to be the only significant predictor of overall adherence in the quantitative study, it may be useful to test an intervention aimed at increasing positive outcome expectations. This may be a simple educational intervention that informs and educates patients (or parents of young patients) about how prophylaxis works, and how it improves outcomes.

The quantitative study found that non-adherence was more likely to be due to forgetting than skipping. Although it is likely that young people's busy lifestyles are partially responsible for this, findings from the qualitative studies also indicate that patients may find it easier to admit to forgetting than skipping. This may be because they are more likely to be 'told off' if they admit to intentionally skipping treatments, whereas they tend to get a more understanding response when they admit to sometimes forgetting.

The increasingly flexible approach to prophylaxis can at times make it confusing for patients to work out when their next injection is due, leading to unintentional non-adherence that is not 'forgetting'. It can also make it more challenging for the haemophilia team to ascertain the extent to which individual patients adhere to their treatment regimen and the reason why they miss injections. Therefore, dichotomising non-adherent patients into 'forgetters' and 'skippers' may not very useful when designing interventions aimed at improving adherence. As treatment regimen are now often tailor-made for individual patients, it follows that approaches aimed at improving adherence may also need to be tailored around individual circumstances. It appears that in many circumstances this

is already the case, as haemophilia teams appear to make an effort to work with individual patients in a way that suits their personal situation.

10.4 Future research

The findings of the studies described in this thesis have informed the design of a new study which is currently being undertaken in the NHS, recruiting participants in haemophilia comprehensive care centres across England and Wales. The primary aim of the new study is to test a new device that helps clinicians to personalize treatment regimens by calculating what happens to factor treatment once a patient has injected it (a process called pharmacokinetics).

The study consists of several blood tests (to determine a patient's individual pharmacokinetic level) and an educational session that explains what pharmacokinetics (PK) is, and what the implications of a PK-guided regimen may be for individual patients. At the end of the (one-to-one) educational session the clinical team and patient will together agree a PK-guided treatment regimen which also takes a the patient's lifestyle and bleeding history into consideration.

Participants will be invited to complete several questionnaires (before and just after the educational session and then 6 and 12 months later). This questionnaire will assess participants' self-reported Health-related Quality of Life, Annualized Bleeding Rate, Adherence, and Patient Activation (a measure which assesses the underlying knowledge, skills and confidence integral to managing one's own health and healthcare). This study is not a randomised controlled trial, but a naturalistic evaluation of the impact of the educational session (and PK-guided treatment decisions). The study follows the framework developed during the course of this PhD.

The findings of the research reported in this thesis suggest that the educational session may improve adherence, as it is likely to improve patients' knowledge and believe in the efficacy of prophylaxis (increasing positive outcome expectations). This improvement in adherence may improve patient outcomes (as it may decrease the number of bleeds). The more personalised treatment regimen is also likely to decrease the number of bleeds directly, as it will provide protection at times that patients need it most (e.g. when they are physically active), and will be personalised based on individual PK levels. It is anticipated that health-related QoL will improve indirectly thanks to better adherence and a reduction in bleeds. It is also likely that QoL will improve directly thanks to the personalised treatment regimen. This is because patients may feel less anxious about treatment as they understand it better and are reassured that their regimen is personalised based on their individual circumstances and lifestyle.

10.5 Conclusion

This study has provided evidence that shows that the current approach that haemophilia teams follow to support patients in managing their haemophilia treatment is working well. The increasingly flexible and personalized approach allows patients to tailor their treatment around their lifestyle and personal circumstances. This often means that patients can live the life they want to live, and suffer few bleeds. This in turn motivates them to keep on track with their treatment, which in turn results in reduced bleeding episodes and its associated costs for patients, the NHS, and the wider society. However, it also appears that this more flexible approach can lead to some confusion around treatment frequency, dosing and may lead to accidental non-adherence. Some additional training and education of patients and their families to increase their knowledge and skills around prophylaxis may help to improve adherence among those patients who currently miss occasional treatments due to confusion.

In a time of austerity, with management in the NHS looking to reduce costs, the evidence provided by this study may help haemophilia teams to build their case to continue with their current way of working with patients. Although it may be seen as a very resource intensive and costly approach, it is clear that the current approach keeps the majority of patients on track and as a result reduces bleeding episodes. It therefore reduces bleeding-related costs in the short-term (additional treatment and hospitalization), and the long-term (treatment of joint damage and joint replacements).

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Appendix 4.1: Assessing adherence to prophylaxis among young people with haemophilia questionnaire

About you

Before you start, please write the participant number you were given by the researcher in the box.

Please circle one answer for each of the below questions.

1. Where do you live?

With parents/carers Independently alone Independently with other(s) Other

2. Do you have brothers or sisters?

No Yes, they live in same house as me Yes, they do not live in the same house

3. Do you have any brothers or sisters who have a bleeding disorder?

Yes No

4. Do you?

I go to school I go to college/university I'm in other full-time education

I'm in part-time education I work part-time I work full-time I don't work Other

5. Please describe your current prophylactic treatment regime in the below box. Please describe the **days of the week** and **time of day** that you take prophylaxis, and the **dosage** that you take.

6. What is the name of the prophylaxis you take?

Please circle one answer for each of the below questions.

7. Do you think your treatment is…

Cheap Moderate in cost Expensive Very expensive I don't know

8. Pain in your body

a. How much pain that you feel is caused by your haemophilia, have you had in your body during the past 4 weeks? (this can be new pain or chronic pain you have had for a while)

None Very mild Mild Moderate Severe Very severe

b. During the past 4 weeks, how much did this haemophilia related pain interfere with your activities? (school, work, hobbies, etc.)

Not at all A little bit Moderately Quite a bit Extremely

9. At what age (roughly) did you start helping with your injections? (for instance helping with making up factor or with the actual injection).

Write the age you started helping in the box on the right. Put an X if someone else doe s your injections.	

If you can't remember tick this box ☐

10. At what age did you start doing your injections by yourself?

Write the age you started doing your injections yourself in the box on the right. Put an X if you receive help with your injections.	

If you can't remember tick this box ☐

11. Who usually does your prophylactic injections? (please tick one answer)

☐ Someone else does injections for me
☐ They are done by someone else, and I help
☐ They are mostly done by me, with help from someone else
☐ I do them entirely myself

About managing your haemophilia and treatment

Managing haemophilia is a challenging task. The questions below ask about how you manage your haemophilia and prophylaxis. We'd like to get an idea of how often you have done each of these things in the past three months.

Please answer each question using the following scale:

Always – all of the time, 100% of the time.

Often – most of the time, at least 75% of the time.

