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A pilot study to investigate the muscle strenght of children infected with HIV

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CHAPTER 1

INTRODUCTION TO THE STUDY

1.1 Introduction

The earliest cases of HIV infection in South Africa were identified in the 1980's (UNAIDS, Sub-Saharan Africa Report, 2008). HIV/AIDS has since become a major public health challenge. South Africa has been reported to be the country with the largest number of HIV infections worldwide (UNAIDS, Sub-Saharan Africa Report, 2008). In 2007 it was estimated that 90% of the world's children infected with HIV were living in sub-Saharan Africa (UNAIDS, 2007). The global figure for the number of children living with HIV stood at 2.5 million in 2007; thus the number translated to 1.8 million children infected with the virus in sub-Saharan Africa (UNAIDS, 2007).

One in seven child has been reported to be newly infected with the virus every day; mostly due to mother-to-child transmission (UNAIDS, 2006). Young women, between 25 and 34 years of age, in South Africa are at greatest risk of becoming infected; they account for 90% of new infections (UNAIDS, Sub-Saharan Africa Report, 2008). In 2006 there was an HIV prevalence of 29% among pregnant women attending antenatal clinics in South Africa (UNAIDS, 2007). In 2007, 66% of HIV-infected pregnant women received antiretroviral (ARV) therapy for prevention of mother-to-child transmission (PMTCT) in the country (UNAIDS, SA Report, 2008). Thus the rate of transmission to children still remains high.

In June 2006, 60 000 to 100 000 of the more than 800 000 children in need of ARV therapy (most of them in sub-Saharan Africa) were receiving it (WHO, HIV in Children, 2006). Children with a CD4 count of less than 25% of the normal for their age have been recommended by the WHO to receive ARV treatment (ANECCA, 2005). At South African Paediatric HIV clinics, guidelines state that children above the age of 18 months should receive ARV treatment when CD4 counts decrease to below that of 15%. Children younger than 18 months of age are eligible for treatment when CD4 counts decrease to below that of 20% (Guidelines for the management of HIV-infected children,

2006).

Symptoms common on general examination of children infected with HIV include wasting syndrome, persistent generalised lymphadenopathy, recurrent bacterial infections, bacterial pneumonia, recurrent chest infections, Pneumocystis jiroveci pneumonia (previously known as Pneumocystis carinii pneumonia), lymphoid interstitial pneumonia (LIP), tuberculosis, dermatitis, opportunistic infections (candida, thrush, herpes simplex), blood disorders, neurological syndromes, encephalopathy and developmental delay (Evian, 2000).

Numerous authors have documented the effect of HIV on encephalopathy and developmental delay in children infected with HIV (Baillieu & Potterton, 2008; Blanchette, 2001; Blanchette, 2002; Chakraborty, 2005; Chase et al., 2000; Foster et al., 2006; Gay et al., 1995; Llorente et al., 2003; Lwin & Melvin, 2001; Mitchell, 2001; Parks et al., 1999; Pearson et al., 2000; Potterton, 2006; Raskino et al., 1999; Stein et al., 2005). These studies have analysed physical central nervous system changes, cognitive function, psychomotor skills, visuomotor integration, visuospatial perception, verbally mediated skills, language acquisition, and social contact, as well as gross and fine motor function. A number of these articles have commented on the effect of muscle strength on gross motor function (Baillieu & Potterton, 2008; Bale et al., 1995; Msellati et al., 1993; Parks et al., 1999; Pearson et al., 2000; Potterton, 2006). These articles state that increased force against gravity is a requirement of higher function and so identify weakness as a cause of gross motor performance deficits.

Although ARV therapy has had proven positive effects on developmental delay in children (Chiriboga et al., 2005; McCoig et al., 2002; Mitchell, 2006; Raskino et al., 1999; Tepper et al., 1998), no effects of ARV therapy on muscle strength in children have been documented.

Many studies have been conducted in order to investigate exercise for the purpose of increasing muscle strength in adults infected with HIV (Agin et al., 2001; Biancalana et al., 2007; Grinspoon et al., 1999; Knapp et al., 2008; O'Brien et al., 2008; Roubenoff, McDermott et al., 1999; Roubenoff, Weiss et al., 1999; Roubenoff & Wilson, 2001; Schroeder et al., 2003; Yarasheski et al., 2000). Muscle weakness has been found predominant in this population. In the adult population grades and quantitative measurements of muscle strength have been used to analyse weakness (Biancalana et al., 2007; Grinspoon et al., 1999; O'Brien et al., 2008).

One study using exercise as a means to increase muscle strength was conducted in children infected with HIV (Miller, 2007). No use of grades or quantitative measurements of muscle strength have been used to analyse weakness in children. Rather weakness has been inferred as a consequence of developmental delay or impaired function.

1.2 Problem statement

Very few authors have documented impairment of muscle strength in children infected with HIV. As yet there has been no study that has investigated the extent of muscle strength impairment or the effect of ARV therapy on muscle strength in children infected with HIV.

1.3 Research question

Is the muscle strength of children infected with HIV different for those children receiving HAART compared to children not receiving HAART?

1.4 Aim

To compare the muscle strength of children infected with HIV who have been receiving HAART for three months or more to that of children infected with HIV who are not receiving HAART.

1.5 Objectives

The primary objective of the study was to ascertain the feasibility and requirement of a full study into the muscle strength of children infected with HIV.

Further objectives of the study were to analyse data and determine the relationship which exists between:

- The muscle strength of children infected with HIV, comparing that of those receiving HAART to those not receiving HAART.
- Muscle strength and length of time having received HAART.
- The CD4 count of children infected with HIV, comparing that of those receiving HAART to those not receiving HAART.
- The socio-economic status of children infected with HIV, comparing that of those receiving HAART to those not receiving HAART.
- The height of children infected with HIV, comparing that of those receiving HAART to those not receiving HAART.
- The weight of children infected with HIV, comparing that of those receiving HAART to those not receiving HAART.

1.6 Significance of the study

Research conducted on developmental delay in children infected with HIV has linked decreased muscle strength with delay in gross motor development. It has been shown that ARV therapy has a positive influence on child development. Research into muscle strength of children infected with HIV will provide better understanding of weakness, and will help to establish whether ARV therapy has an effect on muscle strength in these children. It will promote further research into this area.

CHAPTER 2
LITERATURE REVIEW

2.1 Introduction

In this chapter a discussion of current literature pertinent to the subject of muscle strength in children infected with HIV will be made. Literature for this review has been gathered using key words: HIV, HIV infected children, muscle strength, developmental delay, nutrition, socio-economic status and antiretroviral therapy. Search engines on the World Wide Web included; CINAHL, Cochrane Collaboration searches, MEDLINE, Pedro, Pubmed and Science Direct. A hand search was done at the University of the Witwatersrand, Health Sciences Library.

