Perceived burden, lived experiences and experiences of learning processes and illness management

in parents of children with severe or moderate haemophilia

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Cover illustration: Drawn by a sibling of a boy with haemophilia

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For my family

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ABSTRACT

Haemophilia is a complex condition to manage, especially for parents of newly diagnosed children, and the illness affects the whole family. The parents are deeply involved in the child's treatment, as they frequently have to administer intravenous injections at home.

The overall aim was to investigate perceived burden, lived experiences and to explore experiences of learning processes and illness management in parents of children with severe or moderate haemophilia.

In studies I-III, a qualitative approach was motivated to describe experiences of parenting a child with haemophilia. Study III employed a longitudinal design to explore the learning process, while study IV employed a quantitative method with a cross-sectional survey.

The results reveal that the mothers often needed to become reconciled both with the fact of the child's illness and their own carriership. However, having a child with severe or moderate haemophilia was life changing for both fathers and mothers. The parents were forced into a situation where they had to learn about and manage their child's illness in daily life. Thus, a desire to become independent of health care professionals in this respect emerged as a key incentive for learning. How this learning process developed and how long it took depended on different factors. For example, parents of children with past or present inhibitors reported higher perceived burden than parents of children without a history of inhibitors. Nevertheless, independently managing home treatment was essential for the parents to feel in control of their life-world again.

One conclusion is that female carriers need more knowledge about their carriership and would benefit from counselling before starting a family. One suggestion is that acceptance of the child's illness and reconciliation with the new complex family situation could be promoted with person-centred care. Furthermore, the findings underline that health care professionals need to be aware of an increased burden on parents of young children and particularly the burden on parents of young children with inhibitors.

Keywords: Haemophilia, child, parent, family, learning, experiences, disease/illness burden

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SAMMANFATTNING PÅ SVENSKA

Blödarsjuka (hemofili) är en ärftlig sjukdom som beror på en medfödd brist på koagulationsfaktor VIII vid hemofili A eller koagulationsfaktor IX vid hemofili B. Hemofilisjukdomen är könsbundet recessivt nedärvd och drabbar (i svår form) nästan enbart män. Både hemofili A och B finns i svår, moderat och mild form. Personer med obehandlad hemofili drabbas av (tillsynes) spontana och traumatiska blödningar på grund av låga faktornivåer. För att behandla sjukdomen ersätts den saknade koagulationsfaktorn. Behandling med koagulationsfaktor kan ske förebyggande eller när en blödning uppkommer. I Sverige ges förbyggande behandling med koagulationsfaktor till alla barn med svår form och behandlingen startar när barnet är cirka 12 månader. Profylaxbehandling med koagulationsfaktor ges intravenöst (direkt in i blodet) och vanligen varannan dag i hemmet. Hemofiliteamet stödjer föräldrar att hantera och sköta barnets sjukdom och de intravenösa injektionerna i hemmet.

Avhandlingens syfte är att undersöka föräldrars erfarenheter av att ha ett barn med hemofili, deras lärprocess samt och sjukdomshantering, de första åren efter barnets diagnos. Vidare är syftet att kartlägga föräldrars upplevda börda av sjukdomen

I studie I intervjuades mammor till barn med svår och moderat hemofili. Alla inkluderade mammor var bärare av hemofilianlaget. I studie II intervjuades pappor till barn med svår hemofili. Studie III var en longitudinell intervjustudie, där upprepade intervjuer med föräldrarna genomfördes under ett år, efter profylaxbehandlingsstart. Studie IV var en kvantitativ studie, där ett frågeformulär skickades till samtliga svenska föräldrar till barn under 18 år med svår och moderat form.

Resultatet från avhandlingen påvisar att föräldrar till barn med hemofili upplevde att erfarenheten var livsförändrande och att sjukdomen påverkar alla delar av familjelivet. Mammor som var obligata bärare eller som hade känd hemofili i släkten förstod inte till fullo att de var bärare eller hade risk att vara bärare av anlaget förrän de fick beskedet om barnets diagnos. Föräldrarna beskrev sig som sårbara och att de var i ett existentiellt kaos som krävde mycket stöd från hemofiliteamet de första åren efter hemofilidiagnosen. Om barnet utvecklade antikroppar ökade föräldrarnas börda ytterligare och de upplevde en nästintill ohanterlig familjesituation. Resultatet påvisade vikten av ett intensivt lärande för att kunna hantera barnets sjukdom i det dagliga livet. Föräldrarna poängterade att självständig

hembehandling var nödvändig för att kunna hantera barnets sjukdom och minska beroendet av sjukvården. Papporna beskrev att de kände sig som kapabla pappor först när hembehandling kunde ske utan hjälp av sjukvårdspersonal. Föräldrars börda ökade om barnet utvecklade antikroppar eller om barnet hade övervikt/fetma. Föräldrars börda minskade ju äldre barnet blev.

En konklusion av resultatet är att den anlagsbärande kvinnan bör få möjlighet till information och rådgivning innan barnafödande planeras. Vidare att föräldrars accepterande av barnets sjukdom och försoning med den nya komplexa familjesituationen kan främjas med ett person-centrerat stöd från vårdpersonalen. Föräldrar och hemofiliteamet kan tillsammans utveckla ett sätt som främjar och underlättar familjens resa mot en självständig hembehandling. Vidare bör sjukvårdspersonal inom hemofilivården vara medvetna om den ökade bördan för föräldrar till barn som utvecklat antikroppar.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Myrin-Westesson L., Baghaei F. and Friberg F. (2013). The experience of being a female carrier of haemophilia and the mother of a haemophilic child. *Haemophilia*, 19 (2): 219–224.

II. Myrin Westesson, L., Sparud-Lundin, C., Wallengren, C. and Baghaei, F. (2015). A tortuous route to a capable fatherhood: the experience of being a father to a child with severe haemophilia. *Haemophilia*, 21(6): 799–805.

III. Myrin Westesson, L., Wallengren, C., Baghaei, F. and Sparud-Lundin, C. (2018). Reaching Independence Through Forced Learning - Learning Processes and Illness Management in Parents of Children Affected by Hemophilia. *Qualitative Health Research*, 28(14): 2142 –2154.

IV. Myrin Westesson, L., Sparud-Lundin, C., Baghaei, F., Khair, K., von Mackensen, S., Acuña Mora, M. and Wallengren, C. Burden on parents of children with severe or moderate hemophilia - the impact of sociodemographic aspects and the child's medical condition on perceived parental burden. *Submitted.*

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CONTENTS

ABBREVIATIONS

ABR	Annual Bleeding Rate
BMI	Body Mass Index
CVAD	Central Venous Access Device
EAHAD	European Association for Haemophilia and Allied Disorders
ED	Exposure Days
EHCC	European Haemophilia Comprehensive Care Centre
EHL	Extended Half Life
EUHANET	European Haemophilia Network
FVIII	Factor eight
FIX	Factor nine
GT	Grounded Theory
HCP	Health Care Professional
HEMOCAB	HEMOphilia associated CAregiver Burden scale
HIV	Human Immunodeficiency Virus
HTC	Haemophilia Treatment Centre
ITI	Immune Tolerance Induction
IU	International Unit
PCC	Person-centred care
PTP	Previous Treated Persons

r	Recombinant
QoL	Quality of Life
UK	United Kingdom of Great Britain and Northern Ireland
USA	United States of America
VAS	Visual Analogue Scale
WFH	World Federation of Haemophilia

1 INTRODUCTION

When a child with severe or moderate haemophilia is diagnosed, the whole family becomes affected by the illness. They must have frequent contact with the Haemophilia Treatment Centre (HTC) and are themselves deeply involved in the child's treatment. As a haemophilia nurse at HTC, Sahlgrenska University Hospital, I have long experience of meeting children with haemophilia and their families on a daily basis.

Children with haemophilia need a high level of supervision and care. Haemophilia is mainly treated with intravenous injections of clotting factor, and these injections are usually administered by the child's parents at home every other or every third day. According to Swedish practice, the child is usually between 10-18 months of age when prophylactic treatment with clotting factor begins. In practice, the parents have often learned to administer the clotting factor within one year from the prophylactic start. They will then take over the advanced care of the child and manage it independently at home.

Today, Swedish haemophilia care has no clear structure or plan of how to educate and support families with haemophiliac children. Based on my experiences of working with these families, several questions arise. What are the parents' experiences of having a child with haemophilia? How do the parents learn to handle their child's illness? What is the perceived burden on parents of children with haemophilia in Sweden? How do sociodemographic aspects and the child's illness impact on perceived parental burden? And what can the HTC do to support the parents' efforts to understand and manage their new life situation? My thesis intends to generate knowledge about this complex situation, and I hope the findings will be useful to Health Care Professions (HCP) in haemophilia care in improving the care and support offered to affected families.

2 BACKGROUND

The background describes haemophilia, its prevalence and treatment, and the structure of haemophilia care in Sweden for children with severe and moderate haemophilia. Previous research regarding the impact of the illness on parents is also summarized.

2.1 Haemophilia

Haemophilia is an inherited x-linked recessive disorder with a reported incidence of 1/5 000 males born with haemophilia A and 1/30 000 males born with haemophilia B (1, 2, 3). The incidence is the same in all ethnic groups. The affected gene is located on the X chromosome, and the disease occurs mainly in men. Women carry the gene and their sons develop the disease (2, 3).

A person affected with haemophilia A has a deficiency of factor VIII, while a person affected with haemophilia B has a coagulation deficiency of factor IX. The disease is characterized by partial or total deficiency of factor VIII or factor IX, which causes the blood to coagulate poorly or fail to clot, leading to spontaneous (apparent) and post-traumatic haemorrhaging (2, 4).

A cohort study (5) reported similar severity and variation in bleeding phenotype in young children with haemophilia A and B. However, the pharmacokinetics differ between clotting factor VIII and IX (4). The mean half-life for clotting factor VIII is shorter than for clotting factor IX, and consequently, people with haemophilia A need treatment more frequently than people with haemophilia B (2).

2.1.1 History

The earliest known description of haemophilia is from the 2nd century AD. In the Babylonian Talmud it is written that the third son is exempted from circumcision, if the mother has lost her first two sons due to bleeding after circumcision (6). In 1803, the first modern description of haemophilia was made by the American physician, John Conrad Otto. He recognized that only men had bleeding symptoms and that unaffected females passed the disease to their sons (7).

Haemophilia has been known as “the royal disease”, as several members of the European royal family were affected by severe haemophilia B. Queen

Victoria (1837–1901), was a carrier and her son, Leopold died of a brain haemorrhage in early adulthood. Haemophilia spread to other royal families in Europe (most prominently in the German, Russian and Spanish royal families) through Queen Victoria's daughters (8).

In the first half of the 1900s, people with haemophilia were treated with whole blood or fresh plasma transfusions. Unfortunately, whole blood or fresh plasma do not contain enough factor VIII or factor IX to achieve effective haemostasis. For this reason, most persons with severe hemophilia died in childhood or in early adulthood due to internal bleedings or bleedings after trauma (9, 10). In the 1960s, plasma-derived clotting factor VIII and IX became generally available in Sweden. Home treatment and self-infusing started in the 1970s (4). Clotting factor was manufactured from large plasma pools, with plasma from several thousand donors for each batch of factor VIII and factor IX (11, 12). As a result of these large plasma pools and ineffective virus inactivation, the clotting factor transmitted viral diseases like hepatitis and human immunodeficiency virus (HIV) in the 1980s. In the early 1990s, manufactured recombinant clotting factor became available and in the 2000s, recombinant clotting factor with no human albumin or other human proteins was introduced (9). In recent decades, the volume of clotting factor needed has drastically decreased and is today between 2.5-5 ml diluents depending on the product (6).

2.1.2 Inheritance and prenatal diagnosis

The daughter of a man with haemophilia is an obligate carrier. Her sons have a 50% risk of being affected with haemophilia. Likewise, her daughters have a 50% risk of being carriers and potentially have sons with haemophilia. A father with haemophilia will pass on the Y chromosome to his sons and the boys will not be affected by the disease nor pass on the disease to the next generation. The severity of haemophilia and the type will remain the same in the affected family through generations. Nevertheless, when a child is diagnosed, approximately 50% of the families have no apparent previously known family history of haemophilia (13-16). This includes both sporadic cases that are caused by novo mutations and cases were the disease has been inherited but is unknown to the family. The disease can be inherited through generations of women without any boy being born with haemophilia.

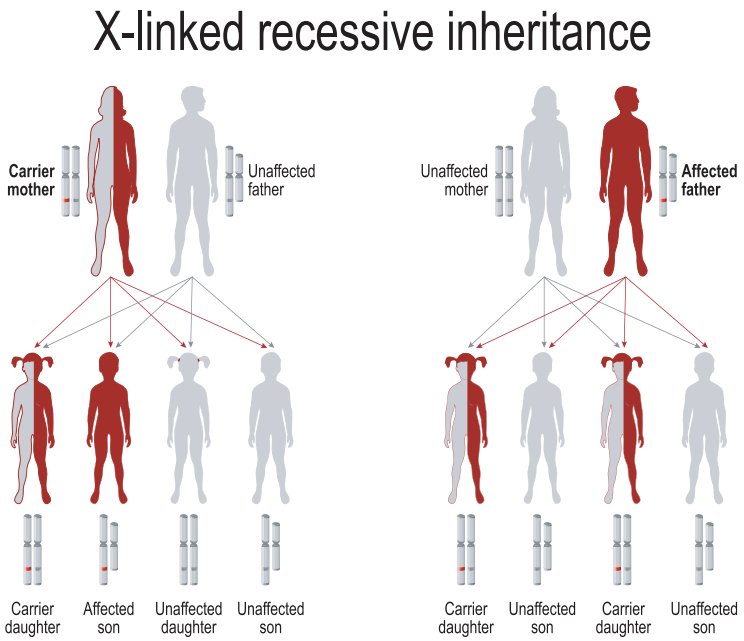

Figure 1. Inheritance of haemophilia (reprint with permission from Shutterstock).

