

AN INVESTIGATION OF MUSCLE STRENGTH, ENDURANCE AND QUALITY OF LIFE IN SOUTH AFRICAN CHILDREN WITH HAEMOPHILIA: A PILOT STUDY

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ABSTRACT

Haemophilia is an X-linked genetically transmitted disorder that is characterised by a deficiency in a circulating blood clotting factor (Falk et al 2000) and presents with intra-articular and intramuscular bleeding. Haemophilia A is the most common and results from a deficiency of clotting factor VIII (Barlow et al 2007). Haemophilia B results from a deficiency of clotting factor IX. Haemophilia A and B are described as having an incidence of approximately 1:10 000 and 1:60 000 people respectively (Engelbert et al 2007). Both haemophilia A and B are rare disorders, but are the most common, severe inherited bleeding disorder (Price et al 2007).

The haemostatic defects of haemophilia lead to spontaneous and post-traumatic internal bleeding events (Von Mackensen et al 2004). Hilberg et al (2001) and Ghosh et al (2004) reported on the consequences of repeated bleeds and immobilization resulting in muscle atrophy, chronic synovitis, chronic haemophilic arthropathy, contractures, unequal leg lengths and loss of proprioception. Considering the musculoskeletal implications of haemophilia, Bradley et al (2006) reported that haemophilia may have a significant impact on the quality of life (QoL). Varni et al (2006) stated that children with chronic health conditions were reported to not only experience lower physical functioning, but also manifested lower emotional, social and school functioning in comparison with healthy children.

The main aim of this study is to compare the muscle strength, endurance and QoL of a group of children with haemophilia to a group of aged matched healthy peers. Children between the ages of five and sixteen years were included in the study.

The MicroFET 2 dynamometer has been used to assess the muscle strength of each subject and the Six Minute Walk Test has been used to test submaximal endurance levels of each group. The PedsQL is one of the quality of life assessment tools used to compare both groups, where the HAEMO-QOL has been used specifically to test the subjects with haemophilia. The first group of participants consisted of children having a diagnosis of haemophilia (n=15), and the second comparative group consisted of normally developing children (n=18).

The results were analysed and compared using the student t-test and the Pearson's correlation coefficient. The two groups were well matched for all anthropometric data. With regards to muscle strength, the haemophilia group showed significant weakness with regards to their left

(L) elbow extensors and right (R) knee extensors in comparison to control group, with p values as $p < 0.01$ and $p < 0.05$ respectively. In contrast the haemophiliac group showed significantly greater strength in the (L) and (R) ankle dorsiflexors, in comparison to the control group with p values as $p < 0.02$ and $p < 0.00$ respectively. No statistical significance was demonstrated in the 6MWT and QoL measures used between the two groups.

The children with haemophilia in comparison to a healthy sample of age matched peers demonstrated almost equal abilities in measured muscle strength and submaximal endurance levels, and almost equal scores in the PedsQL of 75.5% and 77.7 % questionnaire indicating high perceived quality of life in both groups. There was a positive correlation between the Haemo-QoL questionnaire and the PedsQL questionnaire in the haemophilia group, indicating, again, high perceived quality of life with no discrepancies between the two questionnaires used.

The findings of this study demonstrate a need for further research on haemophilic subjects in a South African context. However, the results have shown that both the groups in this present study have reduced muscle strength and poor endurance in comparison to international trends. With regards to perceived QoL, the boys with haemophilia had scores which were similar to those obtained in other studies.

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DECLARATION

I declare that this research report is my own unaided work, except to the extent indicated in the reference citation and acknowledgements. It is being submitted in partial fulfilment of the requirements of the degree of Master of Science (Physiotherapy) at the University of the Witwatersrand. It has not been submitted before for any other degree or examination in any other University.

Donna Theresa Faris

.....day of.....2011

LIST OF ABBREVIATIONS

APTT	-	Activated Partial Thromboplastin Time
CHBH	-	Chris Hani Baragwanath Hospital
DCD	-	Developmental Co-ordination Disorder
HA	-	Haemophilia A
HB	-	Haemophilia B
Haemo-QoL	-	Haemo-Quality of Life Questionnaire
HHD	-	Hand Held Dynamometer
HR-QoL	-	Health –Related Quality of Life
HR	-	Heart Rate
HIV	-	Human Immunodeficiency Virus
ICF	-	International Classification of Functioning
INR	-	International Normalised Ratio
ICF	-	Intracranial Haemorrhage
L	-	Left
N	-	Newton
PA	-	Physical activity
PedsQL	-	Pediatric Quality of life
PNF	-	Proprioceptive Neuromuscular Facilitation
R	-	Right
RR	-	Respiratory Rate
ROM	-	Range of Movement
6MWT	-	Six minute walk test
SA	-	South Africa
SD	-	Standard Deviation
SES	-	Socio-economic Status
WFH	-	World Federation of Haemophilia
WHO	-	World Health Organisation
UK	-	United Kingdom

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Chapter 1: INTRODUCTION

Haemophilia is an X-linked genetically transmitted disorder that is characterised by a deficiency in a circulating blood clotting factor (Falk et al, 2000) and presents with intra-articular and intramuscular bleeding. Approximately 80% of the bleeds occur within joints (Hilberg et al, 2001). The severity of haemophilia is classified under three recognised levels: mild, moderate and severe. They are defined by the level of measurable plasma coagulation factor activity in the circulation; >5% is mild, 1-5% moderate and <1% severe (Bradley et al, 2006). This classification system serves as a guide to the expected frequency of bleeding (Price et al, 2007). Price et al (2007) reports that even patients with mild haemophilia who develop trauma-related musculoskeletal bleeds can acquire permanent damage to a particular muscle group or joint if not treated promptly or properly.

Haemophilia A is the most common and results from a deficiency of clotting factor VIII (Barlow et al, 2007). Haemophilia B results from a deficiency of clotting factor IX. Haemophilia A and B are described as having an incidence of approximately 1:10 000 and 1:60 000 people respectively (Engelbert et al, 2008). Both haemophilia A and B are rare disorders, but are the most common, severe inherited bleeding disorder (Price et al, 2007).

The haemostatic defects of haemophilia lead to spontaneous and post-traumatic internal bleeding events (Von Mackensen et al, 2004). Price et al (2007) describe examples of bleeding, such as intracranial haemorrhage, deep muscle and joint haemorrhage, hematomas, retroperitoneal haemorrhage, post surgical bleeding, easy bruising and mucosal bleeding. Hilberg et al (2001) and Ghosh et al (2004) reported on the consequences of repeated bleeds and immobilization resulting in muscle atrophy, chronic synovitis, chronic haemophilic arthropathy, contractures (caused by repeated bleeds and abnormal postures), unequal leg lengths caused by repeated joint bleeds resulting in varus or valgus deformity, and loss of proprioception. Considering the musculoskeletal implications of haemophilia, Bradley et al (2006) reported that haemophilia may have a significant impact on the quality of life (QoL), including: life style issues such as restrictions in physical activities, parental concerns, development of high-titre inhibitors, and now much less frequent, therapy related infectious complications such as hepatitis, and HIV. Varni et al (2006) stated that children with chronic health conditions were reported to not only experience

lower physical functioning, but also manifested lower emotional, social and school functioning in comparison with healthy children. The treatment of haemophilia as well as related complications might influence the QoL of children and their families (Von Mackensen et al, 2004).

Health Related QoL can be seen as a subjective representation of health, including the physical, mental, social, emotional and everyday life dimensions in terms of wellbeing and function from the patient's perspective (Bullinger et al, 2004). Von Mackensen et al (2004) reports that 13% of approximately 20 000 publications in QoL focused on children, and Bullinger et al (2004) agreed that QoL research in children is still rare.

The Haemo-QoL was one of the first attempts to generate a targeted instrument for QoL assessment in children with Haemophilia (Bullinger et al, 2004). Pollak et al (2006) describe the Haemo-QoL as a set of disease-specific and age related questionnaires to measure QoL in children and adolescents with haemophilia.

The Pediatric Quality of Life Inventory, PedsQL was designed as a modular approach to measuring pediatric health-related QoL in children from the ages of two to 18, with generic core scales and disease-specific modules (Varni et al, 2002). Varni et al (2001) report that the PedsQL, with its generic core scales, includes the ability to conduct comparisons across pediatric acute and chronic health conditions, as well as to enable benchmarking with healthy population norms. It further states that it reflects those items that are of universal concern across age groups.

According to van der Net et al (2006), when children with haemophilia participate on the same level of physical activities as their healthy peers today, it is relevant to know if this coincides with a good level of health-related QoL. Falk et al (2000) mention that despite the agreement regarding the benefits of preservation of well-developed musculature in haemophilia patients; it is still evident that there are no quantitative reports of muscle strength and endurance in such patients compared with healthy individuals.

Muscle strength can be estimated and measured using different methods, ranging from observation without equipment to laboratory examinations with isokinetic instruments. In clinical practice, the most common method is manual muscle testing. Eek et al (2006) and Li et al (2005)

both state that manual muscle testing is subjective and is not sensitive enough to distinguish subtle differences and changes in strength. It has been recognised that traditional manual muscle testing using a 5-point grading scale has poor validity and reliability (Li et al, 2005). A portable, hand-held dynamometer (HHD) has been shown to be a reliable and easy-to-use method to measure muscle strength in clinical practice (Eek M et al, 2006). Ghosh (2004) identified that acute bleeding into major joints such as elbow, knees and ankles is common presentation of severe haemophilia.

Li et al (2005) and Li et al (2007) stated in different studies conducted that an individual's response to exercise is an important clinical assessment tool, as it provides a combined assessment of their respiratory, cardiac and metabolic systems. They describe the six-minute walk test (6MWT) as a quick, easy and inexpensive way to assess the physical function of an individual. The 6MWT is easier to administer, is a better indication of daily activities, is a useful measure of functional capacity and better tolerated than any other walk test (Li et al, 2005). Both Li et al (2007) and Enright (2003) found the (6MWT) to be an important component of perceived QoL as it demonstrates the ability to perform daily activities.

PROBLEM STATEMENT:

It is not known what impairments in terms of muscle strength, endurance and perceived QoL South African children with haemophilia have in comparison to their healthy peers.

AIM OF THE STUDY:

The aim of this study is to compare the muscle strength, endurance and QoL of a group of children with haemophilia to a group of aged matched healthy peers

STUDY OBJECTIVES:

The objectives of this study are as follows:

1. To establish the muscle strength of elbow flexors and extensors, knee flexor and extensors and ankle plantarflexors and dorsiflexors in haemophiliac patients compared to their healthy peers.
2. To establish the endurance of haemophiliac patients and compare this to the endurance of healthy peers.
3. To ascertain the perceived QoL of haemophiliac patients in comparison to the perceived QoL of healthy peers.
4. To determine whether there is a correlation between the PedsQL and Haemo-QoL scores in boys with haemophilia

SIGNIFICANCE OF THE STUDY

Despite there being large amounts of literature on haemophilia worldwide, there are limited studies done in South Africa. There is a need to investigate children with haemophilia within South Africa in order to understand how the condition is impacting on the health and well being of these children so that appropriate management programmes can be developed.

The haemophiliac clinic at Chris Hani Baragwanath Hospital (CHBH), which is run on a monthly basis represents a typically run clinic found in tertiary hospitals in South Africa. Good quality rehabilitation is an integral part of effective long term treatment of the disease (Milhalova, 2007). Results obtained from this study will contribute to the advancement of more extensive rehabilitation programs for children with haemophilia. A comprehensive approach provides ongoing assessments and continuity of care, thereby decreasing the amount of complications for individuals with haemophilia (Price et al, 2007).

Chapter 2: LITERATURE REVIEW

Despite there being large amounts of literature on haemophilia worldwide, there are limited studies done in South Africa. This literature review serves to discuss haemophilia in a South African context, with regards to strength, endurance and perceived quality of life. The literature was obtained through comprehensive searches on major data bases (Pubmed, Medline, MD Consult). Keywords used in the searches were: haemophilia, quality of life, muscle strength testing, endurance training, Six-Minute Walk Test.

2.1 Introduction

Haemophilia is an x-linked genetically transmitted coagulation disorder that is characterised by a deficiency in a circulating blood clotting factor VIII (haemophilia A) or factor IX (haemophilia B) (Falk et al, 2000, Douma-van Riet et al, 2009). Haemophilia A and B are clinically indistinguishable (Brown, 2005). Due to the hereditary pattern of haemophilia, patients are almost invariably male, while women can be carriers of the disease (Plug et al, 2005). Males with haemophilia predominantly inherit the haemophilia gene from their carrier mothers (Brown, 2005). Although haemophilia is an x-linked inherited disorder, 30% of cases occur as a spontaneous mutation, and therefore, there is no family history of the disease in such cases (Price et al, 2007; Mahlangu et al, 2008). Haemophilia has one of the highest mutation rates among genetic disorders (Luck et al, 2004).

2.1.1 Incidence

The true incidence of haemophilia is unknown, but is estimated to occur in approximately 1 in every 50 000 male births (Carlos Rodriguez-Merchan, 1997; Peerlinck et al, 2010). With regards to haemophilia A and B, the frequency is approximately 1:10 000 and 1:60 000 respectively (Douma-van Riet et al, 2009). Haemophilia A and B are found in populations throughout the world and do not appear to have any ethnic or racial predisposition (Brown, 2005). However, the reported prevalence of the disease shows major differences worldwide depending on economic status and reporting procedures (Peerlinck et al, 2010). The number of people with haemophilia

worldwide is estimated to increase from approximately 350, 000 in 1990, to 440,000 by 2020 (Barlow et al, 2007).

2.1.2 Severity

The clinical manifestation of bleeding in haemophilia depends on the severity of the disease (Mahlangu et al, 2008). The severity of haemophilia can vary from mild to severe according to the functional plasma levels of the clotting factor and the severity of bleeding. This classification system serves as a guide to the expected frequency of bleeding (Price et al, 2007). Mild haemophilia is characterised by functional plasma levels above 5% of normal factor VIII levels. Bleeds rarely occur, and are most common following significant trauma or surgery (Carlos Rodriguez-Merchan, 1997). In the moderate form plasma levels are between 2 and 5% of normal levels and bleeding characteristically occurs several times a year, usually after some trauma. In the severe form of haemophilia, plasma levels are below 1% of normal, and patients suffer from spontaneous bleeding even in the absence of trauma (Carlos Rodriguez-Merchan, 1997; Falk et al, 2000; Tiktinsky et al, 2009). The clinical severity of haemophilia is inversely related to circulating clotting factor (Mahlangu et al, 2008). In severe and moderate haemophilia, the bleeding tendency appears early in childhood (Lindvall et al, 2006). In severe haemophilia patients, 15%-20% develop antibodies to therapeutic and prophylactic factor replacement (Santavirta et al, 2001; Ghosh, 2004). The critical level of factor necessary for hemostasis to occur is recorded to be 30% (Carlos Rodriguez-Merchan, 1997).

2.1.3 Life Expectancy

The mean life expectancy of patients with haemophilia was less than 30 years prior to the introduction of clotting factor preparations (Rosendaal et al, 1990; Plug et al, 2005). Overall patients with severe hemophilia had a 5-fold higher risk of death than men in the general population (Plug et al, 2005). Life expectancy in haemophiliacs has increased with advances in haemophiliac treatment, such as clotting factor preparations over the past few decades. (Oldenburg et al, 2009).

2.2 Pathophysiology

The term bleeding disorder refers to a condition of the blood clotting system, in which bleeding is prolonged and excessive (Barlow et al, 2007). Prolonged activation of partial thromoplastin time (APTT) is generally found in haemophilia (Peerlinck et al, 2010).

2.2.1 Haemarthrosis

Haemarthrosis frequently starts early in life where children with haemophilia generally experience their first joint bleed before the age of two years (Sherry, 2008). Due to this early onset, unless haemarthrosis is successfully managed, hypertrophy of the epiphyseal growth plates may occur, resulting in the development of significant structural deformities (Sherry, 2008).

The pathogenesis of haemophilic arthropathy is to some extent misunderstood (Carlos Rodriguez-Merchan, 1997; Sherry, 2008). However, what is known is that persistent haemarthrosis results in a vicious cycle of chronic synovitis leading to chronic joint destruction (Sherry, 2008). The pathogenesis is multifactorial, including general and local physical, chemical and inflammatory factors (Carlos Rodriguez-Merchan, 1997).

Under normal circumstances, the healthy synovial membrane is thin (being made up of two layers of cells), white and avascular. After repeated bleeds, the synovial membrane undergoes hypertrophy which is one of the first changes to occur due to the reabsorption of blood and the absorption of the iron pigment. This causes the tissue to swell and become filled with blood vessels, thus the membrane becomes villous with intense neovascularization. It also becomes thicker, with an irregular surface. Furthermore, a rich capillary network develops beneath the synovial membrane so as to increase the blood flow and remove the breakdown products of blood. Further bleeding generally occurs due to the hypertrophic tissue which occupies the space within the joint, which is more likely to be damaged. Due to recurrent bleeding, the synovium begins to produce enzymes which cause further inflammation in the joint. In addition to this, inflammatory cytokines are released causing increased perfusion and weakness of the intra-articular vessels. The chemical reactions related to the breakdown of blood in the joint damages the articular cartilage, and causes bone erosion and bone remodelling, which eventually begins to

peel off, leaving exposed bone (Buzzard et al, 1988; Gilbert, 2000; McGee, 2006; Sherry, 2008). Eventually the bleeding causes destruction of the synovium and is replaced with scar tissue (Gilbert, 2000).

In due course, chronic synovitis is established with pannus thinning of the cartilage bony changes, and eventually joint dysfunction such as reduced range of movement, stiff, painful joints or chronic swelling. In children, synovitis causes hypertrophy of the epiphyseal growth plates, potentially leading to bony hypertrophy, leg length discrepancy, and angular deformities (Sherry, 2008).

2.2.2 Muscle Bleeds

Bleeding into muscles can occur in both skeletal and smooth muscles (Beeton et al, 1998). Acute muscular bleeding episodes are generally related to direct trauma, and may be related to underlying biomechanical factors at the whole limb or to muscle length/strength imbalances in combination with abnormal biomechanics. This predisposes the muscle to abnormal shear torsion forces, causing microtrauma and intramuscular bleeding (D'Young, 2009). Bleeding into the muscles induces a local inflammatory response, which may cause fibrosis or muscle contractures. This may result in mechanical dysfunction, thus inducing further muscle bleeds (Ashrani et al, 2003).

The main complication of muscular bleeds is the formation of cysts or pseudotumours (De Kleijn et al, 2004). The local pathophysiology that results in the encapsulation of a haematoma remains unclear, but most authors agree that the lesion starts with bleeding into the soft tissue with failure of complete resorption (De Kleijn et al, 2004). The term haemophilic pseudotumour describes a localised haemorrhage with the development of a pseudocapsule around the haematoma. If left untreated, it may ossify, with calcific changes around its well defined borders. As pseudotumour has the potential to erode soft tissue and adjacent bone, leading to pathological fractures (D'Young, 2009).

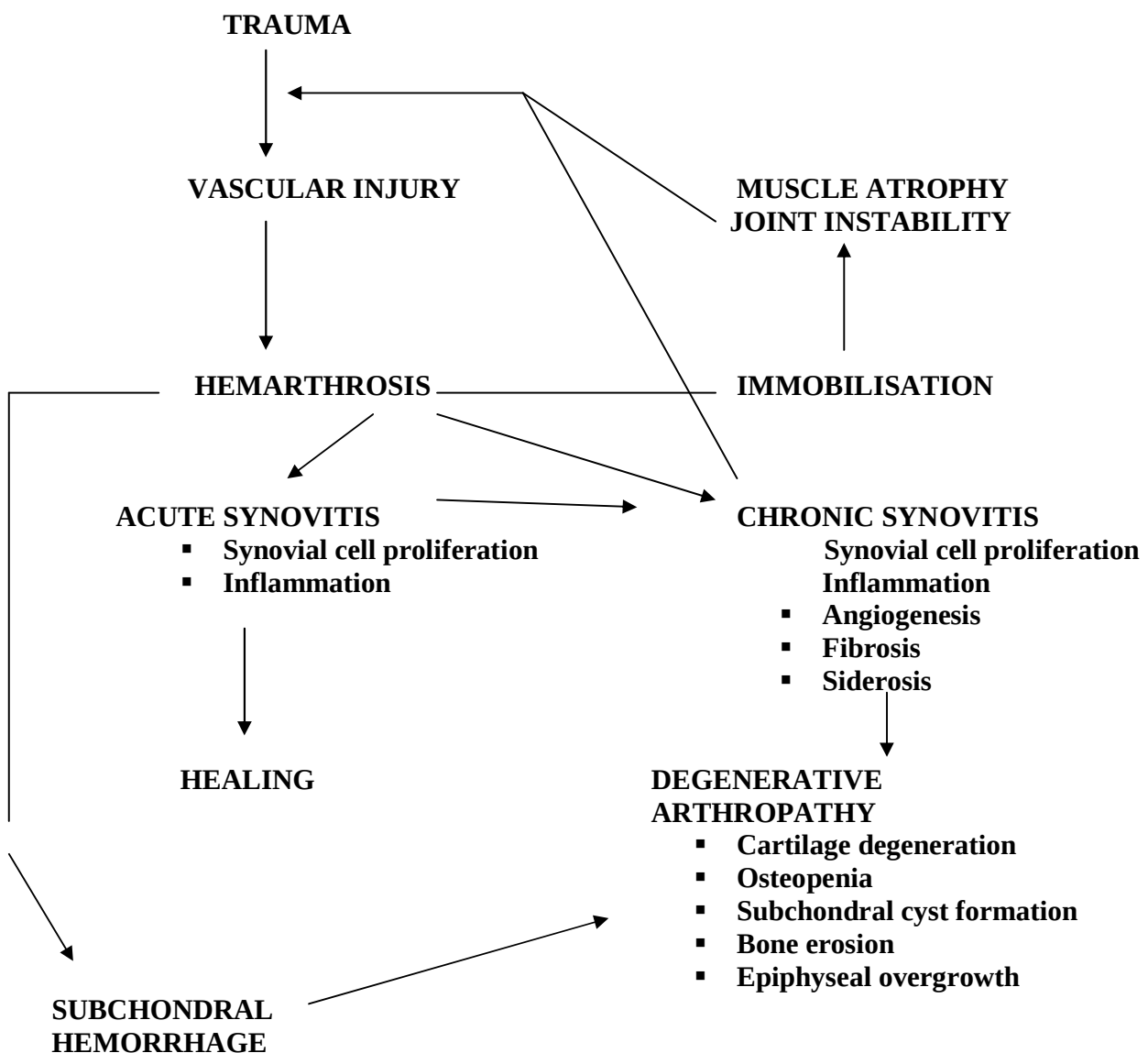


FIGURE Joist and Amens concept of the pathogenesis of hemophilic arthropathy. (Redrawn from Joist JH & Amen, A Pathogenesis of hemophilic arthropathy. In Gilbert MS & Greene WB [Eds]. Musculoskeletal Problems in Hemophilia. New York: National Hemophilia Foundation, 1990 pp. 20-25

2.2.3 Incidence of Inhibitors

One of the major complications of haemophilia is the development of inhibitors; the neutralising alloantibodies against the deficient clotting factor in some patients (van der Bom et al, 2009).

Approximately 15% of factor VIII-deficient patients and even fewer factor IX-deficient patients develop antibodies to their factor replacement (Luck et al, 2004). These alloantibodies act as inhibitors and prevent haemostasis even after factor replacement is given, thus requiring use of bypassing agents (Luck et al, 2004). However, patients who develop inhibitors tend to have bleeding episodes that are difficult to control, even with the use of bypassing agents (van der Bom et al, 2009).

The incidence of inhibitors may depend on genetic factors such as gene mutation, or due to factors such as frequency and dose of clotting factor infusions (van de Bom et al, 2009). For the most part, inhibitors develop early in a patient's treatment life. In haemophilia A, it has been reported that early exposure to FVIII therapy may be linked to subsequent inhibitor development (Santagostino et al, 2009). Inhibitor development in haemophiliacs has been linked to race, nature of mutation and the type of factor used (Ghosh, 2004). Santagostino et al (2009) included other factors such as genetics, challenges to the immune system and environmental influences to be linked to the development of inhibitors.

2.3 Diagnosis

An accurate diagnosis of haemophilia is important to make as this will dictate the nature of therapeutic intervention. The essential fundamentals for making a diagnosis include:

- A comprehensive bleeding history
- A complete physical examination
- Performing screening tests for bleeding diathesis
- Performing confirmatory tests.