2.2 Paediatric HIV

The region of the world most affected by AIDS at present is Sub-Saharan Africa. Ten percent of the world's population live in this region, and 90% of children infected with HIV in the world reside here (UNAIDS, 2007). The sub region of Southern Africa accounts for 35% of all people living with HIV (UNAIDS, 2007). "South Africa is the country with the largest number of HIV infections in the world" (UNAIDS, Sub-Saharan Africa Report, 2008, pg 3). South Africa's Department of Health reported 18, 3% of its adults to be living with HIV in 2006 (UNAIDS, Sub-Saharan Africa Report, 2007). Fifty five percent of South Africans infected with HIV live in the provinces of KwaZulu Natal and Gauteng (UNAIDS, Sub-Saharan Africa Report, 2007). The HIV prevalence among pregnant women stood at 30% in 2005 and 29% in 2006 in South Africa (UNAIDS, Sub-Saharan Africa Report, 2008). In KwaZulu Natal province HIV prevalence among pregnant women stood at 39% (the largest prevalence), in the Northern Cape 15% (the smallest prevalence) and in Gauteng province 25% (UNAIDS, Sub-Saharan Africa Report, 2008). Although prevalence remains high, this figure seems to be reaching a plateau.

A study conducted in sub-Saharan Africa showed that 35% of children who contracted HIV from their mothers died before their first birthday; 53% had died before two years of age (UNAIDS, HIV in children, 2006). In 2004, fewer than 100 children infected with HIV died in the world's high income countries (UNAIDS, HIV in children, 2006).

In sub-Saharan Africa more than 95% of infants contract HIV *in utero*, during delivery or while breastfeeding (UNAIDS, HIV in children, 2006). A fraction of children contract HIV through unsafe needle use, transfusion of infected blood products, sexual abuse, sexual intercourse (in adolescents) or scarification (Lwin & Melvin, 2001). The risk of transmission of HIV from mother to child *in utero*, without effective prevention measures is 15-25%. If the child is breastfed between 18-24 months of age the risk of transmission increases to 30-45%. With effective prevention measures first world countries have limited children born to HIV infected mothers from acquiring HIV to less than two percent. Even in Abidjan, Côte d'Ivoire, a resource poor country, transmission has been limited to between two and four percent (UNAIDS, HIV in children, 2006).

In 2005 South Africa was part of the WHO/AFRO Regional Resolution to declare 2006 a year of accelerated HIV prevention. The Africa Health Strategy, which was adopted by Heads of State and Governments of Africa in 2007, also prioritised prevention of HIV as the key strategy to halt the spread of HIV. Prevention of mother to child transmission (PMTCT) has become a key part of this endeavour. In 2007, 66% of HIV-infected pregnant women received antiretroviral (ARV) therapy for PMTCT in South Africa (UNAIDS, SA Report, 2008). Again, provinces within the country differ with the lowest percentage being shown in the Eastern Cape (53%), Gauteng enrolment being 63% and the largest enrolment being seen in the Western Cape (90%) in 2007 (UNAIDS, SA Report, 2008).

2.3 Antiretroviral therapy

South Africa accounted for one-quarter of all people receiving ARV therapy in sub-Saharan Africa; approximately 207 000 people received treatment in South Africa by the

end of 2005 (WHO, 2006). This still meant that less than 20% of the almost one million South Africans in need of ARV therapy were receiving therapy in 2005 (UNAIDS, 2006). In 2006 the actual number of South African adults and children with advanced HIV infection receiving ARV therapy was 273 400 people (UNAIDS, SA Report, 2008). In 2007 this number increased to 371 731 (UNAIDS, SA Report, 2008). The number of people receiving therapy is increasing but there remain many hundreds of thousands of adults and children who are not yet benefitting from antiretroviral therapy.

The goals of ARV therapy in paediatric HIV infection are to reduce plasma viral loads below the limit of detection, prevent selection of drug resistant strains and maintain good immunological status by repopulation of CD4 and T-cells, to prevent clinical disease progression and to prevent opportunistic infections (Chakraborty, 2005).

Antiretroviral drugs inhibit replication of the HI virus at the level of enzymes known to be involved in this process. The drugs work on the reverse transcriptase enzyme and the protease enzyme. Nucleoside reverse transcriptase inhibitors (NRTIs) attach to the RNA strand to shorten the transcription of DNA from RNA. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) directly inhibit the reverse transcriptase enzyme. Protease inhibitors (PI) prevent new formation of viral particles by inhibiting the protease enzyme. ARV drugs thus work best in a combination of three: combining two NRTI's with either an NNRTI or PI. This combination of ARV drugs is known as highly active antiretroviral therapy (HAART). HAART is expected to reduce viral load to undetectable levels, when treating patients who are ARV-naïve (Guidelines for the management of HIV-infected children, 2006; Nachman et al., 2002; UNICEF, 2006).

ARV drugs are unable to eradicate the HI virus as drugs may not reach lymphoid tissue or the central nervous system where the virus may be present. It is important that adherence to medication is maintained in order that viral genetic material does not mutate and drug-resistant strains do not develop. In order to prevent the emergence of drug-resistant strains, therapy failure and limiting future therapy options, a 95%

adherence to long-term therapy must be maintained (Chesney, 2003).

Children with a CD4 count of less than 25% of the normal for their age have been recommended by the WHO to receive ARV treatment (ANECCA, 2005). As the risk of mortality is increased in a child with WHO stage three or four of disease (See appendix I), it is recommended that these children start ARV therapy regardless of their CD4 count (UNICEF, 2006).

Clinical criteria for ARV therapy at South African paediatric HIV clinics include a confirmation of HIV-infection, recurrent hospitalizations (more than two admissions per year) or prolonged hospitalisation (more than four weeks) for HIV-related illness, or; the patient satisfying the provisional WHO stage three or four disease criteria or; a CD4 percentage of less than 20% for children under 18 months or less than 15% for children over 18 months of age (Guidelines for the management of HIV-infected children, 2006).

First-line drug choices in South Africa for children between six months and three years of age are stavudine (d4T), lamivudine (3TC) and Kaletra®. First-line drug choices for children over three years of age and more than 10 kilograms are d4T, 3TC and efavirenz (EFV). Second-line drug choices for children between six months and three years of age are zidovudine (AZT), didanosine (ddI) and nevirapine/EFV (EFV if the child is more than three years of age, nevirapine if less than three years of age). Second-line drug choices for children over three years of age and more than 10 kilograms are AZT, ddI and Kaletra® (Guidelines for the management of HIV-infected children, 2006).

The effects of ARV therapy are explained in subsequent sections. At this stage it is important to complete an understanding of development of musculature in children in order to better analyse the effects HIV and ARV therapies have on the children infected.

2.4 Development of the muscular system

Muscle is contractile tissue derived from the mesodermal layer of embryonic germ cells. These mesodermal cells differentiate to form myotubes, which in turn develop into primary and secondary multinucleate tubular structures. The primary myotubes are first observed at approximately five weeks of gestational age and develop without neural influence. The secondary myotubes are first seen several weeks later and are highly dependent on neural influence for their development. Lack of neural input to these cells result in malformed, fewer or smaller cells. Muscle fibres form by 20 weeks gestational age. During the last half of gestational development the number and size of muscle fibres increases rapidly in order that skeletal muscle is developed by birth. Division of existing cells or differentiation of myoblasts into secondary myotubes continues throughout the first year of life. Thereafter fibres increase in length and cross-sectional area. Factors such as blood supply, innervations, nutrition, gender, genetics and exercise will determine final muscle size (Campbell et al., 2000; Moore & Persaud, 1998).