Prenatal diagnosis has been available since the 1970s. Before that, female carriers in Sweden were sometimes advised to not have any children. When the sex of the fetuses could be determined in the 1970s, some pregnancies with male fetuses were interrupted even if there was a 50% chance that the fetuses were not affected by haemophilia (17). Today, chorionic villus sampling in gestational week 11-12 is the standard method, if parents want to perform prenatal diagnosis (17, 18). It is important for the parents to have had genetic counselling prior to the decision to undergo prenatal diagnosis to ensure that they can make an informed decision (19). A Swedish study from 2014 (17) revealed that prenatal diagnosis is now more frequently used as psychological preparation for having a child affected by haemophilia than for termination of pregnancies.

2.1.3 Classification of haemophilia

Haemophilia A is prevalent in approximately 80% of cases, and haemophilia B in approximately 20% of cases. In 1958, Biggs and Macfarlane (20) categorized haemophilia as severe, moderate or mild in form, according to

the factor level. The normal range of factor VIII (FVIII) and factor IX (FIX) is defined in the local laboratory, but the lowest normal range is approximately 50-60 IU dL^{-1}. A person with a severe form of haemophilia has <1 IU dL^{-1}, a person with a moderate form has factor levels between 1-5 IU dL^{-1} and a person with mild haemophilia has between >5-40 IU dL^{-1}. Approximately 35% of persons with haemophilia are affected with the severe form, 15% with moderate, and half with mild form (4).

2.1.4 Symptoms

Haemophilia is characterized by (apparently) spontaneous and post-traumatic bleeding events due to low levels of blood clotting factors. In severe haemophilia, the first bleedings usually occur when the child starts to move more actively, at about 6 months of age. Children with moderate haemophilia generally have their first bleedings around 1-2 years of age. There are typically no major traumas that explain the bleedings – they may appear spontaneously. People with mild haemophilia have a wide range of factor levels (>5-40 IU dL^{-1}) and this naturally has an impact on when the first bleedings occur. In cases with mild haemophilia, it is not unusual that the person is diagnosed later in life, e.g. after surgery or tooth extraction (15). For persons affected with mild haemophilia, spontaneous bleedings tend to be unusual.

Haemorrhaging is particularly frequent in joints and causes progressive destruction of articular structures, leading to impairment of joint function and chronic pain (21). The major goal in treating persons with haemophilia is to reduce the frequency of bleeds, and consequently morbidity and joint damage, to prevent future disability but also to reduce mortality due to life-threatening bleeds (22).

2.1.5 Treatment

Treatment is based on replacement of the missing clotting factor when a bleed occurs (on-demand treatment) or regular and continuous treatment (prophylactic treatment). Dose, frequency and type of replacement therapy in haemophilia vary depending not only on the severity of the disease, the person's age, lifestyle, preferences and treatment schemes, but also on the availability of clotting factor in different countries. Untreated or mistreated haemophilia causes painful bleeding, especially in joints. Repeated bleedings in joints lead to arthropathy and joint destruction (2, 4). Additionally, untreated persons are at risk of fatal internal bleedings (23).

There is one exception when clotting factor products may not be necessary to achieve effective haemostasis and that is in persons affected with mild haemophilia A. In these cases, bleedings can be treated with desmopressin, often in combination with tranexamic acid, and this is especially effective if the person has factor VIII levels above 10 IU dL^{-1}. Desmopressin is usually prescribed as an intranasal spray and the person can treat minor bleeding at home (4, 24).

Recently extended half-life (EHL) recombinant (r)FVIII and rFIX products have been developed. With EHL products, the frequency of injections can be decreased compared to conventional clotting factor products, without poorer haemostasis (25, 26). This is especially true regarding EHL rFIX products (27). One major aim of EHL products is to decrease the burden of the illness by reducing the injection frequency for persons on prophylactic treatment (28). Since 2016, EHL rFVIII has been available in Sweden on a state-subsidised prescription basis, but only for previously treated persons (PTP). In October 2018, EHL rFIX also became available on a state-subsidized prescription basis, and likewise only to PTP.

2.1.6 Prophylactic treatment and home treatment

Home treatment implies significant benefits to the child, the family and society (2). Regular, safe and easy access to clotting factor in the child's home is crucial to reduce the impact of the illness. Several decades of research have underpinned that home treatment increases quality of life for families and drastically decreases the need for hospital visits for the child. Children undergoing home treatment are less absent from school, experience less pain, become better integrated with peers and are more active in sports (29, 30). Moreover, home treatment reduces medical costs and means parents are less absent from work (31).

An important task for the haemophilia nurse is to educate persons with haemophilia, parents and other caregivers in home treatment. Home treatment with clotting factor is considered the 'Gold Standard' for persons with severe haemophilia and is part of comprehensive haemophilia care (13, 29, 32, 33). In Sweden, prophylactic treatment with clotting factor for children with severe haemophilia starts when the child is around 12 months of age. The goal is to start prophylactic treatment before the onset of any joint bleeding. At this age, the child starts to place weight on joints and the aim of the treatment is to prevent serious haemorrhaging (22). The prophylactic treatment allows the child to participate in normal social and physical activities throughout childhood, such as sport activities. The World

Federation of Hemophilia (WFH) (13,34) recommend persons with hemophilia to participate in regular non-contact sport activities (e.g. table tennis, swimming, sailing, badminton and golf). Furthermore, WFH point out that persons with haemophilia can participate in high contact and collision sports (e.g. downhill skiing, soccer, ice hockey, rugby and wrestling) if they are covered by good prophylactic treatment.

Haemophilia treatment with clotting factor requires a safe and easy venous access, which is a major challenge when treating children. Venous access is especially difficult in children on immune tolerance induction (ITI) treatment. In Sweden, the injections are usually given peripherally, whereas in other countries, Central Venous Access Devices (CVAD) are more common (15, 35, 36). The choice of venous access depends on many aspects e.g. venous status of the child, the child's age, the parents' skills, clotting factor product (volume), inhibitor development, psychosocial situation and the HTC experiences (37). CVAD is associated with risk of infections and thromboses (38-40). The reason for removal of CVAD in children with haemophilia is mostly infections (69.9%), whereas thrombosis only stands behind 4.1% of the cases (41). In 2004, there was an international consensus (42) that peripheral veins should be the first choice and CVAD should only be used when there was clear need and that the injections in the CVAD should continue no longer than necessary.

Families with children with severe haemophilia have close contact with the HTC and are deeply involved in the child's treatment (43, 44). Newly diagnosed children and parents visit the HTC or local hospital several times per week the first year after the prophylactic treatment start. The parents eventually take over the preparation and administration of the clotting factor under the supervision of the haemophilia care team. It is important that parents recognize signs of bleeds, know how to treat bleeds, understand how the clotting factor works in the child's body over time and that they are aware of which situations the child should avoid. After a year, most parents are ready to manage the intravenous injections at home and can handle the haemophilia illness in daily life (35).

In Sweden, the practical conditions when teaching parents to perform home treatment are usually that one parent would have the child in her/his lap while the other performs the injection, helped and guided by the haemophilia nurse. The peripheral injections are conducted with a 23- or 25-gauge butterfly needle, the child's blood fills the tube and thereafter the clotting factor is administered. Immediately after the clotting factor is administered, the needle is removed from the child without saline flushing.

The time needed for administering the clotting factor is between a few seconds to several minutes depending on product and dose. At the beginning of the treatment, the parent (not holding the child) is observing what the nurse does and how he/she handles the child, the needle and the clotting factor. As the learning process moves on, the parents get more and more hands-on involvement. Either the parents take turns to have the child in their lap or one parent learns before the other. in Sweden, the aseptic non-touch technique (45) is used for children with a CVAD. The CVAD needle is removed after the injection, even though the child has daily or twice daily treatment.

A Dutch study has reported that in 77% of the cases, the mother is the first parent to learn how to do the injections (46). The time needed before parents can independently perform home treatment depends on several factors. Factors that impact the time needed include the child's age at treatment start, whether the venous access is peripheral or central, difficulties with venous access, whether the family lives close to a HTC, whether the child develops inhibitors, and the parents' experiences of haemophilia and education level (47). Due to varying individual circumstances, the time needed for learning to perform home treatment has been reported to be between 9 weeks (46) and 12 months (35).

2.1.7 Complications

Developing inhibitors is a severe complication related to the standard treatment with clotting factor. Inhibitors neutralize the infused clotting factor and the treatment is no longer effective. Over 30% of children with severe haemophilia A develop inhibitors (antibodies) against clotting factor (48). Children affected with haemophilia B are at less risk of developing inhibitors, and the incidence is reported to be between 3-5% in this population. Most persons with severe haemophilia who develop inhibitors do so after an average of 9-12 exposure days (ED) with clotting factor. The risk of developing inhibitors decreases after 50 ED (49). It is therefore rare for adults with severe haemophilia to develop inhibitors in high income countries where prophylactic treatment is standard. For children with moderate haemophilia, the risk of developing inhibitors is significantly lower than for children with a severe form (50).

To eradicate inhibitors, the child is given immune tolerance induction (ITI) treatment, which usually involves daily administration of clotting factor in high doses over a long time (6-24 months). To secure venous access and for

practical reasons, children with inhibitors usually get a central venous access device (CVAD) implanted (2, 22, 38, 50).

2.1.8 Co-morbidities and mortality

In high-income countries, the life expectancy of persons with haemophilia is expected to be close to normal (51). Advances in haemophilia care has improved life expectancy from only 11 years at the beginning of the 1900s to an age that is almost the same as the general population (52, 53). In low-income countries with less or no access to clotting factor, life expectancy is much lower (54). Apart from the symptoms and consequences of the disease, a person with haemophilia faces the same co-morbidities as the rest of the general population. However, hypertension, as well as acute and chronic renal failure, have been reported to be higher in the haemophiliac population than in the general population (55, 56).

Although the modern management of haemophilia has improved significantly over recent decades (4), persons with haemophilia may still suffer from the burden of the illness in regard to clinical (i.e. treatment complications, presence of inhibitors, pain, and arthropathy), psychological (stress and coping, anxiety and depression, stigmatization and discrimination), and economic aspects (57).

2.1.9 Haemophilia care

According to the World Federation of Haemophilia (WFH), haemophilia comprehensive care should be centralized (13). In Sweden there are three European Haemophilia Comprehensive Care Centres (EHCCC): Karolinska University Hospital in Stockholm, Sahlgrenska University Hospital in Gothenburg and Skåne University Hospital in Malmö. To be certified as an EHCCC by the European Haemophilia Network (EUHANET), several criteria need to be fulfilled. EHCCC provide a wide range of services to persons affected by haemophilia, from genetic counselling to parents before the birth of the child to the complex care of elderly persons with haemophilia and comorbidities. EHCCC are consequently multidisciplinary by nature (58). EHCCC are more commonly known as Haemophilia Treatment Centres (HTC) in Sweden and are consequently referred to as HTC, as they have in this thesis as well as in all four studies.

The Guidelines for the Management of Haemophilia (13) have emphasized the importance of the family's involvement in haemophilia comprehensive care. The guidelines state that families need education and support from the HTC. In 2015, The European Association for Haemophilia and Allied

Disorders (EAHAD) wrote a curriculum for haemophilia nurses in Europe (59) naming the domains for the haemophilia nurse as follows:

> *Applied biological science; treatment and management of haemophilia and associated disorders; genetic practice; care management of affected carriers and women; the impact of living with bleeding disorders; evidence base and applied research in haemophilia practice; and, the specialist role of the haemophilia nurse.*
> Harrington et al., p. 109 (59)

The guidelines and curriculum state what should be included in good haemophilia comprehensive care but do not clarify or specify what methods constitute best practice.

2.2 Parenthood

Entering parenthood is a definitive stage in life which has a profound effect on every aspect of a person's life. Parenthood brings new love, joy, challenges and demands on the couple. Personal growth, new values and perspectives on life are commonly described as an effect of parenthood (60). The transition to parenthood is a special and unique journey since it is experienced both jointly and individually. Parents need to find a balance in the relationship between the demands of the child, household chores and professional work. The relationship between the new parents changes as they enter parenthood (61). Despite changing gender relations in society, both international and Swedish studies report that mothers take more responsibility for the day-to-day care of children than the fathers (61-64).

2.2.1 Experiences of being a parent of a child with a chronic illness

When a child is diagnosed with a chronical illness the parents face the demands of the illness while managing their own sorrow. Handling daily family life with a chronically ill child means the parents need to some extent be an active part of the treatment of the illness. Parents of children with chronic illness report higher levels of stress than parents of healthy children. The child's illness impacts the whole family in many aspects (65, 66). High levels of stress could also affect the parents' ability to manage the child's illness and thus have an effect on the child's health-related outcome (67). Higher parental stress is associated with greater parental responsibility for the management of the child's illness and similarly, when the child experiences recurrent pain episodes (65). Burnout is also more common in

parents of children with chronic illness than parents of healthy children (68). It is known that mothers report more intense or more significant experiences of sorrow due to their child's illness than fathers (69). Coughlin and Sethares' (69) literature review on the topic showed that mothers experience more feelings of guilt or self-blaming, depression, fear and emptiness than fathers of children with chronic illness.