These screening tests include measurement of platelet count, international normalised ratio (INR) and activated partial thromboplastin time (aPTT). Bleeding time should also be determined if bleeding is suspected to be due to platelet dysfunction or blood vessel abnormality.

The screening tests are followed by confirmatory tests, which include specific factor assays, inhibitor assays, platelet function tests and von Willebrand factor assays, where indicated. Since haemophilia A and B are indistinguishable clinically and on screening tests, their diagnosis must

be confirmed by specific factor assays. Factor assays allow classification of haemophilia as severe, moderate or mild depending on the plasma concentration of FVIII or FIX (Kitchen et al, 2000; Hemophilia of Georgia U.S.A, 2000; Simon et al, 2008).

2.4 Presentation

The presentation of patients with haemophilia will be described according to the International Classification of Functioning (ICF) model.

2.4.1 Impairments:

According to the ICF model, impairments can be described as the problems in body functions and structure (McGee, 2006).

Patients with haemophilia experience a variety of bleeding manifestations, which usually, but not always, are in keep with their baseline level of clotting factors. Haemarthrosis, synovitis and bruising are the most frequent complications for patients with haemophilia and are frequently accompanied by marked muscle atrophy around the joint, possible due to the poor use of that muscle (Gomis et al, 2009). Examples of bleeding include intracranial haemorrhage, deep muscle and joint bleeds, hematomas, postsurgical bleeding, easy bruising and mucosal bleeds (Price et al, 2007). Up to 80% of bleeding episodes occur in the joints, but in infants under 2.5, soft tissue haematomas are more common (Bladen et al, 2007).

2.4.1.1 Intracranial Haemorrhage (ICH)

Intracranial haemorrhage (ICH) is a relatively uncommon, but very serious complication of haemophilia that may impair the life expectancy and impact the long term prognosis of patients with haemophilia (Revel-Vilk et al, 2004; Ljung et al, 2008).

ICH occur in 2 to 14% of haemophilia patients included in survey data, with an incidence between 54 and 200 per 10,000 person's with haemophilia per year, and is associated with 18%

mortality. It is more common in severe haemophilia patients, but is not excluded in patients with mild haemophilia (Revel-Vilk et al, 2004; Brown, 2005).

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ICH is a significant cause of mortality, and morbidity in patients with haemophilia (Ljung et al, 2008; Bladen et al, 2009). The prevalence and cause of ICH in children with haemophilia is unclear and varies from 3.58% to 12% in the literature, with mortality varying between 0.6% and 21.9%.

The majority of ICH's in person's with haemophilia occur in the pediatric age group, in which the most common cause of ICH in children is birth trauma (Revel-Vilk et al, 2004; Bladen et al, 2009). The origin of the ICH may be subdural, subarachnoid, intracerebral, or intraventricular (Bladen et al, 2009). Symptoms include severe headaches, vomiting, seizures, mental status changes, blurry vision, and can progress to coma or death (Brown, 2005).

The general outcome from an ICH in childhood can range from no apparent neurological impairment to death, with a range of neurological impairments between those extremes, including psycho-intellectual consequences (Ljung et al, 2008; Bladen et al, 2009).

2.4.1.2 Joints Affected

The musculoskeletal system is the most common site of bleeding among haemophiliac patients and the major source of disease-related morbidity in patients who are incorrectly treated (Brown, 2005).

Today prevention of joint damage is one of the most important goals in haemophilia therapy (Oldenburg et al, 2009).

In order for a joint to be 'stable' as such, it is dependant on three factors:

- (1) Relevant joint congruence
- (2) The integrity of noncontractile peri-articular connective tissue, and
- (3) Muscular function across a joint that produces or prevents motion

(Buzzard, 1998)

Haemarthrosis is the most common musculoskeletal finding in haemophilia, usually involving the joints of the lower limbs (Battistella, 1998; Falk et al, 2000). The most common complication is synovitis of the joints leading to more frequent bleeds and development of target joints (Falk et al, 2000; Price et al, 2007). The definition of a target joint, as described by Price et al (2007) is a minimum of three bleeds into a single joint within a consecutive three month period. The frequent bleeds again cause recurrent synovitis leading to joint degeneration, reactive degenerative bone formation, articular distortion and at times severe disability (Falk et al, 2000; Santavirta et al, 2001). Literature has shown that as few as three joint bleeds over 18 months can cause chronic joint damage (Bladen et al, 2007).

Approximately 80% of recurrent haemarthrosis occurs in the elbows, knees and ankles (Buzzard, 1997; Engelbert et al, 2008). Haemarthrosis predominately occur in these diarthrodial joints, most often in the lower limbs (Santavirta et al, 2001; Brown, 2005; Gomis et al, 2009), with the median age at first joint bleed being 2.2 years (Brown, 2005). These joints are more susceptible to haemarthrosis due to the large amount of synovium within the joint. These joints also lack the protection of muscle coverage and are unable to withstand rotatory and angular stresses (Buzzard, 1997). Today, the ankle joint is the most common site for bleeding in both children and adults with haemophilia (Stephensen et al, 2009). Furthermore, due to chronic joint bleeds, ROM limitations begin at an early age which can ultimately affect participation in physical activities (Soucie et al, 2004)

Due to episodes of bleeding, periods of decreased activity that follow and restrictions on participation in physical activity, people with haemophilia are predisposed to impaired strength, balance and proprioception (Wittmeier et al, 2007). Impairments of the musculoskeletal system will in turn limit activities of daily living and restrict participation in social activities (Heijnen, 2008), and will account for major long-term complications of severe haemophilia (Manco-Johnson et al, 2002).

2.4.1.3 Muscles Affected

Bleeding into the muscles is said to account for between 10%-30% of all musculoskeletal bleeding episodes in patients with haemophilia (Beeton et al, 2001). Compared to spontaneous

joint haemarthrosis, muscle bleeds are mostly associated with trauma (Beyer et al, 2010). Bleeding can occur in either skeletal or smooth muscles, with the most common sites including iliopsoas, gastrocnemius and the forearm flexor muscles (Beeton et al, 1998). Muscle bleeds generally need more time for healing than joint bleeds, and can equally impact negatively on range of movement (ROM) (Blamey et al, 2010). Beyer et al (2010) conducted a survey to investigate the current practise in the management of muscle bleeds with participation from 22 haemophiliac patients. It was interesting to note that from this survey it was found that Iliopsoas (55%), calf (18%) and thigh (18%) were scored as the most serious bleeds. Bleeds into the iliopsoas muscle is considered potentially life threatening with significant morbidity, with further complications such as anaemia/hypovolaemia, chronic back pain, groin and thigh pain, femoral nerve compression, as well as contractures at the hip joint (Ashrani et al, 2003).

Muscle bleeds lead to spasms of the affected muscle. Insufficiently treated muscle bleeds may result in several complications such as irreversible damage to the muscle including compartment syndrome, reduced range of motion, loss of function, excessive blood loss, infection, peripheral nerve complications, bruising, swelling and pain (Beyer et al, 2010; Battistella, 1998; Beeton et al, 2001). Pain and muscle spasm can put the adjacent joint articulation in a painful position (Battistella, 1998).

Type II muscle fibre loss is the major component in haemophilic muscle atrophy (Battistella, 1998). Muscle strength recovers before muscle volume (Battistella, 1998). A sufficient muscular strength is necessary not only for range of movement, but also for the control of the joint and the absorption of energy (Hilberg et al, 2003).

As reported by the literature the quadriceps muscle is consequently weak as a result of recurrent bleeds into the knee joint, resting of that joint and inadequate rehabilitation following the bleed (Manigandan et al, 2004; Hart et al, 2010). The quadriceps muscle is the shock absorber for the weight bearing forces that occur on a daily basis. A strong quadriceps muscle is also associated with sufficient strength necessary to reduce strain on the collateral ligaments (Hilberg et al, 2001).

In a study conducted by Falk et al (2000), the muscle strength and anaerobic power was tested in thirteen boys with severe haemophilia in comparison to 16 age matched peers. The Biodex System II dynamometer and the Wingate Anaerobic Test were used during the study. It was found that children and adolescents with haemophilia were characterised by lower muscle strength and anaerobic power when compared to age matched control.

2.4.1.4 Pain

Chronic or recurrent pain is a common incidence among children and adolescents, affecting as much as 25% of the pediatric population. Children with chronic pain have reported on disturbances in sleeping and eating habits, participation in social and schooling events as well as overall a decreased sense of well being (Gold et al, 2009).

Pain is subjective, and many presume that children are unable to reliably report on pain (Sherry, 2008). Thus pain in children is characteristically underrecognised and undertreated. The dictionary definition of pain is any unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in such ways (Sherry, 2008).

‘Pain is of particular relevance on the daily life of a haemophiliac’ (Wallny et al, 2001). It has been shown that pain in haemophilia acts as an important predictor of disability over a longer period of time (Van Genderen et al, 2006). Haemophilia can cause arthritic pain when joints are damaged by repeated joint bleeds, as well as causing acute pain during joint bleeds (Elander et al, 2009). Although pain is often the direct result of a bleed in those with haemophilia, the musculoskeletal system in itself can contribute to, or be the origin of pain (Dalzell, 2005).

Haemophilic patents generally report that pain can negatively impact on everyday physical function, moods and well-being, as well as perceived quality of life (Sherry, 2008) Elander and colleagues (2009) conducted a study to assess whether negative thoughts and pain coping strategies could influence pain intensity and perceived quality of life in 209 men with haemophilia A and B. Although many studies have shown that quality of life can be improved with on-demand treatment and prophylaxis, this study is suggesting that quality of life can

potentially be improved by interventions to promote better acceptance of pain, and reduce negative thoughts about pain.

Van Genderen et al (2006) conducted a study investigating the role of pain in functional limitations in haemophiliac patients as well as the depiction of pain experienced by these patients. Seventy-eight adult haemophiliac patients completed one questionnaire on pain and one on self perceived functional abilities. Two thirds of the patients reported that pain was present in their daily life. It was also shown that pain plays a small but significant role in functional limitations.

Railton et al (1987) studied the clinical features of 158 bleeds in muscle of the upper limb of 44 boys with severe haemophilia over a two year period. Of the 158 bleeds, the authors reported that 99% of the bleeds were treated within two hours of onset. Pain was the presenting symptom in 80% of each bleeding episode, whether on movement or at rest.

Proper pain management is essential in patients with haemophilia to allow for active exercise, proprioception and co-ordination (Buzzard, 2007).

2.4.1.5 Obesity

Obesity has become a global health problem and has been declared an epidemic and ‘public health’ crisis among children worldwide due to an increase in its occurrence (Whitlock et al, 2005; Armstrong et al, 2006).

Children who are overweight are generally less physically active and/or exercise at lower intensities than children who are not overweight (Douma- Van Riet et al, 2009). Literature has shown that obesity is 50% more common among boys, especially those who do not meet the recommended amount of physical activity (Bladen et al, 2007). Children with haemophilia may be at an increased risk for becoming overweight as a result of inactivity due to joint bleeds or overprotection (Douma-van Riet et al, 2009). Obesity leads to overloading of the joints, which may in itself cause further bleeds and joint damage (Salek et al, 2010). Further consequences of

obesity include pulmonary, orthopaedic, neurological, endocrine and gastroenterological conditions as well as cardiovascular risk factors (Whitlock et al, 2005).

One of the most significant short-term morbidities of obesity is the psychosocial problems which include reduced self-esteem, and decreased quality of life (Whitlock et al, 2005).

2.4.2 Activity

The ICF model describes activity as the performance of a task or action by an individual (McGee, 2006).

2.4.1.2 Endurance

Physical fitness has been described by the American Academy of Physical Education as ‘the ability to carry out daily tasks with vigour and alertness, without undue fatigue and with ample energy to engage in leisure time pursuits and to meet the above-average physical stresses encountered in emergency situations’ (Vanhees et al, 2005). Exercise has a direct influence on fitness levels, such as endurance, strength, flexibility, co-ordination and other health parameters such as blood pressure and body composition (Vanhees et al, 2005).

In adults and children, exercise brings about physiological changes in the cardiovascular, pulmonary and metabolic systems. However, in children differences in physiological changes are seen as growth and development occur (McGee, 2006).

Koch et al (1984) assessed the physical fitness of children with haemophilia between 8.3 and 15.5 years and reported a significant reduction on exercise capacity possible due to insufficient intensity during daily physical activities.

Engelbert et al (2008) evaluated aerobic capacity in children between 8.2-17.4 years with haemophilia compared to their healthy peers, and showed that aerobic capacity of children with haemophilia is lower than the normal population, whereas their overall muscle strength is comparable with healthy peers.

2.4.2.2 Gait

Walking involves the repetitive interaction of muscles and joints to propel the body forward at different speeds, over different surfaces while supporting the weight of the body (Stephensen et al, 2009). Literature has shown differences in speed of walking, step length, stride length and step time have been reported in haemophiliac children (Stephensen et al, 2009).

Gait deviations are commonly seen in patients with haemophilia due to frequent immobilisation causing subsequent muscle weakness, shortening and joint changes (McGee, 2006).

Comparisons of biomechanical gait parameters in children with haemophilia compared to their age matched peers were investigated in a study conducted by Stephensen et al, 2009. Fourteen children were used in each group, ranging from 7-13 years of age. Sagittal plane kinematics, kinetic and temporal-spatial data was captured via a motion capturing system and two force platforms. The results suggest that there are early biomechanical changes present in young haemophiliac patients due to recurrent ankle joint bleeds, thus implying that lower limb joint function is more impaired than previous literature indicated.

2.4.2.3 Balance and Proprioception

Proprioception can be defined as the sense of posture, movement and changes in equilibrium, and the knowledge of position, weight and resistance of objects in relation to the body (Hilberg et al, 2003). Proprioceptive deficits have been described by the literature as both a consequence and cause of injury (Buzzard et al, 1998; Hilberg et al, 2001). Proprioception plays a significant role in the afferent and efferent neuromuscular control arcs. These arcs are disrupted by joint and soft tissue injury, which may contribute to micro-trauma and re-injury (Hilberg et al, 2001). Therefore, specialized training for global proprioception would be necessary to compensate for proprioceptive deficits, thus preventing further falls and bleeds. Impaired proprioception may have a negative impact in daily living particularly in conditions where unimpaired proprioception is required (Hilberg et al, 2001).

Hilberg et al (2001) conducted study to investigate the proprioception and maximal isometric strength in the lower limbs of haemophiliac patients compared with anthropometrically matched controls. Proprioception was measured by the one-leg stand test, with eyes opened or closed, posturomed, angle-reproduction and the tuning fork. Lower limb strength was measured by performing a leg press and knee extension. It was shown that global proprioception was impaired as well as a unique isolated weakness to the knee extensor, the quadriceps muscle.

Balance performance is complex and multi-dimensional, involving not only the skill to maintain a static stance, but the ability to maintain equilibrium under a series of dynamic conditions, which classically reflect circumstances when falls occur (Fearn et al, 2010). All motor abilities require a stable control of posture and balance (Austad et al, 2007).

In a study conducted by Fearn et al (2010) balance and related performance was evaluated in 20 adult haemophiliac patients compared to their healthy age matched peers. Static and dynamic balance, mobility, strength, physical activity and fall efficacy was evaluated via a comprehensive suite of clinical and laboratory measures. It was found that the patients with haemophilia have moderate impairments in balance, mobility and related measures, compared to their healthy peers.

Subsequent to the above mentioned study, Austad et al (2007) investigated postural control during the transitional stage between standing and walking by measuring the abilities of healthy children in three different age groups, namely two to three years, four to five years and seven to eight years of age, and compared the results to those of an adult group. The results indicated that the youngest children had the least control over their movements in dynamic standing. Literature has shown that children with haemophilia experience their first joint bleed at a median age of 2.2 years (Brown, 2005). As mentioned previously, bleeding into a joint can affect proprioception (Hilberg et al, 2001), which could further hinder balance in this age group.

2.4.3 Participation

Participation, as described by the ICF, is the involvement in a life situation (McGee, 2006).

2.4.3.1 Quality of Life (QOL)

“Quality of life can be broadly defined as the degree of satisfaction with life in general” (Rosendaal et al, 1990). Health-related quality of life (HRQoL) is an important outcome for the evaluation of haemophilia care, and is defined as a multidimensional construct regarding the physical, emotional, mental, social and behavioural components of wellbeing and function as perceived by the patients and/or observers (Remor et al, 2004).

The debilitating problems of haemophilia often results in restrictions of the patient’s activity and reduction in productivity, thus impacting negatively on the patient’s QOL (Siddiqi et al, 2010).

The disease–related challenges faced by parents, health-care providers and the adolescent patients themselves are made more complex due to the simultaneous physical, social and sexual changes experienced by teenage boys (Petrini et al, 2009). Teenagers tend to focus on the present and may not perceive the prevention of potential future joint disease as a high priority. Thought processes during puberty may include denial of the disease, while emotional reactions may include fear (Petrini et al, 2009).

A physiological approach to the management of patients with haemophilia is becoming increasingly important. In previous studies it has been shown that key factors that influence the quality of life from the physiological perspectives include family, health, education and leisure time (Salek et al, 2010). Functioning and health are not only associated with the underlying disease, but are also influenced by personal and environmental factors (Van Genderen et al, 2005).

2.4.3.2 Academic Achievement

The consequences of haemophilia affect both social and academic activities in children with haemophilia including restriction of activities to prevent trauma, absenteeism from school following a bleed and general inability to participate fully in normal happenings of childhood (Usner et al, 1998). Children who experience more bleeding episodes are more likely to attain lower academic standards than those with fewer bleeds (Sherry, 2008).

In a study conducted by Usner et al (1998) 307 children with haemophilia were assessed for abnormalities in coordination and gait, intellectual ability and academic achievement using data from the Haemophilia Growth and Development Study. The findings of this study suggested that lowered academic achievement is associated with the functional severity of haemophilia. The authors proposed that firstly, frequent and prolonged bleeding episodes could lead to diminished abilities to take advantage of environmental opportunities, and secondly the pain and discomfort associated with bleeds can cause a lack of attention or motivation in academic tasks, thus affecting their academic achievements.

2.5 Management of Haemophilia

2.5.1 Medical Management

Different treatment modalities and dosage of factor concentrate is different worldwide and is dependant on the economic situation of a specific country and their treatment guidelines (Bullinger et al, 2008). Eighty per cent of severe haemophiliacs live in developing countries, where appropriate health resources are severely limited (Srivastava et al, 1998; Ghosh, 2004). The World Federation of Haemophilia has estimated that 75% of the global population of people with bleeding disorders receives either inadequate treatment or no treatment whatsoever (Blamey et al, 2010).

2.5.1.2 Prophylaxis in People with Haemophilia

Children with haemophilia in the western world have unlimited access to factor concentrates and early prophylaxis, which enables a nearly normal lifestyle (Petrini et al, 2009). Prophylaxis in haemophiliac care is defined as the infusion of factor concentrate replacement treatment before the occurrence and in order to prevent further bleeding (Coppola et al, 2009).

Haemophilia is a potentially disabling condition, and can be associated with high financial costs (Beeton, 2002). Financial constraints are the foremost reason for inadequate haemophilia care and prophylaxis in the developing world (Srivastava et al, 1998). The World Federation of Haemophilia (WFH) and the Medical and Scientific Advisory Council of the U.S. National

Haemophilia Foundation recommended prophylaxis as standard therapy for children with haemophilia (Manco-Johnson et al, 2002). Children who start prophylaxis early in life have less bleeding episodes, thus reducing joint damage, which may even lead to reduced factor consumption (Bladen et al, 2007). Those in developing countries without ready access to factor replacement will demonstrate greater joint damage and more restrictions on involvement in physical activities (Wittmeier et al, 2007). The availability of coagulation products for haemophilia, use of home therapy and prophylaxis have a positive influence on the disease course in terms of bleeding control, pain intensity and functional ability (Santavirta et al, 2001). The literature shows that there is a reduction in bleeding incidence in children in prophylaxis compared to those on demand therapy (Mercan et al, 2010).

Haemophilia caregivers in developing countries still see many disabilities of haemophilia that are no longer seen in developed countries (Ghosh, 2007). In South Africa, patients in the smaller centres only receive treatment for acute bleeds for a few days or until pain disappears. Follow up is generally inadequate and no-interval assessments are made (Srivastava et al, 1998).

In a study conducted by Schoenmaker et al (2001) it was investigated whether children with haemophilia on prophylactic therapy differ from healthy aged matched peers in terms of motor performance and disability. It was shown that there was no significant difference with regards to motor performance and ADL between patients with moderate and severe haemophiliacs when compared with their healthy peers.

By using prophylaxis or on-demand therapy, depending on the severity of haemophilia, it is possible for children to be physically active and participate in nearly all sporting activities (Koiter et al, 2009).

Yee et al (2002) conducted a retrospective study of prophylaxis practice in a Haemophilia centre in the United Kingdom (UK). Records from 41 children with severe haemophilia were reviewed. The results showed benefits of the use of prophylaxis in terms of marked reduction in the number of joint bleeds, low clinical joint scores, less hospitalisation, a reduction in school absenteeism and improved participation in physical activity and sport. Parents reported on less anxiety and overall improvement in their family's quality of life.

2.5.2 Treatment

Since the development of clotting factor concentrate in 1966, haemophilia patients have been treated more effectively, where home infusions, prophylactic factor replacement and elective reconstructive surgery have become possible (Luck et al, 2004; De Kleijn et al, 2006).

Haemophilia care should be monitored by specialised centres with comprehensive care teams, which implies the involvement of professionals from different fields (Rosendall et al, 1990).

The aim in haemophilia care has shifted from the treatment of severe bleeds alone to the prevention of further bleeds (Rosendaal et al, 1990).

A comprehensive approach provides ongoing assessment and continuity of care, thus decreasing the amount of complications for individuals with haemophilia (Price et al, 2007).

In the treatment of haemophilia, the most important component is replacement therapy (Lindvall et al, 2006). Treatment consists of i.v. administration of the deficient clotting factor to either prevent or stop bleeding (van der Bom et al, 2009). The World Federation of Haemophilia (WFH) guidelines for the management of haemophilia recommend early assessment and treatment (within two hourly, if possible) of acute bleeds (Salek et al, 2010). By controlling the bleeding rapidly, will also limit the degree of joint destruction by preventing increased exposure to blood in the joint, as well as to the amount of blood deposited (Salek et al, 2010).

Traditional therapies include arthroscopic and open surgical synovectomies to remove hyperplastic synovium and limited joint haemorrhage. Surgical approaches are not really suitable for children for many reasons. Firstly, surgical outcome depends on optimal co-operation with postoperative physiotherapy and activity restrictions, which may prove difficult for many young children. Small joints are less accessible in arthroscopic procedures. Joints of children with haemophilia commonly lose range of motion after surgery (Manco-Johnson et al, 2002).

2.6 Effects of Exercise

With an increase in age expectancy, the aging haemophilic population will be affected with age-related musculoskeletal disease, cardiovascular and cancer (Oldenburg et al, 2009). Regular participation in physical activity is an important component of the management of haemophilia (Wittmeier et al, 2007; Heijen, 2008). Children with haemophilia are encouraged to be physically active, and should have fitness levels comparable to those of their healthy peers (Koch et al, 1984). Chronic joint damage and functional impairment, distinctive of haemophilia, can be largely prevented through the benefits derived from participation in exercise (Wittmeier et al, 2007). For those with haemophilia, better physical condition and good coordination may prevent musculoskeletal problems and may accelerate recovery after muscle and joint bleeds (Tiktinsky et al, 2009).

Exercise contributes to better coordination, balance, endurance, flexibility, proprioception and strength which in effect can reduce the occurrence of injuries or prevent intra-articular haemorrhages, maintain healthier joints, improve muscle-to-fat ratio and enhance quality of life and self esteem (Lindvall et al, 2006; Wittmeier et al, 2007; Heijnen, 2008; Petrini et al, 2009). Research has also shown that exercise can improve bone density and reduce the risk of osteoporosis later on in life. There is also documented evidence of changes in the levels of blood-clotting factors during exercise, which may be vital for the survival of haemophilic individuals who live in countries with limited supply of factor replacement therapy (Buzzard 2007). Finally, it may also provide a sense of achievement and companionship, providing a healthier lifestyle with long term benefits (Koiter et al, 2009).

Proprioceptive deficits has been described by literature as both a cause and a consequence of an injury by either being a cause of injury, and therefore causing a bleed, or the result of repeated joint bleeding (Buzzard, 1998; Hilberg et al, 2001). Therefore, specialized training for global proprioception would be necessary to compensate for proprioceptive deficits, thus preventing further falls and bleeds.