Sometimes – occasionally, at least 50% of the time.

Rarely – not often, 25% of the time.

Never – not at all, 0% of the time

N/A – tick if the question is not relevant to you

Please tick one box next to each of the below statements. Please tick the **Not applicable** box if a statement doesn't make sense to you or if it isn't relevant to you.

1. Timing	Always	Often	Sometimes	Rarely	Never	**N/A**
I do prophylactic injections on the days recommended by my doctor or nurse						
I inject the recommended number of times per week						
I do prophylactic injections at the time of day that was recommended by my doctor or nurse						
I do injections according to the schedule that was given to me by my doctor or nurse						
2. Planning	Always	Often	Sometimes	Rarely	Never	**N/A**
I plan ahead so I have enough factor at home						
I keep close track of how much factor and how many supplies I have at home						
I run out of factor and supplies before I order more						
I have a system for keeping track of factor and supplies at home						
3. Remembering	Always	Often	Sometimes	Rarely	Never	**N/A**
I forget to do prophylaxis injections						
Remembering to do prophylaxis injections is difficult						
I remember to inject on the schedule agreed with my doctor						
I miss recommended injections because I forget about them						

4. Skipping	Always	Often	Sometimes	Rarely	Never	**N/A**
I deliberately miss (skip) prophylaxis injections						
I choose to inject less often than prescribed						
If it is inconvenient to inject, I skip the injection that day						
I miss recommended injections because I skip them						
5. Communicating	Always	Often	Sometimes	Rarely	Never	**N/A**
I call the Haemophilia Centre when I have questions about haemophilia or my treatment						
I call the Haemophilia Centre when I have concerns about my health or when things change						
I make decisions about my treatment myself, without calling the Haemophilia Centre						
I call the Haemophilia Centre before I have medical interventions (for instance dentist treatment, or when you have to visit A&E)						

Outcome expectations

Below are 16 statements that finish the sentence: *If I always did everything I am supposed to do to manage my haemophilia, it would.....*

Please circle ONE number next to each statement to show how much you agree with it, using the following scale:

Don't agree at all 1 2 3 4 5 6 7 8 9 10 **Agree a lot**

If I always did everything I am supposed to do to manage my haemophilia, it would.....												
…reduce the number of bleeds I experience	Don't agree at all	1	2	3	4	5	6	7	8	9	10	Agree a lot
…be too much to think about		1	2	3	4	5	6	7	8	9	10	
…keep me healthy		1	2	3	4	5	6	7	8	9	10	
…help me do better at my studies/work		1	2	3	4	5	6	7	8	9	10	
…be too time-consuming		1	2	3	4	5	6	7	8	9	10	
…make me be admired by my friends		1	2	3	4	5	6	7	8	9	10	
…be difficult to live my life the way I want to		1	2	3	4	5	6	7	8	9	10	
…make me feel good about myself		1	2	3	4	5	6	7	8	9	10	
…be too much responsibility		1	2	3	4	5	6	7	8	9	10	
…make my family proud of me		1	2	3	4	5	6	7	8	9	10	

How confident are you that you can do each of the below things in the future?

Below are 12 statements about things that you may do to manage your haemophilia. Please circle ONE number next to each statement to show how confident you are that you can do this.

Not confident at all that I can do this 1 2 3 4 5 6 7 8 9 10 **Totally confident that I can do this**

Communication			
Talk to doctor/nurse about my treatment	Not confident at all	1 2 3 4 5 6 7 8 9 10	Totally confident
Talk to friends about my haemophilia		1 2 3 4 5 6 7 8 9 10	
Explain my haemophilia to other people		1 2 3 4 5 6 7 8 9 10	
Taking prophylaxis			
Take my prophylaxis myself without help	Not confident at all	1 2 3 4 5 6 7 8 9 10	Totally confident
Get out the equipment I need for taking prophylaxis		1 2 3 4 5 6 7 8 9 10	
Put the needle into the vein		1 2 3 4 5 6 7 8 9 10	
Take the needle out		1 2 3 4 5 6 7 8 9 10	
Apply pressure to the puncture wound to stop bleeding		1 2 3 4 5 6 7 8 9 10	
Dispose of sharps and other materials safely		1 2 3 4 5 6 7 8 9 10	
Record the injection on my treatment record		1 2 3 4 5 6 7 8 9 10	
Your health			
Tell when I need to get medical care and when I can handle a health problem myself	Not confident at all	1 2 3 4 5 6 7 8 9 10	Totally confident
Take actions that will prevent or minimize some symptoms or problems that are associated with my haemophilia		1 2 3 4 5 6 7 8 9 10	

About your prophylaxis

In some situations it may be difficult for you to take your prophylaxis. Below are 10 situations, please circle ONE number next to each situation to indicate **how confident you are that you can take your prophylaxis in that situation,** using the following scale**.**

Not confident at all 1 2 3 4 5 6 7 8 9 10 **Totally confident**

I am confident I can take my prophylaxis…			
1…. when I am tired	Not confident at all	1 2 3 4 5 6 7 8 9 10	Totally confident
2…. when I am busy with other things		1 2 3 4 5 6 7 8 9 10	
3…. when I am on holiday, or away from home		1 2 3 4 5 6 7 8 9 10	
4…. when I skipped or forgot the last injection		1 2 3 4 5 6 7 8 9 10	
5…. when I am stressed		1 2 3 4 5 6 7 8 9 10	
6….when there are guests in the house		1 2 3 4 5 6 7 8 9 10	
7…. when last injection was difficult or painful		1 2 3 4 5 6 7 8 9 10	
8…. when I am experiencing personal problems		1 2 3 4 5 6 7 8 9 10	
9…. when I can't find a quiet/private place to take it		1 2 3 4 5 6 7 8 9 10	
10…when I am worried about my haemophilia		1 2 3 4 5 6 7 8 9 10	

Please describe things that make it difficult for you to take your prophylaxis? (situations, things people do or say, equipment, activities, etc.). If you need more space please use the back of this sheet.

Please describe things that would make it easier for you to take your prophylaxis? (situations, things people do or say, equipment, activities, etc.). If you need more space please use the back of this sheet.

Beliefs about your prophylaxis

Below are 10 statements that other people have made about their medicines. Please tick one of the boxes next to each statement to show us how much you agree/disagree with it.