One consequence of the child's chronic illness is personal suffering for the parent. This personal suffering is termed 'burden' (70). Parental burden includes objective practical problems e.g. time to treat the child, many hospital visits, extra supervision and care, less time for leisure and work and financial impact. Parental burden also includes subjective psychological suffering e.g. disturbed family relationships, depression, anxiety, loss of dreams and expectations (70, 71).

2.2.2 Impact of haemophilia on parents

Haemophilia has an impact on quality of life (QoL) for the affected adult, as has been well-documented in quantitative research and acknowledged in the treatment of haemophilia (57, 72). Studies investigating QoL and parental burden among parents of children with haemophilia are sparse. In one study, using generic instruments, parents of children with haemophilia reported a higher burden than parents of healthy children (73). Furthermore, there are some studies that point out the increased burden on parents of haemophiliac children with inhibitors (74). This is in line with two studies conducted in the United States of America (USA) using an online questionnaire. The studies reported a significantly higher burden on caregivers caring for children with inhibitors compared to caregivers of children with no inhibitors (75, 76). A recent study regarding parental burden on parents of children treated with EHL products states that the burden decreased when the child was treated with an EHL product (77).

One QoL study on parents of children with haemophilia B revealed that mothers have higher levels of depression and anxiety than fathers. Furthermore, parents of children with moderate haemophilia had greater levels of depression and anxiety than parents of children with mild and severe haemophilia B (78).

2.2.3 Impact of haemophilia on siblings

Few studies have explored the impact of having a sibling with a chronic illness in diagnoses other than cancer. Previous research reports that family roles change and siblings are significantly affected if a child in the family is

diagnosed with a serious chronic illness (79). Siblings can suddenly experience that they are getting less attention and care (79-81). There is a positive association between the sibling's level of knowledge of the ill sibling's chronic disease and sibling connectedness: with greater knowledge there is a higher level of connectedness (82).

2.2.4 Measurements on impact and burden

The need for a tool to measure the specific burden on caregivers of persons with haemophilia has recently been addressed. For example, an online haemophilia-specific questionnaire has been developed in the USA to measure caregiver burden (83) and another tool, The Hemophilia Caregiver Impact (HCI) measuring the specific burden on caregivers of persons with haemophilia was developed in 2017 (74). The HCI measures the caregiver burden on several subscales consisting of 36 items. Both instruments are not fully validated, novel and not specifically aimed at parents of children with haemophilia. Additionally, there are validated caregiver burden scales available that are generic instruments designed for use across different diseases and ages (84). Disease-specific instruments that measure the parental burden are less common (85).

A recently developed measurement aimed specifically at parents of children with haemophilia is the HEMOCAB™ questionnaire (Appendix 1). The HEMOCAB™ is a paper-and-pencil instrument, consisting of 54 questions. The first version of the questionnaire contained 59 items but was further revised to 54 items for psychometric reasons. Questionnaire development included item generation by semi-structured focus groups including 11 caregivers, evaluation of existing caregiver burden scales for relevance by 16 HCPs, feasibility testing and cognitive interviews with 12 caregivers and pilot-testing on caregivers of children with haemophilia, with and without inhibitors (86). The instrument was also pilot-tested on 40 caregivers of children with haemophilia in the USA. Additionally, the questionnaire was used in an international European study (*The Burden of Bleeds and Other Clinical Determinants on Caregivers of Children with Haemophilia,* unpublished) in which 144 parents participated. The HEMOCAB™ showed high psychometric characteristics in terms of internal consistency in both the pilot study (Cronbach alfa 0.97) (86) and the European study (Cronbach alfa 0.96) (87).

2.3 Swedish welfare system

The Swedish welfare system is well-funded compared to many other countries. The parental leave insurance system consists of 480 paid days per child. Three months of this parental leave is reserved for sole use by the father and another three months for sole use by the mother. Medical care, medications and treatment is free of charge for children under 18 years of age. If the child is sick or needs medical care, parents are compensated for loss of salary by the welfare system and the employer cannot deny leave. Moreover, if the child has a disability or chronicle illness, the parents can apply for childcare allowance. The childcare allowance compensates for extra supervision, care and expenses e.g. treatment at home, trips to the hospital or special furniture (88).

3 THEORETICAL STANDPOINTS

This thesis takes its point of departure in a human science approach in relation to the learning person. The overall perspective is based on a reflected life-world approach. Life-world theory is characterized by certain ontological, epistemological and methodological assumptions and offers a view of the learning human.

3.1 Life-world

The philosopher and founder of phenomenology, Edmund Husserl (1859-1938) introduced the concept of "Life-world". The life-world is the everyday world that we experience. It is in the life-world we have relationships with others, learn, feel, think and act. Based on our life-world we make choices and assumptions (89). The life-world is generally taken for granted in daily life and one challenge of the life-world approach is to reflect on it and make it visible (90). A life-world ontology approach assumes that life and world is linked together in a complexity that is the foundation of our experiences, thoughts and actions. The life-world is both personal and shared with others. A person's life-world is shared with people, some of whom we have close and daily relationships with, such as family members, and others who we have more distance to.

To develop knowledge of the phenomenon, the haemophilia experience, the researcher must interpret the person's lived experiences and listen to their narrative (91). In life-world research, the researcher has to elaborate on her/his pre-understanding and keep openness and curiosity towards the phenomena studied (91, 92).

Merleau-Ponty (93) describes that the world becomes accessible to the person through her body. The body is a prerequisite for being in the world and being human is being a body. Merleau-Ponty's thoughts about the human started from Husserl's thoughts about the life-world. This view stands in contrast with the dualistic view of human, where the body and soul are divided (94). Merleau-Ponty argues that the lived bodies are always in a social context and in relation with other humans in the world. Merleau-Ponty's view on human existence is in line with Ricoeur's – that the mind and body share an interrelated existence (95).

Haemophilia is an inherited disease and the parents' life-world is significantly affected by the human body. The mother carries the disease in

her genes and likewise, a man with haemophilia passes carriership to his daughters. A parent's life-world consists of subjective experiences and values of what is certain, real, good and bad. This personal life-world motivates the parent to live her/his life the way she/he does. The child's illness is a disruption of the parent's life-world and makes it necessary to change thoughts, feelings and behaviours to manage the challenging situation that the child's illness has created.

Haemophilia is a serious chronic illness which places the family in a new situation that requires learning. The family needs new knowledge and has to develop new skills to be able to handle the situation. Human learning has a starting point in the human body (93) as well as in the person's previous experiences (92). Gadamer (92) describes that humans understand the world through their previous experiences and when a human faces a new complex situation, it is her previous experiences that form the foundation for interpreting the situation. Learning is a gruelling process which requires new questions to be formulated, and the person's previous understanding may be rejected and further developed. With new knowledge and understanding the person experiences the world in a new way and her actions and decisions can be based on new grounds (92, 96). Learning provides an opportunity for the person to control her life on a conscious level (97). Likewise, Ricoeur argues that consciousness is the disposition to act, and not only an awareness of one's existence (95).

The individuality of a person is always an interpretation of the (life-) world and in constant need of new stimulus for existing and changing. In a learning situation, the person brings with her/him both the past, the present, and the future (98). Knowledge is a way for humans to make the incomprehensible understandable (97). Learning is more than taking in information. In a genuine learning process, the person makes the knowledge part of her life-world (97, 99). According to Jarvis (100), learning is an existential process that changes the individual and her life vision. The existential approach to learning provides a philosophical base for looking at learning as a lifelong process. Jarvis emphasizes that the key result of the learning process is a changed and more experienced individual. Jarvis' theory of lifelong learning (100, 101) offers an approach to the complex existential situation that parents of children with haemophilia are facing. Learning has a positive impact on the person in such a way that the individual becomes more involved and has an opportunity to influence the impact of the illness on her life (99).

The life-world perspectives in this thesis are regarded as the parents' personal and shared experiences of their everyday life-world in which relationships, learning and actions take place, thus forming and shaping the parenthood of a child with severe or moderate haemophilia.

4 RATIONALE

Haemophilia care has undergone significant improvement in recent decades. In high income countries, prophylactic treatment with effective clotting factor is standard and most children with severe haemophilia have home treatment. Home treatment implies significant benefits to the child, the family and society and is essential to reduce the impact of the illness. The parents are deeply involved in the home treatment. However, guidance on how the haemophilia team should meet, support and educate families with children affected by haemophilia is not available today. There are limited studies with focus on lived experiences and experiences of learning processes and illness management in families affected with severe and moderate haemophilia. Furthermore, little is known about the perceived burden on parents of children with haemophilia. There is a need to increase knowledge and understanding of the families' experiences and life situation to further develop and assure quality of care.

Increased knowledge generated from this thesis may be beneficial in developing a more structural way of supporting parents in the first years after the child's diagnosis, thereby improving the care of families affected with haemophilia.

5 AIM

The overall aim was to investigate lived experiences and perceived burden and to explore experiences of learning processes and illness management in parents of children with severe or moderate haemophilia.

5.1 Specific aims

Study I — The aim of this study was to describe the lived experience of being a carrier of severe or moderate haemophilia and being a mother of a child with haemophilia.

Study II — The aim of this study was to describe the lived experience of being a father of a child with severe haemophilia.

Study III — The aim of this study was to explore learning processes and illness management in daily life during the first year after treatment start in parents of children with severe haemophilia.

Study IV — The aim of this study was to describe the perceived burden on parents of children with severe or moderate haemophilia in Sweden and the impact of sociodemographic aspects and the child's medical condition on this.

6 METHODS

6.1 Design

To achieve the overall aim of the presented thesis, multiple scientific approaches have been used, including both qualitative and quantitative methods. A qualitative approach was motivated in Studies I-III to understand experiences of parenting a child with severe or moderate haemophilia, allowing a deeper understanding of the phenomenon studied. The design was guided by the aims of the studies. A phenomenological hermeneutic method was chosen in Studies I and II to develop a profound understanding of the parents' life-world. This method allows the researcher to integrate the preunderstanding of the phenomena studied in the analysis (102). In Study III, learning processes were explored and a longitudinal design was suitable to explore these over time. Illness management and learning processes among the parents were assumed to take place both individually and in a social context. Grounded theory was chosen in Study III to capture how the parents handle the illness and to explore these processes within their own social context. In a longitudinal qualitative study, the researcher is a part of the phenomenon he/she explores, and constructivist grounded theory underlines the relationship between the participants and the researcher and the interaction between them. Conceptual models are created in the interaction between the researcher and the participants (103, 104).

In Study IV, a quantitative approach was applied by using a cross-sectional design to study the perceived burden among parents of children with severe and moderate haemophilia in Sweden. Between 2016 and 2018, an international study on parental burden was conducted in seven countries throughout Europe: *The Burden of Bleeds and Other Clinical Determinants on Caregivers of Children with Haemophilia* (the BBC Study). This international study was extended with a Swedish study that followed the same design and study protocol as the international BBC study but with a total population sample (Study IV). An overview of the four studies is outlined in Table 1.

Table 1. Overview of studies in this thesis

	Study I	Study II	Study III	Study IV
Design	Qualitative approach, life-world perspective	Qualitative approach, life-world perspective	Qualitative, longitudinal approach, grounded theory method	Quantitative approach, cross-sectional multicentre study
Data collection	Individual interviews	Individual interviews	Repeated interviews, Individual or in pair	Questionnaire, socio-demographic and medical data
Participants	13 mothers (carriers) of children affected with severe or moderate haemophilia	14 fathers of children affected with severe haemophilia	Four families (4 mothers, 4 fathers) with children recently diagnosed with severe haemophilia	102 parents of children affected with severe or moderate haemophilia
Data analysis	Phenomeno-logical hermeneutic method	Phenomeno-logical hermeneutic method	Constant comparative method	Descriptive statistics and linear regression analyses

6.2 Settings and study participants

6.2.1 Study I

In 2010 and 2011, a research project to investigate the bleeding tendency of carriers in Sweden was conducted at the HTC, Sahlgrenska University Hospital (105). A total of 126 women were included in the research project. Participants for Study I were strategically chosen from the above-mentioned project to achieve a span and spread in age and experience (102, 106). The only real criteria common to the participants in Study I were gender,

carriership of haemophilia and the fact and that they had given birth to a child with haemophilia. A total of 13 women were asked to participate and all accepted. The participants were approximately equally distributed from the three HTC in Sweden. The number of participants was not decided in advance (107), the reason for stopping inclusion after 13 interviews being that enough material rich in data and variation had been gathered and no new information was obtained in the last two interviews.

6.2.2 Study II

Participants for Study II were strategically chosen to achieve a variety of experiences (106), the variation intending to reflect socio-cultural diversity, rural/urban areas, inhibitors/non-inhibitors, family situation and educational level. The only real criteria common to the participants in Study II were that they were fathers of children with severe haemophilia. The number of participants was not decided in advance, instead the variation and richness of the data determined the final number of participants (107). Existing haemophilia registry was reviewed and patients <18 years with severe haemophilia were identified. Sixteen fathers from all three Haemophilia Treatment Centres (HTC) in Sweden were asked to participate and fourteen agreed to take part in the study. The reason for completing inclusion after fourteen interviews was that no new information was obtained in the last three interviews.