Restriction of physical activity to reduce the risk of trauma and bleeding is common among children with haemophilia. This restriction accelerates muscle atrophy, which ultimately leads to

lower stability and greater vulnerability of the joints, as well as repeated haemarthroses (Tiktinsky et al, 2002; Tiktinsky et al, 2009). Prevention of injury can be achieved with regular training, as the benefits of physical activity, which include increased self-esteem, social contacts and a normal way of life, generally outweigh the risks with persons with haemophilia (Petrini et al, 2009).

In a study conducted by Tiktinsky et al (2002) the bleeding profile of two severe haemophilia patients who began progressive resistance training was reviewed prospectively. Furthermore, data was collected from three patients who had been training for 11-21 years retrospectively. The results not only supported the importance of resistance training for increasing muscle strength, but it was shown that both the frequency of bleeds as well as pain associated with bleeds decreased by the end of the training programme. It was also found that cessation of training over a period of two weeks was associated with an increased frequency as well as severity of bleeds.

Children who are strong and active have improved self-esteem and confidence, which prevents secondary impediments caused by the feeling of being “different” (Koch et al, 1984).

Exercise has also been shown to provisionally increase the circulating levels of factor VIII in patients with haemophilia, but does not eliminate the needs for factor replacement if a bleed occurs (Wind et al, 2004).

2.6.1 Socioeconomic Status on Physical Activity Levels

In a study conducted by McVeigh et al (2004) the associations between socio-economic status (SES), physical activity (PA), anthropometric and body composition variables, as well as the influence of maternal characteristics on PA in South African children were investigated. Three hundred and eighty-one children living in Johannesburg were assessed via an interview. The sample consisted of 43 white males, 157 black males, 38 white females, and 143 black females. The results showed that white children were more active than black children, and boys were more active than girls. The authors hypothesised that this may be due to lack of physical education offered at schools. All the white children in this study were in a higher SES than the black children.

A number of studies conducted in developed countries have shown that children and adolescents are inactive. Thus in recent years Westernised countries have placed huge emphasis on the promotion of physical activity. However, in developing countries, such as South Africa, not much attention is paid to this problem (McVeigh et al, 2004).

2.7 Education

It is imperative to begin education and training of haemophiliac boys prior to puberty when patients are more socially engaged and open-minded (Petrini et al, 2009).

Previously, children with haemophilia were discouraged from participating in physical activity due to a concern that this would increase the risk of haemarthrosis and intramuscular bleeds (Broderick et al, 2010). Patient education is another great challenge, needing careful implementation in countries where literacy rates are still low (Ghosh, 2004).

Family members should be educated and actively involved in the management of bleeds so that they can assist the haemophiliac patient with rehabilitation and home exercise programmes (Buzzard, 2007).

Achieving adequate education for both the patient and their family members is imperative, especially when working with families in developing countries (Buzzard, 2007).

2.8. Physiotherapy

It is evident that physiotherapy is an imperative and important component of care for patients with haemophilia (Mihalova, 2007).

2.8.1. Examination

A comprehensive multidisciplinary team approach incorporating routine musculoskeletal assessment by a physiotherapist is essential for the appropriate diagnosis and management of patients with haemophilia (Dalzell, 2005).

Following an acute bleed, a thorough assessment needs to be done to ensure that comprehensive and complete rehabilitation is being pursued, and plays a key role in the ongoing evaluation and monitoring of any consequences following previous injuries (Blamey et al, 2010).

2.8.1.1 Subjective data:

The subjective data should include historical information about the location, severity and frequency of bleeding episodes (McGee, 2006). An indepth subjective assessment is imperative in order to achieve tailored haemostatic management (Blamey et al, 2010).

2.8.1.2 Objective data:

A thorough evaluation of the musculoskeletal of each individual must be carried out on a regular basis (Blamey et al, 2010), and must include:

- Active and passive ROM assessment with goniometric measurements
- Assessment of any joint deformities such as genu valgus
- Muscle strength
- Leg length discrepancies
- Girth measurements of joints and muscles
- Gait and posture evaluations
- Balance, co-ordination and proprioception training
- Assessment and management of pain
- Assess overall function and fitness levels

(Mulder et al, 2004; McGee, 2006).

2.8.2 Evaluation

Physiotherapy management of neuromusculoskeletal dysfunction involves the assessment and treatment of the articular system, neural system and muscle system, all of which are affected in haemophilia (Beeton et al, 2001). Musculoskeletal assessment in patients with haemophilia is essential to measure the extent of articular damage and assess therapeutic interventions needed in each particular patient's treatment (Lobet et al, 2010).

2.8.3 Intervention

Depending on the location and severity of the bleed, a period of rest and immobilisation is essential (Pelletier et al, 1987; Buzzard, 2007). Following a bleed, after the infusion of factor replacement, the use of immediate ‘first aid’ modalities such as protection, rest, ice, compression and elevation (PRICE) will aid in resolving the bleed within a relatively short period of time (D’Young, 2009). Immobilisation should be brief, but long enough to provide a sufficient time for healing to occur (Pelletier et al, 1987). At times during acute bleeding episodes Plaster of Paris cast may be used for immobilization purposes (Querol et al, 2002).

2.8.3.1 Cryotherapy

Cryotherapy is described by Lobet et al (2008) as ‘the local or general use of low temperature in medical therapy.’ Cryotherapy is an important component of the management of bleeds in haemophilia as it helps reduce pain, muscle spasm, metabolism and inflammation, as well as improve circulation to the affected area (Pelletier et al, 1987; Buzzard, 2007). Many devices are available to administer Cryotherapy such as general cold/ice packs, ice massage, vapocoolant sprays and compression devices such as the cryocuff (Lobet et al, 2008).

Rehabilitation of haemophiliac patients includes measures aimed at reducing the impact of the disabling and handicapping conditions and enabling disabled and handicapped patients with haemophilia to achieve social integration (Heijnen, 2008). Rehabilitation of a joint or muscle by retraining strength, flexibility, balance and proprioception to assist an individual’s return to full function after an injury or bleed is an essential component of physiotherapy (Wittmeier et al, 2007).

2.8.3.2 Range of Movement (ROM)

If full ROM and strength is not achieved following recurrent haemarthroses, a joint contracture will develop (McGee, 2006). Exercise alone won’t overcome the muscle shortening and intracapsular adhesions that may have formed. Blamey et al (2010) identified individual components of exercise such as flexibility, strength, proprioception and balance in the treatment

of haemophilia. The authors discussed the use of stretching exercises to improve ROM in haemophiliac patients. Stretching techniques include static stretching, ballistic or dynamic stretching, or proprioceptive neuromuscular facilitation (PNF) stretching. In the case of haemophiliac patients the authors recommended the use of static and PNF contract-relax techniques as the best for increasing ROM.

2.8.3.3 Strengthening

The aims of physiotherapy following an acute muscle bleed, besides the relief of pain, is to return to maximal function with full ROM of adjacent joints and to regain maximal strength and length of the affected muscle (Beeton et al, 2001). Strengthening can be achieved through isometric, isokinetic or isotonic exercise, depending on the individual's ability to move the joint without eliciting pain. Progressive resistive exercises (isotonic or isokinetic) in the open chain provides both eccentric and concentric strengthening, and are preferred initially to closed-chain exercises which could cause joint tissue damage from compressive forces (McGee, 2006). High repetition, low-load progressive resistance programmes have been shown to be effective in increasing strength and decreasing bleeding frequency (Tiktinsky et al, 2002). Similarly Falk et al (2000) and Blamey et al (2010) discuss the benefits of resistance training exercises, which include increasing joint stability, increase of muscular strength, endurance and power, decrease in pain and the reduction in the risk of injuries. The physiotherapist can decide according to the musculoskeletal health status of the child with haemophilia, as well as that individual's response to strengthening exercises, on how to progress or modify the training programme (Blamey et al, 2010).

2.8.3.4 Proprioceptive and gait re-education

Proprioception as described by Lobet et al (2008) is the 'unconscious perception of movement and spatial orientation arising from stimuli within the body itself.' Proprioceptive training is generally regarded as an essential part of rehabilitation of musculoskeletal trauma (Buzzard, 1998). Hilberg et al (2003) demonstrated that a rehabilitative programme including core stability and lower limb proprioceptive training can improve overall balance in patients with haemophilia. Buzzard (1998) listed exercises such as unilateral balance, balance on a wobble board, hopping

side to side, lunging as bouncing on a minitrampoline for training of proprioception. Assessment of lower limb functioning is highly relevant in haemophilia care. Gait analysis has been shown to be an important tool in determining biomechanical factors that may influence the outcomes of degenerative joint diseases (Lobet et al, 2008).

2.8.3.5 Postsurgical Rehabilitation

Physiotherapists will usually be involved in postsurgical rehabilitation following synovectomies in children with haemophilia (McGee, 2006). Physiotherapy management is of major importance in any pre and postoperative orthopaedic procedures regardless of which joint is involved, and is the only way patients with haemophilia can return to their highest possible level of function (De Kleijn et al, 2006).

2.8.3.6 Orthoses in Haemophilia

Orthoses in haemophilia are used for the prevention and management of bleeds and their effect on the musculoskeletal system. Each device varies according to the joint to which they are applied, although two basis types are notable; static and functional. The principle aim of orthotics is to immobilise and unburden affected body segments, and to provide stability and assistance for ambulation and other functional activities (Querol et al, 2002). Orthotics can also serve as protection for target joints and can also be used in patients undergoing prophylactic treatment. Crutches and walking frames may relieve lower limb bleeds of weight-bearing following a bleed; however this may overburden the upper limb joints. Thus special consideration and circumstances should be adhered to when requesting orthotics as part of the management of haemophiliac patients (Querol et al, 2002).

As stated by the literature, physiotherapy should be an integral part of comprehensive treatment as therapy can be effective in maintaining function and mobility in patients likely to become handicapped by the musculoskeletal complications of haemophilia (Santavirta et al, 2001; Mihalova, 2007). The ability to identify, treat and recover from bleeds is the ability to manage haemophilia successfully (Wittmeier et al, 2007).

2.9 Home Therapy

Home therapy should be part of the holistic management of haemophilia as it ensures early treatment, improvement in quality of life, reduced pain and disability, fewer hospitalisations, increases independence and maximises opportunities for schooling and employment (Rosendall et al, 1990; Salek et al, 2010). In addition, through home therapy patients also become more empowered to take charge of their own care (Salek et al, 2010).

Previous research has shown the home based therapy has led to significant improvement in the quality of life for children with bleeding disorders (Shaw et al, 2008). Shaw et al (2008) conducted a study to evaluate the impact of the increased use of home-based therapy on parents of children with bleeding disorders. Twenty-seven parents of children between eight and twelve were asked to participate in the study. Of the 27, 24 agreed to be interviewed. Twenty-one of the 24 families interviewed had haemophilia. Interestingly, the study showed conflicting results. Some parents felt that home-based therapy was less disruptive, and helped to ‘normalise’ the impact of the disease, whereas other parents struggled to administer the treatment, and felt they may do something wrong, and bring pain and harm to their child. Although the majority of the parents interviewed felt that home-based therapy had major advantages, some felt that there were even greater parental responsibilities and challenges accompanying this.

2.10. Quality of life in paediatric patients

The World Health Organisation defines quality of life (QoL) as the ‘net consequence of life characteristics on a person’s perception of their position in life, in the context of the culture and value system in which they live, and in relation to their goals, expectation standards and concerns’ (Bradley et al, 2006).

Other definitions of QoL have acknowledged that it is a multidimensional framework pertaining to the physical, emotional, mental, social and behavioural components of wellbeing and function as perceived by the patients and/or observers (Bullinger et al, 2004).

Health-related QoL (HR-QoL) is considered one of the most relevant health outcome measures in medicine (Mercan et al, 2010), and can be influenced not only by disease and treatment, but also by personal characteristics (Bullinger et al, 2004). HR-QoL considerations should also play an essential role in medical decision making (Miners et al, 1999). The QoL of children with haemophilia is expected to vary (Bradley et al, 2006). The treatment of haemophilia as well as related complications might influence the QoL of children and their families (Von Mackensen et al, 2004). Studies have shown that several factors may influence the QoL in patients with haemophilia. These include being HIV positive, having impairments due to arthropathy or repeated bleeds and also a history of orthopaedic history (Beeton, 2002).

General HRQoL measurement instruments allow comparisons across pediatric populations and facilitate benchmarking with healthy population norms, while disease-specific measures improve measurement sensitivity for health domains relevant to a particular chronic health condition (Iannaccone et al, 2009). Although generic HRQoL instruments have been developed for use in pediatric populations, there are few disease-specific measures available (Iannaccone et al, 2009).

The advantage of disease-specific measures for QoL lies in the fact that the content of these instruments are more appropriate for haemophilia patients, because they address relevant issues related to haemophilia (Remor et al, 2004). Literature has indicated an increasing use of HRQoL measures as outcomes in haemophilia treatment (Remor et al, 2004).

2.10.1 Pediatric Quality of Life Inventory (PedsQL)

The PedsQL integrates generic core scales and disease specific modules into one measurement system, and were designed to measure the core physical, mental, school and social health measures (Varni et al 2002; Iannaccone et al, 2009).

The PedsQL 4.0 Generic Core Scales was specifically designed for application in both healthy and patient populations. However, it is not a disease-specific instrument and cannot be used to provide detailed information on the specific factors that influence HRQOL in pediatric patients with haemophilia (Iannaccone et al, 2009).

Three age group versions have been developed:

1. 5 to 7 years
2. 8 to 12 years
3. 13 to 16 years

The 23 item PedsQL 4.0 Generic Core Scales consists of:

- Physical Functioning (8 items)
- Emotional Functioning (5 items)
- Social Functioning (5 items)
- School Functioning (5 items)

A study was conducted by Varni et al (2006) to determine the feasibility, reliability and validity of the 23 item PedsQL 4.0, of which the results were conclusive.

To assess the feasibility of administration, the percentage of missing values were calculated, and a percentage of < 0.001 percent was reported. Internal consistency reliability exceeded the minimum reliability standard of 0.70 required for group comparisons, while the total scale scores across the ages approached or exceeded the reliability criterion of 0.09. The construct validity was measured using the analysis of covariance (ANCOVA) at $p < 0.001$.

2.10.2 Haemo-QoL

The Haemo-QoL is a recently developed disease specific and age-related HRQoL questionnaire designed to measure quality of life children and adolescents with haemophilia (Pollak et al, 2006; Van der Net et al, 2006). The questionnaire was field-tested in six European countries involving 339 children from 20 centres. It is a self-report questionnaire for children (Remor et al, 2004).

Three age group versions have been developed:

- I. 4 to 7 years – this consists of 21 items assessed within 8 domains. The domains included physical health, feelings, view of yourself, family, friends, others, preschool/school and treatment.

- II. 8 to 12 years – this consists of 64 items assessed within 10 domains. Two dimensions; dealing with haemophilia and perceived support, are added.
- III. 13-16 years - consists of 77 items assessed within 12 domains. A further two dimensions are added; future and relationships.

(Remor et al, 2004; Pollak et al 2006; Mercan et al, 2010)

The “physical” dimensions includes questions relating to pain and bleeding, restrictions of movement; the “feelings” dimension asks children how they feel about their haemophilia; the dimension of “view” questions how children perceive themselves; the “family” dimension evaluates interaction and relationships with the family; the “friends” dimension is about the interaction with friends; the dimension “perceived support” is about how children perceive their support they received from others; the “sport and schooling” dimension is about whether the patient is able to participate in sporting activities and social activities at school; the dimension “dealing” is about how the child deals with haemophilia; the dimension “treatment” is about factor injections administered. “Future” and “partnership” dimensions question the older children with haemophilia about their feelings about the future, having a girlfriend and family (Mercan et al, 2010).

Overall summary scores range from 0 – 100, with 0 representing best QL which is opposite of most measures, and may complicate interpretations (Bradley et al, 2006).

A study conducted by Von Mackensen et al (2004) examined the reliability and validity of the Haemo-QoL, and found that there were acceptable internal consistency and retest reliability values as well as sufficient discriminative and convergent validity. The test-retest correlation was measured at a value of 0.92. Convergent validity varied from 0.30 – 0.532 depending on which Haemo-QoL was used.

The Haemo-QoL Index has been shown to be a useful and economical instrument that is able to reflect on the multidimensional nature of HRQoL (Pollak et al, 2006).

2.10.3 Haemo-QoL and PedsQL

Bradley et al (2006) conducted a study comparing the Haemo-QoL and CHO-KLAT questionnaires, as well as comparing correlations between other quality of life measures such as the PedsQL and VAS. It was found that the Haemo-QoL and PedsQL were highly correlated, suggesting that what is measured in the Haemo-QoL may be measured equally well by the generic PedsQL ratings.

2.11 Measuring Muscle Strength in Children

Muscle strength testing is an essential component of any neurological and orthopaedic assessment (Li et al, 2006). Different methods can be used to measure and estimate muscle strength ranging from observation without equipment to laboratory examinations with isokinetic instruments (Eek et al, 2006).

2.11.1 Hand Held Dynamometer

Eek et al (2006) and Li et al (2005) both state that manual muscle testing is subjective and is not sensitive enough to distinguish subtle differences and changes in strength. It has been recognised that traditional manual muscle testing using a 5-point grading scale has poor validity and reliability (Li et al 2005). Literature has shown that a portable hand held dynamometer (HHD) is a reliable and easy-to-use method to measure muscle strength in clinical practice. This tool provides a measurement of isometric contraction. Most clinically important muscle groups can be measured easily using a HHD (Beenakker et al, 2001).

There are two types of measurement techniques:

1. **Make Test:** This test is characterised by the assessor holding the dynamometer in a fixed position with the subject pushing against the device.
2. **Break Test:** This test is described by the assessor pushing the dynamometer against the subject's limb until the subject's maximal effort is overcome and the joint gives way.

(van der Ploeg, 1999; Eek et al. 2006)

The make test has been shown to have more reliability than the break test (Eek et al, 2006).

It is essential that the assessor using the HHD has sufficient muscle strength and is capable of stabilising the tool (Eek et al, 2006).

Many studies world wide have conducted research investigating the muscle strength of children. Although various studies have been done on healthy children, there are no international norms available.

Beenakker et al (2001) conducted a study to establish reference values for muscle force in children aged 4 – 16 years of age. Measurements were taken from 270 normal children using a calibrated hand held dynamometer (HHD). The investigators measured 11 different muscle groups by using the ‘break’ technique. No mention of the validity of the break test or the reasoning as to why this particular method was used was stated. The results from this study can be used as reference values and can be used to quantify muscle weakness in individual muscles groups in children aged between 4-16 years to evaluate effects of therapy.

Similarly, Eek et al (2006) conducted a study to establish reference values of arm and leg muscle strength as measured by isometric torque production in healthy children. One hundred and forty-nine healthy children ranging between five – 15 years of age were used in this study. The investigators used a HHD to measure the isometric muscle torque in 8 lower limb muscle groups and four upper limb muscle groups using the ‘make’ test technique. Thus the muscle strength values of this present study can be compared to the results established in Eek et al (2006).

2.12 Endurance Testing in Children

Walk tests have been typically used to measure functional status, monitoring treatment effectiveness, and establishing prognosis. Many walk tests have been developed, including time-based tests, such as the 6-minute walk test; fixed-distance tests; velocity determined walk tests (e.g. self-paced walk tests); and controlled-pacing incremental tests such as the shuttle walk test (Solway et al, 2001).

These functional walk tests are considered objective measures that provide a means of monitoring a subject's response to treatment. Compared to the more traditional laboratory indexes of exercise capacity such as cycling, or the treadmill, walk test necessitate less technical expertise and equipment, thus making them less expensive and easy to administer. Even more so, they utilize an activity that an individual performs on a daily basis (i.e. walking) (Solway et al, 2001).

Hassen et al (2010) conducted a study to compare the walking distance of haemophiliac, juvenile idiopathic arthritis, and spina bifida to that of their healthy peers, and to decipher the associations with age, height and weight body mass index, and sex. It was found that all three patient groups showed a significant reduction in walking distance compared to health references. It was also shown that anthropometric variables are strongly associated with walking distance.

2.12.1 Six minute walk test (6MWT)

The assessment of an individual's response to exercise is an essential clinical tool, as it provides an overall examination of the respiratory, cardiac and metabolic systems (Li et al, 2005; Li et al, 2007). The 6MWT has been proposed as the best indicator of functional capacity among all submaximal exercise tests (Li et al, 2005). Interestingly Li et al (2007) stated that the 6MWT is also an important component of quality of life as it reflects the ability to undertake day-to-day activities.

2.12.1.1 Description of the 6MWT

The six minute walk test (6MWT) is a self-paced sub maximal exercise test used to assess functional exercise capacity in patients with chronic disease (Paap et al, 2005; Hassan et al, 2010). The 6MWT measures the distance a person can walk at a constant, uninterrupted, unhurried pace in six minutes (Lammers et al, 2008).

2.12.1.2 Reliability and validity of the 6MWT

The study by Li et al (2005) proved the 6MWT to be both a reliable as well as a valid measure of functional capacity in healthy children. Likewise, Moalla et al (2005) stated that the 6MWT has been shown to be reproducible and valid. Enright (2003) and Li et al (2007) similarly stated that the 6MWT is quick, easy, better tolerated and inexpensive way to assess the physical function and reflect activities of daily living of an individual. The 6MWT is well-standardised, is easy to administer in clinical settings (Hassan et al, 2010), and is a self-paced submaximal exercise test which is used as an indicator of functional exercise capacity (Li et al, 2005; Paap et al, 2005; Hassan et al, 2010).

The primary variable measured in the 6MWT is the total distance walked during that period (Enright, 2003). Li et al (2007) conducted a study aiming to establish height-specific reference standards for 6MWT of healthy children aged between 7-16 years.

During the conduction of the test, it is important to use standardised phrases for speaking to the patient, because the amount of encouragement and enthusiasm given can make a difference of up to 30% in the distance of the test (Enright, 2003).

Hassen et al (2010) conducted a study to compare the six minute walk performance in haemophilia, juvenile idiopathic arthritis and spina bifida with that of their healthy peers. The walking distance of all three patient groups showed significant reductions in walking distances to that of healthy references.

Lammers et al (2008) conducted a study to provide normal values for children between four and 11 years of age. Three hundred and twenty-eight healthy children were recruited from two primary schools in the UK. The distanced walked in six minutes, oxygen saturation and heart rate during the 6MWT and three minutes post the test were determined. It was found that age, weight and height correlated with distance walked. The authors also stated on the feasibility and practicality of using the 6MWT in young children. The study provides normative data for healthy children, of which data from sickly children can be compared to.

The 6MWT can be performed by children as young as four years of age, with good explanation and encouragement (Lammers et al, 2008).

2.13 Conclusion

After examining the literature it is evident that more South African studies are needed in order to look at the effect of haemophilia in our population allowing comparisons to be made to similar studies done worldwide.

Chapter 3: METHODS

The methodology used in this research report will be presented in this chapter. Demographic information will be presented first, followed by information on the assessment tool used.

3.1 Location

This study was conducted at the Haemophiliac Clinic at Chris Hani Baragwanath Hospital, Gauteng, South Africa. Boys with haemophilia attending this clinic were recruited into the study. Patients attending this clinic are from similar socio-economic and cultural backgrounds. Boys without haemophilia from the same socio-economic and demographic backgrounds in Johannesburg, South Africa were sought either by asking the family members of the boys with haemophilia if there were any other boys in the family without haemophilia, or from The TLC Orphanage

3.2 Ethical Considerations

3.2.1 Ethical Clearance

Prior to commencement of data collection, ethical clearance was obtained from the Committee for Research on Human Subjects of the University of the Witwatersrand. Clearance certificate number (**M090639**) (Appendix I).

3.2.2 Hospital Permission

Permission from the Chris Hani Baragwanath Hospital was obtained before commencement of the study (Appendix II).

3.2.3 Consent

Consent and assent were received prior to commencement of testing (Appendix III).

