Self-reported activity and participation in persons with haemophilia living in Sweden

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Cover illustration: Ivar Arosenius, Självporträtt med blödande hjärta, 1903. Blyerts och akvarell, 20,6 x 12,2 cm, Göteborgs konstmuseum Foto: Hossein Sehatlou

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“Kunskap är en process, inte ett tillstånd” © Göran Torell (1959-)

”Utan tvivel är man inte riktigt klok” © Tage Danielsson (1928-1985)

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ABSTRACT

Background: Haemophilia is a hereditary disease caused by deficiency of clotting factor VIII or IX. Recurrent joint bleeding episodes can lead to haemophilia arthropathy, a condition affecting daily activities and participation in society. The Haemophilia Activity List, (HAL), is a self-reported questionnaire that provides the person's own view of perceived difficulties in performance of daily activities. The overall aim of this thesis was to describe self-reported activity and participation in adult persons with haemophilia in Sweden and explore their experiences of living with haemophilia.

Methods: All adult persons with haemophilia in Sweden meeting the inclusion criteria were invited by letter to studies I+II and III (84 and 129 participated respectively) to validate Haemophilia Activity List and explore any difficulties in activity and participation. Sixty-one participated twice, first in studies I+II and then in study III. In study IV persons from the Haemophilia Treatment Centre in Gothenburg were recruited for interviews about their experiences living with haemophilia (14 participated). The interviews were analysed according to the empirical psychological phenomenological method described by G. Karlsson.

Main results: The most common difficulties reported were in physical activities involving the lower extremities such as e.g. rising from a chair, riding a bicycle, walking and running. Those with early treatment onset reported fewer difficulties than the group with later treatment onset. Over time the later treatment onset group reported increasing difficulties in leisure activities and sport. This indicates a greater need for rehabilitation for the

later treatment onset group to help maintain their activity level in daily life. The participants interviewed valued the treatment with clotting factor and support from caregivers at the Haemophilia Treatment Centre. Preventing bleeds was a main objective for the interviewees with haemophilia. They adapted their social activities and strived for normality throughout life. The Swedish version of HAL has high internal consistency and excellent to good convergent validity and can be used as a complement to other clinical tests to establish the patient's self-perceived difficulties to perform activities of daily life.

Conclusion: The Swedish persons living with haemophilia reported most difficulties with activities involving the lower extremities and there was a difference between the groups with early and later treatment onset, where the later onset reported more difficulties over all. The interviewees with haemophilia adapted their social activities and strived for normality throughout life. They valued the treatment with clotting factor, and a major objective was preventing bleeds. The Swedish version of HAL can be used in the clinic and in research to gather information about the person´s self-perceived activity and participation in daily life.

Keywords: Haemophilia, activity, participation, lived experiences, HAL, validity, interview, empirical phenomenological psychological method, coping

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SAMMANFATTNING PÅ SVENSKA

Bakgrund: Blödarsjuka är en ovanlig recessivt könsbunden ärftlig sjukdom som överförs av kvinnliga bärare och som oftast drabbar män. Blödarsjuka har tidigare varit förknippat med led och muskelblödningar som leder till funktionshinder ofta redan från barndomen, men även med kort livslängd. Personer med blödarsjuka saknar eller har brist på faktor VIII (hemofili A) eller faktor IX (hemofili B) i koagulationskedjan. Blödarsjuka förekommer i mild (6-40 % faktoraktivitet i blodet), medelsvår (1-5 %) och svår (< 1 %) form. I Sverige lever cirka 1000 pojkar eller män med de två sjukdomsformerna varav 80 procent har hemofili A och 20 procent hemofili B. Drygt hälften av personer med blödarsjuka har den svåra eller medelsvåra formen. Livslängden är numera jämförbar med befolkningen i övrigt.
Som en följd av blödningar kan det uppstå led- och muskelförändringar som kan leda till begränsningar i dagliga aktiviteter. I Sverige har personer med svår form av blödarsjuka haft möjlighet att få förebyggande behandling med faktorkoncentrat sedan 60-talet. Det är vanligt att ortopediska ingrepp görs för att förbättra funktionen och minska smärta från av blödningar angripna leder. Att kunna utvärdera patientens upplevelse av sin aktivitetsförmåga i dagligt liv samt värdera utfallet av olika behandlingsformer t.ex. regelbunden förebyggande behandling, är ett viktigt komplement till kliniska test. Ett sjukdomsspecifikt självskattningsinstrument för att utvärdera svårigheter i aktivitetsförmåga hos blödarsjuka är utvecklat i Holland, Hemofilie Activiteiten Lijst, (HAL).
Syfte med denna avhandling var att säkerställa att en svensk version av HAL fungerar för svenska förhållanden (studie I), och att beskriva vuxna svenska blödarsjukas självskattade aktivitet och delaktighet med tre olika frågeformulär (studie II). Vidare var syftet att beskriva förändringar i aktivitet och delaktighet över tid (ca 2,5 år) och mellan personer med tidig respektive sent insatt medicinering med den saknade koagulationsfaktorn (studie III). Ett ytterligare syfte var att få fördjupad kunskap om hur det är att leva med blödarsjuka och vilka strategier man använder i dagligt liv för att hantera sin blödarsjuka (studie IV).
Metodik: Frågeformulär skickades ut med en inbjudan om deltagande i studie I-II, och III till alla vuxna med blödarsjuka i Sverige som hade svår och medelsvår form av sjukdomen. De som önskade delta skickade tillbaka sitt medgivande tillsammans med de ifyllda frågeformulären. I studie IV skickades en inbjudan om att delta i en intervjustudie ut till vuxna med blödarsjuka inskrivna vid Koagulationscentrum på Sahlgrenska Universitetssjukhuset. Totalt deltog i studie I-II 84 personer och i studie III 129 personer. Av dessa deltog 61 personer både i studie I-II och III. I

intervjustudien deltog 14 personer och berättelserna analyserades med empirisk fenomenologisk psykologisk metod (EPP).

Resultat: Den svenska versionen av HAL är ett frågeformulär som kan användas för att utvärdera svenska blödarsjukas egen uppfattning av svårigheter i utförande av aktiviteter och i att vara delaktiga i dagligt liv. De blödarsjuka anger främst svårigheter i aktiviteter som kräver funktion i nedre extremiteterna. Den grupp blödarsjuka som haft tillgång till medicinsk behandling med den saknade koagulationsfaktorn tidigt under uppväxten upplevde färre svårigheter än de som inte har haft det. Över tid rapporterade den grupp som inte haft medicinsk behandling under uppväxten ökade svårigheter i fritids- och idrottsaktiviteter. Intervjudeltagarna strävade efter normalitet och försökte hitta sin egen nisch i sociala sammanhang i dagligt liv. Att förebygga blödning visade sig vara centralt för den blödarsjuke. De upplevde ett betydelsefullt stöd i den specialiserade vården på hemofilicentrum i Göteborg och utryckte betydelsen av den förebyggande medicineringen och oro över vad som kan hända om subventioneringen skulle försvinna.

Slutsatser och klinisk betydelse: Den svenska versionen av HAL kan användas kliniskt och i forskning för att få information om den blödarsjukes självupplevda svårighet i utförande av aktiviteter och att vara delaktig i dagligt liv. Gruppen blödarsjuka med tidigt insatt behandling med koagulationsfaktorn som saknas hade nästan inga svårigheter i dagligt liv till skillnad från de med senare insatt behandling som från början angav större svårigheter inom nästan alla områden och över tid försämrades i fritidsaktiviteter och idrott. Denna grupp av äldre blödarsjuka kan framöver ha ett behov av rehabiliteringsinsatser för att behålla sin funktion i dagligt liv.

LIST OF PAPERS

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

I. Brodin E, Baghaei F, Elfvinger P, Lindvall K, Sunnerhagen KS.
The Swedish version of the Haemophilia Activity List.
Haemophilia 2011 Jul;17(4):662-8. doi: 10.1111/j.1365-2516.2010.02474.x. Epub 2011 Feb 7.

II. Brodin E, Baghaei F, Sunnerhagen KS
Self-reported activity and functioning in daily life; the perspective of persons with haemophilia living in Sweden.
Eur J Haematol. 2015 Oct;95(4):336-41. doi: 10.1111/ejh.12503. Epub 2015 Feb 17.

III. Brodin E, Hadzibajramovic E, Baghaei F, Sunnerhagen KS, Lundgren-Nilsson Å.
Activity and Participation of Swedish Hemophilia Persons; change over 2.5 years.
Manuscript

IV. Brodin E, Sunnerhagen KS, Baghaei F, Törnbom M.
Persons with Haemophilia in Sweden- Experiences and Strategies in Everyday Life. A Single Centre Study.
PLoS One. 2015 Oct 2;10(10):e0139690. doi: 10.1371/journal.pone.0139690. eCollection 2015.

CONTENT

ABBREVIATIONS

AIMS 2	Arthritis Impact Measurement Scale 2
EPP	Empirical Phenomenological Psychological method
ET	Early treatment onset
EQ-5D	Euro Quality of Life 5 Dimensions
HAL	Haemophilia Activity List
HRQoL	Health Related Quality of Life
HTC	Haemophilia Treatment Centre
I-ADL	Instrumental activities in daily living
ICF	International Classification of Functioning
IPA	Impact on participation and autonomy
LT	Later treatment onset
P-ADL	Personal activities in daily living
PROMs	Patient Reported Outcome Measures
PWH	Persons with Haemophilia
SF-36	Short Form health survey
SPSS	Statistical Package for Social Sciences

DEFINITIONS IN SHORT

Early treatment onset	Born approximately 1965 or later (18-45 years old at the time of assessment). Had the opportunity to get factor replacement therapy at an early age.
Later treatment onset	Born approximately before 1965(over 46 years old at the time of assessment). Have not had the opportunity to get factor replacement therapy at an early age.
Activity	According to the ICF the definition of activity is: "activity limitations are difficulties in executing activities – for example, walking or eating" [1]; a task or action by an individual.
Participation	According to ICF the definition of participation is: "participation restrictions are problems with involvement in any area of life – for example, facing discrimination in employment or transportation"[1]; involvement in a life situation.
Content validity	The extent to which a measurement covers all aspects of the topic it purports to measure[2]
Convergent validity	The extent to which two or more instruments that purport to be measuring the same topic agree with each other.[2]
Inhibitors	Inhibiting antibodies against factor VIII or IX

INTRODUCTION

Haemophilia; causes, prevalence, symptoms, and treatments

Haemophilia causes and prevalence

Haemophilia is a hereditary disease characterized by an increased tendency to bleed/hemorrhage. It is a recessive X-linked hereditary disease caused by deficiency of clotting factor VIII or IX.[3] The inheritance is shown in figure 1. There are two forms, haemophilia A with deficiency of factor VIII and haemophilia B with deficiency of factor IX.[4] Haemophilia is classified as severe (<1% of factor activity), moderate (1-5%) or mild (6-40%) based on the clotting factor levels.[5]

The reported prevalence of haemophilia varies considerably among countries.[6] According to a study from 2009, the reported haemophilia A prevalence for high-income countries was about 12.8 ± 6.0 (mean ± SD) per 100 000 males, and it was 6.6 ± 4.8 for the rest of the world.[6] For haemophilia B the corresponding prevalence for high-income countries 2012 was 2.69 ± 1.61 and for the rest of the world it was 1.20 ± 1.33.[7] Approximately 50% of persons with haemophilia (PWH) have either the severe or moderate form.[8]

In Sweden, there are approximately 1000 males, including children, with haemophilia[9] of whom 80% have haemophilia A and 20% have haemophilia B. Within the same family the type and severity remain the same. Approximately 50% of new cases do not have any family history of haemophilia at the time of diagnosis.[10]

Medical advances in hemophilia care have resulted in increased life expectancy, so that the average lifespan of a man with hemophilia is almost the same as the normal male population.[10,11] Still the all-cause mortality compared to controls is higher for PWH especially the ones with severe form.[12]

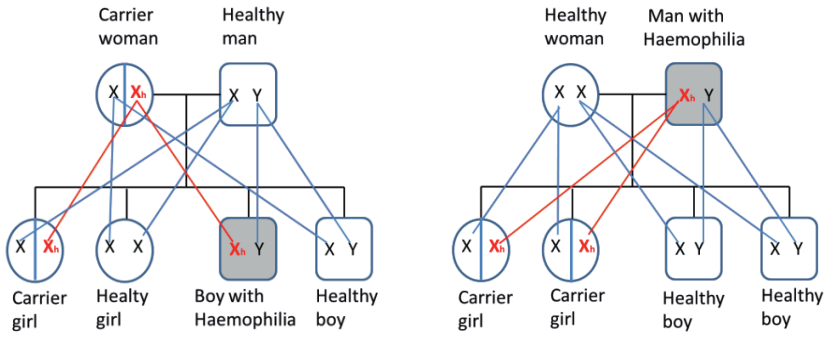

Figure 1. The inheritance of haemophilia: A carrier woman and a healthy man have a 50% risk getting a son with haemophilia and 50% risk of their daughters being carrier. A man with haemophilia and a healthy woman get healthy sons but all daughters will be carriers.

Haemophilia symptoms and treatment

The main symptoms before diagnosis, especially for the severe and moderate forms of haemophilia, are bruises in soft tissue during the first year of life.[13] More serious bleeding occurs in the joints and muscles.[13] Before the availability of treatment with clotting factors a small wound could bleed for weeks.[13] The overall goal for the prophylaxis treatment in Sweden is to prevent bleeds and thereby give the PWH possibility to get healthy joints without hemophilia arthropathy and opportunity to normal activity and participation for an independent life.[10] PWH benefit from an early start of prophylactic factor replacement treatment in order to prevent arthropathy and to reduce the bleeding rates.[14,15] In Sweden, people with the severe form of haemophilia have had access to prophylactic treatment with factor concentrate since approximately the 1960s.[16,17] The first prophylaxis treatment was already in use in 1958 (1 dose/2 weeks) in a small sample of PWH and gradually increased.[17-19] Nowadays replacement therapy with clotting factors as prophylaxis is commonly used in Sweden for the severe and moderate forms of haemophilia to avoid the onset of bleeding.[10] The prophylaxis treatment starts early in life, at approximately one year old, when the boy begins bearing weight more on joints and muscles and it should be initiated before the onset of a serious bleed.[10] The administration of clotting factors by injections is in Sweden mostly done as home treatment by the PWH themselves or by a family member.[20] In 2012 PWH in Sweden used 8.56 units Factor VIII per capita which is highest in Europe.[20] The high dose

prophylaxis treatment had an annual cost per adult PWH (average weight of 74kg) of approximately US$ 297 900.[21]

The PWH residents in high-income countries have access to treatment with clotting factor for on demand or prophylactic treatment to a greater degree compared to those who live in low-income countries.[9] Therefore the numbers of PWH in the world with disability differ a great deal between countries with access to medication with the clotting factor and without.[22] Some PWH develop inhibitors against the clotting factor when treated and a new cohort study has shown that approximately 30 % of children with haemophilia A developed inhibitors against the medication during the first 50 exposure days after treatment with factor concentrate.[23] In a Swedish population 19% of the PWH with the severe form of haemophilia B had developed inhibitors.[24] Increase in inhibitors over time is that more sensitive laboratory tests are available and testing is more frequent.[23]

Treatment options in patients with inhibitors are limited to bypassing agents such as recombinant FVIIa (NovoSeven®)[25,26] or activated prothrombin complex concentrate (FEIBA©).[27] Inhibitor patients have a greater risk for disability both physically and psychosocially.[28] A person with severe haemophilia and an inhibitor was predicted to have an average 1.71% more overall range of motion limitation than an otherwise identical person without an inhibitor among PWH, 2-19 years old.[29]

If untreated, haemophilia leads to frequent bleeds into the joints mainly in the elbows, ankles and knees, and bleeds in muscles.[10,30,31] Muscle hemorrhage usually occurs in the iliopsoas, but also in the thigh and forearm muscles.[31,32] Recurrent bleeding episodes, particularly in the extremity joints, can lead to haemophilia arthropathy and chronic synovitis and joint pain, loss of range of motion and decreased strength.[10,33] Other risk factors for limited range of motion are increased age, increased body mass index and recent orthopedic procedures.[29] As a result, functional changes occur that can lead to disabilities.[10,32]

The first line drug for acute pain for PWH is paracetamol. Non-steroidal anti-inflammatory (NSAIDs) drugs with a short half-life may be considered as the second line treatment, but not salicylic acid because the latter increases the bleeding risk. For adult patients and for chronic pain, COX-2 inhibitors are preferred[34,35] combined with paracetamol.[36] For severe pain different opioids are used if paracetamol is ineffective to maintain function.[35,36]

For chronic pain, non-pharmacological methods can also be used such as behaviour and psychological methods, for example pain coping, pain acceptance, cognitive behavioural therapy and bio feed-back[37,38] and physical strategies such as orthopedic surgery, hydrotherapy,[39] acupuncture,[40] transcutaneous electrical neuro-stimulation (TENS), physical therapy especially increased muscles strength and coordination.[35,37,39]

Physiotherapy

Physical therapy is an important means of preventing functional limitation after bleeding episodes in joints or muscles.[41] Especially in developing countries with low or no factor replacement therapy, physiotherapy has an important role to play in preventing disability.[42,43]

In addition to prophylaxis with a clotting factor, advice regarding physical activity and exercise, guidance to find suitable education and work, and information about the disease are given to parents and boys throughout life. At an early age, a helmet to prevent cerebral hemorrhage due to trauma is recommended. In all sports activities it is important to use the recommended protection for each sport.