2.5 Muscle strength

Skeletal muscle is made up of individual muscle fibres arranged parallel to tendinous endings. Muscle fibres are made up of fibrils divisible into filaments, made up of contractile proteins. These proteins of actin, myosin, tropomyosin and troponin are arranged in bands that move past each other to contract and lengthen a muscle (Ganong, 2005). An individual's strength is determined by genetic inheritance of muscle fibre types as well as training. Factors influencing strength are hormones, nutritional intake, gender, age, weight and pathology (Bohannon, 1997). Studies in children have found that developmental differences between individual children are much stronger factors in determining muscle strength than age or size (Kroksmark et al., 2005; University of Utah, 1988). Another factor affecting muscle strength is medication (Damiano et al., 1999).

2.6 Measurement of muscle strength

Muscle strength is a parameter often measured during a physiotherapy examination of a child. Manual muscle testing techniques are commonly used (Daniels & Worthingham, 1986), which, for the purpose of determining whether a muscle is weak due to early stage pathology or for the evaluation of small physiotherapeutic effectiveness, is subjective (Beenakker et al., 2001; Nyström Eek et al., 2006).

Muscle testing using a handheld dynamometer has been designed in order to objectively document muscle impairment. Objective measures and consistent results have been measured by both a single tester over multiple results and across multiple testers (Bohannon, 2006). A single measurement with poor test re-test reliability has a low validity (Fletcher et al., 1996), thus, test-retest reliability is very important. Not only is it important for validity but also for the function of monitoring muscle strength in children. For this purpose, high test re-test reliability is essential for good sensitivity to change (Van den Beld et al., 2006). Reliability and test-retest reliability have been shown in adult samples (Nyström Eek et al., 2006; Taylor et al., 2004) , as well as in children (Van den Beld et al., 2006). Gadjosik (2005) found that isometric force of children who are still developing, and as young as two years of age, can be measured with fair to excellent reliability, using a hand-held dynamometer and standardised testing procedures.

Two methods of muscle strength testing have been described: the make test and the break test methods (Stratford & Balsor, 1994). The make test method requires the examiner to hold the dynamometer in a stationary position while the subject pushes on the dynamometer. The break test method requires the subject to push to his or her maximal effort until the joint gives way. “The make test has been found to have higher reliability than the break test.” (Nyström Eek et al., 2006, pg 1091).

Bohannon (1993, pg 188) describes muscle strength as: “what we are measuring is the maximum short duration voluntary force or torque brought to bear on the environment

… it represents the final output of the central nervous system… the sum of the agonist torque minus antagonist restraint." Force is defined as a physical quantity that causes a mass to accelerate. This can be explained using Newton's Second Law which can be expressed as a force being the product of mass multiplied by acceleration (F=ma), its metric unit being a Newton (N) (Newton, 1999). Torque is a vector that measures the tendency of a force to rotate an object around an axis (Serway & Jewett, 2003). Torque is the product of force multiplied by the length of the lever arm, where the lever arm is at right angles to the force (Tipler, 2004). Torque is measured in Newton metres (Nm).

2.7 Normative data

Articles describing normative values for muscle strength in children are those of Hosking et al. (1976); Bäckman et al. (1989); Beenakker et al. (2001) and Nyström Eek et al. (2006).

The more recent three studies have been analysed. These studies have used sample sizes of 217, 270 and 149 subjects, respectively. All researchers have divided this sample size into categories of age and gender. Children between the ages of three and a half and 15 years of age were included in the first study; those between the ages of four and 16 years of age in the second; and those between five and 15 years of age in the third study. When divided into categories of age and gender the maximum number of children per group is that of 18 children. The minimum number of children in a group is that of five children. The average number of children per group is 8.8 children.

A myometer and hand held dynamometers were used to obtain muscle strength values in the studies mentioned above. Values of muscle strength were measured in kilograms, Newton and Newton metres respectively. All of these studies included their exclusion criteria as well as detailed reproducible methodology.

More recent studies conducted by Holm et al. (2008), and Macfarlane et al. (2008) have slightly larger sample sizes; a maximum of 41 children and 32 children in the respective

studies. The average number of children per group was 31 and 25 children respectively.

In the study done by Holm et al. (2008) measurements of isokinetic and isometric strength were done in children between the ages of seven and 12 years of age. A Jamar dynamometer was used to measure isometric strength in Newton. The study does not, however, document these results nor does it state any inclusion or exclusion criteria. The study proves irreproducible and useless in providing a normative measure of isometric muscle strength in children.

Macfarlane et al. (2008) used a MicroFET 2 handheld dynamometer to measure strength in pounds; these values were then converted into torque. Exclusion criteria as well as detailed methodology are recorded making the study reproducible. Children between the ages of six and eight years of age were included in this study.

One must compare the strength of a child to a group of the same gender and equal age. None of the studies analysed allow for large enough sample sizes or demographic diversity to obtain statistically significant differences when used as normative data.

2.8 Muscle strength in adults infected with HIV

Myopathy has been found in adults infected with HIV, in the absence of ARV treatment. Derangements found to exist in skeletal muscle due to HIV infection include polymyositis, rhabdomyolysis, tumour infiltrations, Dupytren's contractures, wasting syndromes, severe weakness, and fatigue (Biviji et al., 2002; Bower et al., 1990; Otis et al., 2008). These myopathies have not been associated with any particular stage of immunosuppression (Verma et al., 2004). Myopathy has been documented in adults infected with HIV in the absence of ARV treatment but not yet in children.

The effects of aerobic exercise, resistance training and androgen therapy on muscle strength in HIV infected adults have been well documented. As HIV infection changes course in developed countries causing an increase in disability associated with

improved life expectancy, so exercise has become a key strategy in addressing impairment, activity limitation and participation restriction (O'Brien et al., 2008).

Numerous studies have quantified strength and measured the effects exercise has on it. In O'Brien et al.'s (2008) systematic review and meta-analysis of randomized trials, which analysed effects of progressive resistive exercise in adults living with HIV/AIDS, it was noted that all 10 studies reviewed reported muscle strength outcomes. These outcomes could not be meta-analysed due to differences in outcomes and participants, however, nine of the 10 studies showed improvements in strength in the exercise group. In a study conducted by Grinspoon et al. (1999), participants in the exercise group partook in aerobic and resistance training. No significant muscle strength improvement was shown between the exercise and control group, however, isometric strength measurement was used in this study as opposed to isotonic testing that was used in all the other studies. "Isometric testing is known to underestimate changes in strength" (O'Brien et al., 2008, pg 649).

Articles by Knapp et al. (2008), and Schroeder et al. (2003) showed improvements in strength in adults infected with HIV when given androgen therapy combined with an exercise program. Roubenoff and Wilson (2001) showed similar results when 25 adult men (six wasted and 19 not) were only placed on a resistance training program.

All studies reviewed showed progressive resistance training and aerobic exercise to be safe in HIV infected adults who were medically stable. Shepard (1998) advised intensive bouts of exercise to be avoided. Exercise showed no change in immunological or virological status and improvements in strength and physiological status were limited to those people who continued to exercise (O'Brien et al., 2008). It can be seen that numerous authors have observed impairment of muscle strength, function and quality of life in HIV infected adults, and have thus identified a need to analyse the effects of exercise and therapies on improving these.