3.3 Sample Selection

The data of 15 boys with haemophilia and 18 boys without, between the ages of 5-16 years of age, without any other ailments were analysed over a period of 9 months from August 2009 to April 2010. Informed consent had been obtained from the caregivers prior to assessment

3.3.1 Inclusion Criteria

Subjects who meet the following criteria were included in the study:

- *Inclusion criteria for haemophiliac patients*
 - Boys ranging from the age of 5 – 16 with a diagnosis of either haemophilia A or B
 - Attending the haemophiliac clinic at Chris Hani Baragwanath Hospital
- *Inclusion criteria for boys without haemophilia*
 - Boys ranging from 5 – 16 years of age
 - No physical illness or impairments

3.3.2 Exclusion Criteria

Subjects who did not meet the following criteria were excluded in the study:

- *Exclusion criteria for haemophiliac patients*
 - They have active bleeds in any joint or muscle
 - Children with disabilities other than haemophilia which may affect muscle strength and endurance
- *Exclusion criteria for boys without haemophilia*
 - They have experienced any previous injury or illness in the past month
 - Any musculoskeletal disorder

3.4 The Study Population

The data from 15 boys with haemophilia and 18 boys without fitting the inclusion criteria were analysed. The boys with haemophilia came mainly from Soweto and surrounding areas, and thus had similar socio-economic and educational backgrounds. All children assessed were black, and most were brought to the clinic by their primary caregiver. The boys without haemophilia were either a relation of one of the boys with haemophilia or were from TLC Orphanage which was in the same surrounding area as the clinic.

3.5 Instrumentation:

3.5.1. Hand Held Dynamometer:

A hand held dynamometer (HHD) was used to measure muscle strength in both haemophiliac patients and their healthy peers. A HHD provided measurements of isometric contractions.

A portable HHD has been shown to be a reliable and easy to use method to measure muscle strength in clinical practise (Eek et al, 2006). The make test showed higher reliability than the break test (Eek et al, 2006). Therefore the make test was used in this study.

The MicroFET 2 dynamometer was used to measure muscle strength during the course of this study. Li et al (2006) concluded that the MicroFET 2 is valid and reliable.

3.5.2. Six – Minute-Walk Test (6MWT):

Included instruments:

- Stop watch
- Beacons
- BP and HR monitor

The 6MWT was used to measure the endurance of the haemophiliac subjects as well as that of their healthy peers.

The primary measurement in the 6MWT is the total distance walked. Heart rate, respiratory rate and blood pressure constituted the secondary measurements and are recorded before and immediately after the 6MWT (Li et al 2005; Enright 2002).

3.5.3. Haemo - QoL questionnaire

The Haemo-QoL questionnaire was used as measurement for perceived QoL and self report in only the haemophiliac subjects. The Haemo - QoL questionnaire was developed for the purpose of a more targeted instrument for QoL assessment in haemophiliac patients (Bullinger et al, 2004).

3.5.4. Pediatric Quality of Life Intervention Measurement Model (PedsQL):

The PedsQL was used to measure the self-report and perceived QoL in both children with haemophilia and those without. The PedsQL integrates generic core scales and disease specific modules into one measurement system, and were designed to measure the core physical, mental, school and social health measures (Varni et al, 2002).

3.6 Procedure

Subjects attending the monthly haemophilia clinic were screened against the inclusion and exclusion criteria in order to recruit satisfactory subjects for this study. The subject and caregiver/parent were informed on the purpose of the study and the proceedings to follow.

The age-matched control group were recruited either by asking the consent from the caregivers of the haemophiliac boys participating in the study to bring any male siblings living in their particular household to the next clinic or set appointment date, or by recruiting boys from the TLC Orphanage.

Written consent from the care-giver as well as written assent from the child being tested had been obtained prior to testing.

The boys without haemophilia followed the same procedures as the boys with haemophilia, but did not fill in the Haemo-QoL questionnaire as this is disease specific to haemophilia.

3.6.1 Haemo – QoL and PedsQL

Once the necessary consent and assent had been obtained from parents and children taking part in the study, the children with haemophilia were taken to a quieter, more private room and were asked to complete the Haemo-QoL and PedsQL questionnaires. The parents\caregivers were asked to leave the room while the child completed the questionnaire to minimise bias especially in the questions relating to parental overprotection and clinical support. Although the questionnaires were in English the research assistant translated each question of the questionnaire using a standardised format that she had developed prior to testing. The research assistant was available to answer any questions at all times. The questionnaires were completed first as the other procedures may have fatigued the child, and concentration was required for the answering of the questions.

3.6.2 Hand Held Dynamometer (HHD)

Before the study commenced both the assessor and research assistance acquired practise with the instrument where the assessor will do the actual test and the research assistant will record the readings. The research assistant who had been asked to participate in this study has had previous experience with regards to the use of the HHD in a study conducted in 2008.

Once the study commenced, subjects were asked to get into specific positions in order to measure each isolated muscle group. The make test was used in all measurements

The following muscle groups were tested on both left and right limbs:

- Elbow flexors and extensors
- Knee flexors and extensors

- Ankle plantarflexors and dorsiflexors

The procedure for every muscle group, position and dynamometer position was standardised as follows (Eek et al, 2006):

Elbow

Flexors:

1. The child was asked to lie supine on a firm flat surface with his knees bent, and his arms next to his trunk with forearms in a supinated position.
2. The assessor held the dynamometer against the palmer surface of the hand.
3. The child was asked by the assessor to bend his elbow and pull the instrument as hard as he could.

Extensors:

1. The child was asked to lie supine on a firm flat surface with his knees bent and his elbow flexed to 90° with forearm supination.
2. The assessor held the dynamometer at the distal surface of the forearm.
3. The child was asked by the assessor to straighten his elbow and push the instrument as hard as he could.

Knee

Flexors:

1. The child was asked to lie prone on a firm flat surface with his knees extended.
2. The dynamometer was placed on the posterior distal region of the calf by the assessor.
3. The child was asked to bend his leg by pushing as hard as he could against the instrument.

Extensors:

1. The child was asked to lie prone on a firm flat surface with his knee flexed to 90°.
2. The assessor placed the dynamometer on the anterior distal region of the shin.
3. The child was asked to straighten his leg by pushing as hard as he could against the instrument.

Ankle

Dorsiflexors:

1. The child was asked to lie in supine on a firm and flat surface with the ankle positioned in neutral.
2. The assessor placed the dynamometer on placed on the dorsum of the foot.
3. The child was asked to pull his ankle up, pushing as hard as he could against the instrument.

Plantarflexors:

1. The child was asked to sit in long sitting on a firm flat surface with his knees extended.
2. The assessor placed the dynamometer on heads of the metatarsals of the foot.
3. The child was asked to point his foot, pushing as hard as he could against the instrument.

After each measurement had been taken, the recordings were immediately recorded on the data sheet before commencing with the next measurement.

Each test was performed three times in order to acquire accurate measures. An average of the three measures was calculated.

Time for rest was given between measurements to avoid fatigue. Encouragement to maximum effort was given by standardised words of encouragement.

3.6.3 Six Minute Walk Test (6MWT)

A study conducted by Li et al (2007) on standard reference values for the 6MWT in healthy children documented that before commencement of the test, the subjects were not allowed to perform any 'warm-up sessions' prior to testing, and were seated resting on a chair.

- Subjects to be tested were seated comfortably on a chair and had their resting respiratory rate (RR), heart rate (HR) and blood pressure (BP) taken prior to testing. The assessor explained to the child that he must relax, and that the taking of these measurements was to see how fit he is, and that no pain will be experienced. The heart rate and blood pressure

were taken by using a digital monitor. The respiratory rate was measured by observing the number of breathes taken per minute. All three readings were recorded prior to testing on a data sheet.

- Two beacons were placed 20 meters apart from each other on a flat surface in the an area where there was no interference with other patients, staffing, or distractions. The distance was accurately measured using a tape measure, and was marked with tape on the floor for exact placement of the beacons for future testing.
- Before commencing with the 6 MWT the procedure for the test was explained to the child using the research assistant to translate in their home language if needed.
- Explanation was as follows:
 - This test will help us to know how fit you are. It is not going to cause any pain.
 - You will start by standing in line with the first beacon.
 - When I say “Go”, then you must start walking as fast as you can to the second beacon. You must walk as close as you can around the beacon, and go as fast as you can back to the first beacon. You must keep walking as fast as you can until I say “Stop”.
 - You can walk as fast as you can, but don’t run, because you will fall.
 - While you are walking I am going to count how many times you can walk up and down so I can see how fit your are.
 - As soon as I say stop you must sit in the chair again and I will measure your breathing, heart rate and blood pressure like I have just done.
 - After this you are finished.
- During the test, the assessor verbally encouraged the child using the same words of encouragement; “Keep going,” “You are doing well.”
- Timing of the test was done with a Kenko stop watch. Recording of the number of times the child walked between each beacon was done.
- Once the time was over, the assessor told the child to stop, and sit down. The assessor had a chair ready and placed the chair exactly where the child had stopped. Measurement of where the child had stopped was considered so as to acquire accurate distancing that the

child had walked. Calculations were made with regards to the distance walked by the child, and the distance was recorded on the data sheet.

- The assessor immediately re-measured the child's HR, RR and BP using the same procedures as above, and again recorded this on the data sheet.
- Once 2 minutes had lapsed, the child's HR, RR and BP were measured again, and as before recorded on the data sheet.

A repeat test was not performed in this study.

3.7 Statistical Analysis

All the data collected were analysed by the Medical Research Council of South Africa.

Children available at the clinic who met the inclusion criteria were included in this study. Due to the small number of boys available a pilot study was done.

- A comparison between the boys with haemophilia and those without haemophilia were statistically analyzed using the student's t-test.
- Correlation between the two QoL measures, the Haemo-QoL and PedsQL, were measured by the Pearson's correlation coefficient.
- Demographic information was summarised using descriptive statistics, for example percentages, means and standard deviations.

Chapter 4: RESULTS

In this chapter, the results of the study will be presented. Data analysis of 33 subjects will be presented.

4.1 Demographics

The mean age, height and weight distribution of the sample are shown in the table below.

Table 4.1 Demographics of sample

	Haemophilia n = 15 Mean (SD)	Control n = 18 Mean (SD)	P-value
Age (years)	10.4 (3.22)	10.6 (2.85)	0.9
Height (meter)	1.32 (0.19)	1.43 (0.28)	0.19
Weight (kilogram's)	32.4 (13.97)	33.5 (14.71)	0.83

The age group of the sample of boys with haemophilia ranged between 6.7 – 15.9 years of age. The age group of the sample of boys without haemophilia ranged between 6 – 15.4 years of age.

The height of the sample of boys with haemophilia ranged between 1.1 – 1.7 meters. The height of the sample of boys without haemophilia ranged between 1- 2.3 meters.

The weight of the sample of boys with haemophilia ranges between 18.3 - 73.5 kilograms. The weight of the sample of boys without haemophilia ranges between 17 – 81kg.

According to the p-values, all three of the above values indicated that the two groups of subjects were well matched.

4.2 Type of Haemophilia

The figure below represents the distribution of the types of haemophilia seen in the sample.

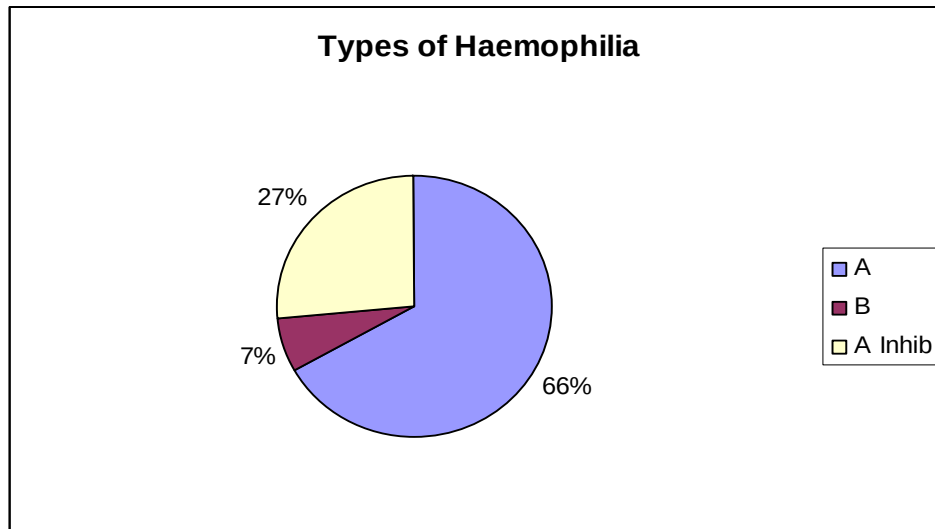


Figure 4.1: Types of Haemophilia

In the sample of boys with haemophilia, 10 out of the 15 boys had haemophilia A, making up 66% of the sample. Only one of the boys had haemophilia B, representing 7% of the sample. Four boys out of the sample had haemophilia A with inhibitors, thus representing 27% of that sample.

4.3 Muscle strength

The muscle strength of the sample was determined using a hand held dynamometer and was measured in Newton (N).

Table 4.2 Muscle Strength

	Haem group n=15 Mean (SD)	Control n=18 Mean (SD)	P value
Muscle Strength Right Elbow Flexion	16.41 (5.12)	16.1 (4.70)	0.84
Muscle Strength Left Elbow Flexion	16.11 (5.12)	16.7 (6.94)	0.78
Muscle Strength Right Elbow Extension	15.01 (4.07)	17.51 (5.46)	0.15
Muscle Strength Left Elbow Extension	12.91 (4.60)	17.20 (4.64)	0.01
Muscle Strength Right Knee Flexion	21.55 (5.52)	23.9 (6.44)	0.27
Muscle Strength Left Knee Flexion	22.43 (3.60)	23.37 (5.86)	0.59
Muscle Strength Right Knee Extension	19.40 (6.70)	24.17 (7.13)	0.05
Muscle Strength Left Knee Extension	22.70 (8.07)	25.33 (7.24)	0.33
Muscle Strength R Ankle Plantar Flexion	23.10 (5.5)	20.56 (5.29)	0.19
Muscle Strength L Ankle Plantar Flexion	21.51 (4.27)	19.1 (5.35)	0.17
Muscle Strength R Ankle Dorsiflexion	17.60 (5.02)	13.48 (4.17)	0.02
Muscle Strength L Ankle Dorsiflexion	17.85 (4.60)	13.19 (4.19)	0.00

As seen in the table above, muscle strength of the left elbow extensors, and muscle strength of the right knee extensors were significantly weaker in the boys with haemophilia ($p=0.01$ and $p=0.05$). In contrast, muscle strength of both left and right dorsiflexors were significantly greater in the haemophilia sample group, with p -values of 0.02 and 0.00 respectively. There was no significant difference between the two groups for any of the other muscle groups assessed.

4.4 Endurance

Endurance was measured with the use of a Six Minute Walk Test (6MWT) where the vitals were measured before, immediately after and 2 minutes after the test. The results are as follows.

Table 4.3 Results preceding Six Minute Walk Test

	Haem group n=15 Mean (SD)	Control n=18 Mean (SD)	P value
Heart rate (beats per min)	76.8 (17.5)	88.3 (20.3)	0.09
Respiratory rate (breathes per min)	22 (2.7)	22.9 (2.7)	0.91
Systolic Blood Pressure (mmHg)	120.9 (16.3)	115.2 (18.5)	0.33
Diastolic Blood Pressure (mmHg)	75.7 (10.5)	82.65 (12.9)	0.12

As seen by the data above there was no significant difference between the two groups in terms of their vital signs prior to the Six Minute Walk Test.

4.4.1 Distance walked

The mean distance walked by the haemophiliac boys during the 6MWT was measured as 589.6 meters with a standard deviation of 81.86 meters. Boys without haemophilia walked a mean distance of 597.08 meters, with a standard deviation of 147.57 meters. No statistical significance was noted, $p = 0.86$, as both groups walked similar distance during the test.

The vital signs as measured immediately and two minutes after the 6MWT are shown in table 4.4 and 4.5 respectively.

Table 4.4 Results immediately after the Six-Minute Walk Test

	Haem group n=15	Control n=18	P value
Heart rate (beats per min)	95.4 (26.8)	100 (22.3)	0.59
Respiratory rate (breathes per min)	29.3 (3.4)	27.6 (3.5)	0.15
Systolic Blood Pressure (mmHg)	131.9 (15.2)	130.8 (16.3)	0.86
Diastolic Blood Pressure (mmHg)	86 (14.9)	89.1 (14.6)	0.55

As seen by the data above, there was no statistically significant difference between the two groups' vital signs immediately after the Six Minute Walk Test.

Table 4.5 Two Minutes post Six-Minute Walk Test

	Haem group n=15 Mean (SD)	Control n=18 Mean (SD)	P value
Heart rate (beats per min)	82.5 (21.2)	92.4 (18.1)	0.15
Respiratory rate (breathes per min)	24.1 (2.0)	23.2 (3.6)	0.43
Systolic Blood Pressure (mmHg)	123.3 (15.1)	122.4 (17.3)	0.87
Diastolic Blood Pressure (mmHg)	80.9 (11.9)	83.6 (15.3)	0.58

As seen by the data above, there was no statistically significant difference between the two groups' vital signs two minutes after the Six Minute Walk Test.

The vitals before the test and two minutes post the test were similar in value in both groups.

4.5 Pediatric Quality of Life Inventory (PedsQL)

Quality of life was measured with both the PedsQL and HAEMQOL questionnaires.

Table 4.6 represents the total score, as well as the subscores for the PedsQL questionnaire

The higher the score is, the better the quality of life with a perfect score being 100.

Table 4.6 PedsQL scores

	Haem group n=15 Mean (SD)	Control n=18 Mean (SD)	P value
PedsQL Total	75.5 (16.3)	77.7 (16.7)	0.71
PedsQL Domain 1 (About my health and activities)	79.2 (21.2)	84.2 (14.7)	0.43
PedsQL Domain 2 (About my feelings)	77.33 (27.4)	69.7 (23.8)	0.40
PedsQL Domain 3 (How I get along with others)	77.33 (21)	75.8 (22)	0.84
PedsQL Domain 4 (About School)	59.7 (19.1)	70.3 (22.5)	0.16

As seen by the data above, there was no statistical significance between the two group's perceived quality of life depicted by the PedsQL questionnaire. The groups were very similar in their total scores as well as for the scores for each domain. The domain where the boys with haemophilia scored the worst was domain 4, which represented questions about school.

4.6 Haemo-QoL questionnaire

Figure 4.2 represents the total and subscores of the Haemo-QoL questionnaire.

Overall summary scores range from 0 to 100 with 0 representing the best QoL.

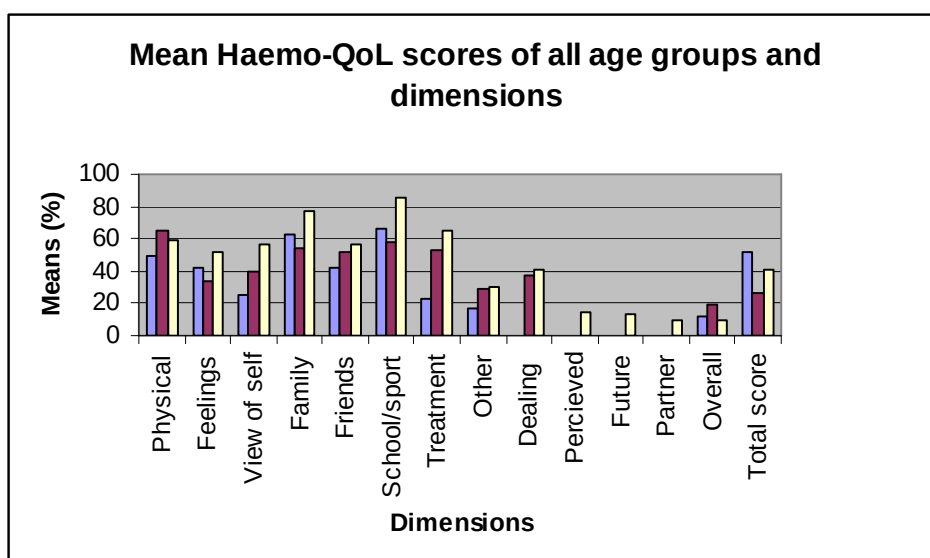


Figure 4.2 Mean HAEMO-QoL scores of all age groups and dimensions

Key:

Blue: Haemo-QoL boys 4-7 years

Red: Haemo-QoL boys 8-12 years

Yellow: Haemo-QoL boys 13-16 years

As shown in Figure 4.2 the youngest children in the age group I (4-7 years of age) were mainly impaired in the dimension 'family' and 'schooling/sport', with scores of 63.2% and 66.5% respectively. Children in age group II (8-12 years of age) were mainly impaired in the dimension 'physical health' with a score of 65.6%. The children in age group III (13-16 years of age) were impaired in dimension 'family' and 'school/sport' with scores of 76.6% and 85.4% respectively. The total overall scores showed the children in age group I showed the highest score of 51.75%, indicating the lowest perceived quality of life compared to the other two age groups II and III with scores of 27.06% and 40.43% respectively.

The overall total scores of the Haemo-QoL questionnaires are represented by the figure below, Figure 4.3. The graph shows that all the subjects answering the questionnaire scored below 50, in a range from 0 – 100, where the higher scores are associated with high impairments.

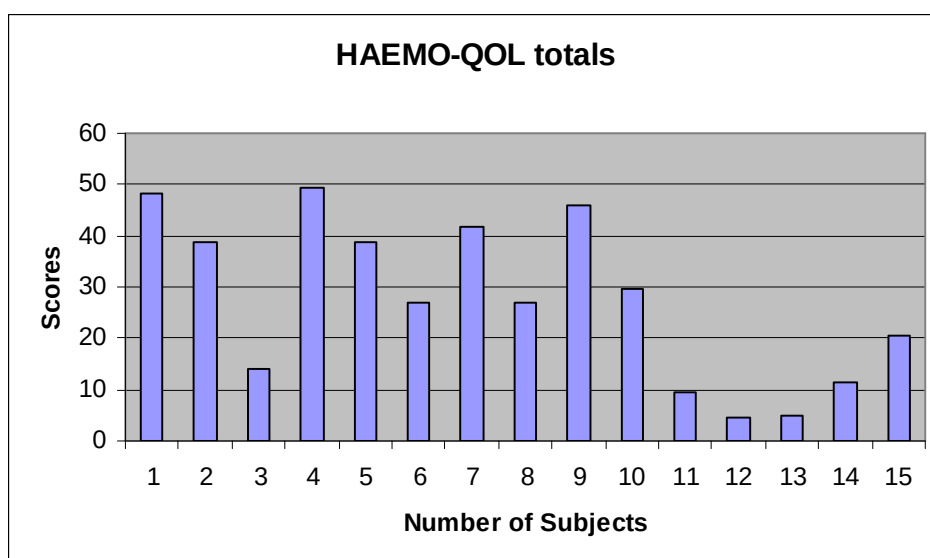


Figure 4.3: Total Haemo-QoL scores

The total Haemo-QoL score was 29.6%. The scores for each domain ranged between 10–55.6 %.

4.6.1 Haemo-QoL questionnaire - Comments

As part of the Haemo-QoL questionnaire, clinical data was obtained by asking questions with regards to the frequency and severity of the bleed, sensation felt before the bleed, the concerns of the subjects during and after their bleeds, their management during bleeds, and informing their parents during their bleeds.

4.6.1.1 Frequency of bleeds during past month:

Figure 4.4 below shows the incidence of bleeds during the past month.

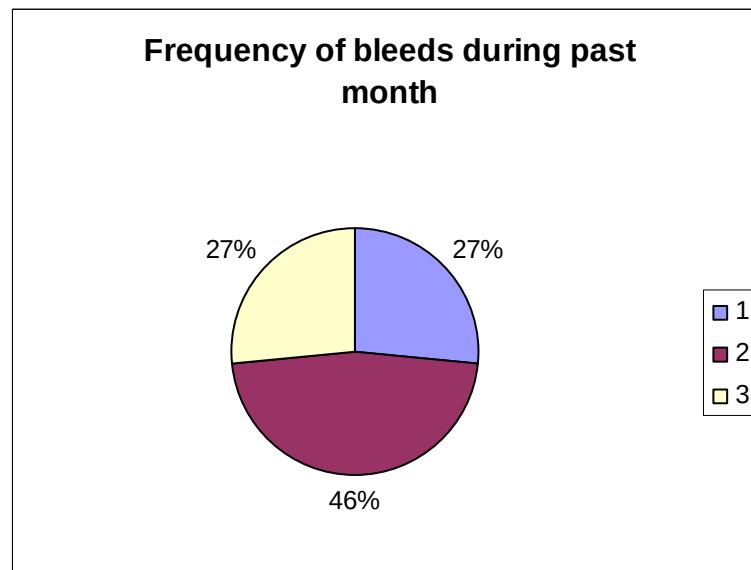


Figure 4.4 Frequency of bleeds during the past month

Key:

- 1- One bleed
- 2- More than 2 bleeds
- 3- No bleeds

As seen by the chart above, the majority of boys with haemophilia, 46.7 % experienced more than two bleeds during the past month prior to the administration of the questionnaire. This may have some effect on the muscle strength and endurance of the subjects in question. Twenty-seven percent of the sample tested experienced no bleeds during the past month, with the remainder of the sample, 27%, experiencing only one bleed.