When an acute bleed occurs in a joint or muscle the focus is on minimizing the bleeding with clotting factor and to mitigate symptoms such as pain and edema by resting in a comfortable position, oral analgesia, local ice application, compression of the joint and elevation of the extremities, and limited weight bearing of the lower limb.[41,44] A plan for an exercise program to restore lost function is devised. The consequences of a joint- or muscle bleed are affected function and mobility and it is important to handle these consequences in a structured way. A theoretical framework for physiotherapy intervention used is the motor control theory by Shumway-Cook and Woollacott to regain a person's functional capacity.[45] Motor control is studied in relation to specific actions or activities and the specific movement is an interaction between the individual, the task that should be performed and in the environment in which it is performed.[45] Exercise improved range of motion and muscle strength in PWH.[46] The physiotherapist guided PWH to do graded exercise, first to increase range of motion and then successively more strengthening of muscles close to the affected joint and thereafter coordination of movement. Several studies show that mobility and strength exercise lead to faster normalization of function and also significantly reduce the risk of permanent disability after a bleed.[44,47,48] Sometimes modification

of activities had to be done and advice be given about leisure activities and sport during the rehabilitation phase.[41] Haemophilia arthropathy with joint pain, reduced range of motion, strength, and balance/coordination can successfully be treated with physical exercise individually adapted to the PWH to increase physical performance and decrease pain.[41,44,39]

Orthopedic surgery

Orthopedic surgery can be performed to improve function and reduce pain from the affected joints with haemophilia arthropathy.[30,49] The most common orthopedic surgery is total joint replacement in the knee but also joint replacement in the hip, elbow, shoulder and ankle have been performed due to haemophilia arthropathy.[50,51] In order to regain function after surgery the physiotherapy intervention is important[8] and follows the intervention protocols used at the orthopedic clinic where the surgery is performed.[52]

Organization of care

Haemophilia care is commonly organized in Europe as comprehensive care in a so called Haemophilia Treatment Centre, HTC. The care is specialized and centralized to a few hospitals per country where staff are organized into multidisciplinary teams.[53]

All countries in Europe nowadays have access to clotting factor concentrate for on demand treatment and it is possible for children to get prophylaxis treatment but not all adults.[53] One of the reasons could be the high pharmaceutical costs and/or differences in national treatment guidelines.

The main goals for the care at the HTC are: maintain expertise and offer trained personnel for delivery of care, make available multidisciplinary comprehensive care teams, offer specialized services, e.g. prenatal diagnosis, orthopedic surgery and genetic counseling, support home treatment for patients, uphold a national network of care and do research to improve care.[54]

According to one study from the United Kingdom, PWH preferred the specialized care-givers at the local hemophilia centre over other health-care providers.[55] In Sweden there are three HTCs providing comprehensive care to all known hemophilia patients living in Sweden and other patients with rare bleeding disorders[8]. The HTCs are located at three University hospitals; Karolinska University Hospital (Karolinska), Skåne University Hospital (SUS) and Sahlgrenska University Hospital (SU). The multidisciplinary

teams consist of physicians, nurses, physiotherapists and social workers all specialized in haemophilia care. The HTC teams take care of the whole life span of the patient due to the bleeding disorder and act as consultant to other health-care providers. The PWH with the severe or moderate form are monitored regularly, 1-2 times a year at the HTC.

International Classification of Functioning Disability and Health (ICF)

ICF is a model within the World Health Organizations classification systems regarding function, disability and health. The classification system of ICF focuses on human functioning and provides a unified, standard language and a framework that captures how people with a health condition function in their daily life. The person is viewed as a resident/participant in society, not simply as a patient or user of facilities. It has its origin in the civil rights for humans to live a life as everyone else even with any disability. ICF does not focus on the diagnosis or presence or absence of disease. Instead the model is used to sort out information that identifies important factors that facilitate as much independence as possible for the person in their life. Definitions and categories are formulated in neutral language. The model tries to explain the complexity of impairment and participation through environmental and personal factors and how a mix of factors affect each other.[56,57]

In the ICF model functioning and disability are to be understood as umbrella terms expressing both positive and negative aspects of functioning from a biological, individual and social perspective. According to ICF the definition for activity is; "activity limitations are difficulties in executing activities – for example, walking or eating"[1]; a task or action by an individual. Participation is defined as; "participation restrictions are problems with involvement in any area of life – for example, facing discrimination in employment or transportation"[1]; involvement in a life situation.

In figure 2 the multidimensional model is described for PWH. The physiotherapists take care of the preventive phase according to activities and participation level of the PWH at the annual check-up at the HTC. But when a physiotherapist provides treatment, it is more as a result of an acute bleeding incident to help restore function. After acute treatment the rehabilitation phase turns more and more towards the activity and participation part of the ICF model. All advice is based on information about the personal and environmental factors prevailing in each case. The HAL

questionnaire identifies problematic activities as a part of the functional health status both as an epidemiological outcome for the group of PWH and also at an individual level to evaluate activity and participation after an intervention.

The ICF places all health conditions on an equal basis. The focus is switches to functioning, which enables comparing different health conditions in terms of related functioning via a shared structure/framework. The ICF model is based on a platform of the two major model views of disability, the medical one caused by the disease and the socially generated one caused by a socially derived problem and merge together to form the biopsychosocial model.[58] The model is built up of an interaction between aspects of the person and elements of the overall context in which the person lives. Some aspects of disability are completely internally generated, while other aspects are totally externally generated. It gives a rational view of different perspectives of health: biological, individual and social.[58]

It is a challenge to assess disability for PWH and compare the results from different countries when using self-reported measurements. The ICF model is useful for interpretation of results into a living context, especially when cross–cultural validating is performed.[59]

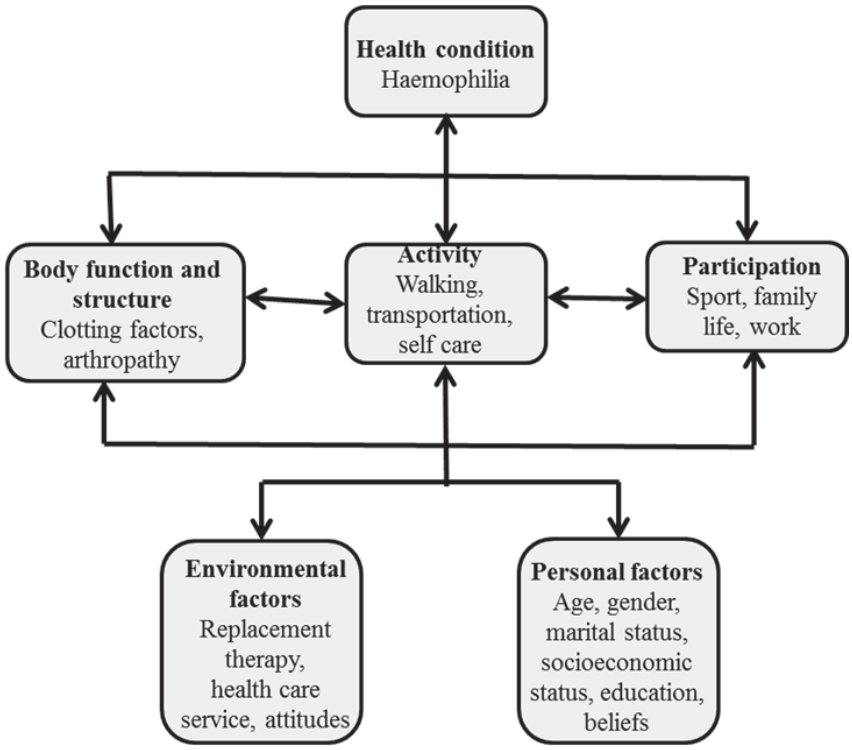

Figure 2. The ICF multidimensional model illustrating the interaction between the various factors from health condition(s) to the contextual factors (environmental and personal factors). In the domains some factors are exemplified due to the haemophilia diagnosis.

Disability

Disability is an umbrella term that covers impairment, activity limitations and restricted participation due to disturbances in human functioning.[58] Disability mirrors an interaction between characteristics of a person's body and features of the society in which they live.[58] There are over 1 billion persons in the whole world experiencing disability of different kinds from visual impairment to neurological and orthopedic disabilities.[1] Interventions are needed in order to overcome environmental and social obstacles. Persons with disabilities have the same needs as non-disabled persons regarding health-care but they are 2 times more likely to be met by insufficient knowledge and inadequate service in health-care, 3 times more likely to be refused health-care and 4 times more likely to be poorly treated in the health-

care system.[1] Globally, about 50% of the persons with disability cannot afford health-care.[1]
Disability increases with age and persons with disabilities more often have limited education and a worse economic situation and report poorer health compared to healthy persons.[60-62] Of the whole Swedish population, 16-84 years old, 23% have disabilities and about a half a million (8%) have impaired mobility.[62] Among men 65-84 years old 18% have impaired mobility and among men 16-64 years the corresponding figure is 3%.
PWH have disability mainly due to arthropathy with impaired mobility which complicates performance of demanding activities of daily life.

Outcome measures in haemophilia care

A variety of assessment instruments are used to monitor PWH over time at the annual check-up. Both disease specific and general instruments are used. These instruments give the opportunity in research to compare the outcome of the haemophilia population in different countries.[63] In table 1 some of the assessments used worldwide are presented. For quality of life assessment, there are both disease specific instruments mostly developed for children and general instruments. For adults the more general applicable questionnaires used are the Euro QoL 5D, (EQ-5D),[64-66] and the Short Form health survey, SF-36,[67] with the purpose of comparing people within the general population in a country or between populations with different diagnoses.[59] In Sweden, the most used QoL assessments are generic instruments and not the disease-specific instruments. One reason is that the disease specific questionnaires have not been translated into Swedish and tested for validity and reliability. Beside medical examination, including various forms of X-rays, annual bleeding rates and joint status (e.g. the Haemophilia Joint Health Score) are used.[68,69] In table 1 the most proposed assessments in haemophilia care regarding body function, activity and participation are listed.[63,68,70-72,73-75]

Table 1. *Some of the different disease specific assessments used in haemophilia care globally.*

Haemophilia disease specific assessments	Body function and structure	Activity	Participation
Annual bleed rate, ABR	**X**		
X-ray, Pettersson score	**X**		
Magnetic resonance imaging, MRI score	**X**		
Ultrasonographic assessment	**X**		
Haemophilia Joint Health Score, HJHS	**X**	**X**	
Functional Independent Score, FISH		**X**	
Haemophilia Activity List, HAL		**X**	**X**

Self-reported measure

With more persons living with diseases and disability in the society, there has been increasing interest in the patient reported outcome measures (PROMs), which refer to self-reports regarding impairments and other aspects of wellbeing and disability, as well as general health perceptions.[76] Questionnaires or instruments that are disease-specific may have greater clinical interest because of their specificity of content. They should be associated with increased responsiveness to specific changes in condition and should appeal to the respondent who would recognize the areas discussed. The results of a questionnaire could be used to evaluate the results of an intervention as a complement to other functional or clinical tests following a person with a chronic disease over time. The patients' self-assessed outcome of an intervention can be more telling than the result of, for example, an X-ray after orthopedic reconstruction surgery of a joint. These instruments could ideally be used in clinical trials, economic evaluation and routine patient care.[77] There is a lack of disease specific outcome measures for the participation level according to the ICF model for PWH. The generic instruments are useful when the purposes are to compare with other populations but may be less sensitive than disease-specific measures. Cross-cultural validity tests are needed for both generic and disease specific instruments because the questions can be interpreted differently in different cultures and in diverse societies.[59]

The questionnaire used in this thesis, the Haemophilia Activity List, HAL, was developed in the Netherlands and is the first questionnaire to assess the activity and participation of PWH[74] according to the ICF using the disability model.[78] The original HAL questionnaire was tested for validity and internal consistent for severe forms of haemophilia.[75] HAL is available in several languages but the different language versions have not been validated. The items in the HAL questionnaire consist of the topics from ICF described in Chapter 4 'Mobility', 5 'Self-care', 6 'Domestic life' or 9 'Community, social and civic life'. All these chapters are examples of personal or instrumental activities of daily living. Personal Activities of Daily Living (P-ADL) and Instrumental Activities of Daily Living (I-ADL), such as transfers, dressing/undressing and toilet hygiene, as examples of P-ADL, and transportation, cooking, purchasing of products for everyday use, leisure activities, and sport as examples of I-ADL.[56] A more detailed description of HAL can be seen in figure 6 of the Methods chapter and in Appendix 1.
A recent article highlighted the importance of using translated and validated assessments for different sociocultural and economic contexts combining health related quality of life instruments with more disease-specific assessments for PWH to better encompass all the dimensions of the ICF model.[79] To evaluate the outcome of prophylaxis treatment of haemophilia it is important to combine clinical/objective and self-reported instruments to capture the whole spectrum of the disease. A study of a cohort of young PWH treated with early prophylaxis showed no correlation between the reported bleeding rate and any clinical/objective and self-reported outcomes parameters besides the HAL sum score and the SF-36 physical function score.[80] Changes in joint structure and function did not immediately result in changes in self-reported limitations in activities or HRQoL.[80] Based on a recently published study describing psychometric properties and limitations of the various clinometric tools used to assess musculoskeletal outcomes in haemophilia, a recommendation for use in clinical practice has been suggested to allow for comprehensive assessment.[81]

The perspective of persons with haemophilia

Experiences of pain and disability are associated with increased age and higher reported bleeding rates leading to lower Quality of Life in PWH[82] in general when compared to the general population.[83] A review article about

psychosocial stressors in PWH showed decreased Quality of Life surrounding education and employment, particularly when medication with a clotting factor was not available as prophylaxis.[83] Most of the literature is from developed countries and aspects from the life cycle of PWH are missing in the literature.[83] A Swedish study showed that compared with a reference population the PWH in the middle age group (45-64 years) experienced lower Quality of Life in physical, physical role and pain domains measured with The Short Form Health Survey (SF-36).[84] In a qualitative interview study the main themes of being a PWH were, in prevalence order "growing up and feeling different from others", "cognitive strategies to manage the illness and find resources", "illness as disability and stressor event", and "learned to manage emotions and action toward normality".[85] Interview studies with PWH from the UK showed the benefits of replacement therapy, [86] the risk of discrimination due to haemophilia and the disease had an impact on education, work, and social activities.[55] From Finland a qualitative diary study showed that the haemophilia disease was always present in everyday life and the home treatment with infusion of clotting factor influenced their daily life.[87]

Coping strategies

According to the psychologists Lazarus and Folkman, coping can be defined as the sum of cognitive, emotional and behavioural efforts, which aim to handle particular demands.[88] These demands can be either internal or external and might be experienced as stressors to the individual. The assessment of what is demanding and frustrating is made by the individual, the person will first of all decide whether the challenge is a problem and/or a threat. Thereafter, the individual must assess what resources he or she has to cope with the event/the disability etc. Learned behaviour and their own experiences will predict how the person copes. How the individual assesses the stressors is crucial in order to understand how he/she will cope with the situation. No coping strategy should be categorized as good or bad. The context must be taken into account when evaluating coping, that is to say that both personal and situational aspects are relevant.[88] Health and energy levels facilitate coping efforts. It is easier to cope when one is feeling well than when one is not. People who are ill and exhausted can usually mobilize adequately to cope in a difficult situation.[88]

Lazarus and Folkman summarized the two main categories of coping, problem-focused and emotion-focused strategies. Problem-focused strategies are those that modify or alter the behaviour of the person. They occur when conditions are appraised to be changeable, for example altering work if a chronic condition affects your body in a negative way. The emotion-focused strategies are used when conditions are assessed to be not mutable. These strategies include the regulation of one´s emotions to tolerate or eliminate stress, for example rejection, self-control, seeking social support, distraction or relaxation techniques.[88]
The psychological alteration to chronic disease contains at least five elements for success, the successful performance of adaptive tasks, the lack of psychological disorders, the presence of low negative affect and high positive affect, sufficient functional status and the satisfaction and well-being in various life domains.[89]

Relevant to this thesis is how PWH manage to cope with pain due to acute bleeds mostly in joints and chronic pain due to arthropathy.[90] The most used coping strategies for the PWH feeling pain, described in the literature are emotion focused or passive coping[91-93] and the strategies are similar to other persons feeling chronic pain.[94] Adult PWH of working age used task oriented coping as frequently as controls in their daily life but PWH with less participation and with poor psychological health commonly used more emotion focused coping strategies to deal with their disease.[95] PWH have good psychological adaptation to their disease but a greater tendency to lower self–esteem than healthy controls.[96]

Lack of knowledge

Although there are a lot of PROMs used in health-care for PWH there is a lack of knowledge how these instruments and assessments function in terms of validity and reliability. Recently an overview of the lack of validity, reliability and responsiveness of Health Related Quality of Life assessments has been published.[97] They found just one disease specific questionnaire, the Haemo-QoL-A, which met the claim of being validated through standard linguistic validation procedures.[97] In December 2015 a simple search on PubMed for publications with the terms “self-reported limitations” and “haemophilia” gave six matches, “haemophilia” and “self-reported

participation" gave nine and "haemophilia" and "self-reported activities" gave twenty. Some of them were doublets. When adding the terms validation/reliability to the search, they reduced to six matches. This showed the lack of knowledge about the measurements properties of self-reported questionnaires concerning activity and participation for the haemophilia diagnosis. Further, there is limited data of how commonly used questionnaires have been implemented in other cultures and languages. Firstly, questionnaires used are sometimes translated to another language just forward and not backward, i.e. without validation of translation. Secondly, the assessments are neither adapted to the country nor to the context where they will be used.

Self-reported questionnaires comprising activity and participation are important to capture the PWH perspective. To ensure a true description of the patients´ views it is essential that questionnaires are validated and reliable in the context where the PWH are living. When HAL was developed in the Netherlands 2004, a Swedish version and tests for its validity seemed to be a good idea to get a PROM for evaluating Swedish PWH with good measurements properties. Once HAL was validated it could be used to investigate the usefulness of the instrument, to see what happens over time with the cohort assessed with HAL. There is no published long term follow up using HAL thus far. The recent published data is an overview about the correlation between the more objective and the self-assessed instruments in a young haemophilia cohort, showing the low correlations between HAL and objective measures.[80] The importance of participation and the factors that influence the levels of participation are highlighted as very important for the PWH and their families and it is a challenge to develop measurements to meet these expectations[98] From the patients´ perspective, it is also important that collecting the measurements is not time consuming.[98] Studies that capture the experience of being PWH are few and they often focus at one subject such as prophylaxis treatments[99,100] or ageing-related issues.[101] There is no published interview study from Sweden to our knowledge. Therefore studying Swedish PWH seemed to be necessary in order to increase knowledge about how PWH experience life and various contacts in their community and health-care since social contexts, laws and regulations vary between countries.

AIM

The overall aim of this thesis was to describe self-reported activity and participation in adult persons with hemophilia in Sweden and explore their experiences of living with haemophilia.

Specific aims

The specific aims were:

Study I To test the validity of the Swedish version of the Haemophilia Activity List, HAL.