2.9 Muscle strength and development in children infected with HIV

Impairment of strength in HIV infected children has, thus far, not been well documented. One article to study the effect of exercise on muscle strength in children is that of Miller (2007). The participants in this study were two persons aged 10 and 17 years of age. They participated in a 12-week hospital based resistance training program. The article reports improved muscle strength as well as decreased abdominal adiposity post training. Although this preliminary data suggests supervised exercise to be safe and feasible for children, it can be suggested that a statistically viable sample size be drawn and a generalisable result be obtained by choosing children of a larger age range and younger age; between six and 15 years of age.

Development in younger children infected with HIV with a mention of muscle strength as a component of development has, however, been better reported. In a neurodevelopmental study testing gross motor skills, fine motor skills, language acquisition and social contact done in Rwanda, authors found that HIV infected children were more frequently delayed than HIV-uninfected children born to HIV-seropositive mothers, or children born to HIV-seronegative mothers. These delays were observed in children with severe HIV-related symptoms and were noted to be mostly as a result of gross motor delay (Msellati et al., 1993).

Parks and Danoff (1999) in their analysis of children and preadolescents, using the *Bruininks-Oseretsky Test of Motor Proficiency (BOTMP)*, noted a lower gross motor subtest score than fine motor subtest score. They postulated that this finding might be as a result of lower muscle force and a need for more precise movements for fine motor movements. In contrast, gross movements require higher force outputs and are thus affected by overall loss of muscle strength, which may be the reason for gross motor performance deficits.

Pearson et al. (2000) noted measures of neuropsychological and motor functioning to be powerful indicators of later disease progression. They further documented that

decreased muscle strength along with poor muscle tone and decreased muscle bulk were significantly associated with increased risk of disease progression. The study, however, states that: “for this analysis, motor function, which was defined as the presence or absence of abnormalities in muscle tone, muscle strength, and muscle bulk at baseline and week 48, was the sole focus” of the study.

A further article to document muscle strength was that of Bale et al. (1995) who compared neurologic and examination results of subjects with HIV-1 and haemophilia. They found that these subjects did not differ in abnormalities of cranial nerve function, sensation, muscle strength, or coordination to HIV-1 status, HIV-seronegative and HIV-seropositive subjects. Subjects with HIV-1 and haemophilia did however have abnormal muscle stretch reflexes and muscle bulk, which could be related to either haemophilia or HIV disease progression.

Research conducted in South Africa documenting muscle strength are those by Baillieu and Potterton (2008), and Potterton (2006). These studies did not primarily investigate muscle strength, but rather development. Baillieu and Potterton (2008) in their report of the extent of language, motor and cognitive development in HIV infected infants found them to have significant mental, motor and language delays. They postulated that as gross motor development was the most affected skill in the sample, that this may be attributed to decreased muscle strength. Potterton (2006) found children to improve in cognitive and motor development with the intervention of a basic home stimulation program. Although improvement was seen in the children, a residual delay remained; long-term management was required. After developmental assessment, teaching of a home program and five follow-up visits, it was commented that, “Improved muscle strength due to improved general health may be responsible for the improvement in motor development seen in these children.” (Potterton, 2006, page 161)

As seen in the above study, general health may have a significant impact on gross motor development and possibly muscle strength in children infected with HIV. Other

factors affecting muscle strength in these children will now be highlighted.

2.10 Factors affecting muscle strength in children infected with HIV

Child growth in South Africa is measured against National Centre for Health Statistics growth charts. Although a representation of children in the USA, the use of these charts has been endorsed around the world by the World Health Organisation based on evidence that growth patterns of pre-school children from different ethnic backgrounds are in fact very similar (Chantry & Moye, 2005).

Nutritional studies have found that malnutrition is globally common in paediatric HIV infection (Ball, 1998; Hsu et al., 2005). In sub-Saharan Africa studies have shown 25% of children with malnutrition to be infected with HIV (Ball, 1998). Malnutrition results initially in wasting, however, stunting is associated with prolonged malnutrition (Chantry & Moye, 2005). Weight loss and malnutrition are likely to accelerate disease progression and so increase mortality as a result of their impact on immunity (Hsu et al., 2005). In a study done in Tanzania that investigated HIV infection, malnutrition and socio-economic status, authors found HIV infection, malnutrition, inadequate water supply and anaemia to be strong indicators of mortality in children aged six to 60 months of age (Villamor et al., 2005).

Inadequate intake, malabsorption and increased energy expenditure are three factors contributing to malnutrition in HIV/AIDS (Hsu et al., 2005). Feeding problems noted in HIV infected children include nausea, vomiting, diarrhoea and sores in the mouth (oral thrush or herpes simplex) (Ball, 1998; Guidelines for the management of HIV-infected children, 2006). Loss of appetite and decreased absorption by the gut will consequentially lead to weight loss and stunting (Arpadi, 2005). When compounded by opportunistic infection children will experience increased energy expenditure (Hsu et al., 2005). An inextricable link between disease status and nutritional status has been established (Ball, 1998). A child given effective ARV therapy will show improved health, including nutritional status (Arpadi, 2005).

Loss of body protein and abnormal protein metabolism has been documented in HIV infected children (Hsu et al., 2005). This in turn leads to weight reduction and decreased muscle bulk. A decrease in muscle bulk can therefore be and has been described to be associated with poor nutrition in children infected with HIV (Pearson et al., 2000). Muscle atrophy secondary to malnutrition and stunting has been described in the South African population (Potterton, 2006). Thirty-two percent of HIV infected children will experience protein malabsorption without clinical symptoms (Arpadi, 2005). Overall evidence suggests that HIV infected persons should increase protein intake by 10% in order to maintain body nutrient stores while asymptomatic. When immunity fails the child is suggested to continue this additional 10% intake, but once immunity is restored to increase this amount to between 30 and 50% in order to recover nutrition (Hsu et al., 2005). It has also been reported that with the prescription of anabolic therapy children experience weight gain and an increase in muscle mass (Fox-Wheeler, 1999). Apart from the fore mentioned nutritional studies, limited research has been conducted on the height and weight of children infected with HIV.

It is therefore important to establish whether a child is receiving adequate nutrition. Adequate nutritional intake can be influenced by socio-economic status (Barbarin & Khomo, 1997; Brown & Lourie, 2000). It has been agreed upon that “a family’s available social resources cannot be ignored, because they have a demonstrable and palpable impact on quality of life both material and social, and they strongly influence developmental outcomes” (Barbarin & Khomo, 1997, pg 198). Efforts made to enhance the home environment will have a positive impact on a child’s cognitive development (Coscia et al., 2001). A study done in the South African population by Barbarin and Khomo (1997) comments that not only are food, shelter and material goods essential for child development, but also concepts of social support, coping, problem-solving, intellectual stimulation, and a healthy portrayal of ethnic and gender foundations. Barbarin and Richter (1999) similarly found socio-economic status in the South African population to affect resilience, affability, maturity and school readiness in six year olds.

There is a need to determine household structure as single mothers living with grandmothers improves social conditions and care-taking environments, due to small but reliable pensions. These “are more effective buffers against hunger for children than the male partners of their mothers” (Barbarin & Khomo, 1997, pg 219).