4.6.1.2 How much were you troubled by your bleeds during the past month?

Figure 4.5 represents how much concern was generated from each bleed from the subjects' perspective.

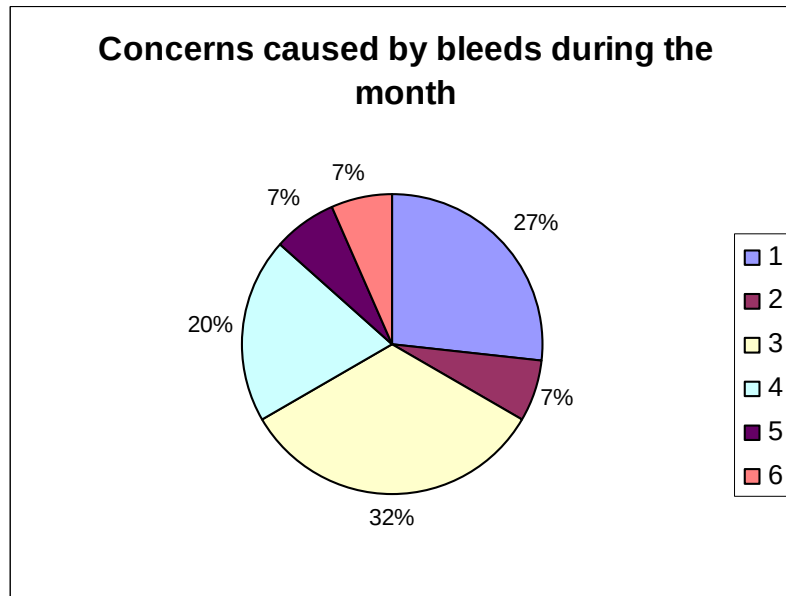


Figure 4.5 Concerns caused by bleeding during the month

Key:

1. Not at all
2. Somewhat
3. Quite a bit
4. Moderately
5. Very much
6. No answer

As depicted by the figure above, almost one third of the sample expressed their concerns about their bleeds with use of the description 'quite a bit'.

4.6.1.3. How severe were your bleeds during the past month?

Figure 4.6 indicates the perceived severity of the bleeds during the past month

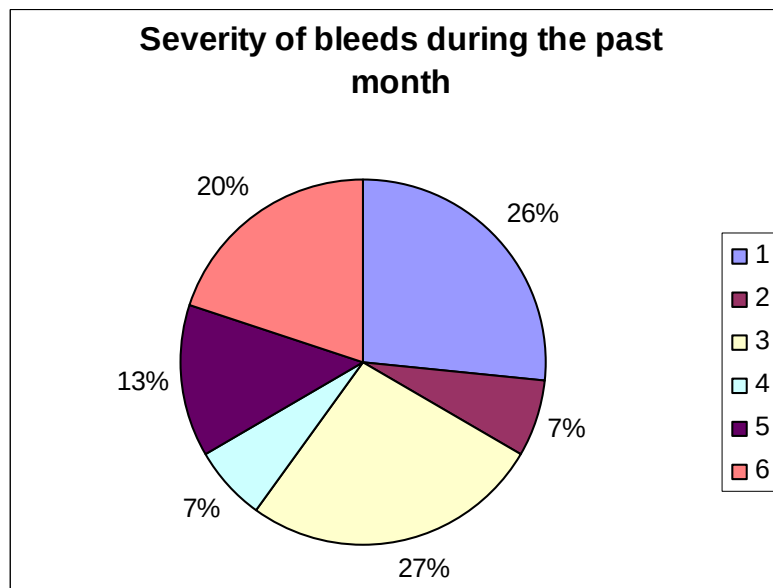


Figure 4.6 Severity of bleeds during the past month

Key:

1. Slight
2. Sometimes
3. Moderate
4. Severe
5. Very severe
6. No answer

The severity of bleeds during the past month, as depicted by the figure above shows varied responses, with 'slight' and 'moderate' showing the most results, 26% and 27% respectively.

4.6.1.4 Did you feel a strange sensation in your joints before you had a bleed?

Figure 4.7 indicated whether the subjects experienced any strange sensations prior to their bleeding episode.

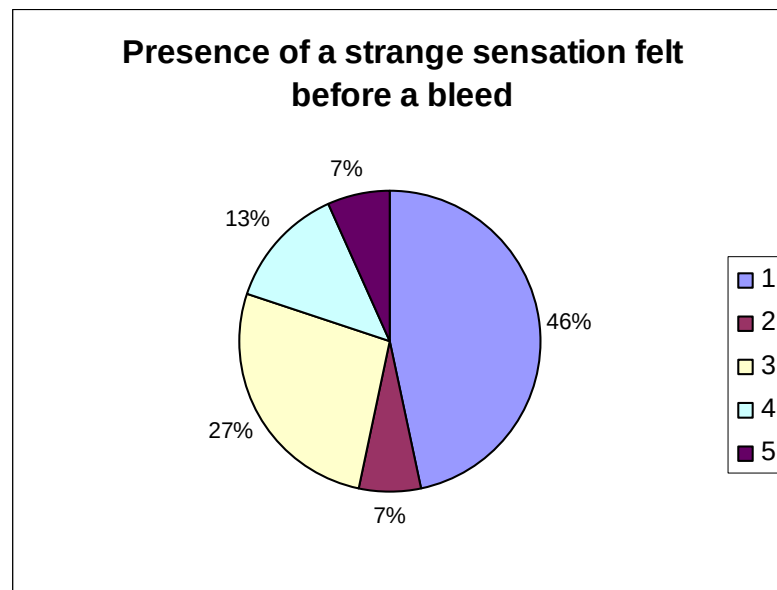


Figure 4.7 Presence of a strange sensation felt before a bleed

Key:

1. Never
2. Seldom
3. Sometimes
4. Often
5. Always

As shown by the figure above, almost half of the sample, 46.7% stated that they never felt a strange sensation before a bleed.

4.6.1.5 Did you have to stay quiet (e.g. lie in bed) when you had a bleed?

Figure 4.8 represents whether the subjects rested during the bleeding episode.

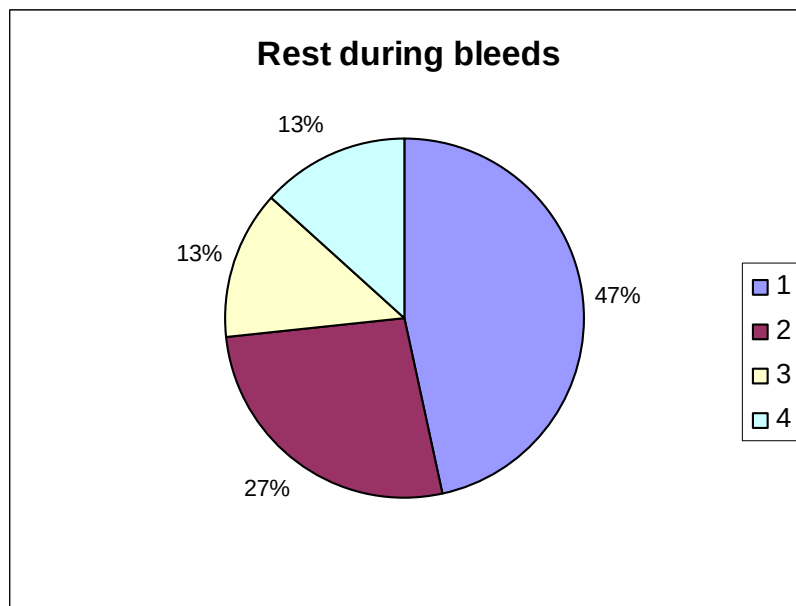


Figure 4.8 Rest during bleeds

Key:

1. Never
2. Sometimes
3. Often
4. Always

The figure above shows that almost half of the sample, 47%, never rested during an acute bleed, which may also have some affect on the recovery of that joint, and consequently affect strength, balance and range.

4.6.1.6 When you had bleeds, did you inform your parents immediately?

Figure 4.9 indicates whether the boys communicated and informed their parents of their bleeding episode.

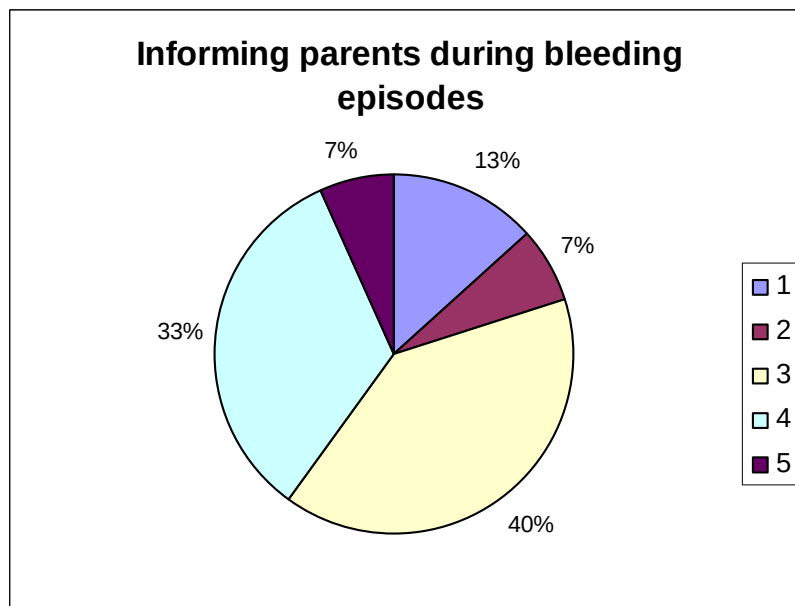


Figure 4.9 Informing parents during bleeding episodes

Key:

1. Never
2. Seldom
3. Sometimes
4. Always
5. No answer

As shown by the figure above, 40% of the sample would 'sometimes' inform their parents of their bleed, 33.3% would always inform their parents, 13.3% never informed their parents and 6.7% would seldom tell their parents of their bleed.

4.6.1.7 How much were you bothered by haemophilia?

Figure 4.10 shows how much hemophilia troubled the subjects.

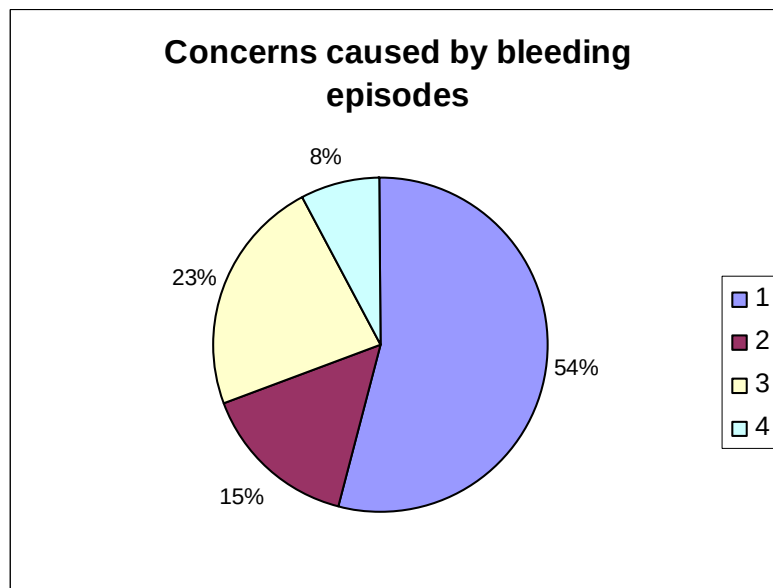


Figure 4.10 Concerns caused by bleeding episodes

Key:

1. Not at all
2. Somewhat
3. Moderately
4. Very much

As depicted by the above figure, more than half of the sample, 54%, stated that they were not bothered at all by their bleeding episode.

4.6.1.8 What bothers you most about haemophilia?

In this section of the questionnaire, the majority of the haemophiliac subjects expressed their frustration for not being able to play soccer and other 'rough' sports with their friends in fear of causing a bleed. One boy expressed his frustration of not being able to ride a bike. Another theme that came out in this section was missing school, especially when being admitted for a bleed. A few disclosed their grievance with being treated differently or being teased by other children. Pain and joint stiffness was also mentioned by 4 subjects as a limitation in their daily living.

4.7 Correlation between the PedsQL and HAEMO-QoL Questionnaires

The results from the PedsQL and HAEMO QoL were compared using Spearman's Rho. The quality of life as measured by the two tests showed only a weak correlation ($r = -0.5$).

Figure 4.11 represents the correlation between the Haemo-QoL and PedsQL

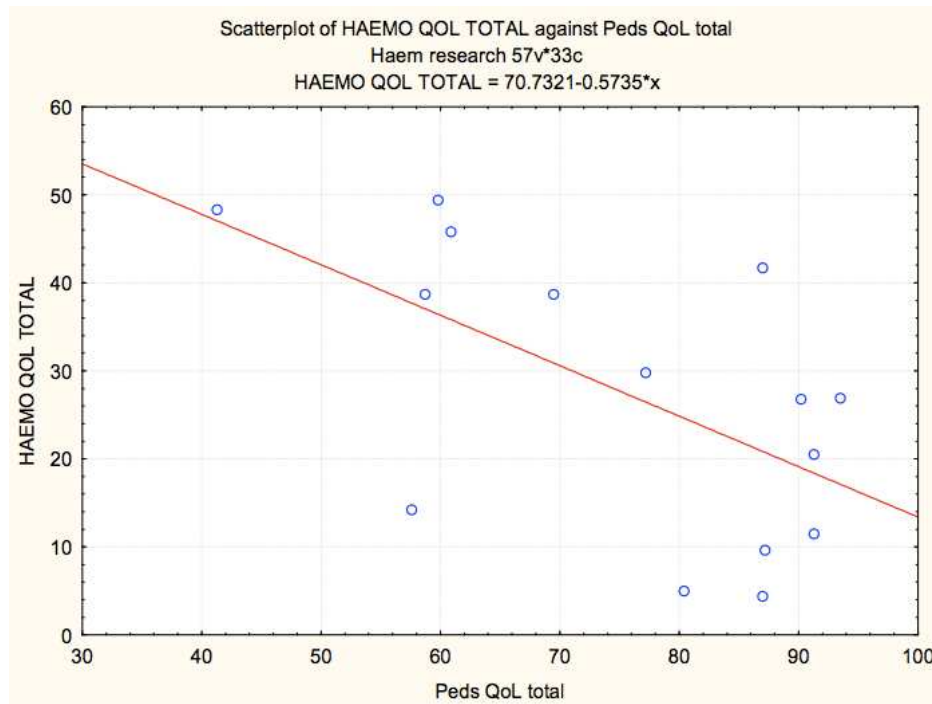


Figure 4.11 Scatterplot of Haemo-QoL total scores and PedsQL total scores

4.8 Conclusion

The boys with haemophilia did well in comparison to their unaffected peers in terms of their strength and endurance. There were also no significant differences between the two groups with regards to the quality of life. The results of this study will be discussed in Chapter 5.

Chapter 5: DISCUSSION

The results obtained in this study will be discussed in this chapter. The results will be compared to those recorded in previous studies. The implications and limitations of this study are highlighted, and recommendations for further research are made.

5.1 Introduction

Haemophilia is a life-long coagulation disorder characterised by spontaneous, post-traumatic and postsurgical bleeding (Mercan et al, 2010). Although the true incidence of haemophilia is unknown, it is estimated to occur in approximately one in every 50 000 male births (Carlos Rodriguez-Merchan, 1997; Peerlinck et al, 2010), with a frequency of 1:10 000 for haemophilia A and 1:60 000 for haemophilia B (Douma-van Riet et al, 2009). As stated by Von Mackensen et al (2004) the haemostatic defects of haemophilia lead to spontaneous and post-traumatic internal bleeding events. Hilberg et al (2001) and Ghosh et al (2004) reported on the consequences of repeated bleeds and immobilization which may ultimately result in muscular atrophy and weakness, contractures, poor balance and proprioception, lower physical functioning (Varni et al, 2006), and may have a significant impact on the quality of life (QoL) (Bradley et al, 2006).

This present study aimed to compare the muscle strength, endurance and QoL of a group of children with haemophilia to a group of aged matched healthy peers with the use of 4 outcome measures, namely a Hand Held Dynamometer (HHD), the Six-Minute Walk Test (6MWT), and two QoL measures, the Haemo-QoL and PedsQL.

It was hypothesised that boys with haemophilia would show muscle weakness, poorer endurance and a poor quality of life in comparison to a group of healthy boys.

5.2 Demographics of the study

The Chris Hani Baragwanath Hospital (CHBH) Haemophilia Centre treats approximately 30 patients with haemophilia from Soweto and other surrounding regions. Fifteen of these patients who were screened against the inclusion and exclusion criteria were included in the study.

5.2.1 Age range of the sample

Studies investigating patients with haemophilia generally have small sample sizes, as the availability of suitable patients is often limited. In this study, boys ranging from five to 16 years of age with, and without haemophilia were used. The Haemo-QoL questionnaire begins at four years of age and ends at 16 years of age, where the PedsQL questionnaires begins at five years of age and also ends at 16 years of age. Thus the age range of this study was chosen in order to accommodate both the PedsQL, and Haemo-QoL questionnaires in the boys with haemophilia.

The boys with haemophilia were recruited from the Haemophiliac Clinic at CHBH, and were all from similar socio-economic and demographic backgrounds.

The majority of the control subjects of this study, 83.3%, were recruited from the TLC orphanage in Soweto. This particular sample group was chosen as they were within close proximity of Chris Hani Baragwanath Hospital, thus with similar socio-economic and demographic backgrounds to that of the haemophiliac sample. It was also possible to specifically age match the control group to the sample group. Initially it was requested that the boys with haemophilia brought a friend or relative without haemophilia or any other medical condition, however, this method was not feasible due to transport, financial and consensual reasoning. However, in light of the above, the location of this particular sample, being that of an orphanage, could pose some limitations to the perceived quality of life questionnaire, as these subjects used may already have other emotional problems which could have had implications on answering the PedsQL questionnaire.

5.2.2 Height and weight

Height measures for the haemophilia group was $1.32\text{m} \pm 0.19$ (SD), and the comparative group was $1.43\text{m} \pm 0.28$ (SD). In relation to each other, the two groups did not vary significantly.

Weight measures for the haemophilia group was $32.4\text{kg} \pm 13.97$ (SD), and the comparative group was $33.5\text{kg} \pm 14.71$ (SD). There was no significant difference between the two groups mean weight values.

In comparison to the World Health Organisation (WHO) growth reference data for children and adolescents aged five to 19 years of age, the height and weight values were within normal ranges in both the haemophiliac and control groups (www.who.int/growthref/en/).

5.2.3 Sample Size

Many studies have been done investigating the perceived quality of life as well as physical fitness and/or muscle strength in children with haemophilia, in comparison to their healthy peers. Most recently, Broderick et al (2010) examined the physical fitness and quality of life in children with haemophilia and von Willebrand. Forty-four boys with haemophilia and von Willebrand were used ranging between 6 – 17 years of age. Although the sample size was large, ($n=44$), the authors did not categorise the subjects into purely haemophiliac or those with von Willebrands. Control data, such as the anthropometric and aerobic fitness data, was obtained by comparing the results to that of previous studies that used school children. Van der Net et al (2006) investigated the physical fitness, functional ability and quality of life in 13 subjects with severe haemophilia ranging between 8-14 years of age. Although the sample size is small, the study was limited to using only boys with severe haemophilia. Both studies investigated similar parameters such as those used in the present study. Age ranges and sample sizes were of similar numbers to that used in the present study, thus the present study results are comparable to previous literature.

5.3 Muscle strength

The results of the present study revealed significant differences in the muscle strength of certain muscle groups only. The haemophilia group showed significant weakness in the muscle strength of the left elbow extensors, and muscle strength of the right knee extensors, with p-values of 0.01 and 0.05 respectively. In contrast, muscle strength of both left and right dorsiflexors were significantly greater in the haemophilia sample group, with p-values of 0.02 and 0.00 respectively.

Beenakker et al (2001) conducted a study to establish reference values for muscle force in children aged 4 – 16 years of age. Measurements were taken from 270 normal children using a calibrated hand held dynamometer (HHD). The investigators measured 11 different muscle groups by using the ‘break’ technique. No mention of the validity of the break test or the reasoning as to why this particular method was used was stated. The results from this study can be used as reference values and can be used to quantify muscle weakness in individual muscles groups in children aged between four -16 years to evaluate effects of therapy.

Similarly in a study conducted by Douma-van Riet et al, 2009, the authors conducted investigations to assess physical fitness, muscle strength and the effect of being overweight in children with haemophilia. The study included 158 boys with haemophilia, ranging between 8–18 years of age. The investigators used the ‘break’ technique to assess muscle strength in the elbows, knees and ankle joints. Again, no mention of the validity of the ‘break test’ was mentioned.

Eek et al (2006) conducted a study to establish reference values of arm and leg muscle strength as measured by isometric torque production in healthy children. 149 healthy children (76 boys and 73 girls) ranging between 5 – 15 years of age were used in this study. The investigators used a HHD to measure the isometric muscle torque in 8 lower limb muscle groups and four upper limb muscle groups using the ‘make’ test technique. In the present study, the ‘make’ technique was used to measure muscle strength in the elbow flexor and extensor muscles, knee flexor and extensor muscles and ankle plantar flexors and dorsiflexors. According to Eek et al (2006) the

‘make’ technique has higher reliability than the ‘break’ technique. Thus the muscle strength values of this present study can be compared to the results established in Eek et al (2006).

Eek et al (2006) represented the mean muscle strength of each particular muscle group separately in each age group ranging between five -15 years of age. In order to compare values to the present study, the mean for each specific muscle group across all age groups was calculated and a new mean for that particular muscle group was calculated. The mean values for elbow extensors, knee extensors and ankle dorsiflexors muscle groups, across all age groups were calculated to 18.5N, 58.28N and 21.99 N respectively.

5.3.1 Muscle strength of control group

The control group in the present study showed significance with regards to their left (L) elbow extensors, with a mean strength of 17.2N, in comparison to the haemophiliac sample with a mean strength of 12.91N. With reference to right (R) knee extension, the control group had muscle strength of 24.17N compared to the haemophiliac group of 19.4N. Muscle strength of the control elbow extensors were of similar value to that of Eek et al (2006), where as the haemophilia group showed much weaker strength in comparison to both groups. Both the control group and haemophilia group showed significant weakness of their knee extensors when compared to the mean value of the knee extensor strength in a study conducted by Eek et al (2006).

In a study conducted by McVeigh et al (2004) the authors investigated the relationship between socio-economic status (SES) and physical activity in 381 children living in Johannesburg, South Africa. The sample comprised of 43 white males, 157 black males, 38 white females and 143 black females. All the white children were in the highest SES bracket. The results showed that the white children were more active than the black children in this sample. The authors contributed this to physical education in schools, as well as parental support for after school activities. As all the children in this present study were black, it can be thought based on the results of the mentioned study, that their levels of physical activity are not adequate, thus contributing to reduced muscle strength, especially in the lower limb muscles, such as knee extensors.

5.3.2 Muscle Strength of Haemophilia Group

The haemophiliac group were significantly stronger in their (L) and (R) ankle dorsiflexors of 17.85N and 17.6N respectively in comparison to the control group showing strengths of 13.14N and 13.48N.

In a study conducted by Fox and Colleagues (2008), isokinetic eccentric torque measures of the musculature of the ankle joint was measured in participants with ankle instability and those without. Ankle instability in this particular study was due to inversion ankle sprains. It was found that there was a deficit in plantar flexion torque in the functionally unstable ankle, thus indicating that plantar flexor strength is an important contributing factor to functional ankle instability. When weakness is present in the plantar flexor muscles, excess anterior sagittal plane tibial rotation (i.e. dorsiflexion) is presented in mid and late stance (i.e. the foot remains dorsiflexed and heel strike is lost) (<http://courses.washington.edu/anatomy/kinesiologySyllabus/PathGait/Ortho.Pdf>). This could account for the increase in dorsiflexion strength in the present study's haemophilia sample, as these particular muscles may be compensating for the weakness in plantar flexors due to instability of the ankle joint caused by bleeds.