	Strongly Disagree	Disagree	Neither agree nor disagree	Agree	Agree Strongly
My health, at the moment, depends on my prophylaxis					
Having to take prophylaxis worries me					
My life would be impossible without prophylaxis					
Without my prophylaxis I would be very ill					
I sometimes worry about long-term effects of prophylaxis					
My prophylaxis is a mystery to me					
My health in the future will depend on my prophylaxis					
Prophylaxis disrupts my life					
I sometimes worry about becoming too dependent on my prophylaxis					
Prophylaxis protects me from becoming worse					

Your views about your haemophilia

The questions below ask about your views about your haemophilia. Please circle ONE number from 0 to 10 under each statement to describe your view. There are no right or wrong answers; we are just interested in what you think. We will not show your answers to your doctor or nurse.

1. How much does your haemophilia affect your life?

Haemophilia does not affect my life at all	0	1	2	3	4	5	6	7	8	9	10	*Haemophilia severely affects my life*

2. How long do you think your haemophilia will continue?

My haemophilia will last a very short time	0	1	2	3	4	5	6	7	8	9	10	*My haemophilia will last forever*

3. How much control do you feel you have over haemophilia related symptoms?

I have absolutely no control over my symptoms	0	1	2	3	4	5	6	7	8	9	10	*I have an extreme amount of control over my symptoms*

4. How much do you think your treatment can help haemophilia related symptoms?

Treatment can't help with my symptoms at all	0	1	2	3	4	5	6	7	8	9	10	*Treatment can be extremely helpful*

5. How much do you experience symptoms to do with your haemophilia?

I have no symptoms at all	0	1	2	3	4	5	6	7	8	9	10	*I have many severe symptoms*

6. How concerned are you about your haemophilia?

I am not concerned at all about my haemophilia	0	1	2	3	4	5	6	7	8	9	10	*I am extremely concerned about my haemophilia*

7. How well do you understand your haemophilia?

I don't understand my haemophilia at all	0	1	2	3	4	5	6	7	8	9	10	*I understand my haemophilia very clearly*

8. How much does your haemophilia affect your feelings (either good or bad)?

My haemophilia does not affect me emotionally l	0	1	2	3	4	5	6	7	8	9	10	*My haemophilia affects my emotions extremely*

9. Please write in the box below the most important factor(s) that you believe causes haemophilia.

Your feelings

The words below describe different feelings and emotions. Please tick one box next to each word to show us **how much you have felt like this THIS WEEK**.

		Very slightly or not at all	A little	Moderately	Quite a bit	Very much
1	Enthusiastic					
2	Scared					
3	Interested					
4	Afraid					
5	Determined					
6	Upset					
7	Excited					
8	Distressed					
9	Inspired					
10	Jittery					
11	Alert					
12	Nervous					
13	Active					
14	Strong					
15	Proud					
16	Irritable					
17	Attentive					

Social Support

We want to know **how often** you are offered help or support with your haemophilia. Under each statement below, circle the number that indicates **how often you receive help or support** with this. However, everyone has different ideas about what is helpful and supportive. **We want to know what is helpful and supportive for you.** So please also circle the number that shows how supportive each behaviour is for **YOU.**

These are the scales to use in answering the questions:

How often does this happen?

0	1	2	3	4	5
Never	Less than 2x a month	Twice a month	Once a week	Several times a week	At least once a day

When this happens, how do you feel about it?

-1	0	1	2	3
Unhelpful or NOT supportive	Neutral	A little helpful or supportive	Helpful/ supportive	Very supportive

Note: if a behaviour never happens, click '0' for never. Please try to rate how you would feel if this did happen.

How often does anyone…	How does this make you feel?... Or How would you feel?
1. Remind you to take you prophylaxis	
How often 0 1 2 3 4 5	It feels: -1 0 1 2 3
2. Let you know they appreciate how hard it is to take prophylaxis	
How often 0 1 2 3 4 5	It feels: -1 0 1 2 3
3. Give you a hard time when you have skipped or forgotten a prophylaxis injection	
How often 0 1 2 3 4 5	It feels: -1 0 1 2 3
4. Praise you for giving yourself injections correctly or on time	
How often 0 1 2 3 4 5	It feels: -1 0 1 2 3
5. Help when you might be having a bleed	
How often 0 1 2 3 4 5	It feels: -1 0 1 2 3
6. Listen to you when you want to talk about worries or concerns you have about your haemophilia	
How often 0 1 2 3 4 5	It feels: -1 0 1 2 3
7. Encourage you to do a good job in taking care of your haemophilia	
How often 0 1 2 3 4 5	It feels: -1 0 1 2 3
8. Understand when you sometimes make mistakes in taking care of your haemophilia	
How often 0 1 2 3 4 5	It feels: -1 0 1 2 3

Appendix 4.2: revisions to VERITAS-Pro questionnaire

About managing your haemophilia and treatment

Managing haemophilia is a challenging task. The questions below ask about how you manage your haemophilia and prophylaxis. We'd like to get an idea of how often you have done each of these things in the past three months. Please answer each question using the following scale:

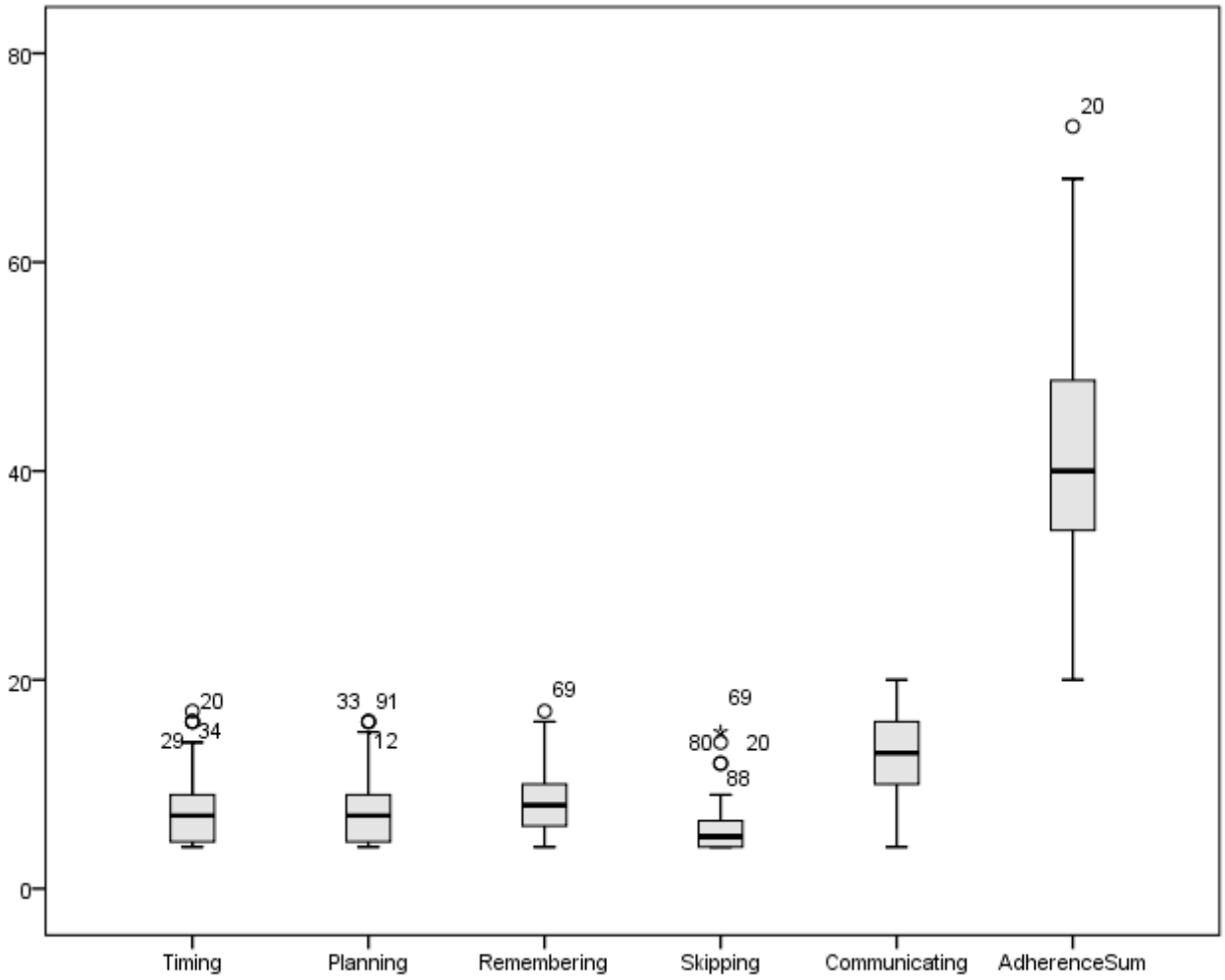
Always – all of the time, 100% of the time.
Often – most of the time, at least 75% of the time.
Sometimes – occasionally, at least 50% of the time.
Rarely – not often, 25% of the time.
Never – not at all, 0% of the time
Not applicable – tick if the question is not relevant to you

Please tick one box next to each of the below statements. Please tick the **Not applicable** box if a statement doesn't make sense to you or if it isn't relevant to you.

Timing	Always	Often	Sometimes	Rarely	Never	Not applicable
I do prophylactic ~~infusions on the scheduled days~~ injections on the days recommended by my doctor or nurse						
I ~~infuse~~ inject the recommended number of times per week						
I do prophylactic ~~infusions in the morning as recommended~~ injections at the time of day that was recommended by my doctor or nurse						
I do ~~infusions~~ injections according to the schedule that was given to me by my doctor or nurse						
~~**Dosing**~~	~~Always~~	~~Often~~	~~Sometimes~~	~~Rarely~~	~~Never~~	~~Not applicable~~
~~I use the doctor-recommended dose for infusions~~						
~~I infuse at a lower dose than prescribed~~						
~~In increase or decrease the dose without calling the treatment center~~						
~~I use the correct number of factor boxes to total my recommended dose~~						
Planning	Always	Often	Sometimes	Rarely	Never	Not applicable
I plan ahead so I have enough factor at home						
I keep close track of how much factor and how many supplies I have at home						
I run out of factor and supplies before I order more						
I have a system for keeping track of factor and supplies at home						

Remembering	Always	Often	Sometimes	Rarely	Never	Not applicable
I forget to do prophylaxis ~~infusions~~ injections						
Remembering to do prophylaxis injections is difficult						
I remember to ~~infuse~~ inject on the schedule ~~prescribed by the treatment center~~ agreed with my doctor						
I miss recommended ~~infusions~~ injections because I forget about them						
Skipping	Always	Often	Sometimes	Rarely	Never	Not applicable
I ~~skip~~ deliberately miss (skip) prophylaxis ~~infusions~~ injections						
I choose to ~~infuse~~ inject less often than prescribed						
If it is inconvenient to ~~infuse~~ inject, I skip the ~~infusion~~ injection that day						
I miss recommended ~~infusions~~ injections because I skip them						
Communicating	Always	Often	Sometimes	Rarely	Never	Not applicable
I call the ~~treatment center~~ Haemophilia Centre when I have questions about haemophilia or my treatment						
I call the ~~treatment center~~ Haemophilia Centre when I have ~~haemophilia-related health~~ concerns about my health ~~or when changes occur~~ or when things change						
I make ~~treatment~~ decisions about my treatment myself, ~~rather than calling the haemophilia center~~ without calling the Haemophilia Centre						
I call the ~~treatment center~~ Haemophilia Centre before I have medical interventions ~~such as dental extractions, colonoscopies, visits to the emergency room, or hospital stays~~ (for instance dentist treatment, or when you have to visit A&E)						

Appendix 4.3: Boxplots for the frequency distribution of the VERITAS-Pro adherence subscales and sum scores



Appendix 4.4a: Statistical power calculation for analyses testing the difference of means (t-test)

Appendix 4.4a. Overview of required sample size to achieve statistical power (70%, 80%, and 90%) and effect size (20%, 15%, and 10%).

	Power					
	70%		80%		90%	
Effect size	2-tailed	1-tailed	2-tailed	1-tailed	2-tailed	1-tailed
20%	620	475	790	620	1060	860
15%	160	120	200	160	270	220
10%	75	55	90	75	120	100

Calculated using Gpower 3.1.9.2 (Faul, Erdfelder, Lang, & Buchner, 2007).

Based on analyses testing the difference of means (t-test, $p<0.05$)

Appendix 4.4b: Statistical power calculation for linear multiple regression analyses

Appendix 4.4b. Overview of required sample size to achieve statistical power (70%, 80%, and 90%) and effect size (20%, 15%, and 10%).

	Power					
	70%		80%		90%	
Effect size	2-tailed	1-tailed	2-tailed	1-tailed	2-tailed	1-tailed
20%	65	50	85	65	110	90
15%	35	26	45	35	55	45
10%	25	20	30	25	40	35

Calculated using Gpower 3.1.9.2 (Faul, Erdfelder, Lang, & Buchner, 2007).