Level of activity is yet another factor which may impact muscle strength. Various studies have found that children leading sedentary lifestyles are at risk of deceased bone density, cardiovascular disease, obesity and psychological imbalances (Behm et al., 2008; Benson et al., 2007; Faigenbaum, 2000; Hass et al., 2001). Improved activity level has been shown to counteract these pathologies and improve muscle strength, endurance, power, balance and co-ordination (Behm et al., 2008; Benson et al., 2007; Faigenbaum, 2000).

2.11 ARV therapy and muscle strength

Multiple articles have documented trunkal adiposity as an effect of ARV Therapy in adults (Agin et al., 2001; Roubenoff, McDermott et al., 1999; Roubenoff, Weiss et al., 1999; Yarasheski et al., 2000). Literature has also shown that ARV therapy causes skeletal muscle abnormality, myopathy and mitochondrial toxicity (Lewis et al., 1992; Panegyres et al., 1990; Sinnwell et al., 1995; White, 2001). Protease inhibitors have been found to decrease the incidence of severe wasting but not affect malnutrition (Agin et al., 2001). Malnutrition results in decreased muscle bulk, which in turn may result in impaired strength. The possibility then exists that ARV therapy may have no effect or a detrimental effect on muscle strength. Further research is needed to establish the existence of any correlation. Other articles have commented on improvement of growth with administration of ARV therapy but no comments on muscle strength have been made (Buchacz et al., 2003; Nachman et al., 2002).

Although Western countries have highlighted the prevalence of developmental delay; prevalence and extent of developmental delay in South African children has not yet been established (Potterton, 2006). Potterton and Eales (2001) found a 40%

prevalence of developmental delay in children under the age of one year. A South African neurodevelopmental study found children to be at risk of severe cognitive and motor developmental delay (Potterton, 2006). In this population, poverty and malnutrition were found to be likely exacerbating factors of developmental delay. Children, antiretroviral naïve at the start of the study who began HAART during the study showed significant improvement in motor development, but not in cognitive development (Potterton, 2006).

Chiriboga et al. (2005) stated: “Progressive HIV Encephalopathy is an infrequent and reversible complication of HIV infection that responds to HAART and that may relapse if control of the virus is lost”. It has also been documented that ARV therapy decreases the frequency of severe forms of encephalopathy and improves neurologic status (McCoig et al., 2002; Mitchell, 2006; Raskino et al., 1999; Tepper et al., 1998). No direct effects of ARV therapy on muscle strength in children have been documented.

2.12 Conclusion

Muscle strength in adults infected with HIV has been extensively documented, especially in light of methods of improving it. Exercise and resistance training has been found to be effective in improving strength in adults infected with HIV. Children infected with HIV have been found to be at severe risk of developmental delay. It has been postulated that these children have decreased muscle strength for their age. Muscle strength in children infected with HIV is a minimally researched subject. Those authors who mention muscle strength in these children have not sited it as the primary subject of their literature. It is essential, therefore, that muscle strength in children infected with HIV be investigated.

CHAPTER 3
RESEARCH METHODOLOGY

This chapter will present the methodology of this research report.

3.1 Location

Children participating in the study were recruited from Harriet Shezi Children's HIV Clinic at Chris Hani Baragwanath Hospital, Gauteng Province, South Africa. This clinic serves to diagnose and then manage disease progression in children who are infected with HIV. The children are seen at regular intervals by doctors, nursing sisters, social workers and dieticians. Children who access clinic services are from similar cultural and socio-economic backgrounds.

3.2 Ethical clearance

Ethical clearance was obtained from the Committee for Research on Human Subjects of the University of the Witwatersrand prior to starting the data collection process. The study ethical clearance number is R14/49 (See appendix II).

The relevant authorities at Chris Hani Baragwanath Hospital gave permission to conduct the study (See appendix III). Prior to participating in the study, children and caregivers received information sheets, which were explained to them as required (See appendices IV and V). Written informed assent and consent was obtained from the child and his or her primary caregiver (See appendices VI and VII).

3.3 Study design

The design of this study was a quantitative cross-sectional correlation pilot study.

3.4 Study population

Subjects were selected from Harriet Shezi Clinic (Paediatric HIV Clinic) at Chris Hani Baragwanath Hospital.

3.4.1 Sample Size

A sample size was calculated, by power calculation, for a full study. This sample size was calculated to be 223 children. Ten percent of this sample size was determined adequate for the present pilot study. The sample size was calculated as 32 children. Sixteen of these children were receiving HAART and sixteen not.

3.4.2 Inclusion criteria

- Children vertically infected with HIV
- Children in the group on ARV therapy must have been receiving treatment for three months or more (these children must have been on Kaletra®, Efavirenz, 3TC or d4T treatments).
- Children vertically infected with HIV attending follow-up at Harriet Shezi Clinic who were antiretroviral naïve.
- Children between four and eight years of age
- Children who were medically stable

3.4.3 Exclusion criteria

- Children who were medically unstable
- Children receiving ARV therapy who had been receiving treatment for less than three months
- Children with any diagnosed joint disorder
- Children with any diagnosed muscular disorder
- Children with any diagnosed disorder affecting muscle tone

3.5 Measurement devices

3.5.1 Hand-held dynamometer

Accurate measurement of strength is important for identifying any impairment of strength. Although manual muscle testing is probably the most versatile and widely used method, recent evidence indicates that handheld dynamometers may yield more precise measurements and are more sensitive to small changes in strength (Campbell

et al., 2000). Using standardised procedures is valid and reliable for testing isometric force of children who are typically developing and as young as two years of age (Gajdosik, 2005).

Therapists should be aware of factors influencing the reliability of strength measurement methods: a children must be able to understand the instructions and follow commands to produce accurate and reliable strength measurements, measurements may vary with time of day (particularly for patients who are fatigued by the end of the day), the level of a child's enthusiasm, the testing environment and the testing clinician's rapport with the child may affect performance (Campbell et al., 2000).

In this study the brand of handheld dynamometer used was the MicroFET 2. This dynamometer measures muscle strength as force, measured in Newton's. The minimum force it is able to measure is that of 3.6 N, the maximum force is that of 660 N. Forces are measured in 0.8 N increments. The dynamometer was manufactured by Hoggan Health Industries and certified on February 19th 2007.

3.5.2 Household Economic and Social Status Index (HESSI)

This four-factor index is simple to administer, easy to calculate, is able to discriminate variations in economic status at the low end of the economic scale, is reliable in accessing information from the informant and is independently verifiable and has high correlations with widely used methods for assessing economic well-being. Its dimensions have cross-cultural, cross-regional, and cross-national relevance. This questionnaire has been found valid and reliable (Barbarin & Khomo, 1997).

For the purposes of this study the questions within the HESSI were divided into seven sections namely: family structure (15), education of caregivers (16), employment and finance (18), housing (18), nutrition (3), well-being of the caregiver (4) and support for the child and his or her primary caregiver (7). These sections were each given a score (that in brackets), the total adding up to 81. The scores given were those indicated by

the index. Where a score was not indicated a higher score was designated to that answer most favouring the child, thus a higher total score would indicate a higher socio-economic status (See appendix VIII). The HESSI has no cut off score.