With regards to the haemophiliac sample, literature has shown that approximately 80% of recurrent haemarthrosis occurs in the elbows, knees and ankles (Buzzard, 1997; Engelbert et al, 2008). Episodes of bleeding ultimately affect activity and participation in physical activities which predispose this population to impaired strength (Wittmeier et al, 2007) and ROM limitations (Soucie et al, 2004). This could account for the significant weakness seen in the haemophilia group's elbow extensors and knee extensors. In addition to this, literature has shown weakness in quadriceps muscle as a result of recurrent bleeds into the knee joint, resting of that joint and inadequate rehabilitation following the bleed (Manigandan et al, 2004; Hart et al, 2010), thus accounting for weakness in knee extensors.

5.4 Six Minute Walk Test

The current study used the 6MWT to establish submaximal endurance levels on both the haemophiliac and control group.

5.4.1 Height and Weight parameters

There were no significant differences between the heights and weights of the two groups in this study. Li et al (2007) conducted a study investigating height-specific standards for the 6MWT for children ranging between 7 – 16years of age. It was stated that height may have an effect on stride length and walking distance, and may have implications on the variables associated with the 6MWT.

Hassen et al (2010) conducted a study to compare the walking distance of children with haemophilia, juvenile idiopathic arthritis, and spina bifida to that of their healthy peers, and to decipher the associations with age, height and weight body mass index, and sex. It was found that all three patient groups showed a significant reduction in walking distance compared to health references. It was also shown that anthropometric variables are strongly associated with walking distance. As there were no significant differences in height between the samples used in this present study, the results from this present study could be compared to normative data such as that of Li et al (2007).

5.4.2 Vital signs

Heart rate, respiratory rate and blood pressure were also taken prior to, immediately after and two minutes following the 6MWT. The results of this present study showed no statistical significance between the two group's vitals before, after and two minutes post the test. HR and RR generally give an indication of an individual's response to exercise thus are important measures in clinical decision making (Benjamin, 2009).

Wallis et al (2005) conducted a study in Plymouth, UK to investigate and produce reference values for resting heart rate and respiratory rates in healthy children aged between four - 16 years

of age. The sample size consisted of 1109 children, a size that was fairly representative of children in the UK.

Similarly, Wallis et al (2006) conducted a study in Cape Town, South Africa (SA) to establish whether physiological reference values of resting heart rate and respiratory rate that were derived in the United Kingdom (UK) could be applied to socially disadvantaged school children in SA. Three hundred and forty-six children ranging between five - 16 years of age from a township school in Cape Town were included in this study. The South African children showed similar values with regards to heart rate compared to the UK sample. The respiratory rate was slightly higher in comparison; however Wallis et al (2006) felt this was not of clinical significance.

5.4.2.1 Baseline values

The present study included children aged between five - 16 years of age. The mean age of the present study was 10.4 years. From Wallis et al (2006), the HR and RR values for children aged 10 years were 84 beats per minute (Bpm) and 18 breathes per minute (bpm) (Appendix VII). At baseline the heart rates for the children in both groups of the current study are similar to those in Wallis et al (2006) study on children in South Africa. Before commencement of the current study all children were screened for any other illnesses. No cardiac abnormalities were suspected.

The children evaluated in the study conducted by Wallis et al (2006) were at lower altitudes than those children included in this present study. At higher altitudes, respiratory rate is increased due to reduced arterial PO_2 levels, which causes the peripheral chemoreceptors to become more responsive to increases in PCO_2 levels. The body compensates for this by increasing respiratory rate in an attempt to restore normal gaseous exchange (McGee, 2006). This could account for the slight increase in respiratory rate in both the haemophiliac and control subjects.

5.4.3 Distance walked

With regards to distance walked, this present study revealed no significant difference in the mean distance covered by the subjects in both groups. The haemophilia group covered a mean distance

of 589.6 m $\pm$ 81.86 (SD), and the comparative group 597.08m $\pm$ 147.57 (SD), with a p-value of 0.86.

However, when the values are compared to a study undertaken by Li et al (2007) it was found that in a sample of 805 boys, aged between 7 -16 years, the walking distance was measured to be 680.9 meters. They valued 600 meters to be the reference percentile for boys with the shortest measured height in their study being 1.20m. Therefore, it is indicative that both the haemophilic subjects as well as the control sample showed a reduction in walking distance compared to the reference value showed in the above mentioned study, with all subjects that participated falling below the 25th percentile, indicating a significant deficit in submaximal endurance levels (Appendix VIII).

In a more recent study by Lammers and colleagues (2008) in the UK, both height and age were used as references to determine normal values (Appendix IX). Three hundred and twenty-eight children (178 males and 150 females) between the ages of four - 11 years of age were used in this study. The total mean distance walked was 470m $\pm$ 59(SD), which, when compared to the present study, shows a reduction in walking distance. In comparison to Li et al (2007), the mean height and mean total distance walked also fall below the 25th percentile, thus indicating that Lammers et al (2008) would be a better predictor for comparison in the present study.

Recently Benjamin (2009) conducted a study in South Africa comparing submaximal endurance levels with the use of a 6MWT between children with Developmental Co-ordination Disorder (DCD) and normally developing children between the ages of seven to ten years of age. The total mean distance of the children with DCD was 375.89m $\pm$ 73.33(SD) and the control was 430.48m $\pm$ 60.85 (SD). The results of the mentioned study also fall below the 25th percentile in comparison to Li et al (2007) and are still smaller values in contrast to the present study.

As mentioned above, McVeigh et al (2004) found that black children in Johannesburg, South Africa demonstrated less physical activity levels to white children. This could account for the reduced endurance levels, thus resulting in a decreased distance walked in the 6MWT.

5.4.4 Post test results

The vitals post the 6MWT showed no significance between the two groups. However, it was interesting to note that the HR and RR in both groups were of similar values.

Moalla and Colleagues (2005) investigated the exercise tolerance and cardiorespiratory responses of children with congenital heart disease in comparison to their healthy peers by conducting a 6MWT. It was stated in the study that similar kinetics of the vitals before and two-minutes post the 6MWT is an indication of a better exertion tolerance and changes in autonomic tone as a result of endurance training (Moalla et al, 2005). This could indicated that, although both groups showed decreased distances walked in comparison to Li et al (2007), their general exercise tolerance and fitness levels could be within normal ranges for their particular age groups.

5.5 Quality of Life (QoL)

Health-related quality of life (HRQoL) is considered one of the most relevant health outcome measures in medicine (Mercan et al, 2010). Questionnaires to test QoL in chronic diseases must be disease specific, reliable and available for different age groups and various cultures. The Haemo-QoL was tested for these characteristics in a study conducted by Von Mackensen et al (2004) by testing this tool in six different European countries on 339 children with haemophilia and their parents.

Varni et al (2001) conducted a study testing the reliability and validity on a diverse sample on children with acute or chronic health conditions using the PedsQL. The results of the study demonstrated that the PedsQL is both a reliable and valid tool to use in clinical trials.

In the present study the PedsQL and Haemo-QoL were used to establish the perceived quality of life in both the sample and control groups. The PedsQL and Haemo-QoL are scored differently in that the higher the score of the PedsQL, the higher the perceived quality of life, whereas with the Haemo-QoL, the higher the scores, the lower the perceived quality of life.

Bradley et al (2006) conducted a study comparing the Haemo-QoL and CHO-KLAT questionnaires, as well as comparing correlations between other quality of life measures such as the PedsQL and VAS. It was found that the Haemo-QoL and PedsQL were highly correlated, suggesting that what is measured in the Haemo-QoL may be measured equally well by the generic PedsQL ratings.

Although there was no statistical significance between the two group's perceived quality of life depicted by the PedsQL questionnaire, the domain where the boys with haemophilia scored the worst (59.7%) was domain 4, which represented questions about school. The control scored the worst (69.7%) in domain 2, which represented questions about their feelings. In the haemophilia sample group, both the age group I (4 - 7 years) and age group III (13 - 16 years) scored the highest in the school/sport dimension in the Haemo-QoL questionnaire, 76.5% and 85.4% respectively, representing lower perceived – QoL, which correlates with the haemophilia sample scoring the lowest in the school domain in the PedsQL questionnaire. The majority of the boys with haemophilia expressed their frustrations in not being able to play sports and missing school during bleeding episodes. This could explain the relation to the lower perceived quality of life in the schooling/sport dimension in both questionnaires.

Gringeri et al (2004) aimed at describing health status and health care and their impact on QoL in haemophiliac children six West European countries. Three hundred and eighteen children aged between 4-16 years of age participated in this study and were required to answer the respective Haemo-QoL questionnaire. It was shown that the youngest were mainly impaired in the dimension of 'Family' with a score of 34.38%, which the authors correlated to the over-protection of parents. Children in age group II and III showed impairments in 'Friend' (43.91% and 46.12% respectively) and 'Perceived support' (49.41% and 53.00% respectively) dimensions. The children in the age group III also showed impairment in the dimension 'Dealing'. The authors expressed concerns with the children in the older categories personal adaptation to the disease.

Similarly Mercan et al (2010) conducted a study describing the health status, health care received and their impact on the QoL in patients with haemophilia. Both children and adults with haemophilia participated in the study and were required to answer age specific Haemo-QoL

questionnaires. Thirty nine children and 31 adult patients were enrolled in this study. In the age group I the 'Family' dimension showed the highest mean score of 60.4%. In age group II the highest mean scores were that of the dimension 'Physical' scoring 57.5%, the dimension 'Family' scoring 51.4% and the dimension 'Perceived support' with a score of 49.4%. In age group III 'School/sport', 'Physical' and 'Perceived support' scored the highest with mean scores of 46.0%, 42.6% and 40.6% respectively.

Van Der Net (2006) investigated the level of physical fitness, functional ability and quality of life in boys with severe haemophilia. Thirteen subjects were used in this study, ranging from 8 to 14.63 years of age. The Haemo-QoL age groups II and III were used. It was found that the children in age group II scored highest in the dimensions 'Friends' and 'Perceived support'. The children in the age group III scored highest not only in those categories as well, but also reported high scores in 'Physical health', 'Dealing' and 'Treatment'. The authors felt that the subjects did not appreciate the questions or have not been able to address their problems with their healthy peers.

When comparing the mean values for the 'Physical' dimension from Gringeri et al (2004), Mercan et al (2010) and the present study, the scores were 16.50%, 49.67% and 58.29% respectively, thus indicating lower perceived quality of life with regards to the physical aspects of haemophilia in the present study. This could be due to the lack of prophylactic therapy in South Africa. Both studies discuss prophylactic therapy, home therapy and central catheters, all of which are limited in the treatment of haemophiliac patients in South Africa. The literature shows that there is a reduction in bleeding incidence in children in prophylaxis compared to those on demand therapy (Mercan et al, 2010). This could indicate the children with haemophilia in a South African context could therefore have an increased risk of physical impairments, which could account for the lower perceived quality of life in the 'physical' dimension.

In a study conducted by Schoenmakers et al (2001) motor performance and disability was investigated in children with haemophilia on prophylactic therapy compared to their healthy peers. Thirty-nine children aged between four – 12 years were assessed with regards to joint swelling, muscle testing with the use of a hand held dynamometer, motor performance with the use of the Movement-ABC measuring gross and fine motor in children aged between four -12,

and the Childhood Health Assessment Questionnaire (CHAQ). Swelling and muscle strength both showed no significant results, however it was interesting to note that although 90% of the sample indicated no disabilities in activities of daily living, 79% reported on the impact of the disease on their lives. Fifty-six percent reported on restrictions in sports and 21% indicated on having pain.

The total mean scores of the Haemo-QoL from Gringeri et al (2004), Mercan et al (2010) and the present study, were 22.78%, 39.77% and 39.75% respectively. These results, especially Mercan et al (2010), were of similar value to the results of the present study. In the study by Gringeri et al (2004) and the present study the age group I showed the highest total mean scores of 25.56% and 51.75% respectively. This could possible be due to the overprotection of parental care, the pain associated with haemophilia and the inability of being able to play like the other children at school. From the clinical data obtained from the Haemo-QoL in the present study, 40% of the sample indicated that they would 'sometimes' inform their parents of their bleed, where 13.3% said they would never tell their parents. This could possible account for late admissions following an acute bleed, thus increasing the risk for greater joint or muscular damage which can lead to physical impairments.

From this present study 46.7% of the sample experienced more than two bleeds during the month prior to the administration of the questionnaire. Almost one third expressed concerns caused by the bleeds. Interestingly 54% of the sample stated that they were not bothered at all by their bleeding episode. This is of some concern as this could account for late admissions following a bleeding episode, which could have serious repercussions on the treatment and rehabilitation of the particular joint involved.

5.5.1 Correlation PedsQL and Haemo-QoL questionnaires

The quality of life as measured by the two tests showed a weak to moderate correlation ($r = -0.5$). The two questionnaires do not measure exactly the same constructs and this may explain the different scores obtained. As the Haemo-QoL questionnaire was directly related to their disease, the boys with haemophilia may have been more attentive in answering the questionnaire than the

PedsQL, which may have influenced the scoring. Further studies which investigate these two questionnaires and their suitability for use in the South African context need to be conducted.

5.6 Limitations of the Study

The limitations of this study are as follows:

- Language barriers could affect some of the items and the child's understandings of what is being asked of them, even with an interpreter involved.
- Due to the large age range of five to 16 years of age, the sample size of the study may need to be reconsidered
- The length of time taken to test relevant muscle groups had, at times lost the interest of the boys. "Factors like attention and understanding of instructions are potential difficulties that make force testing less reliable in small children than in adults." (Beenakker et al, 2001).
- 83.3% of the control was recruited from the TLC orphanage. Although all the boys were healthy and attending normal schools, the implications of living in an orphanage and understanding that they are orphans may have had an effect on the results of the quality of life questionnaire.
- Analysis of the Range of Movement (ROM) should have been included in the measurements of the study especially as 46.7% of the children in the group with haemophilia have experienced more than two bleeds during the month prior to testing.
- Left verse right dominance of each child should have been recorded as this may have had a possible affect on muscle strength.
- There is a need to compare mild, moderate and severe haemophiliac subjects as it is possible to find differences in each objective measured.

5.7 Implications of the Findings

The results of this study indicate that boys with haemophilia attending the haemophiliac clinic at Chris Hani Baragwanath Hospital have generally 'normal' muscle strength in comparison to their healthy peers. This could be due to the home exercise programmes prescribed after each clinic visited and the continuous re-assessment of their base-line muscle strength and joint range of movement at each visit.

With regards to the endurance of the haemophiliac sample, although their vitals are within normal ranges, there was a significant reduction in distance walked in comparison to healthy peer references. Thus, endurance training should be initiated as a further treatment regime in their rehabilitation.

The perceived quality of life of the haemophiliac sample as measured by both the PedsQL and HAEMO-QoL showed no significant values indicating poor perceived QoL. However, psychologists should still be involved for possible intervention for both the patient and their caregivers during a bleeding episode. Due to the socioeconomic status of these patients, extra-curricular sporting activities may be limited at the schools they are attending, such a swimming, which is considered the best and safest sport for haemophiliac patients. Thus the need for further and continuous physiotherapy intervention is imperative for the rehabilitation of these patients.

5.8 Recommendations Based on Findings

Based on the results of this study, the following recommendations can be made:

- Patients with haemophilia should be screened and assessed from initial diagnosis to prevent complications and consequences of haemophilia
- A multi-disciplinary team involvement is needed in the treatment of these patients, including a clinical psychologist to assist with any emotional stresses caused by the disease, not only for the child involved but the caregivers as well
- The boys with haemophilia may need further education regarding whether or not they inform their caregivers of a bleed, and in what length of time. This may prevent hospital admissions and therefore increase time at school if notification is given appropriately.
- A simple home exercise programme should be given to each haemophiliac subject to help maintain muscle strength and ROM, and to prevent complications caused by bleeds.
- Endurance training should be included in the rehabilitation of the patients with haemophilia.
- It is important to make recommendations to TLC to optimise opportunities for structured physical activity in their daily programme.

5.9 Recommendations in Terms of Further Research

- It would be of great value to establish baseline values for South African children in terms of endurance training such as the 6MWT as well as muscle strength. These values should include parameters such as baseline HR and RR, distance covered and the effect of exercise on vitals for endurance training, and muscle strength values for all muscle groups. The information gained from research as such would be valuable for further research done in South Africa.
- A national study of all haemophiliac patients, across all age ranges, in South Africa should be conducted to establish the epidemiology and demographics of the disease within a South African context to understand how the condition is impacting on the health and well being of the persons infected.
- Balance and proprioception, as well as range of movement, should be included in future investigations.

The conclusions drawn from this study will be presented in chapter six.

Chapter 6: CONCLUSION

The purpose of this study was to examine strength, endurance and perceived quality of life in 15 subjects with haemophilia and compare it to that of 18 control subjects without haemophilia. All subjects were from similar socioeconomic backgrounds with all the haemophilia subjects attending the Haemophilia Clinic at Chris Hani Baragwanath Hospital, Soweto. The MicroFET 2 dynamometer was used to assess the muscle strength of each subject and the Six Minute Walk Test was used to test endurance. The PedsQL was one of the quality of life assessment tools used to compare both groups, where the HAEMO-QOL was used specifically to test the subjects with haemophilia

The findings of this study demonstrate a need for further research on haemophiliac subjects in a South African context. However, the results have shown that both the groups in this present study have reduced muscle strength and poor endurance in comparison to literature conducted internationally. With regards to perceived QoL, the boys with haemophilia showed no significant differences in comparison to previous research investigating QoL in similar studies.

The results of this study are important for all health care practitioners involved in the treatment and rehabilitation of children with haemophilia. There is a need for a multidisciplinary approach for the effective management of acute bleeding episodes in such subjects which could have serious consequences, not only on muscle strength and endurance, but on the psychological well being of the patients as well as their families.

Chapter 7: References

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APPENDIX I: Ethical Clearance

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

R14/49 Miss Donna Theresa Faris

CLEARANCE CERTIFICATE

M090539

PROJECT

An Investigation of Muscle Strength, Endurance
and Quality of Life in South African Children
with Haemophilia: A Pilot Study

INVESTIGATORS

Miss Donna Theresa Faris.

DEPARTMENT

Department of Physiotherapy

DATE CONSIDERED

09.05.29

DECISION OF THE COMMITTEE*

Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 09.05.29

CHAIRPERSON


(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Dr J Potterton

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.

I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

APPENDIX II: Hospital permission form



GAUTENG HEALTH

Physiotherapy Dept
Chris Hani Baragwanath Hospital

Post Office Bertsham 2013
Tel: 011-933 8188/8309
Fax: 011-933 8927

PERMISSION FOR RESEARCH

DATE: 11/07/2009
NAME OF RESEARCHER: Donna Theresa Faris
TITLE OF RESEARCH PROJECT:
An investigation of muscle strength, endurance and quality of life
in South African Children with haemophilia: a pilot study
OBJECTIVES OF STUDY(briefly or include a protocol):
Please see attached protocol
METHODOLOGY (briefly or include a protocol):
Please see attached protocol
CONFIDENTIALITY OF PATIENT MAINTAINED:
Confidentiality will be upheld at all times
COSTS TO HOSPITAL:
No costs to hospital
APPROVAL BY UNIVERSITY ETHICS (attach proof): Please see attached form
APPROVAL OF HEAD OF DEPT: SIGN: *[Signature]* DATE: 20/07/2009
Haemophilic Clinic have been informed and have indicated full
PERMISSION OF SUPERINTENDENT: Support of study.
SIGN: *[Signature]* DATE: 23/07/2009
SUBJECT TO ANY RESTRICTIONS:
A very interesting. My office needs a written copy
of permission from Haemophilic Clinic.
Kindly let us know about your results.

APPENDIX III: Informed Consent

Information sheet for Parents with boys with haemophilia
An investigation of muscle strength, endurance and quality of life
in South African children with haemophilia: a pilot study

Dear Parent

By way of introduction, my name is Donna Faris and I am a qualified physiotherapist working at Chris Hani Baragwanath Hospital. I am currently studying towards a Masters degree in physiotherapy at the University of the Witwatersrand.

I am asking for your permission to allow your child to participate in a research study that I will be doing at the haemophilia clinics at both Chris Hani Baragwanath Hospital and Charlotte Maxeke Johannesburg Hospital

The study looks at your child's muscle strength, how fit he is and how he feels about his health. The findings of this research will assist us as physiotherapist to help and understand your children better than before.

The study will involve the use of 4 tools:

1. A hand held dynamometer – this machine helps to measure how strong your child's muscles are.
2. The 6 Minute Walk Test – your child will walk for 6 minutes between 2 beacons to measure how fit he is.
3. The Haemo-QoL – this is a questionnaire that only the boys with haemophilia will be answering. It asks questions about their feelings on having haemophilia, and how they think their friends and family feel.
4. Paediatric Quality of Life Intervention Measurement Model (Peds QL) – this is also a questionnaire which will be answered by all boys who are taking part in this study. It is a quick questionnaire that asks the children questions on their health.

These tools will not hurt your child in any way. Your child may however feel tired after I have done all the necessary testing. You as caregivers of the child will be given a summary of the findings from the study once it is finished.

Your child's personal information will be kept a secret at all times, and all information collected will only be looked at by me. I will only need your child's age, hemophilia type, his last bleed and hospital number so I do not mix papers, but once I have finished these papers will be destroyed.

Participation is voluntary and refusal to participate will not result in any bad feelings towards you or your child. Physiotherapy is a normal part of treatment for your child. If you don't want your child to be part of this study, I will not treat your child differently and he will still receive normal physiotherapy. You may also choose to remove your child at any point during the course of the research.

If I am unable to test your child while he is at the clinic, I may need to call him back for an assessment on another day. I will pay for transportation in a case like this. However, it needs to be made clear that if I do see your child during the time at the clinic, I will not be giving money for transportation.

Please feel free to ask me any questions about the study, and I will answer them as best as I can. Please don't hesitate to contact me.

With Thanks

Donna Faris

Contact Details

Cell number: 082 538 2189

Work number: 011 933 8309

Information sheet for Parents with boys without haemophilia
An investigation of muscle strength, endurance and quality of life
in South African children with haemophilia: a pilot study

Dear Parent

By way of introduction, my name is Donna Faris and I am a qualified physiotherapist working at Chris Hani Baragwanath Hospital. I am currently studying towards a Masters degree in physiotherapy at the University of the Witwatersrand.

I am asking for your permission to allow your child to participate in a research study that I will be doing at the haemophilia clinics at both Chris Hani Baragwanath Hospital and Charlotte Maxeke Johannesburg Hospital

The study looks at your child's muscle strength, how fit he is and how he feels about his health. The findings of this research will assist us as physiotherapist to help and understand children with haemophilia better than before.

The study will involve the use of 4 tools:

5. A hand held dynamometer – this machine helps to measure how strong your child's muscles are.
6. The 6 Minute Walk Test – your child will walk for 6 minutes between 2 beacons to measure how fit he is.
7. The HAEMO_QOL – this is a questionnaire that only **the boys with haemophilia** will be answering. It asks questions about their feelings on having haemophilia, and how they think their friends and family feel.
8. Paediatric Quality of Life Intervention Measurement Model (Peds QL) – this is also a questionnaire which will be answered by all boys who are taking part in this study. It is a quick questionnaire that asks the children questions on their health.

These tools will not hurt your child in any way. Your child may however feel tired after I have done all the necessary testing. You as caregivers of the child will be given a summary of the findings from the study once it is finished.

Your child's personal information will be kept a secret at all times, and all information collected will only be looked at by me.

Participation is voluntary and refusal to participate will not result in any bad feelings towards you or your child. Physiotherapy is a normal part of treatment for your child. If you don't want your child to be part of this study, I will not treat your child differently and he will still receive normal physiotherapy. You may also choose to remove your child at any point during the course of the research.

Please feel free to ask me any questions about the study, and I will answer them as best as I can.
Please don't hesitate to contact me.

With Thanks
Donna Faris

Contact Details

Cell number: 082 538 2189

Work number: 011 933 8309

Information Sheet for children with haemophilia

Hello!

My name is Donna Faris, and I am a physiotherapist working at Chris Hani Baragwanath Hospital. You have been chosen to take part in a project which I am doing in the Haemophiliac Clinic at this hospital.

I have chosen children like you who are 5 to 16 years old, who have haemophilia, and have not had any bleeds for a few weeks. I have also chosen children the same age as you who do not have haemophilia and who have not been sick before to take part in this project.