6.2.3 Study III

The parents were strategically chosen (103) from an existing haemophilia registry at the HTC Sahlgrenska University Hospital, Gothenburg, Sweden. The families were chosen to reflect a variety of experiences of learning processes and illness management in parents of children with severe haemophilia. Four families with children starting prophylactic treatment were asked to participate. All four families (eight parents) agreed to participate in the study. Two parents (same family) had recently received a residence permit and came from a war-torn country. The two parents had limited knowledge of Swedish at study start so the study information and informed consent was translated to the parents' native language.

6.2.4 Study IV

All children (aged 0 to 17 years) with severe or moderate haemophilia were identified by nurses at the three HTC in Sweden: Karolinska University Hospital, Sahlgrenska University Hospital and Skåne University Hospital and a total of 142 families were found. The inclusion criterion was being a parent of a child with severe or moderate haemophilia. Parents with limited knowledge of the Swedish language were excluded since they could not read the questionnaires, so parents who needed an interpreter when their children had their last annual check-up were excluded.

Twelve families were excluded due to limited knowledge of Swedish and two families due to invalid addresses. The questionnaires were consequently sent out to 128 families (Figure 2). One parent per family could participate in the study, independently of how many children with haemophilia they had. The parents chose who should participate in the study. Families that did not respond to the initial mail within one month received duplicate questionnaires. Parents who returned the questionnaires were given a cinema gift card, worth 12 EUR.

The questionnaires were completed by a total of 102 parents (79.7%) (Figure 2) of which 53 were parents with children treated at HTC in Karolinska University Hospital, 25 with children treated at HTC in Sahlgrenska University Hospital and 24 with children treated at HTC in Skåne University Hospital. In the sociodemographic questionnaire the participants were asked if they were the 'father', 'mother' or 'other caregiver'. All 102 participants were fathers or mothers.

The 21 parents first included from the HTC at Sahlgrenska University Hospital were also included in the international study *The Burden of Bleeds and Other Clinical Determinants on Caregivers of Children with Haemophilia* (the BBC study) using the same questionnaires and study design. Duplicates of the parents' questionnaires and medical data of the children were sent to the principle investigator of the BBC study.

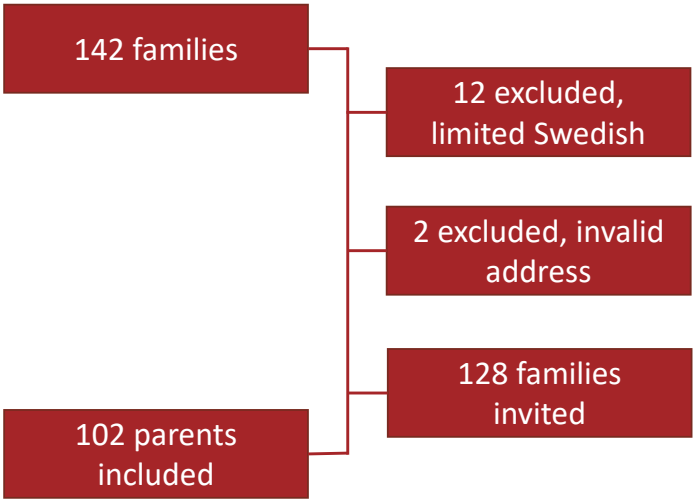

Figure 2. Flow chart of study population study IV.

6.3 Data collection

6.3.1 Study I

A pilot interview was conducted before Study I to ensure that the author had enough knowledge to perform open narrative interviews (108). In order to achieve sufficient quality, the co-authors (of Paper I) reviewed the pilot interview and the interview was then included in the study, thus being judged to have sufficient quality (106). The interviews were conducted between March and October 2010. The length of the interviews varied between 35-76 minutes, the average length being 52 minutes. The interviews all started with a general question: "Can you tell me what it's like to be a carrier of haemophilia". Follow-up questions were asked when clarification or reflections were needed (106, 108). All interviews were conducted by the author.

Eleven of the interviews were conducted in a secluded meeting room at the outpatient clinic, Department of Haematology, Sahlgrenska University Hospital. One interview was carried out in the participant's workplace and

one interview was conducted in the participant's home. The interviews were transcribed verbatim as fully and as closely as practically possible by the author. Pauses were marked with " ..." and laughter, tears, sobs and other emotional expressions were in brackets e.g. (tears). If the participant pointed at a body part, it was similarly marked in parentheses.

6.3.2 Study II

Study II also began with a pilot interview that was reviewed by the three co-authors (of Paper II) (106). The open narrative interview was judged to have the necessary quality and was included in the study. In Study II the 14 interviews were conducted between March 2013 and December 2014, with a mean duration of 42 minutes. Open interviews were used to collect the data and all interviews started with the question: 'Can you tell me about the experience of being the father of a child with severe haemophilia?'. All interviews were conducted by the author.

Six of the interviews took place at the outpatient clinic, department of Haematology, Sahlgrenska University Hospital, four at the participants' workplaces and four at the participants' respective homes. As in Study I, the interviews were transcribed verbatim as closely as possible. The same method as in Study I was used to mark emotional and non-verbal expressions. All interviews were transcribed by the author.

6.3.3 Study III

In Study III, 30 open-ended interviews were conducted between September 2014 and September 2016, with a mean duration of 31 minutes. The first interview with each family or parent began with an open-ended question: "Tell me what it's like to be a parent of a child with haemophilia and starting prophylactic treatment". In the follow-up interviews, the open-ended questions were developed from previous narratives to deepen the previously initiated analysis and to secure focus on the research question (103). The parents were interviewed every second to third month during the study period, depending on when the parents had opportunity. Holidays, busy working schedule and other practical issues for the parents meant that the interviews needed to be postponed on a few occasions. However, the interviews were conducted as evenly throughout the year as possible.

The interviews were conducted in the parents' home, at their work or in a secluded room at the outpatient clinic, department of Haematology,

Sahlgrenska University Hospital. The parents decided if they wanted to be interviewed together or individually. Approximately half of the interviews were individual: 17 of the 30 interviews. One family was interviewed jointly in all seven interviews and one family chose to have all ten interviews individually. For the rest of the families there was a mix of individual and joint interviews. The same method as in Studies I and II was used to mark emotional and non-verbal expressions. All interviews were conducted and transcribed by the author.

The interviews with the family who had just received a residence permit were carried out with the help of an authorized interpreter. Efforts were made to have the same interpreter throughout the study period to maintain continuity in the interview situation. Six out of seven interviews were conducted with the same authorized interpreter. The parents' Swedish improved rapidly during the study and in the last three interviews they spoke more and more Swedish despite the present of the interpreter.

6.3.4 Study IV

Parents were included between November 2016 and February 2018. The HEMOCAB™ questionnaire, along with a sociodemographic questionnaire (Appendix 2) was sent by post and the parents were asked to complete both the questionnaires.

HEMOCAB™ is a haemophilia-specific self-rated questionnaire completed by the parent and consisting of 54 questions pertaining to 13 domains. In the BBC study, the English version of HEMOCAB™ showed high psychometric characteristics of internal consistency (total HEMOCAB™ score Cronbach's a= 0.963) (87). The scores in all domains range from 0-100 and higher scores on the HEMOCAB™ indicate a greater perceived burden for the parent.

Prior to the study, HEMOCAB™ was translated into Swedish using principles developed by *The Translation and Cultural Adaptation* (TCA) group (109). Principles of good practice for the translation and cultural adaptation process for Patient-Reported Outcomes (PRO) includes ten steps. The ten steps in the method are:

1. Preparation

2. Forward translation

3. Reconciliation

4. Back translation

5. Back translation review

6. Harmonization

7. Cognitive debriefing

8. Review of cognitive debriefing, results and finalization

9. Proofreading

10. Final report

The project management group for the translation was the author (LMW), Catarina Wallengren (CW) and Carina Sparud Lundin (CSL). Permission from the instrument developer was obtained for the translation into Swedish.

The preparation, forward translating and reconciliation of the instrument into Swedish were performed by LMW, CW and CSL. The forward translating was done in two independent versions, which were then reviewed and merged together by LMW, CW and CSL. Back translation was conducted by an external professional translator. The back-translation review and harmonization compared the new version of the instrument with the original to reveal discrepancies and similarities between the versions. This step of the translating process was conducted by LMW, CW and CSL. During the cognitive debriefing, the instrument was tested in a small group of parents of children with mild haemophilia and in a small group of parents of young adults aged 18-19 years with severe or moderate haemophilia (in total 10 parents). This was done to check understandability, cultural relevance and alternate wording of the translation. Review of cognitive debriefing, results and finalization of the final version of the Swedish HEMOCAB™ was conducted by LMW, CW and CSL. In the next step, the instrument was reviewed and proofread by a haemophilia physician. The instrument developer of the HEMOCAB™ was an active part throughout the process and acknowledged the final version of the Swedish HEMOCAB™.

For collection of sociodemographic data, a structured questionnaire specifically developed for the study was used (Appendix 2). The questionnaire included data about who mainly takes care of the child, age, living status, number of children, number of children with haemophilia, educational level, occupation, family income, impact of haemophilia on

parent, impact of family economics due to haemophilia, if haemophilia restricted what the child could do, known haemophilia in the family, chronic illness in other family members and the responding parent, time spent on injecting clotting factor for the child and the parent, time spent on hospital visits, chronic pain in the child and absence from work and school due to haemophilia. Some of the data from the sociodemographic questionnaire is not included in Paper IV since the data is planned to be presented elsewhere.

Clinical data was collected from the National Haemophilia Register by haemophilia nurses at each HTC (Appendix 3). Clinical data included type and severity of haemophilia, history of inhibitors, bleeding history, treatment, hospital visits and body mass index (BMI). If the parent had two or more children affected by haemophilia, clinical data was collected on the youngest of these.

6.4 Data analysis

6.4.1 Study I and II

Based on Ricoeur (110) philosophy, Lindseth and Norberg (102) have developed a phenomenological hermeneutic analytical method which means that the text is analysed in three steps (naïve reading, structural analysis and comprehensive interpretation). A constant movement between description and interpretation of the phenomena continues throughout the analysis process in both Study I and II. The thoughts and feelings that the interviews elicited were written down as soon as possible after the interviews, and summarized and saved for inclusion in the naïve reading of the transcribed text from the interviews (102).

The analytical process started with the naïve reading, which aimed to grasp the overall meaning of the haemophilia experiences captured in the spoken word (102). The naïve reading was formulated in phenomenological 'language' so that it could be recognised against the emerging units of meaning. During the reading, openness to the text and its meaning is necessary to be able to capture the phenomenon (102). When the phenomenon was captured, the analysis moved forward into the second phase: structural analysis. The text was divided into units of meaning that were condensed with the aim of preserving the essence, and then divided into sub-themes and main themes. A unit of meaning could be a paragraph, a sentence or a part of a sentence. The analysis alternated between

methodical reading and re-reading the text as a whole to ensure that the sub-themes and main themes that emerged mirrored the naïve understanding of the text (102).

Lindseth and Nordberg explain that the structural analysis can be performed in several ways. In Study I, main characters, arenas and timelines were identified during the first structural reading (102). This first step of structural reading was integrated in the structural analysis in Study II.

The third phase, the comprehensive understanding, aimed to achieve a deeper understanding of the phenomenon, the carriership and haemophilia experience. The text was critically read while the themes that emerged, the naïve reading, previous research, related literature and preunderstanding were included in the analytical process. In other words, the analysis entered the hermeneutical spiral which includes a movement between closeness and distance. The hermeneutic spiral is an ongoing bidirectional process between naïve reading and structural analysis to capture the comprehensive understanding of the phenomena, experiences of being a carrier and experiences of being a parent of a child with haemophilia. The hermeneutic spiral led to a new, deeper insight and a more profound understanding of the parental experiences (102). Quotes from the interviews were integrated into the presentation of results, with the intention of illustrating and validating the meanings of the results in the studies (106).

To achieve high trustworthiness according to Lindseth and Norberg (102), all authors (of Paper I and II) were involved in the data analysis and discussion of the emerging findings continued in Studies I-II. Furthermore, trustworthiness of the findings was ensured by familiarity with the research topic and time spent listening to the parents' experiences.

In study II, NVIVO 10 software for computer-assisted qualitative data analysis was used to manage the data.

6.4.2 Study III

The constant comparative method is a process in which the data collection and the analysis process is carried out simultaneously (103, 104). Throughout the study, memos were consistently written directly after each interview. In this way, early impressions, feelings and assumptions were preserved and at the authors' disposal throughout the analysis process.

The complexity of the longitudinal design and the extent of interviews required a systematic analysis process in order to capture emerging processes within each case (family/parent). A narrative report was written after each interview to summarise the processes and illness management at that time and to keep track of the parents' individual phases in the learning process (111).

At the end of the study, a narrative report was also written for each parent and for each family as a whole to summarise the learning process and illness management over time. Open coding of the interviews was achieved by examining the text data to identify illness management and learning processes as closely as possible to the moment of the interview. Memos, narrative reports and data from the interviews were constantly compared by the authors (of Paper III) within and across cases to identify themes and concepts. The emerging themes were analysed, discussed and reversed to reach a more abstract level of exploring processes and management among the parents. Patterns and themes within and across cases were explored and categories developed as the study progressed. The analytical process continued by merging categories together into theoretical categories, which allowed data to be reduced and condensed. In the final step, the essential findings were summarized in the core category and depicted in a conceptual model (103, 112).