3.5.3 CD4 count

CD4 count is used as a marker of disease progression. In adults an indication of immune suppression is absolute CD4 count. In children a percentage is used. A percentage of more than 25% indicates that there is no immune suppression; 15-24% indicates moderate immune suppression, and less than 15% indicates severe immune suppression. At Harriet Shezi Clinic CD4 count is taken when children are first registered at the clinic. Thereafter a measure is taken six monthly, unless the child's condition is compromised. CD4 count is also used to determine a child's eligibility for ARV treatment as well as the child's response to therapy (Guidelines for the Management of HIV-infected Children, 2006).

3.5.4 Anthropometric measurements

Height and weight are measures taken at each visit to Harriet Shezi Clinic. Children's height was measured standing bare-foot against a wall-mounted scale (Hottain Ltd, Crymych, Dyfed), which measured height in centimetres. Children's weight was measured in kilograms using a Seca Standing Digital Scale.

3.6 Procedure

Children attending follow-up at Harriet Shezi Clinic are routinely examined by doctors, routine measurements of height and weight are done, and routine blood tests are done. Children who met the inclusion and exclusion criteria of the study were selected. These children, together with their caregiver, were seen by the physiotherapist. An information sheet, consent and assent forms were given and the contents explained to caregivers and children. A translator was employed as needed. A once-off measure of muscle strength was done using a hand-held dynamometer. Muscle strength measurements were established in the standard positions, as described below. These positions

eliminated gravity, so as to allow children to push with ease against the dynamometer (Gajdosik, 2005). All tests of muscle strength were done by the researcher.

- Muscle strength measurements included:
  - Shoulder abduction strength
    - The child was positioned on a firm flat surface in supine, knees flexed and arms at his or her sides.
    - The assessor held the dynamometer against the dorsal surface of the forearm midway between the wrist and elbow joints.
    - The assessor asked the child to push as hard as he/she could up to the side.
  - Shoulder forward flexion strength
    - The child was positioned on a firm flat surface in supine, knees flexed and arms at his or her sides with forearms supine.
    - The assessor held the dynamometer against the palmer surface of the forearm midway between the wrist and elbow joints.
    - The assessor asked the child to push up as hard as he/she could keep his/her arm straight.
  - Elbow flexion strength
    - The child was positioned on a firm flat surface in supine, knees flexed and arms at his or her sides with forearms supine.
    - The assessor held the dynamometer against the palmer surface of the forearm, on the most distal quarter of the forearm surface.
    - The assessor asked the child to bend his/her elbow as hard as he/she could.
  - Elbow extension strength
    - The child was positioned on a firm flat surface in supine, knees flexed, elbows flexed to 90 degrees, with forearms supine.
    - The assessor held the dynamometer against the dorsal surface of the forearm, on the most distal quarter of the forearm surface.

- The assessor asked the child to straighten his/her elbow as hard as he/she could.

- Hip flexion strength
  - The child was positioned in side-lying with both knees flexed to 45 degrees.
  - The assessor held the dynamometer on the supra-patella region of the thigh.
  - The assessor asked the child to push forward as hard as he/she could
  - The alternate leg was done as above in alternate side-lying.
- Hip extension strength
  - The child was positioned in side-lying with both knees flexed to 45 degrees.
  - The assessor held the dynamometer on the distal posterior region of the thigh, just above the popliteal fossa.
  - The assessor asked the child to push back as hard as he/she could.
  - The alternate leg was done as above in alternate side-lying.
- Knee flexion strength
  - The child was positioned in prone with the knee in full extension.
  - The assessor placed the dynamometer on the posterior distal third of the calf.
  - The assessor asked the child to bend his/her knee pushing as hard as he/she could.
- Knee extension strength
  - The child was positioned in prone with knee flexed to 90 degrees.
  - The assessor placed the dynamometer on the anterior distal third of the shin.
  - The assessor asked the child to straighten his/her knee pushing as hard as he/she could.

  - Measurements were taken three times and the maximum was recorded on the data collection sheet after each measurement was taken.
- The height and weight of the child was taken from that measured by the nursing sisters on the day on which muscle strength was tested.
- The most recent CD4 count was obtained from the child's file.
- Information as to whether the child was receiving ARV therapy and the duration which they had been taking the treatment was obtained from the file.
- The Household Economic and Social Status Index (HESSI) was administered to the caregiver by the researcher.
- Translation to the child or caregiver was provided by a trained counsellor where needed.
- All information on the data collection sheet was filled in (See appendix IX).

3.7 Statistical analyses

All data collected was analysed in consultation with the South African Medical Research Council using STATA, Release 8.0, for Windows. Further analysis was done using SPSS 16.0 for Windows.

3.7.1 Descriptive and inferential statistics

Descriptive statistics were used to summarise collections of data into a coherent and simple representation.

Inferential statistics were employed to determine the nature and statistical significance of relationships between the variables, and to statistically contrast these relationships. T-tests were used to analyse the differences between the means for the two groups. The type of t-test used to analyse means in this experimental design was that of a two sample student's t-test, also known as an independent samples t-test. This test is used where there are two different experimental conditions (the group not receiving HAART and the group receiving HAART), and different participants are assigned to each group (Field, 2005). Assumptions made for a two sample t-test are that variances within the

sample are equal (homogeneity of the sample) and scores are independent (different children in each group) (Field, 2005).

Two-tailed t-tests (or non-directional tests) were employed as the objectives sought not to determine the direction in which a significant difference may exist (either greater or less than zero), but only whether or not there was a significant difference (Howell, 2002). Two-tailed t-tests yield a probability value (p-value) which has been employed in order to determine whether or not the noted relationships were statistically significant.

Data was summarised, for descriptive purposes, using means, standard deviations, percentages, minimum and maximum values. The groups (those receiving HAART and those not receiving HAART), their demographics and anthropometrics were compared using two sample student's t-tests.

3.7.2 Correlation statistics

The Pearson Product Moment-Correlation Coefficient is an example of a bivariate correlation coefficient. A bivariate correlation is a correlation between two variables. Pearson Product Moment-Correlations (r) are used in order to determine the magnitude of covariance (degree of relationship) between variables (Field, 2005). Two-tailed t-tests, which yield a probability value (p-value), were employed in order to determine whether or not these relationships are statistically significant. The two-tailed t-tests allow for the statistical determination as to whether or not the computed Pearson Product Moment-Correlations (r) are significantly different from zero (or no correlation) (Howell, 2002). Additionally, two-tailed t-tests are used to ascertain the significance (or non-significance) of the differences between two correlations.

Pearson correlation analyses were done in order to determine the relationship between muscle strength and length of time on HAART. Further, Pearson correlation analyses were done to determine the relationship between disease progression (CD4 count) and muscle strength between groups on HAART and those not receiving HAART.

Backward regression analyses were done for both groups together to determine which variable (height, weight, CD4 count, HESSI, family structure, education of caregivers, employment and finance, housing, nutrition, well-being of the caregiver or support from the caregiver) had the greatest impact on muscle strength.

The results obtained will be presented in the following chapter.