Why am I doing this?

I want to find out what special problems boys like you with haemophilia have. I want to see how strong your muscles are and how long you can walk for. I will also be asking you how you feel about having haemophilia, how you think your friends and family feel and how you feel about your bleeding. All the information I get from this project will help us physiotherapists to see if we can help you more and understand you better. All the boys without haemophilia will also have a chance to see how strong their muscles are and how fit they are.

How am I going to do this?

I will test how strong your muscles are with a special machine, that won't hurt you. To see how fit you are, I will be making you walk up and down the corridor of the clinic for six minutes. I will also give you questions to answer to see how you feel about having haemophilia, and how you think your friends and family feel. The tests will be done during the time you are at the haemophiliac clinic and they will not make you sore.

If you do not want to take part in this project you must tell me. Your caregiver also has to sign a piece of paper saying that you may take part in the tests.

Just to make sure that the information stays a secret I won't put your name on the piece of paper with all the test results. If you are confused or have questions just ask me and I'll try my best to answer them so that you understand. You may decide at any time that you don't want to be in the study and that is OK. You will still be seen at the clinic as usual.

Thank you

Donna Faris

Contact Details: Cell: 0825382189

Work: 011 933 8309

Information Sheet for children

Hello!

My name is Donna Faris, and I am a physiotherapist working at Chris Hani Baragwanath Hospital. You have been chosen to take part in a project which I am doing in the Haemophiliac Clinic at this hospital.

I have chosen healthy children like you from 5 to 16 years old to be part of this project. I have also chosen children who are the same age as you, but have a special bleeding disease called haemophilia to also take part in this project.

Why am I doing this?

I want to find out what special problems boys with haemophilia have. I need to see how strong your muscles are and how long you can walk for so I can see if the boys with haemophilia can do the same. All the boys with haemophilia will also have a chance to see how strong their muscles are and how fit they are. I will also be asking you questions on how you feel about your own health.

How am I going to do this?

I will test how strong your muscles are with a special machine, that won't hurt you. To see how fit you are, I will be making you walk up and down the corridor of the clinic for six minutes. I will also give you questions to answer to see how you feel about your health. These tests will be done at the haemophiliac clinic at the hospital.

If you do not want to take part in this project you must tell me. Your caregiver also has to sign a piece of paper saying that you may take part in the tests.

Just to make sure that the information stays a secret I won't put your name on the piece of paper with all the test results. If you are confused or have questions just ask me and I'll try my best to answer them so that you understand. You may decide at any time that you don't want to be in the study and that is OK. You will still be seen at the clinic as usual.

Thank you
Donna Faris

Contact Details:

Cell: 0825382189

Work: 011 933 8309

ASSENT FORM

I _____ say that it is ok for the physiotherapist to test me in this project. I understand what this project is about and understand what I am expected to do as part of the project. I understand what has been explained to me about the testing on how strong my muscles are, how fit I am and how I am feeling?

All my questions have been answered and I understand that by taking part in this project I will not get hurt in any way. I am aware that I am allowed to say that I do not want to be tested in this project.

Patient

Researcher

Date

Date

CONSENT FORM

Research Problem:

It is not known in South Africa what impairments in terms of muscle strength, endurance and perceived QOL haemophilic patients have in comparison to their healthy peers.

I _____ understand the purpose of this project and give consent for my child _____ to take part in the research. I have read and understand the information and all my questions have been answered and explained to me. I am aware of the procedures and understand that they will not harm my child in any way. I am also aware that I may remove my child from the research without any questions or prejudice towards myself or my child.

Care giver

Researcher

Date

Date

APPENDIX IV: Data Collection sheet

DATA COLLECTION SHEET

Age: _____

Height: _____

Haemophilia type: _____

Last bleed: _____

Weight: _____

Severity: _____

Number of bleeds in past year: _____

Muscle Strength:

Joint	Right	Right	Left	Left
	Flexion/DF	Extension/PF	Flexion/DF	Extension/PF
Elbow: 1				
2				
3				
Knee: 1				
2				
3				
Ankle: 1				
2				
3				

Six-Minute-Walk Test

	Before test	After Test	2 Min post test
HR			
RR			
BP			
Distance			

APPENDIX V: Haemo-QoL Questionnaires

Trial ID:

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VISIT X

Centre ID/No.:

Subject No.:

Visit Date:

D D M M Y Y Y Y

HAEMO - QOL

Questionnaire for Children and Adolescents

Kids' long Version

age: 4-7

Hello there!

We would like to know how you have been feeling during the past few weeks, so we have worked out some questions which we would like you to answer.

This questionnaire was made for young children with haemophilia.

- ⇒ I will now read each question to you.
- ⇒ Think about how things have been for you during the past few weeks.
- ⇒ Please tell me, which answer is the best for you.

There are no right or wrong answers. It's what you think that matters.

For example: 	Never	Some-times	Very often
During the past 7 days, I felt like eating ice-cream.	☐	☐	☒
			

Date of completion:
(day/ month/ year)

Country:

Trial ID:

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VISIT X

Subject No.:

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We would like to know about your physical health...

During the past 7 days...	Never	Sometimes	Very often
1. ... I felt ill.	☐	☐	☐
2. ... I had a headache or tummy-ache.	☐	☐	☐
3. ... I was afraid that my illness might get worse.	☐	☐	☐

... then about how you've been feeling in general...

During the past 7 days...	Never	Sometimes	Very often
1. ... I had fun and laughed a lot.	☐	☐	☐
2. ... I was bored.	☐	☐	☐
3. ... I was sad because of my illness.	☐	☐	☐

... and how you have been feeling about yourself.

During the past 7 days...	Never	Sometimes	Very often
1. ... I was proud of myself.	☐	☐	☐
2. ... I felt pleased with myself.	☐	☐	☐
3. ... I was able to cope well with my illness.	☐	☐	☐

[I, kids, long]

CLHAEMO-001 - South Africa/English - Final version - 16 Jul 07 - Meri Research Institute

Trial ID:

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VISIT X

Subject No.:

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The next questions are about your family...

During the past 7 days...	Never	Sometimes	Very often
1. ... I got on well with my parents.	☐	☐	☐
2. ... I felt fine at home.	☐	☐	☐
3. ... my parents treated me like a baby because of my illness.	☐	☐	☐

... and then about your friends.

During the past 7 days...	Never	Sometimes	Very often
1. ... I played with friends.	☐	☐	☐
2. ... I got along well with my friends.	☐	☐	☐
3. ... I did not want others to notice my illness.	☐	☐	☐

Now, we would like to know about nursery school/kindergarten/playschool.

During the past 7 days...	Never	Sometimes	Very often
1. ... I coped well with the things we did in nursery school/kindergarten/playschool.	☐	☐	☐
2. ... I enjoyed nursery school/kindergarten/playschool.	☐	☐	☐
3. ... I missed something at nursery school/kindergarten/playschool because of my illness.	☐	☐	☐

[I, kids, long]

Trial ID:

Page 4/8

VISIT X

Subject No.:

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NOW WE WOULD LIKE TO ASK YOU SEVERAL QUESTIONS ABOUT YOUR HAEMOPHILIA.

Here we would like to know about your **BLEEDS (JOINT BLEEDS)**.

1.	How frequent were your bleeds during the past month?
	☐ No bleeds ☐ 1 ☐ 2 ☐ More than 2 How many? ____

The following questions should only be answered if the child had bleeds.

2.	How much were you troubled by bleeds during the past month?	☐ Not at all ☐ Somewhat ☐ Very much
3.	How severe were your bleeds during the past month (if you had several bleeds, please answer for the most severe bleed)?	☐ Slight ☐ Moderate ☐ Very severe
4.	Did you feel a strange sensation in your joints before you had a bleed?	☐ Never ☐ Sometimes ☐ Always
5.	Did you have to stay quiet (e.g. lie in bed) when you had bleeds?	☐ Never ☐ Sometimes ☐ Always
6.	When you had bleeds, did you tell your parents immediately?	☐ Never ☐ Sometimes ☐ Always

We would like to know who gave you **INJECTIONS**.

During the past month...	Never	Sometimes	Very often
1. ... I injected myself.	☐	☐	☐
2. ... my mother injected me.	☐	☐	☐
3. ... my father injected me.	☐	☐	☐
4. ... a nurse injected me.	☐	☐	☐
5. ... a doctor injected me.	☐	☐	☐

[I, kids, long]

Trial ID:

Page 5/8

VISIT X

Subject No.:

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Here we would like to know about
haemophilia and your **PHYSICAL HEALTH**...

During the past month...	Never	Sometimes	Very often
1. ... my bruises hurt.	☐	☐	☐
2. ... it was difficult for me to move my arms or legs.	☐	☐	☐
3. ... I was afraid of bleeds.	☐	☐	☐
4. ... I was afraid of hurting myself.	☐	☐	☐

... and now about how you have been **FEELING** because of your haemophilia.

During the past month...	Never	Sometimes	Very often
1. ... I was in a bad mood because of my haemophilia.	☐	☐	☐
2. ... I was sad because of my haemophilia.	☐	☐	☐
3. ... my haemophilia made me angry.	☐	☐	☐

How does haemophilia affect your **VIEW OF YOURSELF**?

During the past month...	Never	Sometimes	Very often
1. ... I was jealous of healthy boys my age.	☐	☐	☐
2. ... I felt embarrassed about my haemophilia.	☐	☐	☐

[I, kids, long]

Trial ID:

Page 6/8

VISIT X

Subject No.:

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The next questions are about haemophilia and your **FAMILY**...

During the past month...	Never	Sometimes	Very often
1. ... my mother protected me too much.	☐	☐	☐
2. ... my father protected me too much.	☐	☐	☐
3. ... my parents got cross with me when I hurt myself.	☐	☐	☐
4. ... my parents would not let me do certain things because of my haemophilia.	☐	☐	☐

... and then about haemophilia and your **FRIENDS**.

During the past month...	Never	Sometimes	Very often
1. ... I could not do as many things with my friends because of my haemophilia.	☐	☐	☐

These questions are about your haemophilia and **OTHER PEOPLE**.

During the past month...	Never	Sometimes	Very often
1. ... I felt different from others because of my haemophilia.	☐	☐	☐
2. ... I felt left out when others did things together.	☐	☐	☐

[I, kids, long]

CI-HAFMO-QOI - South Africa/English - Final version - 16 Jul 97 - M&D

Trial ID:

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VISIT X

Subject No.:

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These questions are about **NURSERY SCHOOL/KINDERGARTEN/PLAYSCHOOL...**

During the past month...	Never	Sometimes	Very often
1. ... I could not play games that I enjoy because of my haemophilia.	☐	☐	☐
2. ... I did just as much sport as any other kid.	☐	☐	☐
3. ... I was able to take part in games at nursery school/kindergarten/playschool in spite of my haemophilia.	☐	☐	☐

... and what about your **TREATMENT?**

During the past month...	Never	Sometimes	Very often
1. ... I did not like going to the haemophilia unit.	☐	☐	☐
2. ... the injections irritated me.	☐	☐	☐

And your **OVERALL HEALTH?**

In general, ...	Excellent	Good	Bad
1. ... would you say your health is...	☐	☐	☐

[I, kids, long]

Trial ID:

Page 8/8

VISIT X

Subject No.:

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Open Questions.

1. How much are you bothered by your haemophilia?

☐ Not at all

☐ Somewhat

☐ Very much

2. What bothers you most about haemophilia? Please write down some things:

- _____
- _____
- _____

3. How did you like the questionnaire?



Did not like it



Ok



Good

4. Have we forgotten anything that is important to you?

- _____
- _____
- _____

5. How long did it take to fill in the questionnaire? About _____ minutes.

Well done!

THANK YOU FOR YOUR HELP!

[I, kids, long]

CI-HAEMO-QOL - South Africa/English - Final version - 16 Jul 07 - Mapi Research Institute.
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Trial ID:

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VISIT X

Centre ID/No.:

□ □ □ □

Subject No.:

□ □ □ □ □ □ □ □

Visit Date:

□ □ □ □ □ □ □ □
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HAEMO - QOL

Questionnaire for Children and Adolescents

Kids' long Version

age: 8-12

Hello there!

We would like to know how you have been feeling during the past few weeks,
so we have worked out some questions which we would like you to answer.

This questionnaire was made for children with haemophilia.

- ⇒ Please read each question carefully.
- ⇒ Think about how things have been for you during the past few weeks.
- ⇒ Choose the answer that fits you best and tick (✓) the appropriate box.

There are no right or wrong answers. It's what you think that matters.

For example: 	Never	Seldom	Some- times	Often	All the time
During the past 7 days, I felt like eating ice-cream.	☐	☐	☐	☒	☐

Date of completion: □ □ □ □ □ □ □ □
(day/ month/ year)

Country: □ □ □

Trial ID:

Page 2/12

VISIT X

Subject No.:

--	--	--	--	--	--

We would like to know about your physical health...

During the past 7 days...	Never	Seldom	Some-times	Often	All the time
1. ... I felt ill.	☐	☐	☐	☐	☐
2. ... I had a headache or tummy-ache.	☐	☐	☐	☐	☐
3. ... I was tired and worn-out.	☐	☐	☐	☐	☐
4. ... I felt strong and full of energy.	☐	☐	☐	☐	☐
5. ... I was afraid that my illness might get worse.	☐	☐	☐	☐	☐

... then about how you've been feeling in general...

During the past 7 days...	Never	Seldom	Some-times	Often	All the time
1. ... I had fun and laughed a lot.	☐	☐	☐	☐	☐
2. ... I was bored.	☐	☐	☐	☐	☐
3. ... I felt alone.	☐	☐	☐	☐	☐
4. ... I felt scared	☐	☐	☐	☐	☐
5. ... I was sad because of my illness.	☐	☐	☐	☐	☐

[II, kids, long]

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... and how you have been feeling about yourself.

During the past 7 days...	Never	Seldom	Some-times	Often	All the time
1. ... I was proud of myself.	☐	☐	☐	☐	☐
2. ... I felt on top of the world.	☐	☐	☐	☐	☐
3. ... I felt pleased with myself.	☐	☐	☐	☐	☐
4. ... I had lots of good ideas.	☐	☐	☐	☐	☐
5. ... I was able to cope well with my illness.	☐	☐	☐	☐	☐

The next questions are about your family...

During the past 7 days...	Never	Seldom	Some-times	Often	All the time
1. ... I got on well with my parents.	☐	☐	☐	☐	☐
2. ... I felt fine at home.	☐	☐	☐	☐	☐
3. ... we quarrelled at home.	☐	☐	☐	☐	☐
4. ... my parents stopped me from doing certain things.	☐	☐	☐	☐	☐
5. ... my parents treated me like a baby because of my illness.	☐	☐	☐	☐	☐

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... and then about your friends.

During the past 7 days...	Never	Seldom	Some-times	Often	All the time
1. ... I played with friends.	☐	☐	☐	☐	☐
2. ... other kids liked me.	☐	☐	☐	☐	☐
3. ... I got along well with my friends.	☐	☐	☐	☐	☐
4. ... I felt different from other children.	☐	☐	☐	☐	☐
5. ... I did not want others to notice my illness.	☐	☐	☐	☐	☐

Now, we would like to know about school.

During the past 7 days...	Never	Seldom	Some-times	Often	All the time
1. ... doing my schoolwork was easy.	☐	☐	☐	☐	☐
2. ... I enjoyed my classes.	☐	☐	☐	☐	☐
3. ... I looked forward to the weeks ahead.	☐	☐	☐	☐	☐
4. ... I was afraid of getting bad marks.	☐	☐	☐	☐	☐
5. ... I missed something at school because of my illness.	☐	☐	☐	☐	☐

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NOW WE WOULD LIKE TO ASK YOU SEVERAL QUESTIONS ABOUT YOUR HAEMOPHILIA.

Here we would like to know about your **BLEEDS** (JOINT BLEEDS).

1. How frequent were your bleeds during the past month?
☐ No bleeds ☐ 1 ☐ 2 ☐ More than 2 How many? ____

The following questions should only be answered if you had bleeds.

2. How much were you troubled by bleeds during the past month?
☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
3. How severe were your bleeds during the past month (if you had several bleeds, please answer for the most severe bleed)?
☐ Slight ☐ Moderate ☐ Severe ☐ Very severe
4. Did you feel a strange sensation in your joints before you had a bleed?
☐ Never ☐ Seldom ☐ Sometimes ☐ Often ☐ Always
5. Did you have to stay quiet (e.g. lie in bed) when you had bleeds?
☐ Never ☐ Seldom ☐ Sometimes ☐ Often ☐ Always
6. When you had bleeds, did you inform your parents immediately?
☐ Never ☐ Seldom ☐ Sometimes ☐ Often ☐ Always

We would like to know who gave you **INJECTIONS**.

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I injected myself.	☐	☐	☐	☐	☐
2. ... my mother injected me.	☐	☐	☐	☐	☐
3. ... my father injected me.	☐	☐	☐	☐	☐
4. ... a nurse injected me.	☐	☐	☐	☐	☐
5. ... a doctor injected me.	☐	☐	☐	☐	☐

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Here we would like to know about
haemophilia and your **PHYSICAL HEALTH**...

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... my bruises hurt.	☐	☐	☐	☐	☐
2. ... I had pain in my joints.	☐	☐	☐	☐	☐
3. ... it was painful for me to move.	☐	☐	☐	☐	☐
4. ... my joints felt stiff.	☐	☐	☐	☐	☐
5. ... it was difficult for me to move my arms or legs.	☐	☐	☐	☐	☐
6. ... I had difficulty walking as far as I wanted to.	☐	☐	☐	☐	☐
7. ... I was afraid of hurting myself.	☐	☐	☐	☐	☐

... and now about how you have been **FEELING** because of your haemophilia.

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I was in a bad mood because of my haemophilia.	☐	☐	☐	☐	☐
2. ... I was sad because of my haemophilia.	☐	☐	☐	☐	☐
3. ... my haemophilia was a burden (real problem) for me.	☐	☐	☐	☐	☐
4. ... my haemophilia made me angry.	☐	☐	☐	☐	☐
5. ... I was worried because of my haemophilia.	☐	☐	☐	☐	☐
6. ... I felt lonely because of my haemophilia.	☐	☐	☐	☐	☐
7. ... I was afraid of bleeds.	☐	☐	☐	☐	☐

[II, kids, long]

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How does haemophilia affect your **VIEW OF YOURSELF?**

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I envied healthy boys my age.	☐	☐	☐	☐	☐
2. ... I felt physically weaker than other boys.	☐	☐	☐	☐	☐
3. ... I felt as well as other boys my age.	☐	☐	☐	☐	☐
4. ... I felt contented about my body.	☐	☐	☐	☐	☐
5. ... haemophilia made my life more difficult.	☐	☐	☐	☐	☐
6. ... I felt embarrassed about my haemophilia.	☐	☐	☐	☐	☐
7. ... I had difficulty doing things with other kids my age.	☐	☐	☐	☐	☐
8. ... I was unable to do as much with my friends because of my haemophilia.	☐	☐	☐	☐	☐
9. ... I felt healthy in spite of my haemophilia.	☐	☐	☐	☐	☐

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The next questions are about haemophilia and your **FAMILY**...

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... my mother protected me too much.	☐	☐	☐	☐	☐
2. ... my father protected me too much.	☐	☐	☐	☐	☐
3. ... there were problems at home because of my haemophilia.	☐	☐	☐	☐	☐
4. ... I felt I was causing my family trouble because of my haemophilia.	☐	☐	☐	☐	☐
5. ... my parents limited their time at work or leisure because they had to look after me.	☐	☐	☐	☐	☐

... and then about haemophilia and your **FRIENDS**...

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I was able to talk to my friends about my haemophilia.	☐	☐	☐	☐	☐
2. ... my best friend cared about how I was feeling.	☐	☐	☐	☐	☐
3. ... I had a best friend that I felt very close to.	☐	☐	☐	☐	☐
4. ... my friends took care of me when I felt bad.	☐	☐	☐	☐	☐

[II, kids, long]

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... and then about haemophilia and the **SUPPORT YOU FELT YOU WERE RECEIVING.**

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... others showed special consideration for me because of my haemophilia.	☐	☐	☐	☐	☐
2. ... others showed understanding for my haemophilia.	☐	☐	☐	☐	☐
3. ... I was able to talk to others about problems connected with my haemophilia.	☐	☐	☐	☐	☐
4. ... others stood by me.	☐	☐	☐	☐	☐

These questions are about your haemophilia and **OTHER PEOPLE.**

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I felt different from others because of my haemophilia.	☐	☐	☐	☐	☐
2. ... I was bothered by others knowing about my haemophilia.	☐	☐	☐	☐	☐
3. ... others kids teased me because of my haemophilia.	☐	☐	☐	☐	☐
4. ... people behaved differently towards me because of my haemophilia.	☐	☐	☐	☐	☐
5. ... I felt left out when others did things together.	☐	☐	☐	☐	☐
6. ... some people made silly comments about my haemophilia.	☐	☐	☐	☐	☐

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These questions are about **SPORTS AND SCHOOL**.

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I could not do sports that I like because of my haemophilia.	☐	☐	☐	☐	☐
2. ... I had to do indoor activities more than other kids because of my haemophilia.	☐	☐	☐	☐	☐
3. ... I could not do sports like rugby or soccer.	☐	☐	☐	☐	☐
4. ... I did just as much sport as any other kid.	☐	☐	☐	☐	☐
5. ... I participated in sports classes at school in spite of my haemophilia.	☐	☐	☐	☐	☐
6. ... I was able to go to school in spite of my haemophilia.	☐	☐	☐	☐	☐
7. ... I could not go to special school events (e.g. outings) because of my haemophilia.	☐	☐	☐	☐	☐
8. ... I found it difficult to concentrate at school because I was in pain.	☐	☐	☐	☐	☐

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The next questions are about **HOW YOU DEAL WITH HAEMOPHILIA...**

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I tried to recognise early on when a bleed developed.	☐	☐	☐	☐	☐
2. ... I was careful with my body.	☐	☐	☐	☐	☐
3. ... I was able to tell whether or not I was bleeding.	☐	☐	☐	☐	☐
4. ... I was in control of my complaints due to haemophilia.	☐	☐	☐	☐	☐
5. ... I felt well-informed about haemophilia.	☐	☐	☐	☐	☐
6. ... haemophilia was a normal part of my life.	☐	☐	☐	☐	☐
7. ... I have accepted having haemophilia.	☐	☐	☐	☐	☐

... and what about your **TREATMENT?**

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I was satisfied with the haemophilia unit.	☐	☐	☐	☐	☐
2. ... the medication I got was okay.	☐	☐	☐	☐	☐
3. ... I trusted my doctors and nurses.	☐	☐	☐	☐	☐
4. ... I disliked going to the haemophilia unit.	☐	☐	☐	☐	☐
5. ... the injections irritated me.	☐	☐	☐	☐	☐
6. ... I was irritated about the amount of time spent having the injections.	☐	☐	☐	☐	☐
7. ... I felt interrupted in my activities by the injections.	☐	☐	☐	☐	☐

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And your **OVERALL HEALTH?**

In general, ...	Excellent	Very good	Good	Fair	Bad
1. ... would you say your health is...	☐	☐	☐	☐	☐

Open Questions.

1. How much are you bothered by your haemophilia?
☐ Not at all ☐ Somewhat ☐ Moderately ☐ Considerably ☐ Very much

2. What bothers you most about haemophilia? Please write down some things:

- _____
- _____
- _____

3. How did you like the questionnaire?
(Please put a mark on the line between "0" and "100", to show which most applies to you.)

0		100

Very bad		Very good

4. Have we forgotten anything that is important to you?

- _____
- _____
- _____

5. How long did it take to fill in the questionnaire? About _____ minutes.

Well done!

THANK YOU FOR YOUR HELP!

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HAEMO - QOL

Questionnaire for Children and Adolescents

Kid's long Version

age: 13-16

Hello there!

We would like to know how you have been feeling during the past few weeks,
so we have worked out some questions which we would like you to answer.

This questionnaire was made for adolescents with haemophilia.

- ⇒ Please read each question carefully.
- ⇒ Think about how things have been for you during the past few weeks.
- ⇒ Choose the answer that fits you best and tick (✓) the appropriate box.

There are no right or wrong answers. It's what you think that matters.

For example: 	Never	Seldom	Some- times	Often	All the time
During the past 7 days, I felt like eating ice-cream.	☐	☐	☐	☒	☐

Date of completion: □ □ □ □ □ □ □ □
(day/ month/ year)

Country: □ □ □

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We would like to know about your physical health...