Based on linear multiple regression analysis with 10 predictors

Appendix 4.5: Table 4.9A: Linear regression model of predictors of adherence sum, fixed enter method

Table 4.9A: Linear regression model of predictors of adherence sum scores

	b	SE B	β	P
Constant	33.370	16.317		.045
BMQ Concern	1.053	.438	.351	**.020**
BMQ Necessity	-.782	.315	-.291	**.016**
Positive outcome expectations	-.152	.104	-.164	.151
Negative outcome expectations	.085	.156	.073	.589
Squared Haemophilia-related self-efficacy	.000	.001	.088	.528
Squared Prophylaxis-related self-efficacy	-.001	.000	-.143	.242
PANAS positive affect	-.139	.130	-.125	.287
Log PANAS negative affect	4.778	3.997	.173	.237
IPQ Consequences	.035	.455	.010	.938
IPQ Squared Timeline	.107	.076	.160	.166
IPQ Squared Personal Control	.031	.046	.079	.502
IPQ Squared Treatment Control	.092	.055	.200	.100
IPQ Identity	.316	.486	.077	.518
IPQ Concerns	-.008	.491	-.002	.988
IPQ Coherence	-.253	.788	-.035	.750
IPQ Emotional representations	-1.303	.488	-.367	**.010**
Social support frequency	.030	.183	.031	.868
Social support satisfaction	.071	.246	.047	.775
Social support frequency*satisfaction	-.158	.079	-.381	**.050**

R^2 = .488, p = .001

Appendix 4.6: Table 4.10A: Linear regression model of predictors of Skipping, fixed enter method

Table 410A: Linear regression model of predictors of adherence skipping

	b	SE B	β	P
Constant	-.056	.573		.923
BMQ Concern	.042	.015	.435	**.007**
BMQ Necessity	-.006	.011	-.064	.606
Positive outcome expectations	-.003	.004	-.101	.396
Negative outcome expectations	.011	.005	.296	**.033**
Squared Haemophilia-related self-efficacy	.000	.000	.158	.291
Squared Prophylaxis-related self-efficacy	.000	.000	-.089	.486
PANAS positive affect	-.003	.005	-.094	.442
Log PANAS negative affect	.315	.138	.342	**.026**
IPQ Consequences	.006	.016	.057	.689
IPQ Squared Timeline	-.001	.003	-.048	.690
IPQ Squared Personal Control	.000	.002	.038	.760
IPQ Squared Treatment Control	.000	.002	.031	.804
IPQ Identity	.008	.017	.062	.622
IPQ Concerns	-.005	.017	-.047	.751
IPQ Coherence	.086	.028	.363	**.003**
IPQ Emotional representations	-.045	.017	-.383	**.010**
Social support frequency	.003	.006	.098	.614
Social support satisfaction	.003	.009	.060	.727
Social support frequency*satisfaction	-.004	.003	-.268	.187

R^2 = .415, p = .008

Appendix 4.7: Table 4.11A: Linear regression model of predictors of Remembering, fixed enter method

Table 4.11A: Linear regression model of predictors of adherence remembering

	b	SE B	β	P
Constant	-1.819	4.868		.710
BMQ Concern	.448	.126	.517	**.001**
BMQ Necessity	-.173	.095	-.220	**.072**
Positive outcome expectations	-.045	.031	-.164	.160
Negative outcome expectations	.008	.044	.025	.851
Squared Haemophilia-related self-efficacy	.000	.000	.274	**.060**
Squared Prophylaxis-related self-efficacy	.000	.000	-.186	.145
PANAS positive affect	-.030	.039	-.094	.442
Log PANAS negative affect	-.140	1.102	-.017	.899
IPQ Consequences	-.049	.137	-.049	.722
IPQ Squared Timeline	.042	.023	.225	**.067**
IPQ Squared Personal Control	.004	.013	.039	.748
IPQ Squared Treatment Control	.058	.016	.432	**.001**
IPQ Identity	-.054	.145	-.044	.713
IPQ Concerns	.156	.148	.149	.297
IPQ Coherence	.174	.236	.083	.463
IPQ Emotional representations	-.044	.143	-.043	.761
Social support frequency	.023	.052	.079	.664
Social support satisfaction	-.048	.074	-.110	.519
Social support frequency*satisfaction	-.024	.023	-.199	.297

R^2 = .445, p = .003

Appendix 5.1 a: Interview schedule study one (young people with haemophilia)

Theme 1 Living with haemophilia

1. What does having haemophilia mean to you on a day to day basis?

   Probe differences between

   - at school/work
   - at home with parents/siblings
   - with friends

2. Do you remember when your parents (carer) first told you about haemophilia?
   - What was that like/ what did they tell you?
   - How did you come to understand what haemophilia means?

3. What kinds of things do you do to make yourself feel better?
   - Probe strategies for both physical and emotional wellbeing.

Theme 2 Treatment

1. How often do you have to take prophylaxis?
   - Probe regimen (do they keep to regimen advised by clinicians or do they self-manage based on their daily needs, e.g. exercise etc).
   - Does your doctor encourage you to follow more bespoke dosing around your lifestyle?
2. What is the treatment like?
   - Probe to get to feelings around treatment (difficult, painful, etc.)
3. What kinds of things might interfere with you taking treatment on time?
   - Probe to gauge frequency of missed or not-on-time treatment
   - Probe body image issues (needle marks, impact on body appearance, perceptions of weakness)
   - Probe if/what role relationships with friends/family play
   - What about girlfriends/boyfriends?

Theme 3 Transition of care and responsibility

1. How involved are your parents/carer in your treatment regime? How involved are you?
   - Probe to gauge
     - who takes main responsibility for treatment
     - whether participant thinks he has too much or too little responsibility

2. How often do you attend the haemophilia treatment centre?
    - What is it like going there?
    - What are the staff there like? How do they talk to you?
    - Are there are any challenges directly related to the treatment centre?
    - Suggestions for potential improvements?

3. What do you think is the difference between paediatric and adult care centres?
    - Probe to explore
        - Whether current treatment setting is appropriate for participant
        - If has gone through transition from paediatric care, what was transition like?

4. Is there anything about the illness or treatment that you don't quite understand?

5. Who would you go to with questions about haemophilia?
    - Probe
        - Parents
        - Health care staff
        - Internet
        - Haemophilia society
        - Friends
        - Other people with haemophilia
        - Other

Theme 4 Social support

1. What support do you get in managing your haemophilia? For instance reminding you to take your prophylaxis, listening to you if you want to talk about things, going to the centre with you, etc.
    - Probe to gauge social support from
        - Parents
        - Siblings
        - Friends
        - Girlfriend/boyfriend
        - Other people with haemophilia

2. What effect do you think haemophilia has on your relationship?
    - Probe to gauge impact on relationships with
        - family
        - friends
        - girlfriend/boyfriend

Appendix 5.1 b: Interview schedule study two (parents of young people with haemophilia)

Theme 1 Living with haemophilia

1. Tell us about what an average day is like?
   Probe
   - What influence does haemophilia have on daily life
   - Influence on relationships in the family
   - Influence on parent's work/social life
   - Other things (e.g. finances, holidays, etc.)