6.4.3 Study IV

The data was analysed using SPSS statistics software (Version 24.0; SPSS Chicago, Illinois). Descriptive data of sociodemographic characteristics are shown as frequency distribution and in numbers. According to their distribution, data are presented in absolute numbers, percentages, mean ± standard deviation and range (minimum-maximum). To assess the impact of sociodemographic aspects and the child's clinical condition on perceived parental burden, linear regression analyses were undertaken. The assumptions of linearity of residuals, independence of observations, and absence of multicollinearity were met by assessing Durbin-Watson statistics, variance inflation factor and normal probability plots. Tests were two-sided and $p<0.05$ considered statistically significant. The Swedish HEMOCAB™ showed high internal consistency in the study, with a Cronbach's alpha coefficient of 0.966 (total score).

7 ETHICAL CONSIDERATIONS

This thesis contains three qualitative studies and one quantitative. All the studies were non-interventional and non-drug related. The four studies followed the World Medical Association's Helsinki Declaration (113) guidelines and principles. The guidelines ensure that research involving humans follows basic ethical principles, emphasizing that research must be done with respect for the individual and their autonomy. The research should aim to be of benefit and the researcher must minimise the risk of harm. Moreover, the research must follow the principle of justice, with all participation being voluntary and allowing the person to withdraw their participation at any time without having to specify the reason.

The studies were approved by the Regional Ethical Review Board (Gothenburg, Sweden) with the following identification numbers: Study I: 667- 09 Study II: 120-13; Study III: 517-14; Study IV: 827-16.

Written information for the different studies emphasized the voluntary aspect of participation and the right to withdraw at any time, without any impact on the child's haemophilia care. In Studies I-III, both verbal and written information were given to all participants before inclusion; in Study IV only written information was given (114). Participants signed informed consent before inclusion according to applicable regulatory requirements and Good Clinical Practice (GCP). The confidentiality requirement was adhered to for all four studies. No names or places were used in the transcriptions of the data in Studies I-III; instead they were replaced with a unique study number. In Study IV the participants' names were replaced by a number before the data was entered in the SPSS file.

Studies I-IV did not involve any physical risks, but the data collection could elicit questions and emotions among the participants that they had not previously reflected upon. During or after the data collection, they could be reminded of unpleasant situations or emotions. The author was alert to possible reactions from the participants during all the interviews. In Studies I-II the participants were offered free contact with a psychotherapist (BSc Social Work) working at Sahlgrenska University Hospital, if they needed to discuss feelings that might have arisen during or after the interview. The written information included details about the psychotherapist and how to contact her if they felt psychological discomfort. None of the participants asked for psychotherapist counselling so the offer of contact with a

psychotherapist was not included in the written information for Studies III and IV.

Participants in Study III were parents of children treated at the HTC at Sahlgrenska University Hospital, Gothenburg, Sweden. In order to separate my professional and researcher role, I have tried as far as possible not to be involved in the children's treatment. Unfortunately, this has not always been possible and sometimes I have been the only haemophilia nurse on duty and I have then had to treat the child and his family as a haemophilia nurse. Two of the families lived some distance from the HTC and their prophylactic treatment with factor concentrate took place at their local hospital. Colleagues have mainly had responsibility for all the children whose parents was included in Study III.

In Study IV, informed consent was obtained from both parents and children aged 15 years or older. If the parent had sole custody, the informed consent was only obtained from that parent. In Study IV, participants were given a cinema gift card, worth 12 EUR. The study information and informed consent form for the 21 parents included in the BBC study was different to that for the other participants in Study IV. Thus the questionnaire, sociodemographic data and medical data of the child reported in Study IV (for this, 21 parents) was duplicated and likewise included in the international BBC study.

The results from all four studies were presented with complete confidentiality to guarantee that no parent or child could be identified.

8 RESULTS

The main findings from Study I-III are summarized and presented together. The main results from Study IV are presented separately, followed by a summary of all four studies.

8.1 Studies I-III

The findings in Study I revealed that the mothers needed to simultaneously reconcile with both the illness and their own carriership. In this study, the mothers who were obligated carriers had not fully realized this until the child's diagnosis. Likewise, most of the mothers with a family history of haemophilia had not understood that they were at risk of bearing the gene. Suddenly, the mothers had to face both their carriership and sorrow over the child's illness. The knowledge that they had transmitted a serious illness to the child created guilt and existential questions among them (Study I).

The results from Studies I-III revealed that becoming a parent of a child affected with severe or moderate haemophilia was life changing. After the child's diagnosis, the parents' life-world fell apart and they experienced a chaotic and almost unmanageable situation. The parents described the situation as initially involving great fear, worries and distress. It was a new life situation they had never experienced before, and they entered an existential chaos. The parents were overwhelmed with uncertainties and unknowns about what the illness meant for them, the child and the family as a whole (Study I-III).

The fathers described existential ponderings as to what kind of fathers they would now become. They had dreamed of a 'regular' fatherhood, in which sport and other physical activities were seen as the major foundation of growing a strong father-son bond. They were afraid of losing the opportunity of having this imagined closeness with the child, describing it as the greatest sorrow of being a father of a child with haemophilia. To manage the situation some fathers escaped into practicalities, for example, work. Afterwards, this escape generated guilt for abandoning the child's mother (Study II).

The parents faced a complex social situation in which they were forced to learn and manage the child's illness in daily life. They emphasized that they lacked the resources and ability to manage the complex treatment of the

illness and felt overwhelmed by the situation. They described feelings of powerlessness and helplessness (Study III). The parents had no choice: they were forced into a learning process and incentives for learning were characterized by a longing to reach independence and regain control of their life situation. The emerging key incentive for learning was a desire to become independent of HCP in the daily care of the child, another trigger being the ability to influence the child's health. At the beginning of the learning process the parents were in an existential chaos and needed a great amount of support from HCP. The learning process involved an interaction between the parents and HCP, with a complex relationship between the process, context, and conditions varying over time (Study III). The parents moved from a state of sad, existential chaos to reconciliation with their new situation. How this process developed and how long it took was dependent on different factors, but a sense of being fully informed and supported by the HTC emerged as essential to its realization (Studies I-III).

The parents gradually shifted focus from existential thoughts to practical issues to manage the child's illness and treatment (Study III). Feelings of competence and independence was strongly associated with the conquest of knowledge (Studies I and III). When home treatment functioned without the involvement of HCP, the parents described a sense of feeling empowered, secure, competent and in control of their life situation (Study I-III).

The process of learning required the parents to go to great effort, and they emphasised the important role that the haemophilia team had in supporting that learning (Studies I and III). Support from their partners was also very important in reconciling with the child's illness and coping with their new life situation (Studies I-III).

The parents underlined that the experience of haemophilia was a resource that no-one could take away from them. Personal growth, new values and new perspectives on life were described as a result of the process of becoming a parent of a child with severe or moderate haemophilia (Studies I-III).

8.2 Study IV

A total of 142 families comprising 166 children <18 years with severe or moderate hemophilia was identified by nurses at the three HTC in Sweden. Non-responders and excluded families (Karolinska University Hospital n=28,

Sahlgrenska University Hospital n=3, Skåne University Hospital n=9) are outlined in Table 2.

Most responders were mothers and the mean age of the parents was 40.6 years. The parents included in Study IV had a total of 121 children with haemophilia. If the parent had more than one child with haemophilia, medical data was obtained for the youngest child.

Table 2. Characteristics of children of participant parents and non-responders/excluded parents.

	Characteristics of children of participant parents n = 102	Characteristics of children of non-responders and excluded parents n = 40
Age (mean, range)	9.4 (1–17)	10.7 (1–17)
Haemophilia A	83.3% (85)	90% (36)
Haemophilia B	16.7% (17)	10% (4)
Severe form	79.4% (81)	70% (28)

Parents reported the highest burden related to their children's illness in the dimensions 'Emotional stress' (32.6 ± 17.8), 'Perception of child' (31.5 ± 19.0), 'Medical management' (30.5 ± 19.8) and 'Impact on you' (27.1 ± 23.7) on the HEMOCAB™ scale. The majority of parents (68.6%) reported that haemophilia had an impact on their life in general and 22.5% stated that haemophilia impacted on the family's economic situation. Sixty percent (59.8%) reported that the haemophilia illness restricted what the child could do.

Parents of children with past or present inhibitors showed a significantly higher total score on the HEMOCAB™ than parents of children without a history of inhibitors (p<0.010). Parents of older children had a lower perceived burden than parents of younger children (p<0.015). If the parents mainly injected the clotting factor, the perceived burden was higher than if the child was mainly injected by HCP (p<0.008). Furthermore, a significantly

increased perceived parental burden was reported by parents of children with overweight/obesity (p<0.014).

No significant differences in parental perceived burden were observed for type of haemophilia, if the child had bleeding in the past 12 months, if the child mainly self-infused, had another family member (e.g. father, cousin, brother) with haemophilia or if the parent had more children below 18 years living in the household.

8.3 Summary

Parents of young, newly diagnosed children perceived a high parental burden and the illness affected all parts of family life. The results revealed that parents were vulnerable and in an existential chaos that required a great deal of support from the HTC in the first years after the child's diagnosis. If the child developed inhibitors, the pressure on the parents increased even more and they experienced an almost unmanageable family situation. The findings from the studies emphasized the importance of learning and being able to manage the child's illness in daily life. Both fathers and mothers described that they started to feel competent and independent again only after becoming able to handle the child's illness without the involvement of HCP.

9 DISCUSSION

The main findings of the thesis emphasize the parents' lived experiences, perceived burden and learning process as a parent of a child with severe or moderate haemophilia. The parents participating in the studies describe this as a complex and demanding journey. The pathway to independent home treatment was filled with sorrow, worries, reconciliation, learning, challenges, new perspectives on life, personal growth and happiness. The perceived parental burden was significantly increased if the child developed inhibitors, particularly for parents of young children.

Since haemophilia is an X-linked disease, there are some aspects of parenting that are unique to the mother. She is not only the mother of a child with a chronic illness, but has also transmitted the illness through her genes. Mothers carrying the haemophilia gene expressed guilt about transmitting the illness to the child. This is in line with other studies of mothers in families affected with X-linked disorders (115, 116). In Study I, the mothers described blaming themselves for not realizing that they were carriers of haemophilia before the child was diagnosed. This result was surprising, because the women had been informed of their gene mutation carriership by the health care service. This is a reminder that learning means something more than simply receiving information (100). In genuine learning, a person incorporates the knowledge into her life-world and makes it part of her (97, 100). Lack of knowledge about the inheritance of haemophilia needs to be addressed by the HTC. One conclusion of Study I was that carriers may benefit from a counselling meeting at the HTC before they consider starting a family. A genetic counselling meeting is different from giving information about the inheritance of the disease. In a genetic counselling meeting, the HCP actively involve the counselees and help them make informed choices (117, 118). In a counselling meeting, advice is not given – the HCP is an active listener and the feelings of the counselees are explored (119). The counselling can help the woman understand her carriership more, as well as her feelings, needs and thoughts, thus giving her a sense of control and later, the opportunity to influence the impact of haemophilia on her life, for example, by choosing whether or not to have prenatal diagnosis. Harrington et alt. (59) argues that one key point of the haemophilia nurse role is genetic counselling. Counselling meetings with carrier women could be beneficially facilitated by the haemophilia nurse, with support from the rest of the haemophilia treatment team. Research on other inherited diseases shows that persons who have received genetic

counselling from nurses have reported positive experiences and were satisfied with the genetic counselling (120). Studies of mothers in families with other x-linked diseases show that feelings of guilt for the child's illness are associated with higher risk of depression and feelings of helplessness (115, 121). Clearly then, a counselling meeting could help potentially reduce feelings of guilt by increasing understanding of the genetic condition among carriers. Moreover, during counselling, the carriers can process feelings and reflect on what carriership means for them, thereby minimizing potential psychological harm in the future. Study I only includes mothers who were carriers of haemophilia (DNA tested). The feeling of guilt might not be an issue for mothers of children with new mutations.

Regarding gender role division of labour, the parents' description of family life in Study III was different to that of the parents in Studies I and II. For example, in Study III, fathers and mothers equally administered injections with clotting factor. Although gender role division of labour in the family has become more equal in recent decades, research reports that mothers usually remain the primary caregivers of young children (122, 123). The mothers are more likely to have reduced working hours (124), be more involved in the child's health care (125) and spend more overall time with the child than fathers (124). Different gender roles between parents may be one explanation for why mainly mothers participated in Study IV. During the period of time that the participants (in Studies I-IV) were parents of minors, gender role divisions had become more equal (126-128). The data in Study I was collected in 2010 from participating mothers with a wide range of ages. The data in Study II was collected between 2013 and 2014 from participating fathers with children who had a mean age of 11.9 years, whereas in Study III, the participants' children were aged between 10-31 months. The differences between the fathers' and mothers' experiences of gender roles should be interpreted with this in mind, especially since the experiences of some of the participants in Study I were from decades previous to the 2000s.

The transition to parenthood is a challenging and demanding phase that involves major changes in life for all parents (129). Becoming a parent of a child with a serious chronic illness obviously places an extra strain on the transition; earlier dreams and ideas about parenthood are shattered and new ones must be created. The parents entered the learning process with their previous experiences, knowledge, values, attitudes, emotions and beliefs about health and the haemophilia illness (98, 100). At the time of the child's diagnosis, the parents' life-world was shattered, and they described a fragmented world filled with overwhelming demands. From a theoretical

learning perspective, this is described by Jarvis (100) as the disjuncture which is the catapult into the learning process. The parents struggled to accept the child's diagnosis and the new complex family life, at the same time being forced to learn. The results revealed that the parents may benefit from increased psychological support to cope with this. By listening to the parents' narratives and by embracing the relationship between the parent and the HCP, the parents' acceptance of the child's illness could accelerate, and this acceptance may propel the learning process. The parent's narrative could be the starting point for a partnership between the parent and the HCP (130). Within the partnership the HCP should encourage and empower the parents to actively find their ability to manage the new complex situation that the child's illness has created.