Study II To investigate the self-reported activity and participation with HAL, AIMS 2 and IPA in the daily life of persons with haemophilia living in Sweden and explore the differences between participants with early treatment onset and participants with later treatment onset.

Study III To describe the self-reported activity and participation using HAL in persons with haemophilia and to explore whether there is a change over time in activity and participation after 2.5 years between the assessments.

Study IV To explore the lived experiences and coping strategies in persons with haemophilia living in Sweden.

METHODS AND PARTICIPANTS

Method

This thesis comprises four studies using different methodologies to explore how activity and participation are influenced in adults with haemophilia living in Sweden. An overview of the study design and included study groups are seen in Table 2.

Table 2. *An overview of the study design and study groups*

Study	I + II	III	IV
Design and data collection	**Quantitative descriptive Convergent Validity study Questionnaires**	**Quantitative descriptive Longitudinal study Questionnaire**	**Qualitative Individual Interviews study**
Analysis	**Non-parametric statistics within and between group comparisons Parametric statistics for data with normal distribution**	**Non parametric statistics for ordinal paired data developed by Svensson**	**Empirical Phenomenological Psychological Method, EPP**
Invited Adult Swedish PWH, haemophilia A and B Severe and moderate form, n	**All available 225**	**All available 261**	**Convenient sample at HTC Sahlgrenska Available PWH, 31**
Study group, n	**84**	**129(longitudinal: 61)**	**14**
Total response rate %	**37**	**49**	**-**

Abbreviations: HTC Haemophilia Treatment Centre, EPP Empirical phenomenological psychological method

All studies were conducted at Gothenburg University, Sahlgrenska Academy. The recruited PWH in studies I-II and III were from all three haemophilia treatment centres (HTC) in Sweden (Karolinska University Hospital, Solna,

Skåne University Hospital, Malmö and Sahlgrenska University Hospital, Gothenburg). The PWH in study IV were recruited from the HTC at Sahlgrenska University Hospital, Gothenburg.

Study Design

The studies I-II in this thesis had a cross-sectional study design and in study III a longitudinal follow up was conducted with those who had answered HAL twice. In study I-II-III all available PWH in Sweden meeting the inclusion criteria were invited by a letter to participate, see table 2 and figure 3. Study IV had an explorative design and a convenient sample were recruited from a single HTC in Sweden, see table 2 and figure 4.

Participants

In all four studies the included PWH were adults, ≥18 years of age. The inclusion criteria were the diagnosis of haemophilia A or B, moderate or severe form and able to read, speak and understand Swedish. In studies I-III all participants were male, with the exception of one female. In study IV all were male. In figure 3 and 4 the populations in each study are illustrated. An overview of the included participants is presented in table 3.

Table 3. *An overview of the included PWH in the studies and Drop-outs for study I-III.*

Study	I + II	Drop-outs I+II	III	Drop-outs III	IV
Study group, n	84	134[a]	129	131	14
Age, mean, SD, years	45±17.7	36±14.2	43±17.6	37±14.9[b]	42±18.6
Treatment onset, n early/ later	43/41	103/31	61 29/32	93/37	7/7
Haemophilia A, %	70	84	78	80	71
Haemophilia B, %	30	16	22	20	29
Severe form, %	72	75	76	69	71
Moderate form,%	28	25	24	31	29

[a]*n=7 missing data* [b] *n=1 missing data*

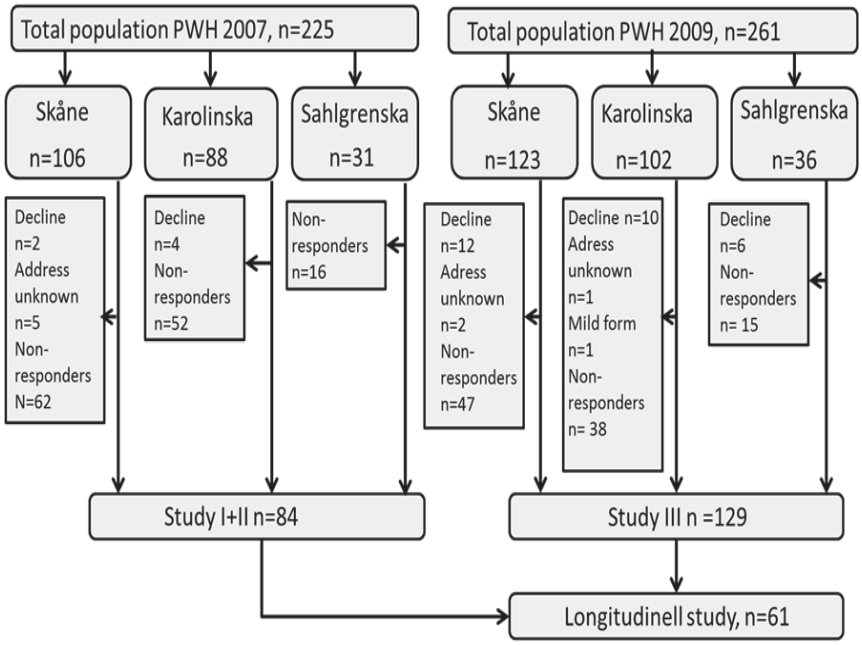

Figure 3. The flow chart over the studied populations in study I, II and III Skåne (Skåne University Hospital), Karolinska (Karolinska University Hospital) and Sahlgrenska (Sahlgrenska University Hospital)

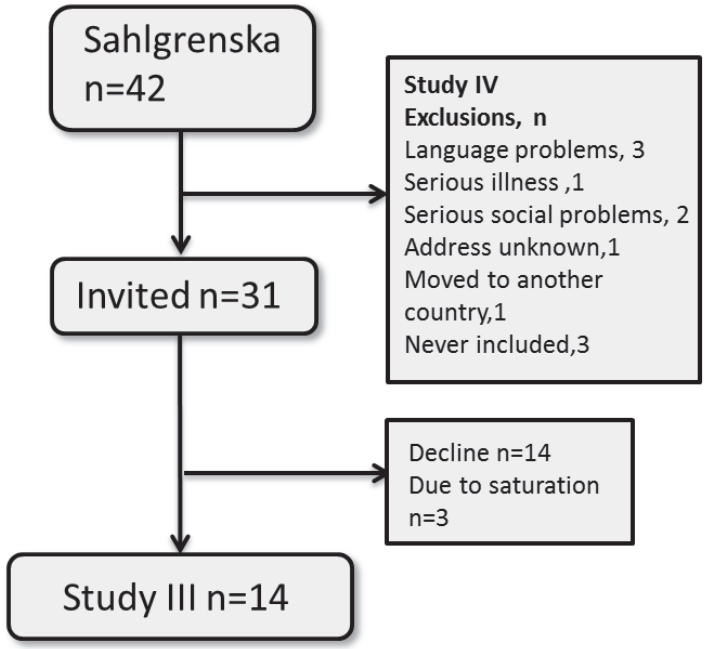

Figure 4. The flow chart over the including PWH for study IV. Haemophilia Treatment Centre, HTC at Sahlgrenska University Hospital, Sahlgrenska

In Sweden, in the mid 1960s PWH received treatment with the clotting factor.[17-19] In studies II-IV the study group was divided into two groups; an early (born approximately 1965 or later, 18-45 years old) and a later treatment onset group (born before 1965, ≥46 years old). Of the population in studies I-II 61 PWH also participated in study III. In study IV a convenience sample was gathered of the 42 available PWH at HTC, Sahlgrenska University Hospital due to severity of the disease, age, and place of residents. Thirty-one received a written invitation and 17 agreed to participate. There was a wide age span and participants lived in a wide variety of places from the area around the HTC. Fourteen PWH were interviewed to get saturation of data.[102]

Drop-Outs

In studies I-II six patients declined to participate without any explanation and five patients could not be reached by mail. Of the available population (n=214) the response rate was 39%. The remainder, were non responders (n=130) (58%).
In study III 28 PWH (11%) declined to participate, 3 of the drop-outs had an unknown address and one person had the mild form of hemophilia and did not fulfill inclusion criteria. The response rate of the available population (n=229) was 56%.The non-responders were 100 persons (38%), figure 3.
In table 3 all known (n=134) drop outs in studies I-II and study III are presented together with the participants. The drop-outs range of age in study I-II was 18-89 years and in study III 18-91 years. In both cohorts one of the drop outs was female. The non-responders were significant younger than the participants in both studies I-II and III and in studies I-II there was a significant difference in diagnosis between hemophilia A and B, where the haemophilia B was more common among the participants.
Of the 42 available PWH to be included in study IV, 11 PWH were not invited due to different reasons; three had language difficulties, one was seriously ill, one had an unknown address, two had serious social problems, one had moved to another country, and three were never included due to an error in the inclusion procedure. Of the 31 PWH invited to participate 14 (45%) declined. The available population and the PWH that were not interviewed are described in the interview study (study IV).[103]

Measurements properties

When constructing a new questionnaire the measurements properties should be as good as possible meeting the purpose of the assessment. Self-reported questionnaires are often constructed as a multi-item questionnaires measuring general or disease specific phenomena such as health, symptoms, disability etc. The questionnaires are mostly built up with response options from the extremes, worst and best with a number of scale steps in between. It is a rank ordered ordinal scale; the distance between the scale steps is not known and cannot be treated as a ratio scale statistically.[2] There are four classical scale types which need to be considered when using statistics. These are nominal,

ordinal, interval and ratio scales.[2,104] HAL is an ordinal scale. Before a new scale can be used some properties have to be examined. First the ***validity*** meaning the degree to which the questionnaires measures what they intend to measure.[105] The validity term could be split into different components with various degrees of strength. In this thesis the content validity was investigated for the Swedish version of HAL by convergent validity relating HAL to scales in other questionnaires measuring similar constructs. The second, the ***reliability,*** indicating the extent to which a measurement gives consistent result when repeated.[106] Reliability describes the precision that can be expected under comparable conditions.[2] The variability in test scores is due to errors in measurement.[2,104] A good assessment has high validity and high reliability, as shown in figure 5.[2] The reliability of the HAL scale was analyzed through internal consistency using Chronbach´s alpha of the HAL domains. Also the Bland Altman's graphs were used to visualize the limits of agreements as systematic variations around zero.[106]

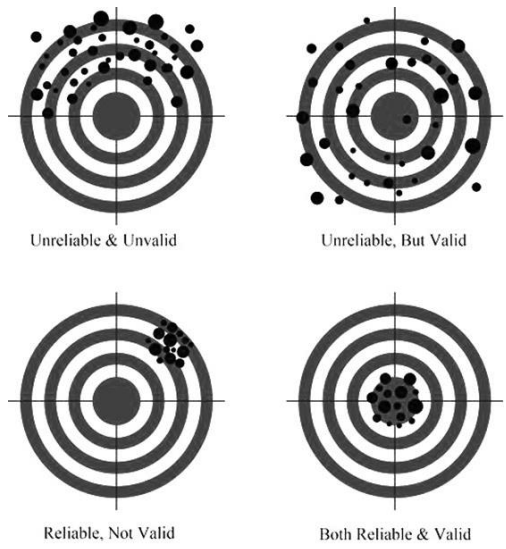

Figure 5. A visualization of the variations of validity and reliability of different assessments. The black dots illustrate the individual measures.

Outcome measures

Haemophilia Activity List, HAL

The Haemophilia Activity List is a haemophilia disease specific self-reported questionnaire developed in accordance with ICF,[74] for PWH measuring the activity and participation.[75] The questionnaire has 42 items with 6 possible answers in an ordinal scale ranging from impossible to never. In some questions not applicable can also be chosen. It was developed in the Netherlands and is available in several languages. It is divided into 7 domains: *Lying/sitting/kneeling/standing* (8 items), *Function of the legs* (9 items), *Function of the arms* (4 items), *Use of transportation* (3 items), *Self-care* (5 items), *Household tasks* (6 items), and *Leisure activities and sport* (7 items). There is a sum score; *HAL overall* (42 items) and 3 complex domains; 1/ *Basic lower extremity function* (6 items), 2/ *Complex lower extremity function* (9 items) and 3/ *Upper extremity function* (9 items), see figure 6.[75] It

has been developed according to the biopsychosocial model presented in the ICF.[57] Each item is classified according to domain 'd' of the ICF: activities and participation.[57,78] HAL has a normalized scoring system adjusted for missing values ranging from 0-100 where 0 is bad and 100 is good. The Swedish version of HAL is presented in Appendix 1.

Arthritis Impact Measurement Scale 2, AIMS 2

The Arthritis Impact Measurement Scale (AIMS) is designed for measuring the disease-specific outcome in arthritis measuring physical, social, and emotional well-being.[107] The extended version, AIMS 2[108] has been translated into Swedish and is shown to be reliable and valid for individuals suffering from rheumatoid arthritis.[109-111] The Swedish version used in these studies includes 78 items and evaluates the following 3 complex domains: *Physical* (33 items), *Social* (9 items), *Psychological* (10 items) and 12 health status scales: *Mobility level* (5 item), *Walking and bending* (5 items), *Hand and finger function* (5 items), *Arm function* (5 items), *Self-care* (4 items), *Household activities* (4 items), *Social activities* (5 items), *Support from family and friends* (4 items), *Arthritis pain*(5 items), *Work* (5 items), *Level of tension* (5 items) and *Mood* (5 items)[109,110,111] The score is a 5 step ordinal scale. Higher scores indicate greater disability. The Swedish version of AIMS 2 does not use a sum score.

Impact on participation and autonomy, IPA

The IPA assesses the person's participation according to the ICF.[112-115] In this study, a Swedish version of the IPA was used containing 41 items divided in the following domains: *Autonomy indoors* (7 items), *Autonomy outdoors* (5 items), *Family role* (7 items), *Social activities* (6 items), *Work and education* (6 items).[116] IPA is a generic instrument that can be used for adults with different chronic diseases to measure self-reported perceived participation and experienced problems. The score is an ordinal scale from 0-4 or 0-2 respectively. A higher score represents more restrictions in participation or greater experienced problems. The Swedish version of the IPA does not use a sum score. The Swedish version has been validated for spinal cord injuries.[116]

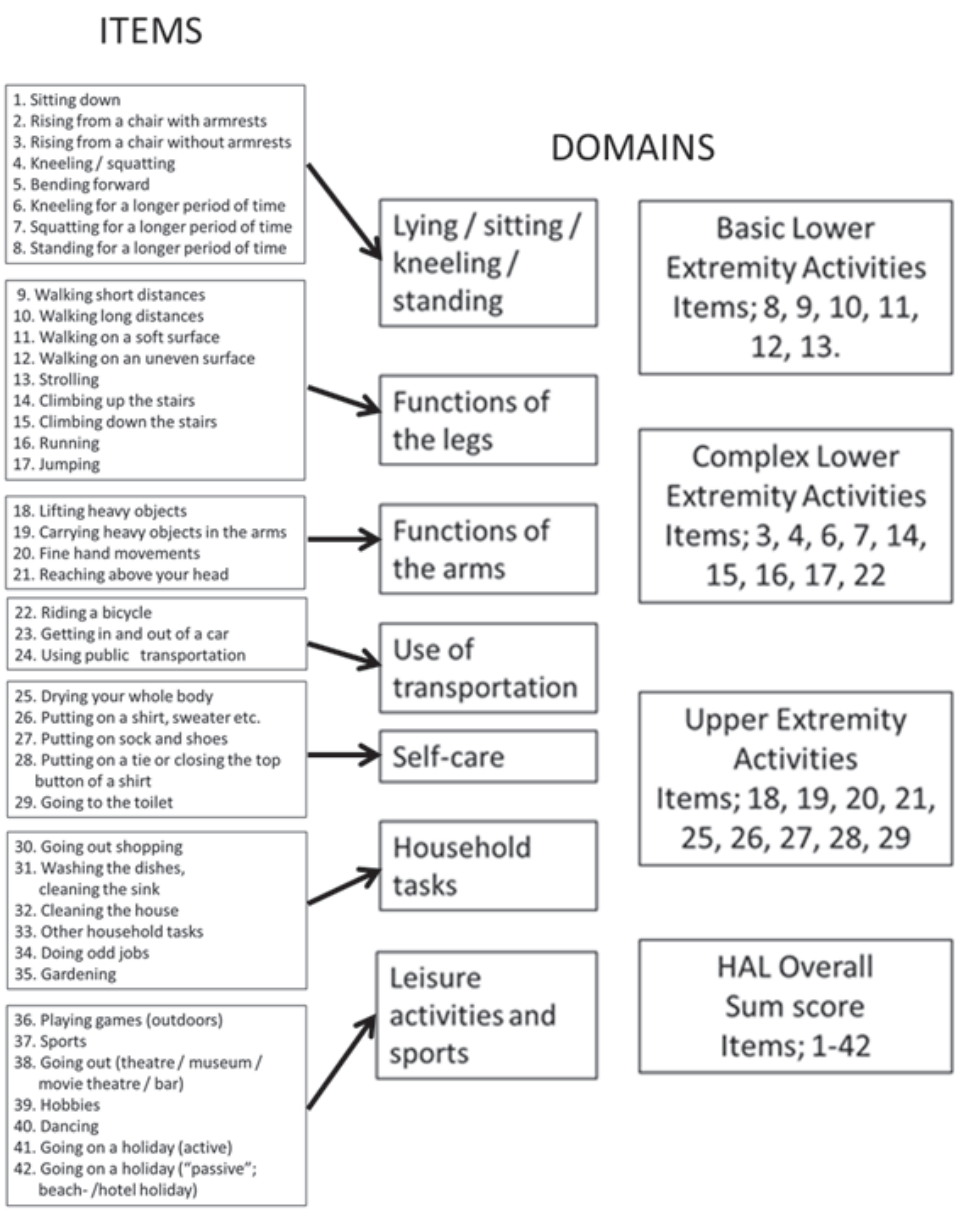

Figure 6. The Haemophilia Activity List. Items and domains. The overall question is: In the previous month, did you have any difficulty due to haemophilia with:….