CHAPTER 4
RESEARCH RESULTS

4.1 Introduction

This chapter serves to present the results laid out by the objectives of the study and of statistical data analyses discussed in chapter three. They will be presented in the order described in 3.7. Interpretation and discussion of the results will follow in chapter five.

4.2 Descriptive and inferential statistics

For the purposes of this study these descriptive statistics include percentages, means, standard deviations, minimum and maximum values. Two-tailed t-tests were employed in order to determine whether or not the noted relationships were statistically significant.

4.2.1. Gender demographic

Figure 4.1 depicts the gender composition of the realised sample. It shows the predominance of females over males in each group; 75% and 62.5% respectively.

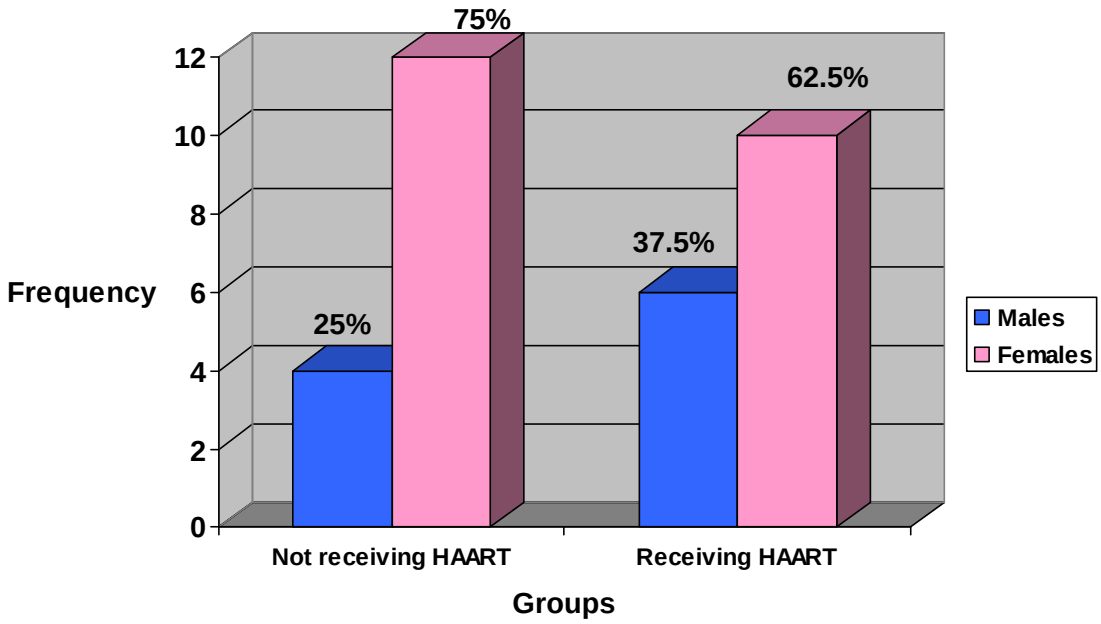

Fig 4.1 Realised sample gender compositions

4.2.2 Age Demographic

Table 4.1 indicates the age distribution of children in the groups receiving and not receiving HAART. Groups were well matched in terms of age.

Table 4.1 Age demographic information for groups not receiving and receiving HAART

	Not receiving HAART n=16			HAART n=16			
	Mean (SD)	**Minimum**	**Maximum**	**Mean (SD)**	**Minimum**	**Maximum**	**Probability Value (p)**
Age (years)	6.44 (1.09)	4	8	6.00 (1.21)	4	8	0.292

4.2.3 Demographic information

Further demographic information for both groups is given in Table 4.2. Relevant information from the demographic questionnaire and HESSI were extracted. Information from the HESSI has been quantified according to the method described in 3.5.2. Factors not included in the scoring included service charges (rent or bond), electricity charges, appliances owned, anxiousness or depression not requiring medication in the primary caregiver, and neighbourhood safety. Primary caregivers were not always able to provide the fore-mentioned information and thus, the most relevant and complete information was scored. Means, standard deviations, minimum and maximum values are included. A two sample student's t test of equal variance has been used to compare groups.

Table 4.2 Demographic information for groups not receiving and receiving HAART

	Not receiving HAART n=16			HAART n=16			
	Mean (SD)	**Minimum**	**Maximum**	**Mean (SD)**	**Minimum**	**Maximum**	**Probability Value (p)**
HESSI (total score = 81)	44.75 (10.77)	30	67	42.81 (9.77)	29	63	0.598
Nutrition (score = 3)	2.38 (0.50)	2	3	2.44 (0.81)	1	3	0.795
Family Structure (score = 15)	7.44 (2.66)	3	14	8.06 (2.24)	5	14	0.477
Employment and Finance (score = 18)	9.13 (4.15)	1	16	8.44 (3.98)	2	15	0.636
Education (score = 16)	8.06 (2.84)	2	12	6.88 (2.09)	3	10	0.188
Housing (score = 18)	11.06 (4.61)	4	17	9.63 (4.46)	3	18	0.377
Well-being (score = 4)	3.06 (1.12)	0	4	2.75 (1.18)	1	4	0.450
Support (score = 7)	3.63 (2.12)	1	7	4.56 (1.97)	2	7	0.205

There were no significant differences found between the two groups. The groups were well matched. Children came from poor backgrounds, the average HESSI scores being just above half of the potential score in both groups, an average of 54%. Fifty percent of primary caregivers were unemployed, and 31.25% of primary caregivers had formal

employment. Two families relied solely on a grandparent's pension as a monthly income. The remainder supplemented grants with that earned from "piece jobs" (sporadic work). Child support grants were received by 56.25% of families. The majority of families lived in houses, with the average number of people residing there amounting to 13 people. The average number of persons over the age of 18 years living in a home was six; whether their relationship to the child was aunt, uncle or older sibling. One family had 22 people living in the house, eight persons being over the age of 18 years. One father and three mothers lived in a room or shack alone with one or two children, living on a child support grant and having no support from any family. Seven of the total 32 primary caregivers had passed matriculation examinations, one a university degree and one a technical diploma. The majority of caregivers had completed only a grade seven to nine level of schooling. Two caregivers had never received any formal education. Fifty percent of caregivers could state that the children always had food to eat. Three stated that the children often go hungry, one of which stated that the children would not have food at least once every week.

4.2.4 Primary caregiver demographic

Figure 4.2 depicts the primary caregiver of both groups. The group not yet receiving HAART is depicted in blue and the group receiving HAART in red. Percentages shown were calculated for both groups together, as represented above the green columns.