2. Do you remember when you first told your son about haemophilia?
   - What was that like/ what did you tell him?

3. How have things changed as he has got older?
   - Probe what has become better and also key challenges

4. What kinds of things do you do to make things better for your son and yourself?
   - Probe strategies for both physical and emotional wellbeing.
     - E.g. going to school, going to work, going on holiday, going out

Theme 2 Treatment

1. How often does your son take prophylaxis?

2. What is the treatment like?
   - Probe to get to feelings around treatment (difficult, painful, etc.)

3. What kinds of things might interfere with him taking treatment?
   - Probe to gauge frequency of missed or not-on-time treatment
   - Probe body image (needle marks, impact on body appearance, perceptions of weakness)
   - Probe technical skills needed to administer treatment (probe needle phobia if it comes up)
   - Probe if/what role relationships with friends/family play
   - What about girlfriends/boyfriends?

4. Who would you go to with questions about haemophilia?
   - Probe
     - Health care staff
     - Internet
     - Haemophilia society
     - Friends
     - Other parents of young people with haemophilia
     - Other

Theme 3 Responsibility for care

1. How involved are you in his treatment regime? How involved is he?

2. If son still lives at home: probe to gauge
    - who takes main responsibility for treatment
    - whether parent thinks their son has too much or too little responsibility

3. How often do you attend the haemophilia treatment centre with your son?
    - What is it like going there?
    - What are the staff there like? How do they talk to you?
    - Are there are any challenges directly related to the treatment centre?
    - Suggestions for potential improvements?
    - What was the transition from paediatric to adult care like?
    - Suggestions for potential improvements to help with transition?

Theme 4 Social support

1. What support do you get in managing your son's haemophilia?
    - Probe to gauge support from
        - Husband/wife
        - Family
        - Son with haemophilia
        - Other children
        - Friends
        - Treatment centre
        - Social care

2. What support are you able to offer your son in managing his haemophilia? For instance reminding him to take his prophylaxis, going to the treatment centre with him, etc.

3. What effect do you think haemophilia has on your relationships?
    - Probe to gauge impact on relationships with
        - Husband/wife
        - Son with haemophilia
        - Other children
        - family
        - friends

Appendix 5.1 c: Interview schedule study three (haemophilia healthcare professionals)

Theme 1 The treatment centre

1. Tell us about what an average day is like in the treatment centre (both in the day unit and on the wards)?
   Probe:

   - How many patients do you see?
   - What age range?
   - Collaboration with colleagues
   - Do you deal with many parents of patients
   - Split routine check-ups/ad-hoc treatment

2. In what way have things changed in haemophilia care since you started?
   Treatment and prescription probes:
   - How are prescriptions generated in your centre?
   - How are treatment schedules assessed?
   - Do you ask for treatment sheet returns?
   - Do you use Haemtrack? And if yes, in what way? Do you use it as a clinical tool?
   - Does your department encourage patients to follow more bespoke dosing around their lifestyle?
   - If yes, do all the clinicians in your centre do this?
   - Potential conflicting messages for staff and patients if not all clinicians follow the same practice?

3. How much time are you able to spend with each patient?
   Probe:
   - Able to meet patients' needs and expectations?
   - Would you like to spend more or less time with them?
   - Are there any changes you would like to see?

Theme 2 Treatment

1. How well does prophylaxis work for your patients?
    - Probe: main problems and challenges, and what works well

2. How well do you think your patients adhere to their prophylaxis?
    - Probe: how do you find out that someone doesn't keep to their treatment plan?

3. What kinds of things do you think might interfere with your patients' adherence?
    - Probe to gauge estimated adherence levels in the treatment centre
    - Probe perceptions of the influence of:
        - body image issues (needle marks, impact on body appearance, perceptions of weakness)
        - Technical skills needed for treatment (also needle phobia)
        - family/friends of patients
        - girlfriends/boyfriends?
        - School/work
        - Relationships with doctors and nurses

Theme 3 Improvements to care

1. What do you think would help patients keep to their treatment plan?

2. Are there any improvements you think are needed?

3. Are there any improvements directly in the treatment centre you think are needed?

Appendix 5.2: Example page first hermeneutic cycle (study one, young people with haemophilia)

Code	Number Of Coding References	Example text	Notes / reflections on what participant said and what this may mean	Additional notes/researcher's reflections
Forgetting	22	*P: And I know some people say oh it's not something you easily forget, while I've been taking it so long now–P: –that it's kind of second nature. Yeah, I occasionally do forget it. R: Yeah, how often would you say that happens? P: [laughs] Unfortunately more often than not, but [laughs] more often than not, /but– P:-- if I have forgotten during the day mum would say have you done it? If not, right, you do it tomorrow morning then--*	I wonder if the patient was reporting some of the missed treatments as 'forgotten' whereas it may have been closer to 'skipping'. *R: --/Does that happen that you miss three four in a row? P: No I– I won't deliberately miss two three or four in a row, and if– if-- the problem is if I forget one-- R: Hm. P: --the little dull aches a bit, yeah ok, if I miss two then they get worse, then it– then that's it. R: Hm. P: Because you realise, yeah I've missed two, I need to get it done.*	Participant still lives at home and his parents are very involved with his treatment, and they remind him every time or check later if he has taken the treatment. *very supportive, and if I've forgotten mum will always say in-- in an evening, have you done your injection today? And I'll – it's either hm yes, or if I just hadn't done, no, I've forgotten* Patient believes he suffers severe physical symptoms as a result of missing treatments. P: If I miss four then it is very difficult to carry out day-to-day activities. Ask Dr Hart about symptoms as a result of missing treatments (nothing in literature).
Support from parents and siblings most important	21	*But as a family we-- we do share it. I mean, if I've put medication together mum will sometimes say, sure do you mind if I do it, just so she's-- she's still got the chance-- she's got her eye in and she knows what she's doing*	participant refers to **'we'** rather than **'I'**, indicating that he shares the burden and responsibility of haemophilia with his parents. He's 19 and starting full-time work, but his parents still remind him to take his treatment daily, and are involved with the scheduling of hospital appointment and treatment deliveries. they also still come to check-up appointments with him.	mother insisted to keep the door between the dining room (where I interviewed the participant) and the sitting room (where she was watching tv) open.
Haemtrack	15	*P: I think it's, eh, extremely useful. Because that-- Dr. can em log onto it, look me up and see right – you've done all your prophylaxis for the month and then he can look at another month and go, 'actually he's done his prophylaxis but he's had a problem in the middle--- Is it a serious problem?' there's so much detail you have to put in when, em, typing up the bleed-- you have to put the joint, severity of the pain, em, if it's a minor or a major injury, was a spontaneous trauma and that sort of thing, but it's long winded process but it's very useful--*	p feels that the haemophilia centre should use the haemtrack data more pro-actively to check how he is doing and picking potential problems up by looking at his haemtrack entries. *It would be nice if I'm having a problem, if they'd picked up that I've done two three injections in a row-* he is positive about using the app, which he was not aware of until recently. *P: --so if there's an app for the iphone now I will use that because it's easier and in that retrospect I can do it injection by injection that way.*	I wonder if for patients who are keen to avoid risk, and like having close contact with the centre, haemtrack is a good thing because it makes them feel more looked after. They seem to like the idea of the centre checking up on them via haemtrack. Ask Dr Hart for access to Haemtrack.