Phenomenology

To enhance knowledge of what it is like being a PWH a phenomenological method was selected for a deeper understanding. Phenomenology is a philosophy but also a method to describe and elucidate individual experiences.[117] Phenomenology is characterized by perceiving phenomena in a specific cultural and societal context.[118] The most important focus is a person´s own 'lifeworld' that is the person´s directly experienced phenomena and goes "back to things themselves".[118] The phenomenological approach describes the meaningful world of individuals´ experiences.[118] The importance of bracketing presuppositions during the research process and to finding the essence of the phenomena have been described as important.[119] 'Lifeworld' research emphasizes on knowledge in everyday life, as experienced before theorization.[117,119] 'Lifeworld' is studied in a non-reductionist way, as it is shown in all its variation and complexity.[119] Giorgi suggested a four step procedure; reading the entire description to get a general grasp of the contents; to find meaning units; finding psychological insight of the meaning units; synthesizing meaning units into a statement regarding the person´s experiences.[119] Merleau-Ponty highlighted that fundamental to his epistemological approach is the belief that the 'lifeworld' paves the way for knowledge and thus founds scientific knowledge about the lives of humans and the world.[120] Furthermore, he also stated that the human body is not an object but a center for carrying experiences.[120] This can be interpreted as we are our bodies when experiencing the 'lifeworld' but we also have a body and can examine and communicate about that body. This means that the body is both a subject and an object and this is expressed by "the lived body".[120] It is through our body that we live and comprehend the world. "The lived body" is purposeful and gives access to the world and there is no perceived separation between body and self.[120]

Empirical phenomenological psychological method, EPP

The method used in the interview study was the Empirical Phenomenological psychological method, EPP according to G. Karlsson.[117] EPP is a descriptive qualitative method with a 'lifeworld' perspective in which the purpose is to answer the question of what the phenomenon is and how it is experienced. The 'lifeworld' is characterized by intersubjectivity, that is that the world is shared by persons but could be experienced differently.[117] In this thesis, the meaning structure of PWH´s lived experiences of their life-long disability

due to hemophilia was in focus, with the aim to understand and deepen the knowledge about how PWH experienced their situation and what strategies they used to cope with their disability. The imbued meanings of the collected facts are the purpose of the analysis. The researchers strived to be as open as possible to the interview text to discover experiences and coping strategies. Further, the analysis has an inside perspective, the purpose is to avoid to explain or describe a concept or a theory of the experience itself. The EPP method is also characterized by hermeneutical elements. These elements are the researcher´s pre-understanding of the phenomenon and the hermeneutical circle is the understanding of the whole and the parts. Reduction of the objects is performed in a way that results into the construction of meaningful units.[117] The analysis in EPP is divided into 5 steps searching for the meaning structure of the experiences. The results are mentioned as general characteristics for the experiences all interviews articulated and as typologies when the experiences differed between the interviews. The 5 steps are:

Step 1. The transcribed interviews are read until a good grasp of the contents are obtained. The analyses started in an unbiased open manner in order to understand the whole.

Step 2. The interview texts are divided into smaller meaning units where a shift in meaning is identified in accordance to the purpose of the study. The meaning units are to be regarded as parts of the coherent wholeness.

Step 3. Eidetic induction that is transforming what the participants supplied to a significant and implicit meaning of the phenomena in objectivised psychological terms.

Step 4. The transformed meaning units are organized into coherent categories and with repeated consultation with the interviews. This step means synthesizing the transformed meaning units into a situated structure of each interview that is what the phenomenon is. Also the process is described, that is how the phenomenon is lived.

Step 5. The final step according to the method is to move from the situated structure of each protocol to a so call “general structure”. The eidetic constituents of all situated structures were called “general characteristics” in this study. It was discovered that the phenomenon

contained some "types" of situated structures so called "typological structures" named "typologies" here.

Also in the interview study (study IV) coping strategies were looked for in every transcribed individual interview, identifying task and emotional coping strategies.[88]

Procedure and data collection

In all four studies the PWH were invited to participate by mail. In studies I-III, if they wanted to participate, they returned the questionnaires and the written informed consent at the same time. Those who did not respond after the first invitation received a reminder letter after 4–6 weeks. In study IV the PWH who wanted to participate replied by returning their written informed consent forms and after that they were contacted by phone to book the location and time for the interview. Demographic data were collected in a separate sheets included in the survey (studies I-III), and together with the individual interviews in study IV. In studies I-II the demographic data sheet included: age, gender, marital status, children living at home, assistance from the community for daily activities, social situation which included options for; working, studying, receiving a disability pension, retired, unemployed and sick-leave. For social situations more than one option could be ticked except for retired. Comorbidity was also asked for. Haemophilia form and type, data regarding treatment with clotting factor either prophylaxis or on demand, was gathered in study I and II. In study III, history of inhibitors and orthopedic surgery for the common joints, knees, elbows, ankles as well as hips and shoulders, were gathered in the demographic questionnaire. In study IV the demographic questionnaire did not include social situation or treatment. In study IV the haemophilia form and type was gathered from medical record. The three demographic sheets are shown in Appendices 2,3,4.

Study I

Translation

First, permission from the original HAL developer sought for creating the Swedish version. Two versions of HAL were used, the original HAL in Dutch and a version available in English. The forward-backward translation

procedure according to Ware JE[67] was used and conducted in following manner:

- The forward – backward translations of the Dutch version to Swedish was performed by 2 bilingual native Dutch speaking persons.
- The translation from English to Swedish was performed by the author (native Swedish speaker) and then backward was performed by a bilingual person, a native English speaker.
- The original developer of the HAL recommended a translator who reviewed the two translated versions in Swedish critically and made comments on the content before they were translated back into Dutch and English.
- The two Swedish versions were merging to one after the above procedure and another Swedish native speaking person gave feedback on the vocabulary used and grammar before the Swedish final version was made and set.

The original HAL scoring system was retained in the Swedish version of HAL.

Validity

The validity (convergent) testing of the Swedish version of HAL was performed in the same way as the original Dutch validity study.[75] Internal consistency of the HAL domains and systematic changes in the mean values between the different domains of the different questionnaires comparing HAL with the already-established one were calculated.

Study II

The self-reported difficulties in activities and participations were presented from the PWH by the three different questionnaires; HAL, AIMS 2 and IPA. The results are presented both for the whole group and divided in early and later treatment onset groups.

Study III

Of the respondents in study III, 61 PWH had also answered HAL in study II. The result from the HAL questionnaires for the whole group and the result

over time for PWH, who answered twice, 2.5 years in between, were presented divided into early and later treatment onset groups.

Study IV

The PWH were interviewed during the spring of 2012. All interviews were performed individually by one of two persons with knowledge of interview technics[121] but with no specialist knowledge of haemophilia. When fourteen PWH had been interviewed no new aspects appeared. We assessed that enough information was gathered for the purpose of the study and due to saturation.[102,122,123] The participants chose the time and place for their in-depth interview. Each interview lasted from 1 to 1.5 hours. The interviews were performed using an interview guide with open-ended questions such as; "How do you experience living and dealing with haemophilia?" "How does haemophilia influence your life situation now and during your childhood?" "How do you experience your health-care?", see Appendix 6. The interviews were recorded with a digital tape recorder and transcribed word by word. No repeat interviews were performed and no transcripts were returned to participants.

Statistical analysis

The ordinal scales (studies I-III) of the measurements were analyzed with non-parametric statistics. Data were presented as the median and measures of dispersion used were range or min-max for each domain from the different questionnaires or a 95% confidence interval. For comparisons between groups the Mann–Whitney U-test, was used with a significant level of $p \leq 0.05$. Box plots were used to illustrate the differences between the two PWH groups. No power-analyses were performed due to the small sample of the total PWH population in Sweden. Parametric analysis was used for continuous variables. The results were expressed as mean and standard deviation (±SD) for data with normal distribution was used, e.g. the age of the PWH.

For HAL, the normalized score for the domains from the raw score was performed according to the mathematical formula 100-((Σ of the item raw score - number of valid item)*(100-/(5*number of valid item)).[75] If an item had been answered "not applicable" it was defined as not valid in the formula. In study I and II a conversion of the score was also done to facilitate

the comparison. For IPA and AIMS 2 the Swedish manuals were used and the scores were then normalized proportionally so the scale was 0-100 for each domain proportionally. Spearman's rank correlation was used for validation, assessing the correlation between HAL and AIMS 2 and IPA. Excellent correlation was defined as $r \geq 0.8$. [75] Good correlation was defined as $0.6 \geq r < 0.8$. [75] Low correlation was defined as $r < 0.6$.[75] The internal consistency of the HAL domains was calculated with Cronbach's alpha. Bland–Altman graphs were used to assess systematic changes in the mean values between the different domains of the different questionnaires, comparing the new diagnostic tool with the already established one. The Bland Altman graphs are commonly used for quantitative ratio scale to compare two different methods. The differences between the normalized result of HAL and the other questionnaires were plotted against the mean of the normalized result of HAL and the other questionnaires. The graphs illustrate variations around zero. The graph displays a scatter diagram of the differences plotted against the averages of the two measurements. Horizontal lines are drawn at the mean difference and at the mean difference ± 1.96 times the standard deviation of the differences.[124] In study III changes over time were analyzed item by item by pairing off the assessments of each item for the two time points. The percentage agreement (PA) of identical pairs was calculated and differences were evaluated by a method that identifies and measures the group-related systematic disagreement separately from the additional individual variability by the Svensson method.[125] A more detailed description of this method is found in the study III. An overview of the statistical methods used is shown in table 4.

Table 4. *An overview of the used statistical methods in the studies.*

Methods	Study I	Study II	Study III	Study IV
Descriptive statistics				
Mean (SD)	X	X	X	X
Median (Min-Max) (Range)	X	X	X	
Percent	X	X	X	
Numbers		X	X	X
Differences between groups and over time				
Mann Whitney U test	X	X	X	
Rank invariant analys method á Svensson			X	
Convergent Validity				
Spearman´s correlation coefficient	X			
Reliability: (Internal consistency) (systematic differences)				
Cronbach alfa	X			
Bland Altman plot	X			

Data analysis

Data were analyzed using the IBM Statistical Package for Social Sciences (SPSS version 15-19) Inc, Chicago, Ill, USA (SPSS,). Statistical significance level was defined as $p < 0.05$. In study III the 95% confidence interval (CI) of relative position (RP), relative concentration (RC), and relative rank variance (RV) and the construction of rank-transformable pattern of agreement (RTPA) were calculated using free software.[126]

Ethical Considerations

All studies were approved by the Regional Ethical Review Board in Gothenburg, Sweden, Dnr.653-06 (studies I-III) and Dnr.1057-11 (studies IV). Written and oral information about the studies were given to the participants and informed written consent was obtained from all participants in connection to their participation. The PWH were allowed to withdraw their participation from the studies at any point without giving a reason.

RESULTS

Demographics of participants

The demographic data of the participants in studies I, II and III are presented in table 5 and the corresponding information for study IV are presented in table 6. In studies I-II 78 PWH were born in Sweden. One was born in another Nordic country, one was born in an oversea country and 4 were born in another European country. The level of education and household income before tax are seen in table 7. In the Manuscript of study III the demographic data are seen for the PWH divided in the two treatment groups.

Table 5. *Demographic data for the entire study group (studies I+II and III).*

		Study I+II n	Study III n
Marital status n=81 (I-II) n=126	Married/de facto	47	79
	Single/divorced	34	47
Children living at home n=81(I-II) n=129	Yes	19	35
	No	62	94
Assistance from the community for daily activities n= 82(I-II) n=127	Yes	2	3
	No	80	124
Social situation *	Working	46	77
	Studying	11	16
	Disability pension	19	25
	Retired	13	22
	Unemployed	5	14
	Sick-leave	6	7
Educational level n=80	University	27	
	Secondary school (2 or 3 year)	37	
	Training school	3	
	Elementary	7	
	Community college	6	
Household income before taxes (year 2007) SEK n=82	0-100 000	10	
	100 001-200 000	14	
	200 001-300 000	15	
	300 001- or more	43	

*n=number of respondents answered. *Possible to give more than one response.*

Table 6. *The demographic data for the PWH in the interview study (study IV).*

	Participants	LT	ET
Individuals with haemophilia, all male (n)	**14**	**7**	**7**
Marital status (n)			
Married	**6**	**5**	**1**
De Facto	**2**	**1**	**1**
Single	**6**	**1**	**5**
Working (n)	**6**	**2**	**4**
Studying (n)	**3**	**0**	**3**
Sick-leave (n)	**2**	**2**	**0**
Disability pension (n)	**3**	**3**	**0**
Retired (n)	**2**	**2**	**0**
Concomitant diseases (n)	**6**	**4**	**2**

LT=later treatment onset, ET=early treatment onset

Concomitant diseases, comorbidities, mentioned by the participants in the interview study IV were hepatitis, diabetes mellitus, kidney disease, hypertension, psoriasis arthritis, kidney stones, pollen allergy, depression, and attention deficit hyperactivity disorder (ADHD). In study II the main concomitant diseases for the whole group were hypertension (30%), liver disease (27%), back pain (20%) and other diagnosis (29%). Activity limitations were specified particularly in other diagnosis (12%) and in back pain (9.5%). In the ET group 86% had prophylaxis and most common was 2-4 times/week and in the LT group the corresponding figure was 76% and 2-3 times/week. In the manuscript of study III corresponding figures are presented for the study population divided in ET and LT group for comorbidity, prophylaxis, inhibitors and orthopedic surgery. The pattern of comorbidities follow the above in the whole group, but the ET group has fewer comorbidities generally, see study III.

Validity of the Swedish version of Haemophilia Activity List

The Swedish version of HAL had a high convergent validity and is comparable to the original Dutch version. Spearman's rho for the different compared domains are presented in study I.[127] The HAL domains were compared initially with the AIMS 2 *Walking*, AIMS 2 *Physical*, IPA domains *Family role*, *Mobility indoors* and *outdoors* with correlations that were excellent or good (r=0.91-0.72, P < 0.01). The correlation analyses between *Function of the Arms* and *Upper extremity* domain of HAL showed good correlation with AIMS 2 domains of *Hand and Finger function* (r = 0.68) and *Arm function* (r = 0.68). *Self-care* domain of HAL correlated well with *Hand finger function* (r = 0.68) and *Arm function* (r = 0.71) of AIMS 2, but showed a poor association with AIMS 2 *Self-care* domain (r = 0.48). The domain of *Self-care* from AIMS 2 did not show any good correlations with any domains of the HAL questionnaire. The convergent validity of the different domains of HAL, AIMS 2 and IPA in the subgroups of patients divided in moderate and severe forms of haemophilia respectively were equal. The results showed that domains that involved the lower extremities demonstrated good correlation in contrast to the domains that involved the upper extremities.

There were no significant differences in any domains regarding the results of HAL score between the moderate and severe haemophilia patients, see study I.[127]

Reliability of the Swedish version of the Haemophilia Activity List

According to the Cronbach´s alpha the internal consistency of the Swedish version of HAL was high. The highest internal consistency was shown in the two domains involving the lower extremities; *basic* and *complex* f*unction of the legs* and the *HAL Overall sum score*, while *Transportation* demonstrated the lowest value, see table 7.

Bland–Altman graphs for HAL and the domains AIMS 2 physical, IPA indoors, outdoors and family visually illustrated the systematic variation around the zero line for the different domains of the questionnaires.[127] The

visual analysis showed a proportional and systematic difference between the scales and individual variations between the HAL sum score and the AIMS 2 physical domain, see figure 7. Systematic difference between the scales was also demonstrated for the IPA indoors domain and *HAL Sum Score*. However, regarding the two domains of IPA outdoors and family role, there were no large differences between the scales.

Table 7. *The internal consistency of the Swedish version of HAL*

HAL: Domains	Items (n)	Cases (n)	Cronbach's α
HAL: overall	**42**	**75**	**0.98**
Lying/sitting/kneeling/standing	**8**	**82**	**0.95**
Function of the legs	**9**	**82**	**0.98**
Function of the arms	**4**	**84**	**0.90**
Use of transportation	**3**	**82**	**0.71**
Self-care	**5**	**83**	**0.91**
Household tasks	**6**	**82**	**0.92**
Leisure activities and sport	**7**	**81**	**0.89**
Basic lower extremity function	**6**	**81**	**0.98**
Complex lower extremity function	**9**	**81**	**0.96**
Upper extremity function	**9**	**83**	**0.93**

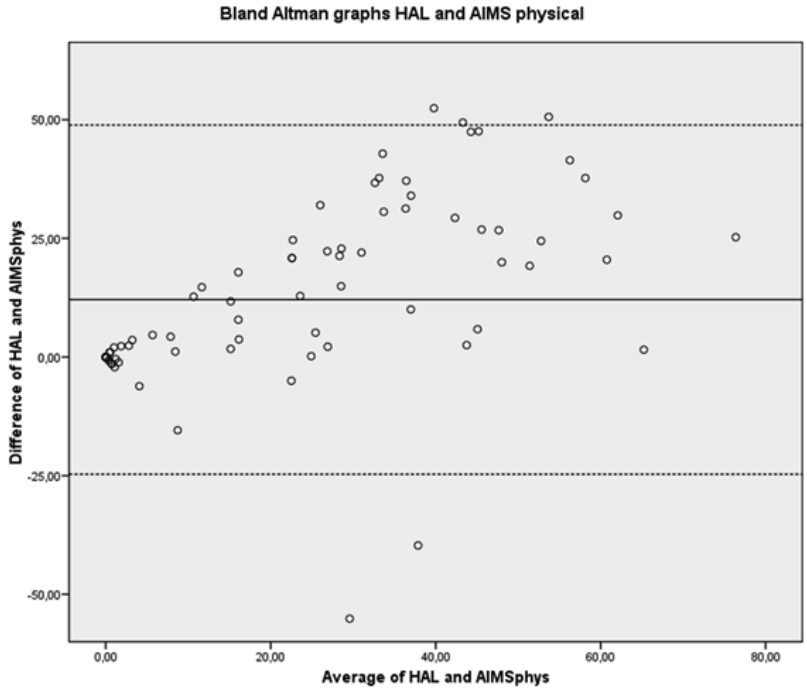

Figure 7. Bland Altman illustrating the systematic error between the HAL sum score and AIMS 2 Physical. The dots are mostly located in the upper field of the graph, which illustrate the lack of agreement.

The reliability of the Swedish versions of IPA and AIMS 2 for Persons with Haemophilia

The internal consistency for IPA and AIMS 2 is presented in table 8 and 9. IPA for Swedish PWH showed high internal consistency in all five domains (0.96-0.77). The lowest value was for work and education (0.77)

Similar numbers presented for AIMS 2 with high values for internal consistency (0.95-0.72) in 14 of 15 domains. Domain number 15, *Work*, had a Cronbach's alpha of 0.36 and was the lowest overall, see table 9.