Parents reported no lack of medical information given by the HTC, and it was relatively easy for the parents to retrieve information from the internet. In the first phase of the learning process it was more important for the parents to be recognized and listened to than to receive lots of information. As mentioned above, being acknowledged as a person was important to move the learning process forward, and this is in line with a life-world approach to the learning human (92, 98, 100, 101, 110) and an essential part of person-centred care (PCC) (130). The PCC recognizes that a person has will and capability and that her/his actions are a result of her/his experiences, thoughts, values and perceptions. PCC assumes that the person is a narrative being that understands the world through her/his own life-world, in relationship with significant others (131, 132). PCC emphasizes the person needs to be heard and recognized as a whole person with a unique narrative (including needs as well as resources) in the meeting with HCP (experiences and evidence-based knowledge) (130, 133).

Jarvis (101) explains that learning occurs in an integration of two different processes. The external interaction process is between the learning person and the social, cultural and material context around it. The internal learning process is within the learning person and is a psychological process of acquisition and elaboration. The two processes in learning continuously intertwine with each other (101). Because of this intertwined process, the parents' learning may be inhibited if they are occupied by sorrow for the child's illness. By recognizing and listening to the parent narrative in the early phase of the learning process, the parent's reconciliation with the new situation can be promoted. As a consequence, the parents' internal learning process need to be attended and then be supported.

The parents commented that information that was not immediately recognizable in their unique family context did not appear to be relevant. In order to become familiar with the parents' narrative and recognize what is relevant to them as a family there must be continuity of care. The parents need to be able to form lasting relationships with HCP, both in the HTC and at the local hospital. The importance of continuity of care for children with chronic illness has been emphasised in research as one key element in good health care provision (134-136). When a relationship has begun to develop, HCP could actively involve parents in shared decisions and thus promote learning. Likewise, it is important that enough time is allocated during visits to the HTC to promote the trajectory towards independent home treatment.

Being able to independently manage home treatment was essential for the parents to feel in control of their life-world again. This turning point was strongly associated with the conquest of knowledge and skills, especially the need to acquire skills to handle the injection technique. HCP were important actors in the parents' learning process towards independent home treatment of the child. The European curriculum for haemophilia nurses (59) addresses the specific and important educational role of the haemophilia nurse. In the three qualitative studies of this thesis, the parents emphasize the importance of the haemophilia nurse in their learning process and see them as an important rescuer, guide and standby for the parents in the different learning phases. When the parents are in the first phase, the HCP need to act as a rescuer in a frightening new life-world. By listening to the parents, HCP can create relationships and provide psychological support, thus promoting acceptance of the child's illness, and the parents can move on to the next phase in the process.

When learning the hands-on practical management of the child's haemophilia, the HCP need to act as a guide. In this phase of the learning process, the parents could only focus on one task at a time. By acting as a hands-on step-by-step guide, the HCP could enhance the parents' learning. The parents request realistic, reasonable, practical and short-term goals. In this phase, a practical learning plan could propel the learning process forward. In the last phase HCP could more actively involve the parents in decisions, thus promoting the emerging independence. With the HCP as a standby in the background, the parents can start independent home treatment with the knowledge that they can receive help if a difficult situation arises.

By listening to how the parents want to learn home treatment and illness management, the nurse can facilitate the parents' learning and problem

solving. When the parents and the nurse have identified the parents' resources, abilities and difficulties in achieving independent home treatment, they can create and document a learning plan together to reach independent home treatment.

In Study II, the fathers experienced the loss of an envisaged fatherhood consisting of physical and sports activities. One conclusion of this finding is that HCP need to listen more to the father's possible thoughts and concerns regarding the child's future physical activity. Moreover, the results from Study IV revealed that 60% of parents restricted what the child could do, mainly in regard to physical activity and sports activities. Schoenmaker et al (32) reported that children with haemophilia perceived a higher impact of the illness when they were restricted from participation in sport. The results (Study II and IV) indicate that HCP need to more actively address the positive aspects of physical activity as soon as the child is diagnosed and starts prophylactic treatment. The benefits of physical activity in childhood is well known (137, 138). Children with haemophilia specifically benefit from physical activity since it has been shown to reduce the incidence of bleeds, joint problems and improve the child's quality of life (37, 139-142). However, the importance of physical activity for children with haemophilia must be weighed against the risks, especially the risk of joint bleeding (143). Haemophilia does not contraindicate with physical activity and sports participation, if the child has good prophylactic treatment (34). However, the timing of prophylactic treatment needs to be adjusted and adapted to when the child is most physically active in order to achieve high clotting factor levels while they are participating in sport (34, 144). The results from the studies (II and IV) suggest that HCP could involve the parents (and later the child) in decisions about options for safe physical activity and sports participation. HCP could encourage the parents to support the child's physical activity and thereby promote the health of the child.

Study IV revealed that 89% of children in Sweden with severe or moderate haemophilia had home treatment and the parents reported rather low impact on parental burden in several domains of the HEMOCAB™ questionnaire. The high percentage of children on home treatment may probably contribute to this low parental burden. Contradictory to this, however, parents who performed the injection actually reported a higher burden than parents for whom HCP was performing the injections. One explanation could be that most children who were not treated at home were affected with moderate haemophilia. There is a correlation between factor level and bleeding tendency. A person with moderate haemophilia has factor levels between 1-5 IU dL^{-1} (22). Collected medical data in Study IV

did not include factor levels, only type and severity of haemophilia. The parental burden may differ if the child has 1 or 5 IU dL^{-1} factor level. Another explanation for this contradictory result is that the burden might be higher for parents of children who need home treatment than for parents of children who do not. As several decades of evidence shows, prophylactic home treatment is superior to on-demand treatment (145-148), and the parents of children who require home treatment have no real alternative than to learn and perform it.

When a child is diagnosed with haemophilia, it affects the whole family. Living in a family with a seriously chronically ill child creates emotional demands on both parents and siblings (79, 80). The family context in which the child-parent relationship exists changes profoundly and a new family dynamic is necessary (81, 149). Parents in Studies I-III described feeling that siblings were often overlooked as the affected child required all their available time and energy. They were aware of the situation but described themselves as being too exhausted to change it. Learning to manage haemophilia required a great deal of emotion, energy and concentration of the parents. It is well known that siblings of seriously ill children are at risk of declining psychosocial health (150). Despite feeling tired and exhausted, the parents actively tried to find time and energy for siblings as the learning process progressed. Nevertheless, this was a great challenge and the parents expressed guilt for neglecting siblings around treatment start. HCP can remind the parents that as the learning process proceeds, there will be more time for siblings again.

In Study IV the parents reported that 17% of the children had chronic pain. This result was unexpected as the annual bleeding rate (ABR) in the population was low. Similar findings about pain were reported in two other studies of children affected by severe haemophilia (151, 152). Research has shown that HCP often underestimate chronic pain among persons with haemophilia. Moreover, HCP lack sufficient knowledge and understanding of pain management in children with haemophilia (151). The results from Study IV suggest that HCP at HTC need further education in pain management for children with haemophilia.

This thesis has largely focused on the parents' learning. The results underpin the learning process that was required by the parents to manage their children's haemophilia in daily life. In a learning process, the outcome is a changed person. The person reflects on the world in new ways, with new values and thoughts (100). The parents described the haemophilia experience as having enriched their lives, this in line with Robinson's (153)

study on parents of chronically ill children. The haemophilia experiences made the parents understand what was important in life and this insight resulted in personal maturity. They also described a greater empathy and understanding of others in distress than they did before experiencing haemophilia.

10 METHODOLOGICAL CONSIDERATIONS

The researcher needs to be guided by preunderstanding and previous research of the phenomenon studied, have a scientific approach and be able to be surprised (107). It is essential to have awareness of one's own preunderstanding and experiences of the field studied. Using one's preunderstanding while being aware and restraining it at the same time is a balancing act (107). For example, when formulating research questions and designing the studies, it was beneficial to have clinical experience of haemophilia care and treatment. Professional experience from working as a haemophilia nurse for several years contributed to a greater preunderstanding of the field studied and was of value when data was collected and analysed. On the other hand, knowledge and preunderstanding of the field can limit one's ability to find new perspectives and reduce curiosity (102, 112). To prevent this limitation, all authors (of the four papers) contributed to the study design and data analysis, and pilot interviews were conducted (106, 108). The preunderstanding of the context varied among the authors and this contributed to restraining preunderstanding and to maintaining openness (102).

Haemophilia is a rare illness and the population of children in Sweden with the disorder is relatively small (1, 154, 155). The decision to exclude mild haemophilia in the thesis further narrowed the studied population. However, this exclusion was judged necessary, as parents of children with mild haemophilia face different challenges to a greater extent than parents of children with severe and moderate forms of the disease. Children with mild haemophilia rarely have prophylactic treatment and spontaneous bleedings are unusual (156). Another major difference is that persons with mild haemophilia A can treat minor bleedings with a desmopressin intranasal spray (22, 24).

The parents in Study I and II were partly recruited from the HTC where I work as a haemophilia nurse. However, the parents came from all three HTC in Sweden and I had never met most of the included parents before the interview situation. In Study III, the parents came from the HTC where I work, and my intention was to refrain from participating in the direct care of these families. As the study was ongoing for two years, I met some of them (Study III) on a few visits, when no other haemophilia nurse was available. On these occasions, I tried to clearly distinguish between the two roles in the meetings. This may have had some impact on the degree to which the parents felt free to describe their feelings and opinions about the

haemophilia care, HTC and HCP. It might have been easier for them to freely talk about negative aspects, feelings and criticise the haemophilia care if the interviewer was not a member of the HCP team at the HTC.

A qualitative research method was used to describe and understand the lived experiences and experiences of learning processes and illness management in parents of children with severe or moderate haemophilia. The data collected in qualitative research does not aim to achieve statistic validity through large sample size, instead it aims to capture data that is rich and relevant to the topic studied (106). Including parents who had a wide variety of experiences of the phenomenon studied strengthened trustworthiness in Studies I-III (103, 112). The number of participants in Studies I-III was not decided in advance, instead the richness and variation of the collected data determined when inclusion stopped (103, 107). Data saturation in qualitative research can be understood as "when collected data stops giving new information" (157). Saturation in qualitative research is complex – how do we know when to stop collecting data? In the qualitative studies of this thesis, data collection stopped when enough deep and rich data was found to be able to answer the research questions. Moreover, no new information was obtained in the last interviews of Study I and II.

The intention of Study IV was to include one parent from every family in Sweden with children aged <18 years, affected with severe or moderate haemophilia. The response rate in the study was high (80%) and there were no major differences in responding parents and excluded and non-responding parents regarding the children's age, type and form of haemophilia. A limitation was that it was mainly mothers who participated in Study IV. Internal validity was secured by both the high response rate and the non-responder analysis. External validity was increased by the multi-centre design of Study IV and the results can likely be generalizable to other settings in high-income countries. Statistical conclusion validity was partly threatened by the small size of samples in Study IV. Differences between some groups could not be analysed due to the small size (parents of children with present inhibitors, treated with EHL, severe haemophilia B, ITI treatment and the child's sex).

Families with same-gender parents and multi-generational caregivers are missing among the participants in Studies I-III. In Study III, no family structure other than nuclear two-parent families were included, whereas in Study I and II, voices from both two-parent and single-parent families were heard. The included mothers in Study I had a wide range of ages (28-83

years). Haemophilia care has greatly developed in recent decades, meaning that the care of children with haemophilia has drastically improved (4, 9). It is likely that this fact has affected the mothers' experiences of the illness. The results may have differed if only mothers of children under the age of 18 were included. However, the focus of the study was the unique experience of being a carrier of haemophilia and this experience remains throughout different stages of life. In contrast to Study I, only fathers with children under 18 years of age were included in Study II.

The interview method used in Studies I-III was based on open-ended questions, allowing the parents to freely talk about their experiences (108). A benefit for the participants was that they actively had the opportunity to share their experiences and thoughts during the interviews (158). In some cases, the interviews created strong feelings, were emotionally intense and some of the topics were painful to talk about for the parents. However, participating in qualitative research is an active and reflexive practice. A possible advantage of this is that participants have the opportunity to reflect on themselves, their experiences and their lives (159). Parents in Study III stated that the repeat interviews were rewarding in this sense as it allowed them to reflect on the experience of having a child affected by haemophilia. Several parents said they wished that the study period would continue for longer than the 12 months.

In Study III, one family had limited knowledge of Swedish at study start. The use of an interpreter had a limiting effect on the interviews, although several measures were taken to reduce its impact (160). All seven interviews were conducted with the help of authorized interpreters. Two additional interviews were conducted to compensate for the time taken to translate, and the interviewer used shorter sentences and longer pauses and was sensitive to body language (161). Trustworthiness would have been improved if the audio recording of the interviews conducted with an interpreter had been listened to by another interpreter to confirm the quality of the translation. However, in the last three interviews, the parents spoke more and more Swedish despite the presence of the interpreter. Swedish qualitative studies with data from non-Swedish speakers are rare. Despite the limitations of using an interpreter, I perceive the benefits of capturing experiences from these parents to far outweigh the limitations.