Appendix 5.3: Full list of themes after first hermeneutic cycle (study one, young people with haemophilia)

Superordinate theme	Theme	Number Of Coding References across all participants	Number of participants with this coding reference
Haemophilia, bleeds and pain are part of life	Bleeds	51	10
reported adherence is high	I forget to take treatment occasionally	46	9
I tailor my treatment around my lifestyle	Regimen	44	7
Support from mum and dad is key	Support from parents/siblings most important	42	5
I try to be positive	haemophilia is not really an issue	30	8
Support from the haemophilia centre is great	Haemophilia team are nice	30	9
Avoiding risk is key	Avoiding risk	27	7
Haemtrack	Haemtrack	26	4
Most take over gradually from a young age but parents stay involved until they leave home	taking over responsibility for treatment from parents	24	8
I tailor my treatment around my lifestyle	Tailored treatment regimens	20	6
venepuncture issues	venepuncture issues	17	9
Social support	Social support - friends	17	4
Patient is haemophilia expert	Understanding of haemophilia and treatment	16	4
Treatment is no problem and part of my routine	Treatment has improved lots	16	5
Bleeds and pain are part of life	activity related bleeds	15	7
Taking treatment is inconvenient and no fun	Wish treatment was like diabetic injection or oral medication	15	4
Social support	social contact with other patients and their families and staff	14	4
Support from mum and dad is key	mum does my treatments	14	2
Deliberately skipping treatment is very rare	Skipping	13	5
Haemophilia, bleeds and pain are part of life	haemophilia is part of me and who I am	12	7
haemophilia- and treatment related anxiety	It is hard to take treatment when I am anxious or stressed	12	4

Superordinate theme	Theme	Number Of Coding References across all participants	Number of participants with this coding reference
practical solutions to remember to take treatment	visual prompts and other things that help remember	12	6
Taking treatment is no problem, it's part of my routine	Treatment is part of my day-to-day routine	12	7
Treatment protects me so I can live a normal life	Treatment allows me to live the life I want	12	5
Patient is haemophilia expert	I am an expert in haemophilia and treatment	11	2
Taking treatment is no problem, it's part of my routine	Taking treatment is easy and quick	11	5
Haemophilia care in the UK is second to none	coming to the UK has improved my life immensely	10	1
Barriers to adherence	Barriers to adherence	9	10
Support from the haemophilia centre is great	The haemophilia team encourage me to take treatment	9	1
design of treatment and packaging	new treatment doesn't have all the bits I need	8	2
Taking treatment is inconvenient and no fun	treatment is annoying	8	1
Taking treatment is no problem, it's part of my routine	You've got to get on with it	8	5
I tailor my treatment around my lifestyle	Topping up	7	3
Patient is haemophilia expert	time of day i take treatment is important	6	4
reported adherence is high	I hardly ever miss a treatment	6	4
Taking treatment is no problem, it's part of my routine	It's just one of those things (treatment)	6	3
Support from the haemophilia centre is great	I am very happy with the support I receive	6	4
Haemophilia, bleeds and pain are part of life	Pain	5	2
Taking treatment is no problem, it's part of my routine	at first it was difficult but now things have settled down	5	3
haemophilia- and treatment related anxiety	I am anxious about having to start doing injections myself	4	2
Inhibitors have a significant impact on my treatment and health outcomes	I use a Hickman line or port	4	1
School and Work are usually not an issue	Taking treatment at work is no problem	4	2

Superordinate theme	Theme	Number Of Coding References across all participants	Number of participants with this coding reference
Taking treatment is no problem, it's part of my routine	generally things work really well\generally taking my treatment goes without issues	4	2
Treatment protects me so I can live a normal life	Treatment makes me feel protected	4	2
Haemophilia care in the UK is second to none	i can't think of anything that needs to improve	4	2
Support from the haemophilia centre is great	I know the haemophilia team are there for me if I need them	4	3
haemophilia- and treatment related anxiety	sometimes i have felt inadequate because of the way girls respond to my haemophilia	3	1
practical solutions to remember to take treatment	a digital reminder (text or diary) would help	3	3
Taking treatment is inconvenient and no fun	I don't like taking treatment but accept I need to do it	3	1
Treatment protects me so I can live a normal life	treatment prevents or stops most bleeds	3	2
Social support	I prefer to be self-sufficient and don't ask for help much	3	1
Haemophilia care in the UK is second to none	introduction of prophylaxis has resulted much better outcomes	3	1
Inhibitors have a significant impact on my treatment and health outcomes	inhibitors are a big issue for me	2	2
School and Work are usually not an issue	advancing my education and career are priority	2	1
Taking treatment is inconvenient and no fun	treatment is time consuming	2	1
Taking treatment is no problem, it's part of my routine	it used to hurt but is fine now	2	2
Treatment protects me so I can live a normal life	Treatment prevents long-term problems	2	2
Support from mum and dad is key	sometimes someone else does my treatment for me	2	2
Haemophilia care in the UK is second to none	I feel lucky to have been born in the UK	2	2
I tailor my treatment around my lifestyle	Concern about over-using factor treatment	1	1