Table 8. *Reliability for the different domains in the Swedish version of IPA*

IPA domains	Items (n)	Cases (n)	Cronbach's α
Autonomy Indoors	7	83	0.96
Autonomy Outdoors	5	80	0.89
Family role	7	79	0.96
Social life and relationship	7	80	0.86
Work and education	6	62	0.77

Table 9. *Reliability for the different domains in the Swedish version of AIMS 2*

AIMS 2: Domains	Items (n)	Cases (n)	Cronbach's α
Physical	33	70	0.94
Social	9	79	0.75
Psychological	10	81	0.89
Mobility level	5	84	0.79
Walking and bending	5	82	0.87
Hand and finger function	5	82	0.95
Arm function	5	82	0.72
Self-care	4	82	0.95
Household activities	4	81	0.94
Social activities	5	84	0.82
Support from family and friends	4	79	0.88
Arthritis pain	5	75	0.94
Work	4	49	0.36
Level of tension	5	81	0.83
Mood	5	83	0.82

Self-reported Activity and Participation

The score of the different domains in HAL, IPA and AIMS 2 is presented in in study II as median for the total group.[128] The median value indicates no severe difficulties in activities however the individual spread in the answerers indicating a wide range of disability in the group. In general fewer difficulties are reported in activities involving the upper extremities in the HAL domains of Self-care and Household tasks.

When the group of PWH was divided into the ET, (n=43, 30 ±8.3 years) and LT (n=41, 61 ±9.0 years) groups some differences were seen. The ET group reported fewer difficulties than the LT group which were significant in all domains between the two groups ($p \leq 0.05$) but the ranges were wide in almost all domains. Figure 8 shows the differences between the two groups reported with HAL. For AIMS 2 and IPA corresponding figures can been seen in study II.[128]

The self-reported activity and participation at the first time point are seen for the whole group (n=84) in table 10 and the second time point in table 11. The range was wide but it showed that the domain of *Self-care* had a good result for the whole population with a median of 100, saying that at least 50% scored the best result. In study III, the group was divided into the ET and LT groups and showed significant difference between the two groups, where the LT group had reported more difficulties in activities than the ET group in accordance with the same results in study II.

A ceiling effect was present in the ET group in several of the domains. At first time point 37% reported the maximal score of the HAL Overall sum score for the ET group. By comparison, only 7% of the LT group scored the maximum. For the domain Self-Care, 77% of the ET group reported maximum score and the best score for the LT group was in the domain of transportation where 24% reported the maximum score. In IPA the reported "no problems" was more common among the ET group than in the LT group, see table 12.

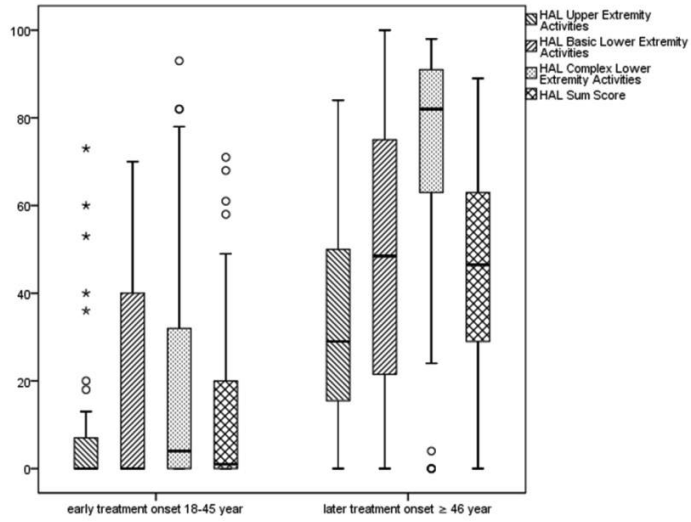

*Figure 8. The main HAL domains shown as BOXPLOT for the participants with early treatment onset and later treatment onset. In the early treatment onset group, the outliers/extreme points represent the severe form of haemophilia; these points represent the moderate form for the later treatment onset group. According to SPSS, the * are extreme points that extend more than 3 box-lengths from the edge of the box and the ° are outliers that extend more than 1.5 box-lengths from the edge of the box. 0= good and 100= bad. There were significant differences ($p<0.05$) between the two groups for all domains presented.*

Table 10. *The results of the HAL domains at the first time point for the whole study group (n=84) normalized score 0=the worst functional status and 100=the best possible functional status*

HAL domains	n	Median	Min-max
Lying/sitting/kneeling/standing	**83**	**70**	**10-100**
Function of the legs	**83**	**60**	**0-100**
Function of the arms	**84**	**85**	**10-100**
Use of transportation	**77**	**93**	**7-100**
Self-care	**84**	**96**	**8-100**
Households tasks	**82**	**97**	**13-100**
Leisure activities and Sport	**80**	**81.5**	**6-100**
Upper extremity Activities	**84**	**90**	**16-100**
Basic Lower Extremity Activities	**83**	**70**	**0-100**
Complex Lower Extremity Activities	**84**	**63**	**2-100**
Sum score	**84**	**79.5**	**11-100**

n= numbers of PWH that have answered the questions in each domain.

Table 11. *The results of the HAL domains at the second time point for the whole study group (n=129) normalized score 0=the worst functional status and 100=the best possible functional status*

HAL domains	n	Median	Min-max
Lying/sitting/kneeling/standing	**126**	**80**	**8-100**
Function of the legs	**128**	**77**	**0-100**
Function of the arms	**127**	**90**	**5-100**
Use of transportation	**121**	**93**	**7-100**
Self-care	**128**	**100**	**20-100**
Households tasks	**125**	**93**	**20-100**
Leisure activities and Sport	**113**	**86**	**0-100**
Upper extremity Activities	**128**	**93**	**16-100**
Basic Lower Extremity Activities	**128**	**87**	**0-100**
Complex Lower Extremity Activities	**127**	**76**	**0-100**
Sum score	**128**	**85**	**14-100**

n= numbers of PWH that have answered the questions in each domain

Table 12. *Reported "no problems" in the IPA domains for the two groups of PWH.*

IPA "no problem"	ET %	LT %
Mobility	**70**	**29**
Self-care	**83**	**51**
Family role	**77**	**36**
Work and education	**70/86**	**39/44**

ET= early treatment onset and LT= later treatment onset

The domains of AIMS 2 showed no significant differences between the two groups in the domains for *Mobility* level, *Self-care* tasks, *Social activities* and *Mood*. All other domains presented significant differences between the ET and the LT groups of PWH as well as the domains of HAL and IPA.

Over time the self-reported activity and participation, as measured with HAL, was almost stable over 2.5 years for all participants. The LT group showed more disability compared to the ETgroup, but over time their score was stable except for individual activities and the domain *Leisure activities and sport*. In this domain the difficulties decreased over time and were assessed as worse in some activities at the second time point. The results in this small sample showed a wide range of difficulties in a majority of activities especially obvious for the LT group and therefore individual changes over time could be obvious both as increased and decreased difficulties. The LT group compared to the ET group reported more difficulties in participation in more challenging activities over time, see study III. Figures 9,10,11 and 12 show the results over time for the ET and LT group respectively in the domains *Self-care* and *Function of the legs*. The LT group showed more individual differences and major disability in the activities but the significant changes over time were in the activity HAL 25, *dry your whole body* and 27, *putting on socks and shoes* over time, being both better and worse.

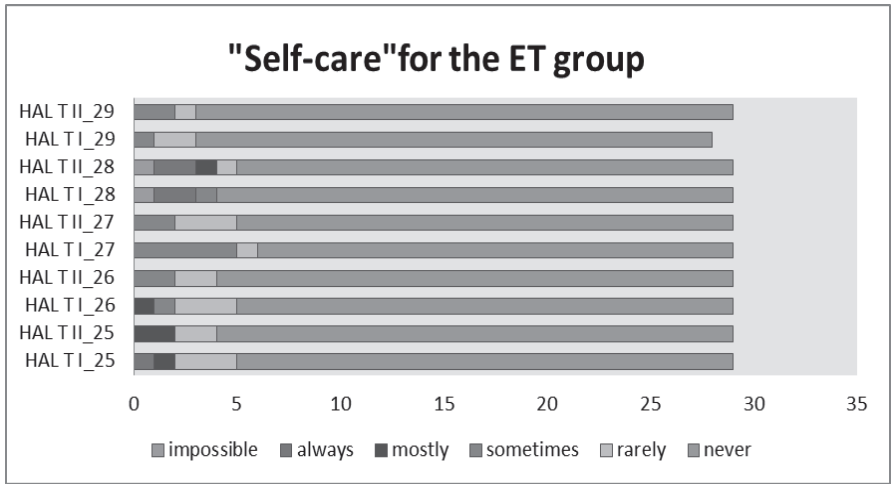

Figure 9. The results question by question for the early treatment (ET) group for the domain "Self-care". No significant changes over time. n=29 except for question no 29 (HAL T I) n=28

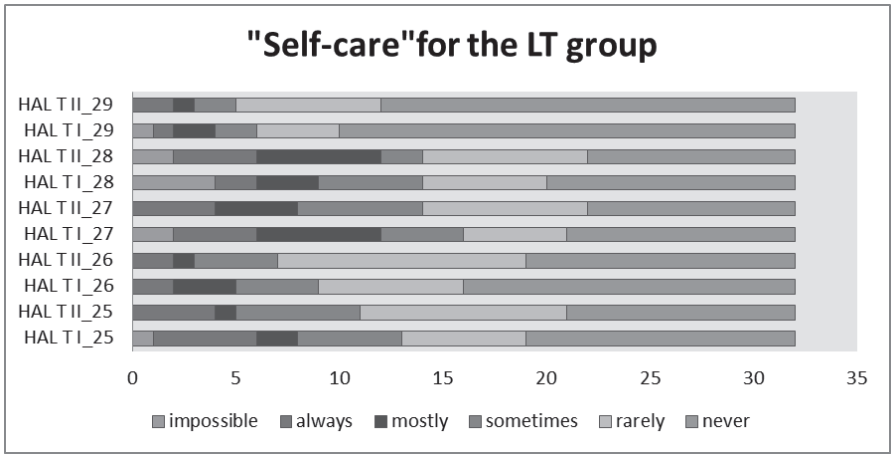

Figure 10. The results question by question for the later treatment (LT) group for the domain "Self-care". Significant changes over time in relative concentrate (RC) in HAL 25 (drying your whole body) and 27(putting on socks and shoes). n=32

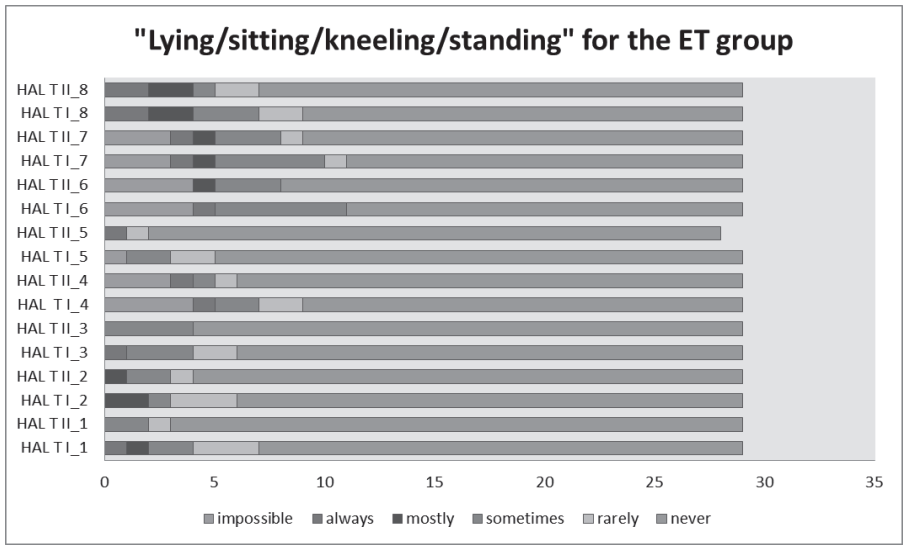

Figure 11. Domain "lying/sitting/kneeling/standing" for the early treatment onset (ET) group with significant changes over time at group level being better in HAL 1 "sitting down" and 4 "kneeling/squatting". n=29 except forHAL II 5 n=28

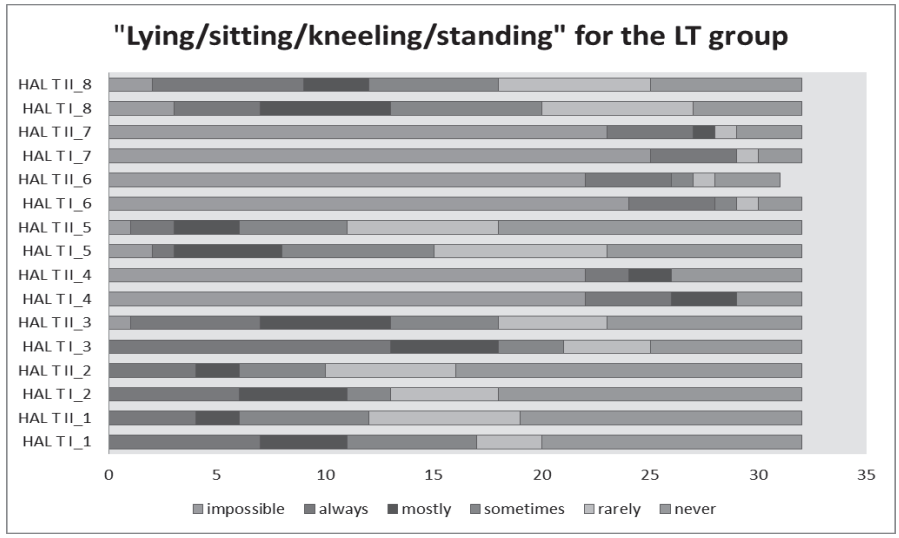

Figure 12. Domain "lying/sitting/kneeling/standing" for the later treatment onset (LT) group with significant changes over time in no 3"rising from a chair without armrest"being better at group level (RP) and no 4"kneeling/squatting" at relative rank variance (RV). n=32 except for HAL T I 6 n=31

For function involving the legs there are some changes over time in both groups but the baseline difficulties differ between the groups. The LT group had more difficulties than the ET group from baseline. The ET group had significant changes over time in 3 of the activities (*sitting down, kneeling/squatting and walking short distances*) each being better as a group and one activity (*rising from a chair without armrest*) being better for the LT group. Individual changes towards the group for the LT group are seen in the activities bending forward, walking short distances and climbing up the stairs. More detailed information for the ET and LT group in all HAL activities, see Appendix 5.

Experiences and Strategies in everyday life in persons with haemophilia

"*It´s painful to exercise but not dangerous*, *so what I've done is, I've started daily exercise instead. This means that I don´t take the car to work but I walk." (middle age PWH)*

The interview study (study IV) explored the lived experiences of everyday life being a PWH with a lifetime perspective in Swedish society. The phenomenological analysis generates an overall general structure; *prevent bleeds.* All strategies in everyday life are about preventing and dealing with the risk of having a bleed. The experiences and strategies of the Swedish PWH, the general characteristics and also the typologies according to the empirical phenomenological psychological method, EPP, are illustrated in figure 13. The general characteristics identified were shared by all PWH interviewed. Everybody praised the availability of factor concentrate and all also experienced limited participation in athletics during childhood, especially in sports where injuries were common. They all wanted to live a normal life and were coping positively with their disorder. They were prepared for pain if a bleed occurred. They were satisfied with the specialised health-care provided at the HTC and the support from caregivers working in the multidisciplinary team.
The ET group felt that they all could live an almost normal life compared with their peers. The LT group that had experienced limitations with physical activities during their childhood had to give them up due the risk for bleeds.

The four typologies found in the material are presented in Table 13 and figure 13. Strategies and citations expressed from PWH representing both individuals from ET and LT group are presented.

The most explicit strategies were task oriented according to the theory by Lazarus and Folkman. [88] Also emotional and avoidance coping strategies were discovered.[88]

The **task oriented coping** strategies were;

- acting in an assertive way when protected during up-bringing.
- planning and acting to reduce symptoms and chose suitable education and work.
- trying to influence political decisions with relation to health-care.

The **emotional coping** strategies were;

- positive attitudes to prophylaxis
- inner struggles against the disorder
- rising after crises.

One **avoidance** coping strategy was defined;

- did not inform others about being a PWH.

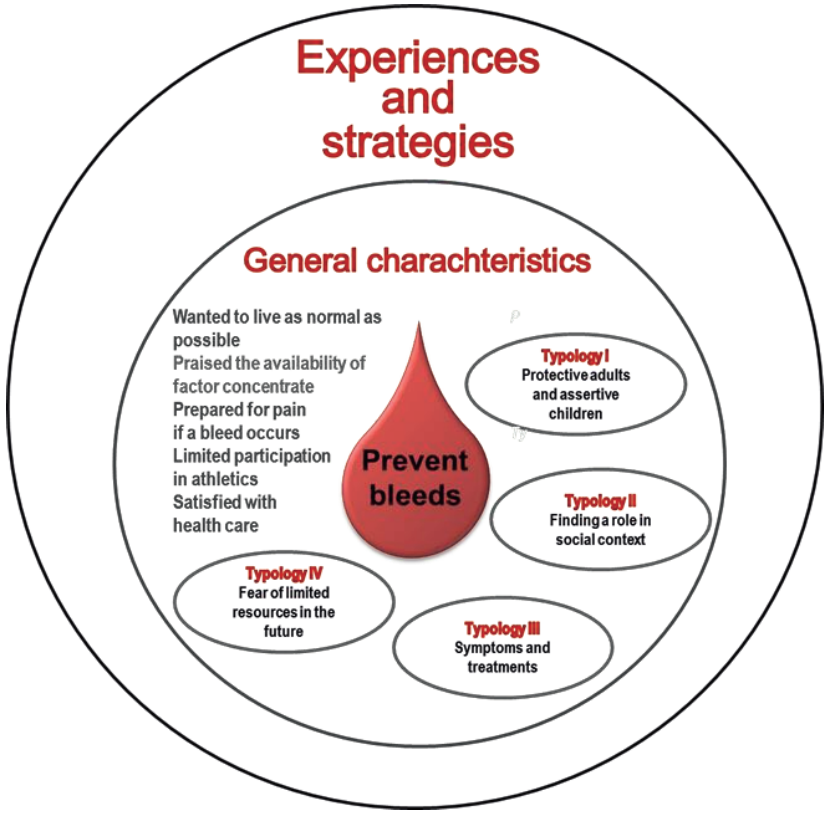

Figure 13. A schematic illustration of the findings in the study of PWH experiences and strategies being a PWH living in Sweden. The general characteristics and the typologies are presented. In the middle the essence or the core in the study of living with haemophilia.