In Study IV, the translating process of the sociodemographic questionnaire was less extensive than the translation of HEMOCAB™, where the principles (109) of good practice for the translation and cultural adaptation process for Patient-Reported Outcomes was used. The cultural adaptation of the

HEMOCAB™ questionnaire was time-consuming and views on the cultural adaptation differed between the developer and the project management group of the translation. However, the final Swedish version of HEMOCAB™ was judged to have sufficient cultural adaption and was achieved by following Wild et al.'s (2005) structured steps for translating.

The questionnaire for collecting medical data (Study IV) was not translated into Swedish (Appendix 3). Nurses at each of the three HTC in Sweden collected the medical data, having been judged to have sufficient knowledge of English. To achieve high reliability, haemophilia nurses (with several years' experience of haemophilia care) collected the medical data. It would have been preferable to abbreviate the medical data and sociodemographic questionnaires (Study IV) as they were rather extensive. Nevertheless, for practical reasons, they needed to be exactly the same questionnaires as in the international BBC study. Part of the collected medical and sociodemographic data in Study IV is planned to be presented elsewhere.

In Studies I, II and III, trustworthiness was strengthened by the rich and extensive variety of experiences that emerged from the collected data. In these same studies, credibility (162) was strengthened through the length of the open-ended interviews (106). Moreover, the fathers and mothers were interviewed individually (Studies I and II), to be able to capture the specific and unique experiences of both fathers and mothers. In Study III, the longitudinal design ensured credibility of the findings and created a unique opportunity to follow the parents during the year after treatment start. The parents were not required to remember previous experiences, instead they described their current life situation. The grounded theory approach allowed follow-up of areas emerging from previous interviews (103, 112). The repeated interviews and the parallel process of data collection and analysis facilitated a deeper understanding of the learning process the parents underwent. Furthermore, by mixing individual and joint interviews, a potentially broader picture of the parents' learning processes emerged (163, 164).

The dependability of the three qualitative studies was improved by presenting each step in the analytical process and illustrating emerging themes by exemplifying quotations (165). By describing the research process and providing quotations from the interviews, the reader can follow the interpretation and understanding of the original data collected (166). However, there is always more than one way to comprehend a narrative text and the results can and should be seen as one possible interpretation

that contributes to a deeper understanding of the parents' experiences, learning processes and illness management.

Transferability of the four studies is limited by contextual factors. Firstly, prophylactic treatment is standard care in Sweden and starts at an early age, with high doses of clotting factor available to all children and adults affected by severe haemophilia. This is not the case in low-income countries. Secondly, the Swedish welfare system is extensive compared to most countries and parental leave is long and well-reimbursed. Thirdly, the role of the father varies in different cultural contexts and over time, which may influence the results. A potential limitation could be that the data reflects specific characteristics of parents in Sweden. To counteract this possible limitation, parent participants in Studies I-III were strategically chosen to achieve a variety of backgrounds. Finally, transferability was strengthened by inclusion of the non-Swedish speaking parents in Study III, which is seldom the case in qualitative studies. In contrast, Study IV was a total population study, which strengthens transferability, although non-Swedish speaking/reading parents were excluded.

11 CONCLUSIONS

This thesis provides a deeper and more profound understanding of parents of children with severe or moderate haemophilia in terms of their lived experiences, perceived burden and experiences of the demand for and process of learning and illness management. The results emphasize what HCP could do to improve the care of families affected by haemophilia. Furthermore, the findings suggest how HCP could act and relate to affected families during the first years after the child's diagnosis. Increased knowledge generated from this thesis could be used to further develop national and international guidelines for haemophilia care.

The findings suggest that:

- Female carriers need more knowledge and understanding about their carriership and would benefit from a genetic counselling meeting before considering starting a family.

- HCP should encourage the fathers to be actively involved in the daily care of the child's illness, support their struggle to feel capable, and reduce the mothers' burden, thus promoting the family health.

- By listening to the parents' narratives and by creating lasting relationships between the parent and the HCP (as a rescuer), the parent's acceptance of the child's illness could accelerate, and this acceptance may propel the learning process.

- Different phases in the learning process towards independent home treatment were identified. By supporting the parents in a person-centred way during these phases (as a rescuer, guide and standby), the HCP can promote the trajectory to independence. These phases could be used for screening to prepare, support, and empower parents as they learn to manage the child's haemophilia and make it a part of their family life.

- Independent home treatment was essential to manage the child's illness and to have a normalized daily family life and constituted the main incentive for learning. The parents and HCP (as a guide) should collaborate to create a learning plan that facilitates the learning process, with the aim of reaching independent home treatment.

- HCP should address and emphasize the positive aspects of physical activity during childhood as soon as the child is diagnosed and starts prophylactic treatment.

- More psychological support from the HCP needs to be directed towards parents of younger children and particularly the parents of young children with inhibitors, thus decreasing the parental burden.

- Parental burden may be reduced if the HTC more actively treat overweight and refer children to appropriate specialists.

- HCP need further education in pain management for children with haemophilia.

12 FUTURE RESEARCH

New knowledge and deeper understanding of a phenomenon usually creates more questions and the results from this thesis are no exception, as several questions are raised.

Firstly, there is a need to explore perceived burden and experiences of learning process and illness management in parents of children in low income countries since their conditions are likely to be different.

Secondly, the voices of parents of children with mild haemophilia have not been heard in this thesis nor of parents with children affected by other bleeding disorders.

Thirdly, the child's experience of taking over responsibility for his own treatment and illness would be another interesting topic to explore and of relevance for HCP.

Fourthly, the relatively high reported prevalence of pain among the children needs to be explained in further studies. Likewise, pain management in children with haemophilia needs to be addressed.

Fifthly, further research is needed to understand the sibling's experiences of living with haemophilia in the family.

Finally, the treatment of haemophilia is rapidly developing with extended half-life products, new medications, new ways of administering the medications and gene therapy. Further research is needed to explore the impact of this development, both for the child, the parent and the family as a whole.

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Appendix 1

Deltagar nummer: |__|__|__| **Initialer:** |__|__|

HEMOCAB™

FÖLJANDE FRÅGOR HANDLAR OM HUR OFTA DU PÅVERKAS AV DITT BARNS BLÖDARSJUKA

1. KÄNSLOMÄSSIG STRESS relaterat till barnets blödarsjuka

Under de senaste 12 månaderna, hur ofta har du upplevt följande?	Aldrig	Sällan	Ibland	Ofta	Hela tiden
1. Jag känner mig uppgiven eftersom jag inte kan göra något p.g.a. mitt barns tillstånd.	☐	☐	☐	☐	☐
2. Jag känner mig förtvivlad p.g.a. mitt barns blödarsjuka.	☐	☐	☐	☐	☐
3. Mina känslor är i kaos p.g.a. mitt barns tillstånd.	☐	☐	☐	☐	☐
4. Jag är rädd att mitt barn ska dö p.g.a. sin blödarsjuka.	☐	☐	☐	☐	☐
5. Jag blir ledsen när jag ser på mitt barn.	☐	☐	☐	☐	☐
6. Jag är rädd att mitt barns hälsotillstånd kan förvärras.	☐	☐	☐	☐	☐
7. Jag är rädd att mitt barn kan skadas i en olycka och att jag inte kan hjälpa honom/henne.	☐	☐	☐	☐	☐
8. Jag gråter mycket p.g.a. mitt barns situation.	☐	☐	☐	☐	☐
9. Jag blir ledsen när jag ser mitt barn med blåmärken och/eller ledskador.	☐	☐	☐	☐	☐
10 Jag undrar om mitt barns tillstånd kommer att bli bättre i framtiden.	☐	☐	☐	☐	☐

Deltagar nummer: |__|__|__| **Initialer:** |__|__|

2. Dessa frågor handlar om EKONOMISK BELASTNING relaterat till barnets blödarsjuka

Under de senaste 12 månaderna, hur ofta har du upplevt följande?	Aldrig	Sällan	Ibland	Ofta	Hela tiden
1. Kostnaden för att behandla barnets blödarsjuka påverkar vårt familjeliv.	☐	☐	☐	☐	☐
2. Jag är orolig över alla extra kostnader kopplade till behandlingen av mitt barn (förutom läkemedelskostnader).	☐	☐	☐	☐	☐
3. Min familj har inte tillräckligt med pengar p.g.a. mitt barns blödarsjuka.	☐	☐	☐	☐	☐
4. Mitt barns blödarsjuka orsakar ekonomiska problem.	☐	☐	☐	☐	☐

3. Följande frågor handlar om dina PERSONLIGA UPPOFFRINGAR OCH BEGRÄNSNINGAR p.g.a. barnets blödarsjuka

Under de senaste 12 månaderna, hur ofta har du upplevt följande?	Aldrig	Sällan	Ibland	Ofta	Hela tiden
1. Jag får ingen paus eller vila p.g.a. mitt barns blödarsjuka.	☐	☐	☐	☐	☐
2. Min hälsa har påverkats av mitt barns tillstånd.	☐	☐	☐	☐	☐
3. Jag har ingen tid för mig själv p.g.a. mitt barns blödarsjuka.	☐	☐	☐	☐	☐

Vänligen besvara följande frågor endast om du tidigare har arbetat. Ifall du aldrig tidigare har arbetat sätt ett kryss i rutan och fortsätt av <u>avsnitt 5!</u>

Jag har aldrig tidigare arbetat ❑

Deltagar nummer: |__|__|__| **Initialer:** |__|__|

4. Följande frågor handlar om samband mellan ditt ARBETE och barnets blödarsjuka

Under de senaste 12 månaderna, hur ofta har du upplevt följande?	Aldrig	Sällan	Ibland	Ofta	Alltid
1. Jag hade problem på arbetet p.g.a. mitt barns blödarsjuka.	☐	☐	☐	☐	☐
2. Jag har blivit särbehandlad på mitt arbete för att jag har haft frånvaro p.g.a. mitt barns tillstånd.	☐	☐	☐	☐	☐
3. Jag har varit tvungen att vara hemma från arbetet/skolan ifall något skulle hända med mitt barn.	☐	☐	☐	☐	☐
4. Jag fick säga upp mig för att jag behövde vara mer flexibel för mitt barn.	☐	☐	☐	☐	☐

5. Dessa frågor handlar om DIN REALTION MED ANDRA relaterat till barnets blödarsjuka

Under de senaste 12 månaderna, hur ofta har du upplevt följande?	Aldrig	Sällan	Ibland	Ofta	Hela tiden
1. Mitt barns blödarsjuka har negativt påverkat vårt familjeliv.	☐	☐	☐	☐	☐
2. Andra familjemedlemmar är avundsjuka eftersom de tycker jag tillbringar för mycket tid med att ta hand om mitt barn med blödarsjuka.	☐	☐	☐	☐	☐
3. Mitt barns blödarsjuka har påverkat mina sociala kontakter negativt.	☐	☐	☐	☐	☐

Vänligen besvara följande frågor endast om du har fler barn. Ifall du inte har det sätt ett kryss i rutan och fortsätt av <u>avsnitt 7</u>!

Jag har inga fler barn ❑

Deltagar nummer: |__|__|__| **Initialer:** |__|__|

6. Dessa frågor handlar om RELATIONEN MELLAN DINA BARN

Under de senaste 12 månaderna, hur ofta har du upplevt följande?	Aldrig	Sällan	Ibland	Ofta	Alltid
1. Mina andra barn känner sig skyldiga för att dom kan göra saker som deras blödarsjuka syskon inte kan.	☐	☐	☐	☐	☐
2. Jag kan inte ge uppmärksamhet till syskonen p.g.a. den tid det tar att ta hand om mitt barn med blödarsjuka.	☐	☐	☐	☐	☐

Vänligen besvara följande frågor endast om ditt barn går i skolan. Ifall ditt barn inte går i skolan, sätt ett kryss i rutan och fortsätt till <u>avsnitt 9!</u>

Mitt barn går inte i skolan ❑

7. Dessa frågor är om barnets SKOLA

Under de senaste 12 månaderna, hur ofta har du upplevt följande?	Aldrig	Sällan	Ibland	Ofta	Alltid
1. Jag är oroad för att skolan inte tar tillräckligt hänsyn till mitt barns tillstånd.	☐	☐	☐	☐	☐
2. Skolan ignorerar det vi har berättat om mitt barns blödarsjuka.	☐	☐	☐	☐	☐
3. Mitt barn har problem i skolan p.g.a. sin blödarsjuka.	☐	☐	☐	☐	☐

Deltagar nummer: |__|__|__| **Initialer:** |__|__|

8. Dessa frågor handlar om hur DU UPPFATTAR BARNET

Under de senaste 12 månaderna, hur ofta har du upplevt följande?	Aldrig	Sällan	Ibland	Ofta	Alltid
1. Mitt barns trotsar sjukdomen.	☐	☐	☐	☐	☐
2. Ju äldre mitt barn blir desto mer utmanande är det att hantera honom/henne.	☐	☐	☐	☐	☐
3. Mitt barn behöver mer kärlek och uppmärksamhet.	☐	☐	☐	☐	☐
4. Mitt barn förstår inte att han/hon inte kan göra allt som andra barn kan.	☐	☐	☐	☐	☐
5. Jag tycker att mitt barns tillstånd innebär en svår situation.	☐	☐	☐	☐	☐
6. Jag känner mig ledsen när jag måste berätta för mitt barn vad han/hon inte får lov att göra p.g.a. sin blödarsjuka.	☐	☐	☐	☐	☐