During the past 7 days...	Never	Seldom	Some-times	Often	All the time
1. ... I felt ill.	☐	☐	☐	☐	☐
2. ... I was in pain.	☐	☐	☐	☐	☐
3. ... I was tired and worn-out.	☐	☐	☐	☐	☐
4. ... I felt strong and full of energy.	☐	☐	☐	☐	☐
5. ... I was afraid that my illness might get worse.	☐	☐	☐	☐	☐

... then about how you've been feeling in general...

During the past 7 days...	Never	Seldom	Some-times	Often	All the time
1. ... I had fun and laughed a lot.	☐	☐	☐	☐	☐
2. ... I was bored.	☐	☐	☐	☐	☐
3. ... I felt alone.	☐	☐	☐	☐	☐
4. ... I felt scared or unsure of myself.	☐	☐	☐	☐	☐
5. ... I was sad because of my illness.	☐	☐	☐	☐	☐

... and how you have been feeling about yourself.

During the past 7 days...	Never	Seldom	Some-times	Often	All the time
1. ... I was proud of myself.	☐	☐	☐	☐	☐
2. ... I felt on top of the world.	☐	☐	☐	☐	☐
3. ... I felt pleased with myself.	☐	☐	☐	☐	☐
4. ... I had lots of good ideas.	☐	☐	☐	☐	☐
5. ... I was able to cope well with my illness.	☐	☐	☐	☐	☐

[III, kids, long]

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The next questions are about your family...

During the past 7 days...	Never	Seldom	Some-times	Often	All the time
1. ... I got on well with my parents.	☐	☐	☐	☐	☐
2. ... I felt fine at home.	☐	☐	☐	☐	☐
3. ... we quarrelled at home.	☐	☐	☐	☐	☐
4. ... I felt restricted by my parents.	☐	☐	☐	☐	☐
5. ... my parents treated me like a baby because of my illness.	☐	☐	☐	☐	☐

... and then about your friends.

During the past 7 days...	Never	Seldom	Some-times	Often	All the time
1. ... I did things together with my friends.	☐	☐	☐	☐	☐
2. ... I was a "success" with my friends.	☐	☐	☐	☐	☐
3. ... I got along well with my friends.	☐	☐	☐	☐	☐
4. ... I felt different from other people.	☐	☐	☐	☐	☐
5. ... I did not want others to notice my illness.	☐	☐	☐	☐	☐

Now, we would like to know about school.

During the past 7 days...	Never	Seldom	Some-times	Often	All the time
1. ... doing my schoolwork was easy.	☐	☐	☐	☐	☐
2. ... I found school interesting.	☐	☐	☐	☐	☐
3. ... I worried about my future.	☐	☐	☐	☐	☐
4. ... I worried about getting bad marks.	☐	☐	☐	☐	☐
5. ... I missed something at school because of my illness.	☐	☐	☐	☐	☐

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NOW WE WOULD LIKE TO ASK YOU SEVERAL QUESTIONS ABOUT YOUR HAEMOPHILIA.

Here we would like to know about your **BLEEDS (JOINT BLEEDS)**.

1. How frequent were your bleeds during the past month?
- ☐ No bleeds ☐ 1 ☐ 2 ☐ More than 2 How many? ____

The following questions should only be answered if you had bleeds.

2. How much were you troubled by bleeds during the past month?
- ☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
3. How severe were your bleeds during the past month (if you had several bleeds, please answer for the most severe bleed)?
- ☐ Slight ☐ Moderate ☐ Severe ☐ Very severe
4. Did you feel a strange sensation in your joints before you had a bleed?
- ☐ Never ☐ Seldom ☐ Sometimes ☐ Often ☐ Always
5. Did you have to stay quiet (e.g. lie in bed) when you had bleeds?
- ☐ Never ☐ Seldom ☐ Sometimes ☐ Often ☐ Always
6. When you had bleeds, did you inform your parents immediately?
- ☐ Never ☐ Seldom ☐ Sometimes ☐ Often ☐ Always

We would like to know who gave you **INJECTIONS**.

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I injected myself.	☐	☐	☐	☐	☐
2. ... my mother injected me.	☐	☐	☐	☐	☐
3. ... my father injected me.	☐	☐	☐	☐	☐
4. ... a nurse injected me.	☐	☐	☐	☐	☐
5. ... a doctor injected me.	☐	☐	☐	☐	☐

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Here we would like to know about
haemophilia and your **PHYSICAL HEALTH**...

During the past month...	Never	Seldom	Some- times	Often	All the time
1. ... my bruises hurt.	☐	☐	☐	☐	☐
2. ... I had pain in my joints.	☐	☐	☐	☐	☐
3. ... it was painful for me to move.	☐	☐	☐	☐	☐
4. ... my joints felt stiff.	☐	☐	☐	☐	☐
5. ... it was difficult for me to move my arms or legs.	☐	☐	☐	☐	☐
6. ... I had difficulty walking as far as I wanted to.	☐	☐	☐	☐	☐
7. ... I was afraid of hurting myself.	☐	☐	☐	☐	☐

... and now about how you have been **FEELING** because of your haemophilia.

During the past month...	Never	Seldom	Some- times	Often	All the time
1. ... I was in a bad mood because of my haemophilia.	☐	☐	☐	☐	☐
2. ... I was sad because of my haemophilia.	☐	☐	☐	☐	☐
3. ... my haemophilia was a burden (real problem) for me.	☐	☐	☐	☐	☐
4. ... my haemophilia made me angry.	☐	☐	☐	☐	☐
5. ... I was worried because of my haemophilia.	☐	☐	☐	☐	☐
6. ... I felt lonely because of my haemophilia.	☐	☐	☐	☐	☐
7. ... I was afraid of bleeds.	☐	☐	☐	☐	☐
8. ... I felt excluded by my friends.	☐	☐	☐	☐	☐

[III, kids, long]

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How does haemophilia affect your **VIEW OF YOURSELF?**

During the past month...	Never	Seldom	Some- times	Often	All the time
1. ... I envied healthy boys my age.	☐	☐	☐	☐	☐
2. ... I felt physically weaker than other boys.	☐	☐	☐	☐	☐
3. ... I felt as well as other boys my age.	☐	☐	☐	☐	☐
4. ... I felt contented about my body.	☐	☐	☐	☐	☐
5. ... haemophilia made my life more difficult.	☐	☐	☐	☐	☐
6. ... I was happy in spite of my haemophilia.	☐	☐	☐	☐	☐
7. ... I felt embarrassed about my haemophilia.	☐	☐	☐	☐	☐
8. ... I had difficulty doing things with other kids my age.	☐	☐	☐	☐	☐
9. ... I was unable to do as much with my friends because of my haemophilia.	☐	☐	☐	☐	☐
10. ... I felt healthy in spite of my haemophilia.	☐	☐	☐	☐	☐

[III, kids, long]

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The next questions are about haemophilia and your **FAMILY**...

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I was treated differently by my family because of my haemophilia.	☐	☐	☐	☐	☐
2. ... my mother protected me too much.	☐	☐	☐	☐	☐
3. ... my father protected me too much.	☐	☐	☐	☐	☐
4. ... my parents criticised me when I hurt myself.	☐	☐	☐	☐	☐
5. ... my parents would not let me do certain things because of my haemophilia.	☐	☐	☐	☐	☐
6. ... there were problems at home because of my haemophilia.	☐	☐	☐	☐	☐
7. ... I felt I was causing my family trouble because of my haemophilia.	☐	☐	☐	☐	☐
8. ... my parents limited their time at work or leisure because they had to look after me.	☐	☐	☐	☐	☐

... and then about haemophilia and your **FRIENDS**.

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I was able to talk to my friends about my haemophilia.	☐	☐	☐	☐	☐
2. ... my best friend cared about how I was feeling.	☐	☐	☐	☐	☐
3. ... I had a best friend that I felt very close to.	☐	☐	☐	☐	☐
4. ... my friends took care of me when I felt bad.	☐	☐	☐	☐	☐

[III, kids, long]

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... and then about haemophilia and the **SUPPORT YOU FELT YOU WERE RECEIVING.**

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... others showed special consideration for me because of my haemophilia.	☐	☐	☐	☐	☐
2. ... others showed understanding for my haemophilia.	☐	☐	☐	☐	☐
3. ... I was able to talk to others about problems connected with my haemophilia.	☐	☐	☐	☐	☐
4. ... others stood by me.	☐	☐	☐	☐	☐

These questions are about your haemophilia and **OTHER PEOPLE.**

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I felt different from others because of my haemophilia.	☐	☐	☐	☐	☐
2. ... I was bothered by others knowing about my haemophilia.	☐	☐	☐	☐	☐
3. ... others kids teased me because of my haemophilia.	☐	☐	☐	☐	☐
4. ... people behaved differently towards me because of my haemophilia.	☐	☐	☐	☐	☐
5. ... I felt left out when others did things together.	☐	☐	☐	☐	☐
6. ... some people made silly comments about my haemophilia.	☐	☐	☐	☐	☐

[III, kids, long]

CIII-HAEMO-QOL - South Africa/English - Final version - 16 Jul 07 - Mapi Research Institute.
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VISIT X

Subject No.:

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These questions are about **SPORTS AND SCHOOL**.

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I could not do sports that I like because of my haemophilia.	☐	☐	☐	☐	☐
2. ... I had to do indoor activities more than other kids because of my haemophilia.	☐	☐	☐	☐	☐
3. ... I could not do sports like rugby or soccer.	☐	☐	☐	☐	☐
4. ... I did just as much sport as any other kid.	☐	☐	☐	☐	☐
5. ... I was treated differently by teachers because of my haemophilia.	☐	☐	☐	☐	☐
6. ... I participated in sports classes at school in spite of my haemophilia.	☐	☐	☐	☐	☐
7. ... I was able to go to school in spite of my haemophilia.	☐	☐	☐	☐	☐
8. ... I could not go to special school events (e.g. outings) because of my haemophilia.	☐	☐	☐	☐	☐
9. ... I found it difficult to pay attention at school because I was in pain.	☐	☐	☐	☐	☐

[III, kids, long]

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VISIT X

Subject No.:

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The next questions are about **HOW YOU DEAL WITH HAEMOPHILIA...**

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I tried to recognise early on when a bleed developed.	☐	☐	☐	☐	☐
2. ... I was careful with my body.	☐	☐	☐	☐	☐
3. ... I was able to tell whether or not I was bleeding.	☐	☐	☐	☐	☐
4. ... I was in control of my complaints due to haemophilia.	☐	☐	☐	☐	☐
5. ... I felt well-informed about haemophilia.	☐	☐	☐	☐	☐
6. ... haemophilia was a normal part of my life.	☐	☐	☐	☐	☐
7. ... I have accepted having haemophilia.	☐	☐	☐	☐	☐

[III, kids, long]

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VISIT X

Subject No.:

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... and what about your **TREATMENT?**

During the past month...	Never	Seldom	Some-times	Often	All the time
1. ... I was satisfied with the haemophilia unit.	☐	☐	☐	☐	☐
2. ... the medication I got was okay.	☐	☐	☐	☐	☐
3. ... I trusted my doctors and nurses.	☐	☐	☐	☐	☐
4. ... I disliked going to the haemophilia unit.	☐	☐	☐	☐	☐
5. ... I felt dependent on others because of my haemophilia.	☐	☐	☐	☐	☐
6. ... the injections irritated me.	☐	☐	☐	☐	☐
7. ... I was irritated about the amount of time spent having the injections.	☐	☐	☐	☐	☐
8. ... I felt interrupted in my activities by the injections.	☐	☐	☐	☐	☐

What do you think about the **FUTURE?**

Recently...	Never	Seldom	Some-times	Often	All the time
1. ... I have been thinking that it will be difficult for me to lead a normal life.	☐	☐	☐	☐	☐
2. ... I have been hoping that things will get better as I grow older.	☐	☐	☐	☐	☐
3. ... I have been worrying about my health.	☐	☐	☐	☐	☐
4. ... I have been sure that I will have a family later on.	☐	☐	☐	☐	☐

[III, kids, long]

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VISIT X

Subject No.:

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What about **RELATIONSHIPS**?

Recently...	Never	Seldom	Some-times	Often	All the time
1. ... I have been finding it difficult to date because of my haemophilia.	☐	☐	☐	☐	☐
2. ... I have been insecure in my relationships with girls because of my haemophilia.	☐	☐	☐	☐	☐

And your **OVERALL HEALTH**?

In general, ...	Excellent	Very good	Good	Fair	Bad
1. ... would you say your health is...	☐	☐	☐	☐	☐

[III, kids, long]

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VISIT X

Subject No.:

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Open Questions.

1. How much are you bothered by your haemophilia?
☐ Not at all ☐ Somewhat ☐ Moderately ☐ Considerably ☐ Very much

2. What bothers you most about haemophilia? Please write down some things:

- _____
- _____
- _____

3. How did you like the questionnaire?
(Please put a mark on the line between "0" and "100", to show which most applies to you.)

0	100

Very bad	Very good

4. Have we forgotten anything that is important to you?

- _____
- _____
- _____

5. How long did it take to fill in the questionnaire? About _____ minutes.

Well done!

THANK YOU FOR YOUR HELP!

[III, kids, long]

CIII-HAEMO-001 - South Africa/English - Final version - 16 Jul 07 - Merit Research Institute

**APPENDIX VI: Paediatric Quality of Life Intervention
Measurement Model (PedsQL) Questionnaire**

ID#	_____
Date:	_____

PedsQLTM

Pediatric Quality of Life Inventory

Version 4.0

YOUNG CHILD REPORT (ages 5-7)

Instructions for interviewer:

I am going to ask you some questions about things that might be a problem for some children. I want to know how much of a problem any of these things might be for you.

Show the child the template and point to the responses as you read.

If it is not at all a problem for you, point to the smiling face

If it is sometimes a problem for you, point to the middle face

If it is a problem for you a lot, point to the frowning face

I will read each question. Point to the pictures to show me how much of a problem it is for you. Let's try a practice one first.

	Not at all	Sometimes	A lot
Is it hard for you to snap your fingers			

Ask the child to demonstrate snapping his or her fingers to determine whether or not the question was answered correctly. Repeat the question if the child demonstrates a response that is different from his or her action.

Think about how you have been doing for the last few weeks. Please listen carefully to each sentence and tell me how much of a problem this is for you.

After reading the item, gesture to the template. If the child hesitates or does not seem to understand how to answer, read the response options while pointing at the faces.

PHYSICAL FUNCTIONING (problems with...)	Not at all	Sometimes	A lot
1. Is it hard for you to walk	0	2	4
2. Is it hard for you to run	0	2	4
3. Is it hard for you to play sports or exercise	0	2	4
4. Is it hard for you to pick up big things	0	2	4
5. Is it hard for you to take a bath or shower	0	2	4
6. Is it hard for you to do chores (like pick up your toys)	0	2	4
7. Do you have hurts or aches (<i>Where?</i>)	0	2	4
8. Do you ever feel too tired to play	0	2	4

Remember, tell me how much of a problem this has been for you for the last few weeks.

EMOTIONAL FUNCTIONING (problems with...)	Not at all	Sometimes	A lot
1. Do you feel scared	0	2	4
2. Do you feel sad	0	2	4
3. Do you feel mad	0	2	4
4. Do you have trouble sleeping	0	2	4
5. Do you worry about what will happen to you	0	2	4

SOCIAL FUNCTIONING (problems with...)	Not at all	Sometimes	A lot
1. Is it hard for you to get along with other kids	0	2	4
2. Do other kids say they do not want to play with you	0	2	4
3. Do other kids tease you	0	2	4
4. Can other kids do things that you cannot do	0	2	4
5. Is it hard for you to keep up when you play with other kids	0	2	4

SCHOOL FUNCTIONING (problems with...)	Not at all	Sometimes	A lot
1. Is it hard for you to pay attention in school	0	2	4
2. Do you forget things	0	2	4
3. Is it hard to keep up with schoolwork	0	2	4
4. Do you miss school because of not feeling good	0	2	4
5. Do you miss school because you have to go to the doctor's or hospital	0	2	4

ID#	_____
Date:	_____

PedsQLTM

Pediatric Quality of Life Inventory

Version 4.0

CHILD REPORT (ages 8-12)

DIRECTIONS

On the following page is a list of things that might be a problem for you. Please tell us **how much of a problem** each one has been for you during the **past ONE month** by circling:

- 0 if it is **never** a problem
- 1 if it is **almost never** a problem
- 2 if it is **sometimes** a problem
- 3 if it is **often** a problem
- 4 if it is **almost always** a problem

There are no right or wrong answers.
If you do not understand a question, please ask for help.

In the past **ONE month**, how much of a **problem** has this been for you ...

ABOUT MY HEALTH AND ACTIVITIES (problems with...)	Never	Almost Never	Some- times	Often	Almost Always
1. It is hard for me to walk more than one block	0	1	2	3	4
2. It is hard for me to run	0	1	2	3	4
3. It is hard for me to do sports activity or exercise	0	1	2	3	4
4. It is hard for me to lift something heavy	0	1	2	3	4
5. It is hard for me to take a bath or shower by myself	0	1	2	3	4
6. It is hard for me to do chores around the house	0	1	2	3	4
7. I hurt or ache	0	1	2	3	4
8. I have low energy	0	1	2	3	4

ABOUT MY FEELINGS (problems with...)	Never	Almost Never	Some- times	Often	Almost Always
1. I feel afraid or scared	0	1	2	3	4
2. I feel sad or blue	0	1	2	3	4
3. I feel angry	0	1	2	3	4
4. I have trouble sleeping	0	1	2	3	4
5. I worry about what will happen to me	0	1	2	3	4

HOW I GET ALONG WITH OTHERS (problems with...)	Never	Almost Never	Some- times	Often	Almost Always
1. I have trouble getting along with other kids	0	1	2	3	4
2. Other kids do not want to be my friend	0	1	2	3	4
3. Other kids tease me	0	1	2	3	4
4. I cannot do things that other kids my age can do	0	1	2	3	4
5. It is hard to keep up when I play with other kids	0	1	2	3	4

ABOUT SCHOOL (problems with...)	Never	Almost Never	Some- times	Often	Almost Always
1. It is hard to pay attention in class	0	1	2	3	4
2. I forget things	0	1	2	3	4
3. I have trouble keeping up with my schoolwork	0	1	2	3	4
4. I miss school because of not feeling well	0	1	2	3	4
5. I miss school to go to the doctor or hospital	0	1	2	3	4

ID#	_____
Date:	_____

PedsQLTM

Pediatric Quality of Life Inventory

Version 4.0

TEEN REPORT (ages 13-18)

DIRECTIONS

On the following page is a list of things that might be a problem for you. Please tell us **how much of a problem** each one has been for you during the **past ONE month** by circling:

- 0 if it is **never** a problem
- 1 if it is **almost never** a problem
- 2 if it is **sometimes** a problem
- 3 if it is **often** a problem
- 4 if it is **almost always** a problem

There are no right or wrong answers.
If you do not understand a question, please ask for help.

In the past **ONE month**, how much of a **problem** has this been for you ...

ABOUT MY HEALTH AND ACTIVITIES (problems with...)	Never	Almost Never	Some- times	Often	Almost Always
1. It is hard for me to walk more than one block	0	1	2	3	4
2. It is hard for me to run	0	1	2	3	4
3. It is hard for me to do sports activity or exercise	0	1	2	3	4
4. It is hard for me to lift something heavy	0	1	2	3	4
5. It is hard for me to take a bath or shower by myself	0	1	2	3	4
6. It is hard for me to do chores around the house	0	1	2	3	4
7. I hurt or ache	0	1	2	3	4
8. I have low energy	0	1	2	3	4

ABOUT MY FEELINGS (problems with...)	Never	Almost Never	Some- times	Often	Almost Always
1. I feel afraid or scared	0	1	2	3	4
2. I feel sad or blue	0	1	2	3	4
3. I feel angry	0	1	2	3	4
4. I have trouble sleeping	0	1	2	3	4
5. I worry about what will happen to me	0	1	2	3	4

HOW I GET ALONG WITH OTHERS (problems with...)	Never	Almost Never	Some- times	Often	Almost Always
1. I have trouble getting along with other teens	0	1	2	3	4
2. Other teens do not want to be my friend	0	1	2	3	4
3. Other teens tease me	0	1	2	3	4
4. I cannot do things that other teens my age can do	0	1	2	3	4
5. It is hard to keep up with my peers	0	1	2	3	4

ABOUT SCHOOL (problems with...)	Never	Almost Never	Some- times	Often	Almost Always
1. It is hard to pay attention in class	0	1	2	3	4
2. I forget things	0	1	2	3	4
3. I have trouble keeping up with my schoolwork	0	1	2	3	4
4. I miss school because of not feeling well	0	1	2	3	4
5. I miss school to go to the doctor or hospital	0	1	2	3	4

APPENDIX VII:

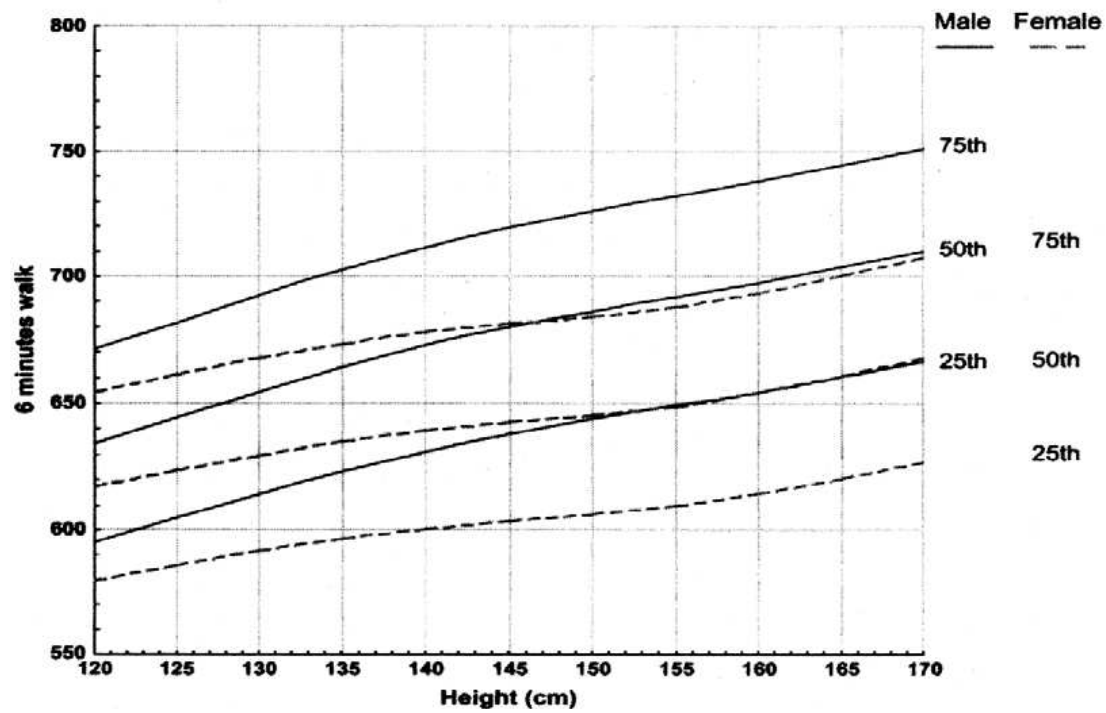
Table 1 Reference values for heart rate and respiratory rate in South African children of four to sixteen years (Taken from: Wallis et al, 2005, pg 1118)

Table 2 Respiration rate and heart rate; median and 2½, 97½ centiles by age						
Age (y)	Heart rate (bpm)*			Respiration rate (bpm)†		
	2½	50	97½	2½	50	97½
4	81	103	131	20	22	26
5	74	95	121	19	21	25
6	69	89	115	18	21	24
7	66	85	111	17	20	24
8	63	83	109	17	19	23
9	62	82	108	16	19	23
10	61	81	108	15	18	22
11	60	80	108	14	17	21
12	59	80	108	14	17	21
13	58	79	107	13	16	20
14	56	77	106	12	15	20
15	54	74	103	12	14	19
16	51	71	99	11	14	18

*Beats per minute.
†Breaths per minute.

APPENDIX VIII:

The following graph is taken from the results of Li and colleagues and it combines centile curves for both genders (Taken from: Li et al, 2007, pg 179)



APPENDIX IX:

The following graph is taken from Lammers and colleagues with reference values for the 6MWT in children of four to eleven years of age (Taken from: Lammers et al, 2008, pg 466)