Table 13. *Summary of Typologies and strategies included quotations from the PWH divided in later (LT) and early treatment onset (ET) group*

Typology	Experiences LT/ET	Strategies LT/ET
I: Protected adults and assertive children during up-bringing	**....”the teacher in my new class told my mates to be careful with me and I found it distinguishing” (code 15)/ ....”I lived in a room lagged with foam rubber” (code 1)**	**….” I became disorderly and fought with all (code 15)/ ….”I looked at my mates when they were playing soccer and was offered the sport clubs tracksuit and participated” (code 1)**
II: Finding a role in social context	**....” I understood that I didn´t manage any longer to work full time” (code 15)/ ....“I had to stop work as a cook because of elbow pain” (code 12)**	**....“I took the role as a judge when the others were doing sport activities” (code 2) /….”Next autumn I think it will be some education”. (code 12)**
III: Symptoms and treatments	**…. “I have still problems with my joints that are painful (because of bleedings)” (code 20)/ ….” I have a crappy ankle (due to bleeding symptoms after a sprained ankle)” (code 30)**	**….” I went in for daily physical activities…..took walks outside” (code 15)/ ….“It is really a trifle (morning ritual taking the medication) compared to not having access to medication” (code 29)**
IV: Fear of limited resources in the future	**….”When you come to an age care facility are there persons who can give you your injections?”…. (code 2)/ ….”sometimes I worry that prophylactic medication is questioned (due to societal expenses)” (code 29)**	**….” started a group in the Swedish Hemophilia Society to retain the interest of the elderly persons” (code 2)/**

DISCUSSION

In this thesis, it has been shown that hemophilia results in decreased activity and participation. This is a problem for persons with hemophilia since there are both limitations of function due to impairment and an impact of the disease on their everyday life. The activity limitations are more pronounced in activities involving the lower limbs. It was also shown that the time at which prophylactic treatment started had an impact on activity and participation as an adult with hemophilia. Those that started treatment in the earlier life reported fewer and less severe problems with activity and participation. The Swedish PWH experienced more disability from arthropathy in the lower extremities than arthropathy in the upper extremities. It was also shown that over time (approx. 2 years), the reported self-capacity in ADL was basically unchanged and about half reported no problems.
The HAL is the only disease-specific questionnaire for self-reported activity and participation in haemophilia care today and the Swedish version of HAL seems to be an useful instrument for measuring difficulties in activity and participation, such as problems with leisure time and sport. This indicates that HAL is the instrument of choice that should be used to measure self-reported activity and participation in haemophilia care and research.

Validity of Haemophilia Activity List, HAL
The validating process of the Swedish version of the HAL questionnaire with respect to convergent validity is a proper assessment tool for Swedish PWH and is comparable to the original version in Dutch. The Swedish version of HAL showed that the domain involving the lower extremities demonstrated good correlation between the domains in AIMS 2 and IPA involving the lower extremities in contrast to the domains involving the upper extremities between HAL and AIMS 2.[127] This can be explained with the disparate joint symptoms PWH and rheumatoid arthritis patients suffer from, such as elbows that are more affected in PWH and not small joints such as fingers and wrists which are commonly affected in patients with rheumatoid diseases[129,130] which the AIMS 2 is developed to evaluate.[111] For Swedish PWH high internal consistency was shown in all five domains of IPA and also for 14 of 15 domains of AIMS 2 which indicates that the domains in the questionnaires are reliable and could be used for this group of PWH. Systematic difference between the evaluated questionnaires and HAL in the validating process was

systematically tested in some domains illustrating the lack of agreement.[127] It seems natural because of the disease specific construction of AIMS 2 and HAL. There were no large differences between the scales in the domains of IPA, outdoors and family role, this is probably because IPA is a more general tool for self-reported participation and can be used for different patient groups.[112,113,115]

In this thesis HAL showed a ceiling effect when scoring the early treatment onset group. Small differences in impairments for e.g. in a single joint are not detected with the HAL instrument. This is in accordance with a study comparing results from HAL with other outcomes used in haemophilia care and the only significant correlation for HAL was with the SF-36 "physical domain".[80]

When self-reported questionnaires are used it is important to choose a validated and reliable instrument that applies to the context in which the participants live.[81,98] Although HAL has been translated into several languages, no published validation studies could be found except for the original Dutch one [75] and the present Swedish one.[127] The World Federation of Haemophilia provides a core set of assessment tools and manuals to be used globally[63] and these tools are promoted for systematically monitoring PWH over time. Due to reasons such as lack of time and resources many centres do not perform these outside clinical trials.[77] The ability of HAL to detect clinically important changes over time has yet to be established.[63]

Activity and participation

In this thesis there were differences regarding the impact of haemophilia within a group. Those that had received treatment earlier reported fewer difficulties in the HAL domains at both time points compared to the later treatment onset group. The same pattern was seen using AIMS 2 and IPA at time point 1.

Some domains for which even the later treatment onset group reported few difficulties were the domains of self-care, household tasks and upper extremity activities in HAL. In IPA, the domains of autonomy indoors, social life and relationships had lower scores than autonomy outdoors and family role. The later domains (autonomy outdoors and family role) are more challenging for persons with disabilities. In AIMS 2, the differences between the groups in the social and psychological domains were lower than in the domains that mainly involved joint and muscle function indicating despite

disability, their life situation could be satisfactory in ways that were unexpected for PWH in the later treatment onset group.
The different questionnaires measure different limitations in life. The disease-specific questionnaire HAL is most appropriate to use for measuring the activity level of PWH. If the main focus for measurement is participation, IPA may be more appropriate to use and gives the opportunity to compare the result with other populations. In the clinic, it is important to use the questionnaire that gives the answer to the questions you wish to address.

To our knowledge this is the first longitudinal follow up study without intervention showing that PWH living in Sweden over 2.5 years' time did not change their self-reported difficulties in activities and participation very much. Many of the PWH with early treatment onset reported a maximal score, having no difficulties at all. Some also reported better function over time in some activities such as sitting down, kneeling and squatting and walking short distances in the early treatment onset group and rising from a chair without armrest in the later treatment onset group. This could be due to treatment such as orthopedic surgery, physical therapy or that some had had a recent bleed the first time they filled in the HAL but not the second time. The ranges of the reported scores were wide and the cohort is small so there were individual differences.
The later treatment onset group reported a statistically significant difference over time with more complex and challenging activities such as sport, dance and managing active holidays. This greater difficulty could be attributed to ageing rather than just haemophilia related disability alone. It could be difficult to effectively evaluate what is the impact of the disease and what is normal ageing.[101] In the later treatment onset group many answered "not applicable" which could reflect that they had had orthopedic surgery to a greater extent and more prominent haemophilia arthropathy and so were no longer doing these activities. This is in accordance with a study that showed difficulties in riding a bicycle, walking at speed and participation in school sports for PWH who did not receive prophylaxis from the beginning of life but had switched to it later in life.[131] PWH with later treatment onset had in many cases already experienced haemophilia arthropathy and had disability with a decreased range of motion, muscle strength and pain when the access to clotting factor was made available.[132] The differences in difficulties of self-reported activities and participation between the persons with later treatment

onset compared with the early treatment onset indicates the need for more pronounced rehabilitation for the later treatment onset group.
This thesis showed that it was essential for PWH to prevent bleeds to make it possible to live normal life of their own choosing. They cope with their disorder, finding their own niche in social interaction. This in accordance with PWH in England where they recollected their more difficult functional level before clotting factors were available and highlighted the benefits of replacement therapy with clotting factors.[86] Many of the PWH in this thesis did not find it extraordinary to take the clotting factor routinely. One of the general characteristics of our study was that everybody praised the availability of clotting factor concentrate. Our findings were similar to two newly published qualitative studies from Canada in some ways.[101,133] The prophylaxis treatment preventing bleeds and also the need to recognize symptoms such as pain and manage risky situations regarding physical activity were highlighted in both of these studies.[101,133] Younger PWH had fewer concerns about the consequences of participating in risky activities.[133]
The PWH experienced overly protective adults throughout their childhoods and many reacted by being assertive as children, they protested against all precautions and showed for example that they could climb trees or perform other risky activities. Many had experiences of wearing helmets and other protection during childhood and participated of limited extent in athletics especially in sports where injuries were common. The young PWH participated in athletics at school on equal terms as others if they had taken the prescribed clotting factor but the older PWH had to take another role as a child to protect themselves from damage and to prevent joint bleeds and pain just like the participants in a study from England.[86]

When education and work were chosen, the PWH chose higher education and more sedentary work due to the risk of bleeding. This has also been pointed out to be more common in the group that had prophylaxis treatment since an early age vs those who received prophylaxis later in life.[131] This choice of education and work is in contrast to a study about ageing with a rare bleeding disease that found participants did not allow their diagnosis to restrict them in living a very full life with labour-intensive work and contact sports.[101]

One of the reasons for disability in spite of prophylaxis is the presence of inhibitors.[29] In this thesis the PWH with inhibitors or a history of them were

not excluded and this could be a reason for the wide range of disability, even in the early treatment onset group. About 30% of severe haemophilia A patients develop inhibitors against factor VIII[134,135] and the treatment of these PWH is more complicated and there can be a risk for more bleeding related disabilities. Over time, the ability to treat the PWH with inhibitors has improved and today with bypassing agents like rFVII, Novo Seven, and FEIBA, orthopedic surgery can be performed despite the presence of inhibitors.[136,137]

To get a more comprehensive picture of the effectiveness of the treatment self-reported bleeding rates can be used.[80] In this thesis the self-reported bleeds were gathered over time between the two time points in study III and showed that some individuals reported many bleeds in spite of prophylaxis and no history of inhibitors in both the early and later treatment onset groups. This indicates some uncertainty about interpretation of the symptoms with regard to differentiation between bleeds and haemophilia arthropathy.
In a recently published study the economic burden from a societal perspective and the health-related quality of life of PWH in Europe was in focus.[138] They concluded that haemophilia is associated with a substantial economic burden but there are differences between countries.[138] Of the annual cost for the care of PWH, 90 % consists of drugs.[138] In Sweden the costs of the clotting factors are subsidized and society pays the majority of the costs. The PWH interviewed in this thesis were concerned that the regulations of subsidized medications would change in the future and become more restricted for the available clotting factors. The fear of future restrictions to medical treatment was obvious in their stories. The ageing PWH were also concerned whether care givers from outside the HTC, in municipal elderly care facilities, would be able to give them the clotting factor if they were unable to do it themselves when elderly.

In Sweden, as well globally, the patients' associations try to lobby for the best practice for PWH to increase activity and participation as well as health related quality of life. Overall the interviewed PWH had a task oriented coping strategy to handle situations while being a PWH. This is in agreement with a study from the Netherlands that studied coping strategies with a questionnaire and concluded the same.[95] A haemophilia diagnosis, as with other chronic diseases, requires a certain adherence to the prescribed

treatment to be able to live an ordinary normal life. Studies showed the benefits of prophylaxis treatment as a success factor to enable being active and participating in society.[139,140] Problem focused or task oriented coping seem to be effective methods for PWH to handle situations in life.

HTC care

The PWH in the interview study pointed out that it was difficult to get the right care at a primary health-care facility and praised the HTC. A study from Canada also established the vital importance of the health-care givers' knowledge of the disease in order for PWH to feel safe when visiting the clinic.[133] One of the general characteristics of our study was that all participants were satisfied with the specialized health care provided at the HTC and the support from caregivers working in the multidisciplinary team. As in a study from Canada,[101] the importance of knowledge at the comprehensive care team members about normal ageing was highlighted even in our study. The subject of "the ageing PWH" has been pointed out earlier from different viewpoints as being a challenge for the care givers at the HTC. A newly published review article pointed out the ageing PWH with a focus on complex age-related issues such as handling arthropathy, cardio vascular disease, malignancy, renal insufficiency, and liver disease.[141] These comorbidities are in accordance with the findings of this thesis and most common was the diagnosis of hypertension especially for the later treatment onset group.

The HTC care in Sweden is already organized according to a recent report from the government's official investigations, (SOU 2016:2).[142] The best option for care of a rare diagnosis with low numbers of those affected justify continuity and concentration of care with specialist teams. This concentrated care contributes to quality and efficiency.[142] The report also highlighted the importance of involving and asking the patients about their own health-care to increase their participation and adherence in said care.[142]

Methodological considerations

Statistics

Haemophilia is a rare disease and so the population of PWH is small. Studies performed that just include PWH living in Sweden, makes it difficult to get a sample size with statistical power when trying to compare groups of PWH.

This indicates that multinational studies should be emphasized if they are possible to expand the sample size and achieve greater statistical power. In this thesis the statistics are used to describe the Swedish population of PWH and the statistical calculations are chosen to suit this.

The statistical calculations had to be adapted to ordinal data of the questionnaires. In the validating study some calculations were done when comparing agreement of the scales in the study using the Bland Altman graph that is normally used for continuous quantitative data.[124] These graphs are performed with the normalized score according to the HAL manual. HAL showed good correlations with IPA and AIMS 2 and the graph used gave a view of the different questionnaires´ compatibility. When the validity study was performed the original HAL questionnaire was prepared for such calculations by normalization of the scale and used as a continuous scale. The agreement analysis was therefore performed with the Bland Altman graphs.

The study of HAL over time used another statistical method when comparing the results of HAL using cross tables, percentage of stable reported value, and the Svensson method[125], a rank-invariant non-parametric method for paired ordinal data. The raw data had an ordered structure and not a numerical value in a mathematical sense. Statistical evaluations of ordinal data must take into account their so-called rank-invariant properties, which means that the methods must be unaffected by a relabeling of the scale categories. The results are attributable to the group change, and the individual categorical changes that are not consistent with the pattern of group changes. Therefore raw data was used in study III according to the method developed by E Svensson[125,143,144] and not the normalized continuous scales as in the manual for HAL.[75] It has been used before for outcomes over time for other ordinal scales for example comparing ADL changes over time[145], social outcome after subarachnoid haemorrhage[146] and memory after surgery intervention in epilepsy.[147] For changes over time or for a reliability study of ordinal data this method is appropriate to use because it captures even individual changes in the measurements and not only systematic changes of the group.[125,143]

Study design

The results of this thesis are based on facts from self-reported questionnaires and in depth interviews.

The original HAL was translated forward-backward[67] to ensure that the linguistic translation was adapted to the Swedish context. The English language version proved to be not validated, which is way the original Dutch version became the main version of the translation process although both versions were translated.

Self-reported outcomes give the patients opportunities to be more involved in their care and balance the more clinical/objective evaluations such as laboratory tests and x-rays. Patient reported outcomes can correlate with the more objective assessments.[148] When the validating tests of the original HAL questionnaire were performed, it was concluded that it didn´t correlate with the functional tests such as button test, 50 meter walking test, timed-up-and-go test and figure-8 walking test.[75] In another study the correlations with HJHS were not significant either.[80] In the validation of the Swedish version no functional tests or joint status assessments were performed. This is because the whole adult Swedish sample of PWH was invited to participate from the three HTC and the investigator did not meet the PWH face to face. The sample was divided into two groups, early and later treatment onset groups. This was performed to show differences between the groups due to the regimes of treatment of the groups. The dividing point, being born about 1965, is specific to the Swedish population because available clotting factors were made available in the 60s.[16,17,19] This study design is unique and has not been used before and allowed comparisons of the differences between early and later treatment onset groups.

The use of qualitative methods as in the interview study of this thesis, are more and more commonly used to get the person's perspective of a subject in a profound way.[149] The analytical methods are many and the choices are guided by the aims of the studies and there are many methods to choose from.[150-152] In this thesis the empirical phenomenological psychology (EPP) method was used as conducted by Gunnar Karlsson.[117] The method was chosen because it seemed to be a structured analytic method for grasping the meaning structure of the respondents` experiences and coping strategies. A primary assumption of EPP is being aware of the researchers pre-understanding of the experiences explored. The researcher was also inspired by colleagues who had used the method.[153-155] Another appealing factor was the concept of general characteristics of the phenomena found in all protocols.[117] The term saturation is not commonly used when describing phenomenological methods. It was and is still discussed and used to decide

the sample size of interview studies[156] and is in accordance with other researchers using a phenomenological approach to study experiences of patients having, for example heart transplants,[157] and haemodialysis patients.[158] It is difficult to prove saturation and it depends on many factors described by Mason, for example, if an aim is narrow or spans over a wide topic, the quality of the data, the resources available and numbers of methods used.[159] The saturation term is discussed to be or not to be, and "the concept and requirement for data to be saturated should perhaps only be applied within the confines of grounded theory of which there is an established framework for its use".[160] The sample size in this thesis before no new topic appeared in the subsequent interviews was 14. There is no guarantee that no new topic would occur if more interviews had been performed. According to Creswell, the sample size could vary from 1-325 in phenomenological studies but more commonly, 5-25 participants having experienced the same phenomenon.[151] The interviews performed in this study were long and adequate and covered a lot of phenomena related to being a PWH.