9. Följande frågor handlar om hur DU HANTERAR barnets sjukdom

Under de senaste 12 månaderna, hur ofta har du upplevt följande?	Aldrig	Sällan	Ibland	Ofta	Alltid
1. Jag har brist på energi p.g.a. mitt barns tillstånd.	☐	☐	☐	☐	☐
2. Jag tycker inte att mitt barns tillstånd innebär några fördelar.	☐	☐	☐	☐	☐
3. Mitt barns blödarsjuka är hanterbar.	☐	☐	☐	☐	☐
4. Jag har svårt att acceptera det faktum att mitt barn har blödarsjuka.	☐	☐	☐	☐	☐

Deltagar nummer: |__|__|__| **Initialer:** |__|__|

FÖLJANDE FRÅGOR HANDLAR OM HUR BESVÄRANDE VISSA SITUATIONER ÄR RELATERAT TILL BARNETS BLÖDARSJUKA

10. Här finner du några frågor om BEHANDLING av ditt barns blödarsjuka

De senaste 12 månaderna, hur besvärad har du varit av följande?	Inte alls	Lite grann	Något	Ganska mycket	Väldigt mycket
1. Jag är bekymrad för den komplexa behandling mitt barn behöver vid blödningar.	☐	☐	☐	☐	☐
2. Jag känner mig uppbunden och stressad eftersom mitt barn inte har lärt sig att ge injektionerna själv.	☐	☐	☐	☐	☐
3. Jag har problem att hantera mitt barns ledblödningar.	☐	☐	☐	☐	☐
4. Jag är orolig för komplikationer p.g.a. mitt barns blödarsjuka.	☐	☐	☐	☐	☐
5. Jag tycker att mitt barns behandling är tidskrävande.	☐	☐	☐	☐	☐
6. Jag är bekymrad över att injektionerna ges så ofta.	☐	☐	☐	☐	☐
7. Jag är rädd för att jag inte kan hantera livshotande komplikationer som mitt barn kan få.	☐	☐	☐	☐	☐

Vänligen besvara följande frågor endast om du arbetar. Ifall du inte arbetar för tillfället sätt ett kryss i rutan och fortsätt till <u>avsnitt 12!</u>

Jag arbetar inte för tillfället ❑

Deltagar nummer: |__|__|__| **Initialer:** |__|__|

11. Följande frågor handlar om din ARBETSSITUATION i samband med barnets blödarsjuka

De senaste 12 månaderna, hur besvärad har du varit av följande?	Inte alls	Lite grann	Något	Ganska mycket	Väldigt mycket
1. Mitt barns blödarsjuka har begränsat mina arbetsmöjligheter.	☐	☐	☐	☐	☐
2. Jag har valt min arbetsplats för att kunna vara nära mitt barns förskola/skola.	☐	☐	☐	☐	☐
3. Min karriär begränsas p.g.a. mitt barns blödarsjuka.	☐	☐	☐	☐	☐

Vänligen besvara följande frågor endast om du är mamma. Ifall du är pappa eller annan vårdnadshavare sätt ett kryss i rutan och fortsätt av <u>avsnitt 13!</u>

Jag är pappa/annan vårdnadshavare ❑

12. Dessa frågor handlar om DIN RELATION till barnets pappa

De senaste 12 månaderna, hur besvärad har du varit av följande?	**Inte alls**	**Lite grann**	**Något**	**Ganska mycket**	**Väldigt mycket**
1. Mitt barns pappa förnekar hans/hennes blödarsjuka.	☐	☐	☐	☐	☐
2. Mitt barns pappa anklagar mig för att vara bärare.	☐	☐	☐	☐	☐

13. Dessa frågor handlar om hur DU PÅVERKAS av barnets blödarsjuka

De senaste 12 månaderna, hur besvärad har du varit av följande?	**Inte alls**	**Lite grann**	**Något**	**Ganska mycket**	**Väldigt mycket**
1. Jag känner att mitt barns situation svänger från den ena ytterligheten till den andra.	☐	☐	☐	☐	☐
2. Jag känner att jag har åldrats p.g.a. den stress som mitt barns blödarsjuka innebär.	☐	☐	☐	☐	☐
3. Jag har behövt anpassa mitt liv p.g.a. mitt barns blödarsjuka.	☐	☐	☐	☐	☐

Tack för din medverkan!

Appendix 2

Deltagar nummer: |__|__|__| **Initialer:** |__|__|

Sociodemografiska FRÅGOR

1. Först av allt vill vi veta lite om dig…

1.	Du är?	☐ Mamma ☐ Pappa ☐ Annan vårdnadshavare Vem? _____
2.	Vem tar huvudsakligen hand om ditt barn?	☐ Mamma ☐ Pappa ☐ Båda föräldrarna tillsammans ☐ Annan vårdnadshavare Vem? _____
3.	Hur gammal är du?	☐☐ År
4.	Ditt civilstånd?	☐ Ensamstående ☐ Gift ☐ Separerad/Skild ☐ Änka/änkling
5.	Är du sambo?	☐ Ja ☐ Nej
6.	Hur många barn har du?	☐☐
6a	Hur många av barnen har hemofili?	☐☐
6b	Hur många av barnen har en annan kronisk sjukdom, förutom hemofili? Vilken sjukdom? _____	☐☐
6c	Hur många barn under 18 år bor hos dig?	☐☐
7.	Vilken utbildning har du?	☐ Grundskola ☐ Gymnasium ☐ Högskola/Universitet
8.	Arbetar du?	☐ Heltid ☐ Deltid ☐ Studerande ☐ Ej yrkesverksam ☐ Arbetssökande

Deltagar nummer: |__|__|__| **Initialer:** |__|__|

8a	Om du inte arbetar heltid är det p.g.a. att du tar hand om ditt barn med hemofili?	☐ Nej ☐ Ja
8b	Har du bytt yrke p.g.a. ditt barns hemofili?	☐ Nej ☐ Ja
8c	Om du arbetar, vilket avstånd och hur lång tid tar det till arbetet?	☐☐☐ Avstånd i km ☐☐☐ Restid i minuter
9.	Var bor du?	☐ I en stor stad ☐ I en förort eller kranskommun till en stor stad ☐ I en mindre stad ☐ I ett litet samhälle ☐ På landet
10.	För att se påverkan av ditt barns hemofili i ett sammanhang, skulle vi vilja ställa en fråga om inkomst. Vänligen fyll i hushållets sammanlagda årliga inkomst före skatt?	☐ < 142, 000 SEK ☐ 142,000–283,999 SEK ☐ 284,000–567,999 SEK ☐ 568,000 – 1,134,999 SEK ☐ > 1,135,000 SEK ☐ Vet inte/Vill inte uppge
11.	Hur mycket har du uppskattningsvis själv betalat de senaste 12 månaderna för ditt barns hemofili vård?	☐☐☐☐ SEK
11a	På vilket/vilka av följande har du spenderat pengar?	☐ Hjälpmedel ☐ Speciella kläder (ex. skor) ☐ Speciella möbler ☐ Sjukvårdsartiklar (ex. sprutor) ☐ Transport (ex. taxi) ☐ Sjukgymnastik ☐ Psykolog ☐ Annat:_____
12.	Är du själv drabbad av en kronisk sjukdom?	☐ Nej ☐ Ja, vilken_____
13.	Är barnets andra förälder drabbad av en kronisk sjukdom?	☐ Nej ☐ Ja, vilken_____

Deltagar nummer: |__|__|__| **Initialer:** |__|__|

2. Påverkan av hemofili

1. Upplever du att ditt barns hemofili har påverkar ditt liv (familj, arbete, annat…)?

   ❑ Nej ❑ Ja Om ja, på vilket sätt?

   _____

   _____

2. Är familjens ekonomi påverkad av barnets hemofili?

   ❑ Nej ❑ Ja

3.Frågor om ditt barns hemofili

1. Finns det någon annan familjemedlem som har/haft hemofili?

   ❑ Nej ❑ Ja Om ja, ange vilket släktskap (ex. kusin, bror m.m.).

   _____

2. Har någon annan familjemedlem fysiskt funktionshinder p.g.a. hemofili?

   ❑ Nej ❑ Ja Om ja, vem?

   _____

3. Finns det saker som ditt barn inte kan göra p.g.a. hemofili?

   ❑ Nej ❑ Ja Om ja, vad?

   _____

4. Under de senaste *12 månaderna*, ungefär hur mycket tid per månad har ditt barn och du lagt ner på att injicera faktorkoncentrat?

   ❑❑ Timmar per månad för dig ❑❑ Timmar per månad för barnet

5. Under de senaste *12 månaderna*, hur mycket tid per månad har ditt barn och du behövt, i genomsnitt, för att ta er till behandling för hemofili (ex. sjukvårdsbehandling, sjukgymnastik, psykolog, specialistvård)?

   ❑❑ Timmar per månad

Deltagar nummer: |__|__|__| **Initialer:** |__|__|

6. Har ditt barn drabbats av kronisk smärta *de senaste 12 månaderna?*

   (Definition: Smärta utan en uppenbar blödning, återkommande minst två gånger i veckan och som varat över 3 timmar utan behandling.)

❑ Nej ❑ Ja

Om ja, vänligen ange den genomsnittliga intensiteten på denna visuella skala

(sätt ett X på linjen)

0 1 2 3 4 5 6 7 8 9 10

|____|____|____|____|____|____|____|____|____|____|____|

(Ingen smärta) (Maximal smärta)

7. *Under de senaste 12 månaderna* hur många dagar har ditt barn missat förskola/skola/arbete p.g.a. sin hemofili?

   _____ Dagar

8. *Under de senaste 12 månaderna* hur många dagar har DU missat arbete/dagliga aktiviteter p.g.a. ditt barns hemofili?

   _____ Dagar

Tack för din medverkan!

Appendix 3

Identification-No.: |__|__|__| **Initials:** |__|__|

Burden of Bleeds
on Caregivers

Medical Documentation

1. Demographics

Patient birth date ☐☐ MM ☐☐ YY

Weight ☐☐ Kg Height ☐☐☐ cm

Type of haemophilia A ☐ B ☐

Severity of haemophilia moderate ☐ severe ☐

2. Bleeding history

Total number of bleeding events *in the previous 12 months* ☐☐

a. how many were joint bleeds ☐☐

b. how many were muscle bleeds ☐☐

c. how many were life-threatening bleeds ☐☐

d. how many were other bleeds ☐☐

Age at **first joint** bleeding event ☐☐ months N.A. ☐

Are there **target joints**?

(Definition: 3 or more bleeds in the same joint in the past 12 months)

☐ NO ☐ YES

Does the patient have joints with reduced range of motion?

☐ NO ☐ YES

3. History of inhibitor

Past or present development **history of inhibitor** ☐ NO ☐ YES

IF NO: GO TO THE NEXT SECTION

IF YES:
A. Age at inhibitor development: ☐☐ months
B. Was the inhibitor titre? ☐low ☐high
C. Is the inhibitor still present? ☐No ☐Yes

D. Has the patient undergone ITI? ☐No ☐Yes
If Yes, was it successful? ☐No ☐Yes
Still on immune tolerance ☐No ☐Yes

4. Concomitant diseases

(Definition: diseases that have required in the past 12 months regular visits or treatment)

☐ No ☐ YES If Yes, specify: _____

5. Surgery

Has the patient had any **surgical procedures** *in the past 12 months*

☐ NO ☐ YES

Type (Specify):

1. _____
2. _____
3. _____

6. Treatment

Is the patient currently on **home treatment**:

☐ NO ☐ YES

Who **has mainly** administered the therapy *in the past 12 months*:

☐ self-administered ☐ a family member
☐ physician at the center ☐ nurse at the center
☐ general practitioner ☐ nurse at hometown ☐ other hospital

How is the patient treated?

☐ on-demand ☐ prophylaxis

☐ switch between on-demand and prophylaxis

☐ ITI

If the patient is on prophylaxis, which type of prophylaxis?

☐ primary *(started before the 2nd bleed or before the age of 2 years)*

☐ secondary *(started after the 2nd bleed or after the age of 2 years)*

If the patient is on prophylaxis, how frequently?

☐ once per week ☐ twice per week

☐ three times per week ☐ more than three times per week

Venous access type *in the past 12 months*:

☐ peripheral vein ☐ arterovenous fistula

☐ central line ☐ Port-a-cath

☐ Broviac/Hickman ☐ Other (specify)_____

Which kind of product does the patient receive *(tick any that apply)*?

☐ plasma-derived product

☐ recombinant product

☐ EHL recombinant product

☐ Other (specify)_____

7. Medical visits

A. Visits at the Haemophilia Center *in the past 12 months* ☐ **None**

|__|__| programmed |__|__| for bleeds

B. Visits at general practitioner/paediatrician *in the past 12 months* ☐ **None**

|__|__| haemophilia-related |__|__| for other problems

C. Number of days of assisted physiotherapy *in the past 12 months* ☐ **None**

|__|__| at home |__|__| at a centre

D. Number of visits at psychotherapist *in the past 12 months* ☐ **None**

|__|__| haemophilia-related |__|__| for other problems

E. Number of visits at other specialist *in the past 12 months* ☐ **None**

|__|__| haemophilia-related |__|__| for other problems

F. Number of hospitalisations *in the past 12 months* ☐ **None**

|__|__| haemophilia-related |__|__| for other problems

G. Number of days of hospitalization *in the past 12 months* ☐ **None**

|__|__| haemophilia-related |__|__| for other problems

G1. Of these how many days in an Intensive Care Unit

|__|__|haemophilia-related |__|__|for other problems