Superordinate theme	Theme	Number Of Coding References across all participants	Number of participants with this coding reference
Patient is haemophilia expert	I am an example for younger patients and their family	1	1
design of treatment and packaging	I didn't used to like mixing it	1	1
design of treatment and packaging	In emergencies sometimes you can't mix or administer treatment yourself	1	1
design of treatment and packaging	long-acting trial treatment is less convenient to take	1	1
haemophilia- and treatment related anxiety	I generally only take treatment in a safe place (home, work or somewhere familiar)	1	1
haemophilia- and treatment related anxiety	I won't take treatment in front of people	1	1
haemophilia- and treatment related anxiety	psychological support	1	1
haemophilia- and treatment related anxiety	when I realise I've forgotten i feel anxious	1	1
I try to be positive	I try to be positive about my haemophilia	1	1
Inhibitors have a significant impact on my treatment and health outcomes	the quantity of treatment is huge because of the inhibitors	1	1
School and Work are usually not an issue	I'm lucky that work is very flexible, so coming to hospital is no problem	1	1
Taking treatment is inconvenient and no fun	don't have time for breakfast because of prophylaxis	1	1
Taking treatment is inconvenient and no fun	I'd prefer to do fewer injections, or not do it at all	1	1
Taking treatment is inconvenient and no fun	sometimes you get fed-up with having to do treatment	1	1
Treatment protects me so I can live a normal life	non-adherence usually results in bleeds	1	1
Treatment protects me so I can live a normal life	treatment makes me feel better	1	1
Support from mum and dad is key	sometimes you just want someone else to do it for you	1	1
Support from the haemophilia centre is great	I trust the NHS with my life	1	1
Support from the haemophilia centre is great	support from the centre makes me feel less alone	1	1
Support from the haemophilia centre is great	the haemophilia nurses regularly contact me	1	1

Appendix 5.4: Example page second hermeneutic cycle (study one, young people with haemophilia)

Superordinate theme	Theme	Number Of Coding References across all participants	Example text	notes / reflections on what participant comments mean	notes/researcher's reflections (reflective diary, not to be included in table but recorded to allow the researcher to 'bracket off' her own interpretations).
Haemophilia, bleeds and pain are part of life	Bleeds	51	*Like they've, bleeds do happen like and just for some reason you'll wake up one morning, you've just slept funny on your arm and you can't move properly or like, because like, because I've had the op and I've been on crutches quite, I've not long come off crutches and I've gained this sore knee over here just because you're weight-bearing more on that side, that was like the same one I dislocated my knee a fewyears back, they said it was probably because I was subconsciously putting more weight through this leg because I'd only just had the cast on and you've gone home and it's just, it's one of them ones where I just ached and it was, and it went. But/ (UHB001i)*	A19G: family are well equipped to deal with bleeds themselves. *I've always either dealt with it here because we-- we're so well equipped if you will.* Severe bleeds seem very rare (he mentioned once or twice it was severe enough to call the hospital). *But that is-- is quite rare now, that these injuries happen and I am very self-dependent, I know what my limits are, as I said earlier, and that's one of the reasons why we've been less dependent on the hospital* BCH13 gets a lot of bleeds, and has already developed a target joint for which he has been operated. he mentioned that he has trouble with walking. *Um, not really, it's just mainly like walking and also because I've got-- Like when I walk, I can't walk for very long because it causes like bleeds in my ankle and like when I get bleeds in my elbowit gets stiff and I can't move it past certain degrees.* However, he feels that his prophylactic treatment is working for him. *P: Yeah, so whenever I have a bleed I'm always topped up on more of my treatment to recover it.* *R: How do you usually notice that you're having a bleed?* *P: Something will swell up or I'll just feel like I can't walk or something or can't lift something up one day, my shoulder's swollen right now so that's just started yesterday.*	P: his focus on risk management means that he doesn't engage in many activities that could cause bleeds, and because of his sedentary lifestyle he probably doesn't suffer many trauma-bleeds. But even though he doesn't have many bleeds, and hardly any severe bleeds, when he is describing how useful Haemtrack is because the hospital can pick up that you've had a bleed, the example he uses is of 'quite a serious bleed' this again indicated to me that perhaps there was quite a lot of anxiety around haemophilia and potential bleeds for this patient.

Appendix 5.5: Example page third hermeneutic cycle (study one, young people with haemophilia)

master themes	Superordinate theme	code	Number Of Coding References Total	participants (number of times referenced for this participant. *means the most frequent code for this participant)	Example text	Notes / reflections on what participant comments mean	notes/researcher's reflections (reflective diary, not to be included in coding table but recorded to allow the researcher to 'bracket off' her own interpretations).
Difficult balance between avoiding risk, managing haemophilia and living a normal life	**Avoiding risk is key**	**avoiding risk**	27	A19G (7), BCH13 (2), A12L (1), A14D (4), A16O(1), NQI13T (**9**), UHB001i (3)	*I just thought to myself, I'm just not gonna be able to do it. It's gonna put too much damage onto my ankles and my knees, /so--* *++++++++++++++++++++++++++++++++++++++Ye ah, like I want-- Sometimes at school I do try and do football and things like that but I mean I've been taught to like stay away from it but it's hard. Because like-- Because I just want to do the same as everyone else and be active and do sports and stuff but like because my illness it kind of stops me a little bit.++++++++++++++++++++++++++++++++++I just uhm, yeah in terms of respecting the haemophilia uhm I just take a little more care with doing anything that is a little more high risk and try and stay away from uhm playing football or rugby with my mates. Uhm I know that I could but it's uhm just a little bit of treating it with a bit of caution.*	It appears that avoiding risk started at a young age, with him not being allowed to go at break time at primary school. *I believe it was the doctors that said--we would advise that he doesn't go out at break or lunch.* For some patients the worry about bleeds works as an encouragement to take treatment and avoid risk. *recently I've done a 10k run and I knew that the week before I'm training for it and make sure you've given yourself plenty of factor, maybe increase the dosage a little bit because you've got a big run coming ahead and if something were to happen it would be good to have that factor in your system I would have been worried just in case something happens or I get a cut or I bang my head or something and you keep on bleeding and bleeding, whereas if you were prepared then you wouldn't bleed as much would you so-- Not leaving anything to chance I'm always with people so and I always make sure that they are aware of my problem and know what to do in an emergency uhm . I think with a haemophilia emergency it's not. Like if I am doing anything active obviously I would have always had my medication uhm. I don't really leave anything to chance. Uhm so as long as I've had that then there is not a huge panic uhm but obviously if I have broken a bone then you're gonna have to go to hospital either way uhm*	It was interesting that this patient explained how doctors told his parents not to allow him to play out. This didn't come out in interviews with other patients of the same age. This highlighted to me that each situation is different, as each doctor has their own approach and each family has their own way of interpreting what healthcare professsionals tell them. I did feel that this family was perhaps quite anxious about haemophilia, which lead them to be quite risk-averse, and this may have contributed to their decision not to let their son play outside.