Generalizability

Care should be taken in generalizing the results of these studies but the differences between the early and later treatment onset groups are obvious. The later treatment onset group had more disabilities than the early treatment onset group overall, even if the participants do not represent the population of all PWH in the world and not even in nearby countries. The studies were performed in Sweden where prophylaxis treatment with clotting factor has been used since the 60s.[16-19] and haemophilia arthropathy has been able to be prevented due to this medical regime.[161] The outcome of activity and participation must be seen in this context and generalizations of the results are not feasible to other populations due to historically different kinds of medical treatment regimes. A study comparing the young adults from the Netherlands and Sweden showed this variability of outcome for PWH born 1970-1994 in HAL score.[21]

Drop-outs of the total sample of the adult PWH in the study I-III were more than 50% and this is a reason to reflect on how the respondent group was composed compared to the non-respondent group. The non-responders compared to the responders differed in age being younger and in study III the moderate form of haemophilia had a higher representation. The result perhaps had more generalizability among older participants due to the responders

being older than the non-responders. If younger PWH had answered, one can assume that more respondents would be in the group who did not perceive themselves to have difficulty in activities and participation. Clinical investigators face difficulties in recruiting appropriate candidates for clinical trials of haemophilia and a recent study concluded that the rate of willingness to participate in clinical research was significantly lower in patients who reported having no knowledge of clinical trial modalities.[162] The study highlighted the relevance of providing improved knowledge to enhance participation in haemophilia trials.[162] The response rate of this thesis in this light of knowledge about the inherent difficulties in getting study participants will therefore be acceptable but not optimal. Results from participants with previous experiences of clinical trials are perhaps not representative for the whole group of PWH. More studies are needed to generalize the activity and participation level to the whole population of PWH in Sweden.

Strengths and limitations

The strength of this thesis is that all adult PWH in Sweden with the severe and moderate form were invited to participate in the studies concerning HAL. The response rate of about 50% in study III is half of all adult PWH who met the inclusion criteria.

It can be assumed that the differences between the early and later treatment onset groups would have become even clearer if the group was divided into three subgroups and excluded the PWH with a history of inhibitors. A study with all those with life-long prophylaxis without any history of inhibitors in one group, those with prophylaxis from a young age in a second one and the elderly without access to clotting factor during childhood in a third will perhaps give more pronounced differences between the groups with less range. Because of the low numbers of PWH in a cohort in one country it might be more feasible to perform research with multinational studies in this field. But then the culture in which you live and the medical regime differs and has differed historically, confounding comparisons. One German study divided the participants into groups according to the prophylaxis regime during childhood and ongoing treatment.[131] This could be a way to allow the possibility of comparing PWH populations between different countries according to activity and participation. In many ways, it is more interesting to compare the activity and participation level between other persons living in

the same country than between countries. Activity and participation depend on the environment in which you grow up and live.

A limitation in this thesis is that no reported information could be validated by the medical record such as prescribed medical regimes. Whether the PWH adhere to the prescribed regime is unknown. Perhaps some have reported what they actually do rather than the prescribed regime. Studies have shown that in less-adherent patients a higher number of haemarthrosis[163] and lower clotting factor consumption is observed.[164]

The statistical rank-invariation method by Svensson[125,165] used in study III would also have been a proper method to use even in study I according to ordinal scales but instead the method chosen by the author allowed comparison between the Swedish version and the original Dutch.

One of the strengths when the qualitative study was performed was that two persons with no detailed knowledge of the experiences of haemophilia performed the interviews. Thus, it was not difficult for them to "bracket presuppositions" during the interview process as it would have been if the author of this thesis had performed the interviews. The author also knows almost all the persons from their childhood. When the analysis was made the author of this thesis easily found relevant themes because of her knowledge, but this knowledge was complemented by reflections and questions from an outsider. The interviews were long and contained a great deal. If the author had interviewed haemophilia persons from another HTC in Sweden perhaps even more relevant questions might have been posed because of her knowledge, but her presuppositions might have influenced her too much.

Clinical implications

The Swedish version of HAL showed to be a valid instrument for both PWH with the severe and moderate form and could be used both as a clinical instrument at check-ups as well as in research to evaluate activity and participation for the PWH. In registers, which are more and more common in western countries, the need for validated and reliable PROMs is crucial. Many registers just evaluate the impairment level and evaluation with suitable assessment on participation level is lacking.[166] Choosing the most

appropriate tests, depending on whether activity limitation or restriction of participation is of most interest to the assessor and patient is essential.
The results showed the differences in disability between the PWH with early and later treatment onset with clotting factor and the importance of taking the PWH's fear of the future limited societal resources into account when planning for the care of the elderly PWH.
Maintaining centralized specialized care at HTC for PWH seems to be a contributing factor to the participants' satisfaction. The possibility for PWH to influence their own care in line with the results of the government report about effective care seems essential.[142] A success for activity and participation for persons with haemophilia is preventing haemarthrosis.

CONCLUSION

The following are the main conclusions from the studies I-IV in this thesis are:

- The Swedish version of HAL is with respect to convergent validation a questionnaire which can be used to assess the self-reported activity and participation for PWH with both the severe and the moderate forms of haemophilia. The HAL had high internal consistency in all domains and a ceiling effect for the early treatment onset group.

- The early treatment onset group reported less difficulty in activity and participation with HAL compared to the later treatment onset group.

- The PWH in both early and later treatment onset groups reported more disability in activities involving the lower extremities compared to activities involving the upper extremities such as self-care and house-hold tasks.
  The later treatment onset group reported worsening activity over time in the domain of leisure activities and sport.

- The interviewed Swedish PWH strived for normality and adaptation in social activities throughout life and to find their own niche.
  The interviewed Swedish PWH praised the availability of prophylaxis treatment with clotting factors to prevent bleeds. They expressed the importance of the knowledge and support from the comprehensive medical team at the HTC.

FUTURE PERSPECTIVES

This thesis explored PWH's views according to activities and participation in the self-estimated questionnaire HAL and about their experiences according to their haemophilia diagnosis in the interview study. In the society today it is important to study care recipients' views of their disease and their treatment in order to involve them in their own care. A newly published report from the Swedish government highlighted the importance of involving patients in their care in order to obtain a higher efficiency of health care provision.[142] It is also a requirement of the national quality registers in Sweden to have patient involvement, and Patient Reported Outcome Measures (PROMs).[167]

The Haemophilia World Federation has an assessment webpage where HAL is the only disease specific instrument measuring self-perceived functional abilities.[63] In the literature there are many diseases specific Health related Quality of Life (HrQoL) questionnaires described but most of them are for children with haemophilia.[79]. For PWH with prophylaxis and minimal bleedings the changes in HrQoL, disease specific or more general, does not evaluate the impact of the disease but rather other factors such as socio-economical.[79] The early treatment onset group of PWH lives an almost normal life compared to their peers relative to the later onset treatment group. The later treatment onset group reported more difficulties in activities due to joint problems such as haemophilia arthropathy and the ageing persons´ comorbidities resulting in a reduced participation. Therefore it is important to use assessments with outcomes sensitive to what is measured. The medical success with prophylaxis treatment with clotting factor gives the opportunity of a change from major disabilities to invisible disability for PWH in Sweden.

The role of the physiotherapist in this light has changed over time since the beginning of the eighties. In the HTC team the role of the physiotherapist becomes in addition to annual assessments more and more consultative for advice regarding proper physical activity, sports and other physical challenges. Suitable education and work are also discussed with the other team members and with the patients. The treatment sessions are mostly for the older PWH who have hemophilia arthropathy and also the ageing person's disability not as a result of bleedings but still where knowledge of haemophilia is an important issue in their care. Therefore the physiotherapist

at the HTC must be a resource for the health-care professionals outside the hospitals as well.
PWH who develop inhibitors against the clotting factor will need a physiotherapist to give treatments even in the future when their bleeding problems can be equivalent to the time before prophylaxis treatment was available to them.
The young PWH with perhaps only one or two bleeds in a specific joint could have problems as a young adult and therefore it is important that the assessments used are sensitive to this. The HAL had a ceiling effect for the young PWH in accordance with a study by Fischer et al.[80] and do not catch small differences in joint assessments.
It is important to have a person's view of their health and function in health-care but we have to consider that the assessments can be time consuming. Therefore the questionnaires used in regular visits in health-care must measure what they are intended for but with a reasonable number of items respecting for the person's time. Therefore further research could be to reduce the items in HAL, retaining the most useful questions to capture changes in longitudinal studies.

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APPENDIX

Appendix 1

Göteborgs Universitet
Institutionen för neurovetenskap och fysiologi/rehabilitering

Hemofili Aktivitets Lista

Datum:……

Namn:…….

Version 2005

Van Creveldkliniek / Afd. Revalidatie
Universitair Medisch Centrum Utrecht

Van Genderen FR, Westers P, Heijnen L, De Kleijn P, Van den Berg HM, Helders PJM, Van Meeteren NLU. Measuring patients´ perceptions on their functional abilities: validation of the Haemophilia Activies List (HAL). Haemophilia 2006;12:36-46

Inledning

*Framför dig ligger frågeformuläret **H**emofili **A**ktivitets **L**istan, förkortat **”HAL”.** I detta frågeformulär beskrivs flera aktiviteter som kan var svåra att utföra för personer med blödarsjuka. Syftet med detta frågeformulär är att se hur det är för dig att utföra dessa aktiviteter.*

Allmänna anvisningar

När du svarar på frågorna är det enbart **dina egna** erfarenheter som är viktiga. Det bygger på att du svarar med det svar som passar bäst in på din situation.
Vid varje aktivitet frågas det om du **till följd av blödarsjuka** haft problem med denna aktivitet. Det finns sex (ibland sju) svarsalternativ. Du ska kryssa för den rutan efter frågan som bäst stämmer in på dig.

Exempel:

Har du under den senaste månaden haft svårighet till följd av blödarsjuka med att:

	Ej tillämplig	Omöjligt	Alltid	Oftast	Ibland	Sällan	Aldrig
Använda kollektiv trafik (buss, spårvagn, tunnelbana, tåg)	☐8	☐1	☐2	☐3	☐4	☐5	☐6

För varje fråga ska du kryssa för endast ett svarsalternativ. Alternativet ”Ej tillämplig” skall endast användas om du aldrig (behöver) utför(a) den specifika aktiviteten. Detta svarsalternativ finns endast vid ett fåtal aktiviteter. Skillnaden mellan ”omöjligt” och ”alltid” är att vid svarsalternativet ”omöjligt” är du oförmögen att utföra aktiviteten medan vid svarsalternativet ”alltid” är att du faktiskt kan utföra aktiviteten men med svårighet. Det är mycket viktigt att du svarar på alla frågorna. Även när en fråga tycks irrelevant för dig eller när du inte har någon åsikt angående frågan så var vänlig och kryssa för den rutan som närmast beskriver din situation. Om du är osäker angående ett svarsalternativ så försök att svara med det svarsalternativ som ligger närmast vad du tycker.

Det tar ungefär 5-10 minuter att fylla i frågeformuläret.

Var vänlig och skriv vad klockan är nu:……tim:min

Ligga/sitta/sitta på knä/stå

Har du under senaste månaden haft svårighet till följd av blödarsjuka med att:

	Omöjligt	Alltid	Oftast	Ibland	Sällan	Aldrig
Sätta dig (ex. på en stol eller bänk)	☐1	☐2	☐3	☐4	☐5	☐6
Resa dig (från en stol *med* armstöd)	☐1	☐2	☐3	☐4	☐5	☐6
Resa dig (från en stol *utan* armstöd)	☐1	☐2	☐3	☐4	☐5	☐6
Sitta på knä/huk (böja knäna)	☐1	☐2	☐3	☐4	☐5	☐6
Böja dig framåt	☐1	☐2	☐3	☐4	☐5	☐6
Sitta på knäna en längre stund (knäna på golvet)	☐1	☐2	☐3	☐4	☐5	☐6
Sitta på huk en längre stund (utan att knäna rör golvet)	☐1	☐2	☐3	☐4	☐5	☐6
Stå en längre stund	☐1	☐2	☐3	☐4	☐5	☐6

Benfunktion

Har du under den senaste månaden haft svårighet till följd av blödarsjuka med att:

	Omöjligt	Alltid	Oftast	Ibland	Sällan	Aldrig
Gå en kortare sträcka (mindre än 1 kilometer/15 minuter)	☐1	☐2	☐3	☐4	☐5	☐6
Gå en längre sträcka (mer än 1 kilometer/15 minuter)	☐1	☐2	☐3	☐4	☐5	☐6
Gå på mjukt underlag(ex. på stranden eller i skogen)	☐1	☐2	☐3	☐4	☐5	☐6
Gå på ojämnt underlag (ex. gatsten, höga trottoarkanter, trösklar)	☐1	☐2	☐3	☐4	☐5	☐6
Flanera/Strosa/ Promenera på stan/ Fönstershoppa	☐1	☐2	☐3	☐4	☐5	☐6
Gå *uppför* trapporna	☐1	☐2	☐3	☐4	☐5	☐6
Gå *nerför* trapporna	☐1	☐2	☐3	☐4	☐5	☐6
Springa (t.ex. för att hinna med bussen)	☐1	☐2	☐3	☐4	☐5	☐6
Hoppa	☐1	☐2	☐3	☐4	☐5	☐6

Armfunktion

Har du under den senaste månaden haft svårighet till följd av blödarsjuka med att:

	Omöjligt	Alltid	Oftast	Ibland	Sällan	Aldrig
Lyfta tunga föremål	☐1	☐2	☐3	☐4	☐5	☐6
Bära tunga föremål	☐1	☐2	☐3	☐4	☐5	☐6
Utföra små fingerrörelser (t.ex. sy, knyta en slips, knäppa manschettknappar)	☐1	☐2	☐3	☐4	☐5	☐6
Ta något ovanför huvud (från en hög hylla)	☐1	☐2	☐3	☐4	☐5	☐6

Användning av transportmedel

Har du under den senaste månaden haft svårighet till följd av blödarsjuka med att:

	Ej relevant	Omöjligt	Alltid	Oftast	Ibland	Sällan	Aldrig
Cykla	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Att gå i och ur bilen	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Använda kollektivtrafik (buss, spårvagn, tunnelbana, tåg)	☐8	☐1	☐2	☐3	☐4	☐5	☐6

Personlig vård

Har du under den senaste månaden haft svårighet till följd av blödarsjuka med att:

	Omöjligt	Alltid	Oftast	Ibland	Sällan	Aldrig
Torka hela kroppen	☐1	☐2	☐3	☐4	☐5	☐6
Ta på dig en t-shirt, skjorta, tröja etc.	☐1	☐2	☐3	☐4	☐5	☐6
Ta på dig strumpor och skor	☐1	☐2	☐3	☐4	☐5	☐6
Knyta en slips eller knäppa översta knappen på en skjorta.	☐1	☐2	☐3	☐4	☐5	☐6
Torka dig efter toalett besök	☐1	☐2	☐3	☐4	☐5	☐6

Hushållssysslor

Har du under den senaste månaden haft svårighet till följd av blödarsjuka med:

	Ej relevant	Omöjligt	Alltid	Oftast	Ibland	Sällan	Aldrig
Att handla	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Att diska, torka av diskbänken	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Att städa bostaden	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Andra hushållssysslor (t.ex. stryka, bädda sängen etc.)	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Att pyssla med huset, inne och ute	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Trädgårdsarbete	☐8	☐1	☐2	☐3	☐4	☐5	☐6

Fritidsysselsättning och idrott

Har du under den senaste månaden haft svårighet till följd av blödarsjuka med att:

	Ej relevant	Omöjligt	Alltid	Oftast	Ibland	Sällan	Aldrig
Spela spel (ute, t.ex. leka med barnen, kubb, krocket)	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Idrotta	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Gå ut (t.ex. på teatern/museum/bio/restaurang och kafé)	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Utöva en hobby	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Dansa	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Åka på aktiv semester	☐8	☐1	☐2	☐3	☐4	☐5	☐6
Åka på mer ”passiv” semester (t.ex. badsemester)	☐8	☐1	☐2	☐3	☐4	☐5	☐6

Anpassningar och hjälpmedel

För att kunna utföra vissa aktiviteter är det möjligt att du har olika anpassningar eller använder olika hjälpmedel. Det är hjälpmedel, som du använder när du inte har några akuta besvär (d.v.s. inte användande av kryckor i samband med en akut ledblödning). Följande frågor gäller de hjälpmedel eller anpassningar som du använder regelbundet.

Har du en bil med anpassningar?

- ☐ Nej, jag har ingen bil
- ☐ Nej, jag har inga anpassningar i min bil

Ja, jag har en bil med (fler svarsalternativ är möjliga):

- ☐ El fönsterhissar
- ☐ Servostyrning
- ☐ Automatisk växellåda
- ☐ Möjlighet att sitta i en rullstol i bilen
- ☐ Broms- och/eller gasreglage vid ratten
- ☐ Annat, nämligen……
- ☐ Annat, nämligen……
- ☐ Annat, nämligen……

Använder du hjälpmedel när du utför vissa aktiviteter

- ☐ Nej, jag använder inga hjälpmedel

Ja, jag använder (fler svarsalternativ är möjliga):

- ☐ En kryckkäpp/käpp
- ☐ Två kryckkäppar
- ☐ Rullstol
- ☐ Rollator
- ☐ Annat, nämligen……
- ☐ Annat, nämligen……
- ☐ Annat, nämligen……

Var vänlig och skriv vad klockan är nu:……tim:min

Detta var alla frågor om aktiviteterna. Till slut ber vi dig att vara vänlig att delge oss viss personlig information i rutan nedan. Informationen som du lämnar ut kommer att behandlas strikt konfidentiellt.

Dagens datum:	……	
Ditt födelsedatum:	……..	
Typ av hemofili *	☐1	Hemofili A
	☐2	Hemofili B
Form/svårighetsgrad av hemofili *	☐1	Mild
	☐2	Moderat
	☐3	Svår
		* kryssa i den rutan som är tillämplig

Tack för din medverkan!

Appendix 2

Persondata till HAL studien

KOD nr:……..

Peronuppgifter: Datum……

Ålder…….Kön: □ Man □ Kvinna

Civilstånd: □ Gift □ Skild □ Änkling/änka □ Sambo □ Ensamstående

Har du hemmavarande barn? □ Ja □ Nej

Har du hemtjänst? □ Ja □ Nej

Arbetssituation:

Yrke:……Ev. tidigare yrke…….

Markera med ett kryss i rutorna som stämmer in på Dig:

Yrkesarbetar Du? □ Ja □ Nej □ Heltid □ Deltid……%

Studerar Du? □ Ja □ Nej □ Heltid □ Deltid……%

Har Du förtidspension/
Sjukbidrag □ Ja □ Nej □ Heltid □ Deltid……%

Har du ålderspension? □ Ja □ Nej Om ja sedan vilket år?…….

Är Du arbetslös? □ Ja □ Nej □ Heltid □ Deltid……%

Om ja sedan vilket år?…….

Är Du sjukskriven? □ Ja □ Nej □ Heltid □ Deltid……%

Om ja sedan vilket år?…….

Ev andra sjukdomar:
Markera med ett kryss det som stämmer in på Dig.

Har Du någon av följande sjukdomar?			Begränsar det din aktivitet?	
Hjärtsjukdom	□ Ja	□ Nej	□ Ja	□ Nej
Högt blodtryck	□ Ja	□ Nej	□ Ja	□ Nej
Lungsjukdom	□ Ja	□ Nej	□ Ja	□ Nej
Diabetes	□ Ja	□ Nej	□ Ja	□ Nej

Njursjukdom	□ Ja	□ Nej	□ Ja	□ Nej
Leversjukdom	□ Ja	□ Nej	□ Ja	□ Nej
Mag-tarm sjukdom	□ Ja	□ Nej	□ Ja	□ Nej
Cancer	□ Ja	□ Nej	□ Ja	□ Nej
Depression	□ Ja	□ Nej	□ Ja	□ Nej
Ryggbesvär	□ Ja	□ Nej	□ Ja	□ Nej
Reumatoid artrit	□ Ja	□ Nej	□ Ja	□ Nej
Annan medicinsk diagnos				
1……	□ Ja	□ Nej	□ Ja	□ Nej
2……	□ Ja	□ Nej	□ Ja	□ Nej
3……	□ Ja	□ Nej	□ Ja	□ Nej

Appendix 3

Persondata till HAL studien

KOD nr:……..

Peronuppgifter: Datum……

Ålder…….Kön: □ Man □ Kvinna

Civilstånd: □ Gift □ Skild □ Änkling/änka □ Sambo □ Ensamstående

Har du hemmavarande barn? □ Ja □ Nej

Har du hemtjänst? □ Ja □ Nej

Arbetssituation:

Yrke:……Ev. tidigare yrke…….

Markera med ett kryss i rutorna som stämmer in på Dig:

Yrkesarbetar Du? □ Ja □ Nej □ Heltid □ Deltid

Studerar Du? □ Ja □ Nej □ Heltid □ Deltid

Har Du förtidspension/
Sjukbidrag □ Ja □ Nej □ Heltid □ Deltid

Har Du ålderspension? □ Ja □ Nej

Är Du arbetssökande? □ Ja □ Nej □ Heltid □ Deltid

Är Du sjukskriven? □ Ja □ Nej □ Heltid □ Deltid

Har du regelbunden förebyggande behandling med faktorkoncentrat?
Markera med ett kryss det som stämmer in på Dig.

□ Ja

Hur ofta?
- □ 2 gånger per vecka
- □ 3 gånger per vecka
- □ Var annan dag
- □ Annat ange:……

□ Nej

Hade du regelbunden förebyggande behandling med faktorkoncentrat även som barn?
Markera med ett kryss det som stämmer in på Dig.

□ Ja □ Nej

Har du antikroppar mot faktor VIII eller IX?
Markera med ett kryss det som stämmer in på Dig.

□ Ja □ Nej, har aldrig haft □ Nej, har inte längre

Är du opererad i någon/några leder med ledprotes?
Markera med ett kryss det som stämmer in på Dig.

Knä	□ Ja	□ Hö	□ Vä	□ Nej
Höft	□ Ja	□ Hö	□ Vä	□ Nej
Armbåge	□ Ja	□ Hö	□ Vä	□ Nej
Axel	□ Ja	□ Hö	□ Vä	□ Nej
Fot	□ Ja	□ Hö	□ Vä	□ Nej

Eventuellt andra sjukdomar:
Markera med ett kryss det som stämmer in på Dig.

Har Du någon av följande sjukdomar?

Hjärtsjukdom	□ Ja	□ Nej	Mag-tarm sjukdom	□ Ja	□ Nej
Högt blodtryck	□ Ja	□ Nej	Cancer	□ Ja	□ Nej
Lungsjukdom	□ Ja	□ Nej	Depression	□ Ja	□ Nej
Diabetes	□ Ja	□ Nej	Reumatoid artrit	□ Ja	□ Nej
Njursjukdom	□ Ja	□ Nej	Ryggbesvär	□ Ja	□ Nej
Leversjukdom	□ Ja	□ Nej	Annan medicinsk diagnos	□ Ja	□ Nej

Appendix 4

KOD nr:……

Persondata till studien: ***Hur handskas blödarsjuka personer med sin kroniska sjukdom i sin vardag? Hur uppfattar de att specialistteamet möter upp deras behov?***

datum:……..

Ålder:…… Kön: ☐ man ☐ kvinna

Civilstånd: ☐ gift ☐ skild ☐ sambo ☐ ensamstående ☐ änkling/änka

Vad stämmer in på dig? Markera med ett kryss det som stämmer in på dig:

Yrkesarbetar du?	☐ Ja	☐ nej
Studerar du?	☐ Ja	☐ nej
Är du sjukskriven?	☐ Ja	☐ nej
Har du förtidspension/sjukbidrag	☐ ja	☐ nej
Har du ålderspension	☐ ja	☐ nej
Är du arbetssökande	☐ ja	☐ nej

Har du någon annan sjukdom än blödarsjuka? ☐ ja ☐ nej

Om du svarat ja ange vilken/vilka :

……
……
……
……
……

Tack för din medverkan!

Appendix 5

Appendix 5 Table. ***In the previous, month did you have any difficulty due to haemophilia with:*** Item by item for the HAL divided in early and later treatment onset group in between 2.5 years. The figures are the measure of percentage agreement (PA), of the systematic disagreement in position (RP) and concentrate (RC), of the individual variability (RV) and corresponding 95%confidence intervals (95%CI). ***significant change**

HAL	***ET***	*Systematic disagreement*		*Individual disagreement*	***LT***	*Systematic disagreement*		*Individual disagreement*
Item number	**PA %**	**RP (95%CI)**	**RC (95%CI)**	**RV (95%CI)**	**PA %**	**RP (95%CI)**	**RC (95%CI)**	**RV (95%CI)**
1. Sitting down	79	0.14* (0.020:0.261)	0.02 (-0.078:0.111)	0.00 (0.000:0.005)	47	0.14 (-0.041:0.321)	0.16 (-0.047:0.364)	0.19* (0.000:0.381)
2. Rising from chair with armrests	86	0.07 (-0.021:0.152)	-0.03 (-0.119-0.059)	0.00 (0.000:0.005)	63	0.11 (-0.032:0.258)	0.09 (-0.079:0.253)	0.09 (0.000:0.207)
3. Rising from chair without armrests	86	0.06 (-0.021:0.150)	-0.04 (-0.165:0.087)	0.00 (0.000:0.002)	44	0.17* (0.023:0.325)	0.09 (-0.161:0.341)	0.08 (0.000:0.170)
4. Kneeling/ squatting	83	0.10* (0.002:0.193)	-0.04 (-0.162:0.073)	0.00 (0.000:0.005)	69	0.03 (-0.135:0.200)	-0.12 (-0.247-0.002)	0.05 (0.000:0.116)
5. Bending forward	82 n=28	0.11 (-0.003:0.217)	-0.01 (-0.218-0.202)	0.000 (0.000:0.000)	44	0.17 (-0.036:0.371)	-0.08 (-0.295:0.128)	0.23* (0.015:0.451)
6. Kneeling for a longer time	79	0.09 (-0.041:0.215)	-0.08 (-0.213-0.046)	0.01 (0.000:0.044)	88	0.07 (-0.045:0.195)	-0.05 (-0.143-0.049)	0.02 (0.000:0.052)
7. Squatting for a longer time	72	0.06 (-0.078:0.197)	-0.05 (-0.205:0.106)	0.02 (0.000:0.056)	84	0.07 (-0.045:0.182)	-0.02 (-0.125:0.083)	0.01 (0.000-0.022)
8. Standing for a longer time	72	0.06 (-0.026:0.155)	-0.04 (-0.208:0.136)	0.01 (0.000:0.033)	41	0.05 (-0.121:0.225)	-0.10 (-0.292:0.096)	0.20 (0.000-0.423)
9. Walking short distances	59	0.16* (0.009:0.305)	0.20 (-0.040:0.439)	0.02 (0.000:0.064)	34	0.07 (-0.096:0.229)	0.06 (-0.169:0.287)	0.17* (0.001:0.341)
10. Walking long distances	59	0.12 (-0.031:0.271)	0.18 (-0.058:0.411)	0.03 (0.000:0.088)	38	0.09 (-0.070:0.255)	0.04 (-0.201:0.277)	0.17 (0.000:0.354)
11. Walking on a soft surface	72	0.13 (-0.004:0.265)	0.08 (-0.125-0.292)	0.01 (0.000:0.018)	41	0.08 (-0.076:0.240)	0.10 (-0.127-0.322)	0.17 (0.000:0.360)
12. Walking on a uneven surface	66	0.12 (-0.027:0.262)	0.04 (-0.140:0.225)	0.02 (0.000:0.053)	47	0.10 (-0.042:0.249)	0.03 (-0.199-0.268)	0.13 (0.000:0.290)
13. Strolling	66	0.10 (-0.051:0.251)	0.25* (0.090-0.415)	0.01 (0.000:0.038)	47	0.05 (-0.117:0.216)	-0.00 (-0.205-0.201)	0.17 (0.000:0.342)
14. Climbing up the stairs	72	0.114 (-0.013:0.241)	0.04 (-0.133:0.212)	0.01 (0.000:0.017)	41	0.07 (-0.128:0.260)	0.09 (-0.117-0.293)	0.24* (0.005:0.477)
15. Climbing down the stairs	76	0.09 (-0.029:0.205)	0.05 (-0.110:0.216)	0.00 (0.000:0.010)	53	0.10 (-0.092:0.285)	-0.00 (-0.212:0.210)	0.22 (0.000:0.450)
16. Running	69	0.06 (-0.060:0.170)	-0.03 (-0.216:0.155)	0.02 (0.000:0.050)	78	-0.01 (-0.142:0.126)	0.02 (-0.087:0.127)	0.04 (0.000:0.090)
17. Jumping	66	0.07 (-0.062:0.192)	-0.03 (-0.223:0.160)	0.02 (0.000:0.044)	69	-0.05 (-0.195:0.090)	-0.04 (-0.186:0.098)	0.03 (0.000:0.072)
18. Lifting heavy objects	79	-0.05 (-0.126:0.036)	0.10 (-0.022:0.230)	0.00 (0.000:0.007)	47	0.05 (-0.075:0.175)	-0.12 (-0.276:0.038)	0.06 (0.000:0.146)
19. Carrying heavy objects in the arms	79	-0.00 (-0.126:0.036)	0.10 (-0.032:0.230)	0.00 (0.000:0.007)	56	0.04 (-0.083:0.169)	-0.08 (-0.231:0.077)	0.07 (0.000:0.162)
20. Fine hand movements	86	-0.03 (-0.091:0.027)	0.02 (-0.054:0.093)	0.00 (0.000:0.002)	63	-0.05 (-0.164:0.068)	0.08 (-0.102:0.256)	0.04 (0.000-0:094)
21.Reaching above your head	83	0.03 (-0.022:0.091)	0.00 (-0.127:0.127)	0.00 (0.000:0.005)	44	-0.04 (-0.191:0.121)	-0.02 (-0.243:0.205)	0.11 (0.000:0.227)

22. Riding a bicycle	79	0.09 (-0.039:0.220)	-0.07 (-0.242:0.104)	0.01 (0.000:0.043)	58 n=31	-0.03 (-0.142:0.079)	-0.10 (-0.269:0.080)	0.01 (0.000:0.031)
23. Getting in and out of a car	79	0.10* (0.002:0.208)	-0.00 (-0.187:0.183)	0.00 (0.000:0.011)	44	0.07 (-0.098:0.241)	0.21 (-0.014:0.435)	0.10 (0.000:0.220)
24. Using public transportation	76	0.10 (-0.015:0.222)	0.01 (-0.149:0.129)	0.02 (0.000:0.067)	41	0.12 (-0.091:0.327)	0.01 (-0.214:0.203)	0.35* (0.072:0.633)
25.Drying your whole body	86	0.03 (-0.027:0.096)	0.00 (-0.109:0.109)	0.00 (0.000:0.002)	53	0.02 (-0.117:0.166)	0.18* (0.009:0.356)	0.10 (0.000:0.136)
26.Putting on a shirt, sweater etc.	93	0.03 (-0.026:0.095)	0.00 (-0.048:0.048)	0.00 (0.000:0.000)	53	-0.03 (-0.177:0.114)	0.16 (-0.052:0.364)	0.04 (0.000:0.083)
27. Putting on sock and shoes	83	0.05 (-0.061:0.161)	0.10 (-0.039:0.242)	0.00 (0.000:0.005)	56	0.07 (-0.057:0.202)	0.19* (0.024:0.347)	0.05 (0.000:0.116)
28. Putting on a tie or closing the top button of a shirt	93	-0.03 (-0.092:0.030)	0.03 (-0.015:0.074)	0.00 (0.000:0.002)	53	-0.05 (-0.139:0.046)	0.07 (-0.111:0.248)	0.01 (0.000:0.022)
29. Going to the toilet	96 n=28	-0.00 (-0.012:0.004)	-0.04 (-0.113:0.035)	0.00 (0.000:0.000)	69	-0.04 (-0.171:0.093)	0.09 (-0.054:0.240)	0.02 (0.000:0.047)
30. Going out shopping	79	-0.01 (-0.112:0.091)	0.11 (-0.026:0.255)	0.00 (0.000:0.006)	45 n=31	0.09 (-0.075:0.258)	-0.00 (-0.238-0.231)	0.12 (0.000:0.243)
31. Washing the dishes, cleaning the sink	90	0.01 (-0.007:0.031)	0.10 (-0.001-0.197)	0.00 (0.000:0.000)	53	0.09 (-0.072:0.246)	0.06 (-0.125:0.245)	0.05 (0.000:0.120)
32. Cleaning the house	76	-0.09 (-0.191:0.020)	0.12 (-0.058:0.292)	0.00 (0.000:0.002)	59	-0.00 (-0.118:0.110)	0.16 (-0.002:0.312)	0.03 (0.000:0.060)
33. Other household tasks	83	0.04 (-0.062:0.143)	0.04 (-0.077:0.153)	0.00 (0.000:0.005)	53	0.04 (-0.061:0.149)	0.12 (-0.055:0.295)	0.01 (0.000:0.029)
34. Doing odd jobs (in and around the house)	66	-0.04 (-0.183:0.095)	0.11 (-0.066:0.293)	0.03 (0.000:0.073)	44	-0.02 (-0.124:0.087)	0.07 (-0.133:0.270)	0.03 (0.000:0.070)
35. Gardening	59	-0.07 (-0.228:0.094)	0.15 (-0.022:0.328)	0.06 (0.000:0.147)	59	-0.04 (-0.161:0.072)	-0.06 (-0.229:0.110)	0.07 (0.000:0.144)
36. Playing games	72	-0.00 (-0.145:0.140)	-0.01 (-0.157:0.141)	0.04 (0.000:0.094)	41	-0.21* (-0.381:-0.047)	-0.03 (-0.168:0.230)	0.17 (0.000:0.344)
37. Sports	54 n=28	0.05 (-0.142:0.246)	-0.06 (-0.253:0.141)	0.13 (0.000:0.290)	41	-0.21* (-0.366:-0.054)	0.09 (-0.163:0.350)	0.09 (0.000:0.187)
38. Going out (theatre/museum /movie etc.	76	0.03 (-0.083:0.140)	-0.02 (-0.171:0.123)	0.01 (0.000:0.027)	53	0.12 (-0.005:0.243)	0.09 (-0.111:0.285)	0.08 (0.000:0.173)
39. Hobbies	72	0.07 (-0.056:0.203)	0.02 (-0.124:0.173)	0.02 (0.000:0.045)	65 n=31	-0.06 (-0.233:0.119)	-0.13 (-0.281:0.030)	0.18 (0.000:0.382)
40. Dancing	66	-0.05 (-0.192:0.094)	-0.06 (-0.238:0.118)	0.05 (0.000:0.118)	38	-0.12 (-0.281:0.047)	-0.05 (-0.263:0.167)	0.18* (0.001:0.369)
41. Going on a holiday (active)	59	0.02 (-0.181:0.219)	-0.05 (-0.229:0.133)	0.15 (0.000:0.314)	41 n=31	-0.24* (-0.440:-0.035)	-0.06 (-0.353:0.231)	0.30* (0.077:0.533)
42. Going on a holiday (passive)	76	0.02 (-0.155:0.195)	0.10 (-0.046:0.246)	0.01 (0.000:0.140)	57 n=30	-0.05 (-0.237:0.139)	0.03 (-0.205:0.256)	0.22* (0.004:0.442)

Appendix 6

Frågeställningar och frågeguide till intervju med blödarsjuka
De övergripande frågeställningarna i studien är:

1. Hur upplever informanterna och hur hanterar de sin blödarsjuka?
2. Hur påverkar blödarsjukan informanternas livssituation nu och hur var det under uppväxten?
3. Hur upplever informanterna omhändertagandet i sjukvården?
4. Kontakten med andra myndigheter (Socialtjänst, FK, bilstöd, parkeringtillstånd, AF Utbildning mm)

Öppna inledningsfrågor och kompletterande processfrågor (hur, vad, på vilket sätt) kommer att användas till dess informanterna har förmedlat allt de har att säga inom respektive tema.

Hur är det för Dig att leva med blödarsjuka?
Vilka sjukdomsupplevelser har Du?
Hur hanterar Du dina upplevelser?
Hur går det med medicineringen?

Hur hanterar ditt nätverk att du är blödarsjuk?

Hur påverkar den eventuella funktionsnedsättningen/blödarsjukan vardagen inom alla livsområden (arbete, fritid, familj, sociala kontakter)?
Hur upplever du tillgänglighet till samhällsfunktioner relaterat till blödarsjukan?
Hur har blödarsjukan påverkat vardagen inom alla livsområden hittills under Ditt liv?

Hur upplever Du kontakten med sjukvården?
Hur upplever du att du blir behandlad på olika mottagningar i sjukvården?
Hur upplever Du kontakten med specialistteamet vid koagulationscentrum?
Skulle du vilja få insatser från detta team som Du inte får idag och i så fall vilka?
Skulle Du vilja ha tätare eller glesare kontakt med specialistteamet än vad som nu är fallet?

Har du kontakter med andra instanser än sjukvården som har att göra med din blödarsjuka?