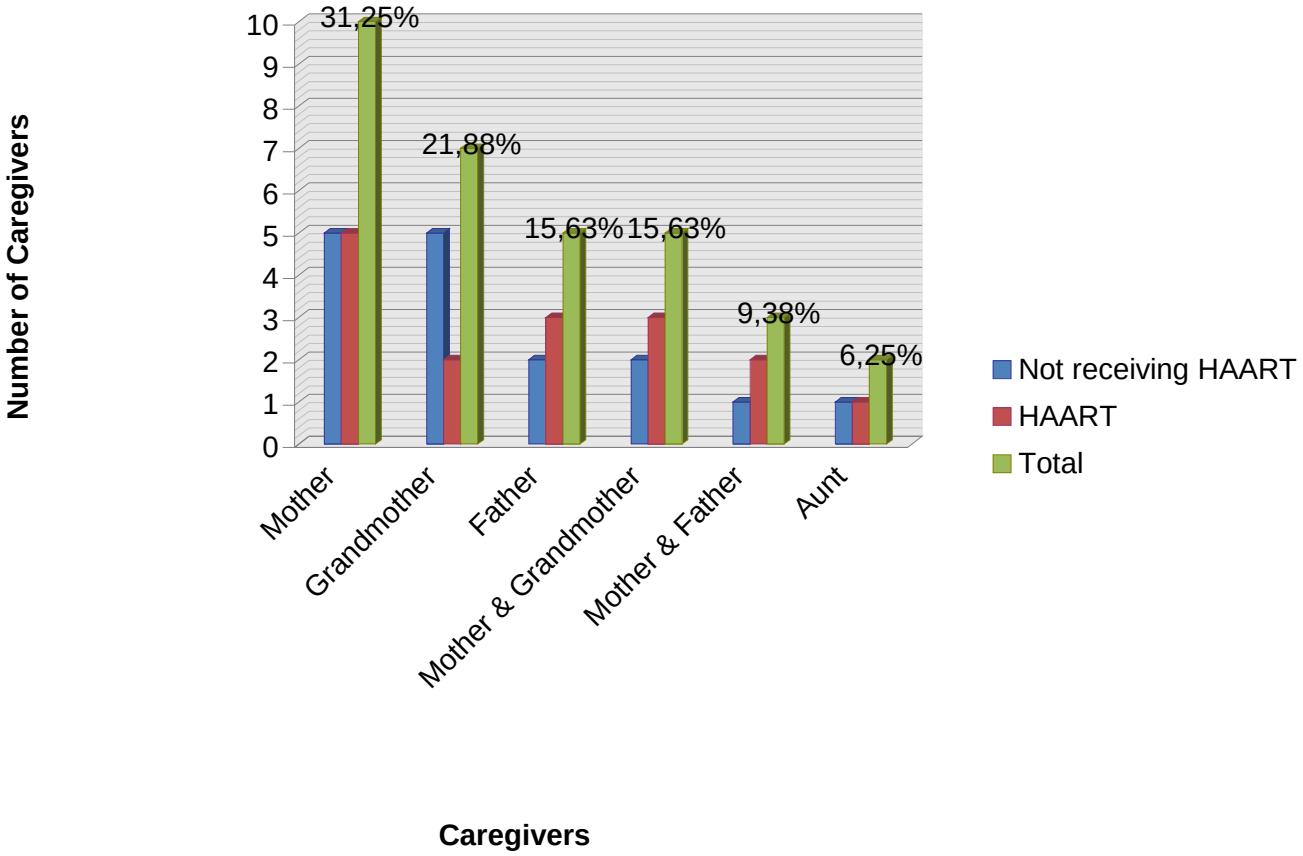

Fig 4.2 Realised sample primary caregiver distribution

Figure 4.2 showed a predominance of the mother as primary caregiver. Grandmothers preceded fathers as sole primary caregiver. One child in each group was cared for by an aunt, as both parents and grandparents had passed away.

4.2.5 Anthropometric data

4.2.5.1 Anthropometric data to compare groups not receiving and receiving HAART

Growth parameters for both groups are given in Table 4.3. Means, standard deviations, minimum and maximum values are included. A two sample student's t test of equal variance has been used to compare the groups.

Table 4.3 Anthropometric data for groups not receiving and receiving HAART

	Not receiving HAART n=16			HAART n=16			
	Mean (SD)	**Minimum**	**Maximum**	**Mean (SD)**	**Minimum**	**Maximum**	**Probability Value (p)**
Height (cm)	111.73 (11.71)	88.0	130.0	108.36 (9.43)	86.7	121.6	0.378
Weight (kg)	20.38 (4.49)	13.20	27.85	18.97 (3.42)	10.85	24.30	0.326

The children in both groups were well-matched with regards to growth parameters. No significant difference between the groups was found.

4.2.5.2 Comparison of height and weight of the children in both groups to the norm for their age

Table 4.4 shows the comparison of all the children's heights and weights to the normative value for their age. A one-sample student's t-test was used to make this comparison. Means, standard deviations and probability values are given. Normative height and weight values were obtained from the National Centre for Health Statistics Growth Charts (1976).

Table 4.4 Comparison of height and weight of the children in both groups to the norm for their age

	Mean (SD) Groups	Mean (SD) Norm	Probability Value (p)
Height (cm)	110.04 (10.59)	125.88 (7.51)	0.000
Weight (kg)	19.68 (3.99)	24.49 (3.10)	0.000

A significant difference was shown between the children's heights to that of the norm, t (31) = 58.76, $p < 0.001$. A significant difference was shown between the children's weights to that of the norm, t (31) = 27.89, $p < 0.001$. Children in both the groups are

underweight and short for their age.

4.2.6 CD4 counts for groups not receiving and receiving HAART

Of the 16 children in the group not receiving HAART, four children were not eligible for ARV therapy. The remaining 12 children had either a CD4 count below that of the required percentage threshold for receiving therapy (less than 15%) and/or presented with stage three or four disease status, qualifying for HAART. The children not eligible for HAART had CD4 counts higher than that of 15% and did not present with symptoms of stage three or four of disease.

CD4 counts (represented as percentages) for both groups are given in Table 4.5. Means, standard deviations, minimum and maximum values are included. A two sample student's t test of equal variance has been used to compare groups.

Table 4.5 CD4 counts for groups not receiving and receiving HAART

	Not receiving HAART n=16			HAART n=16			
	Mean (SD)	**Minimum**	**Maximum**	**Mean (SD)**	**Minimum**	**Maximum**	**Probability Value (p)**
CD4 count (%)	14.65 (8.36)	1.06	25	22.10 (9.77)	8.08	36	0.027

A significant difference was shown between CD4 counts of the groups, t (30) = -2.319, $p < 0.05$. The group receiving HAART showed a higher mean, as well as, higher minimum and maximum values of CD4 count.

4.2.7 Muscle strength

Muscle strength data for both groups are given in Table 4.6. Means, standard deviations, minimum and maximum values are included. A two sample student's t test of equal variance was used to compare groups. Values of muscle strength are represented in Newtons (N).

Table 4.6 Muscle strength data for groups not receiving and receiving HAART

	Not receiving HAART n=16			HAART n=16			
Muscle Group	**Mean (SD)**	**Minimum**	**Maximum**	**Mean (SD)**	**Minimum**	**Maximum**	**Probability Value (p)**
Shld Abd Left	45.06 (13.68)	19	63	36.75 (12.52)	16	62	0.083*
Shld Abd Right	50.25 (18.78)	20	84	40.13 (13.23)	15	64	0.088*
Shld Fwd Flex Left	48.56 (17.49)	15	76	45.25 (16.33)	16	71	0.584
Shld Fwd Flex Right	49.00 (17.54)	16	78	44.69 (17.22)	15	73	0.488
Elb Flex Left	53.44 (16.63)	15	76	45.25 (14.20)	19	67	0.145
Elb Flex Right	64.44 (20.84)	16	89	50.00 (17.88)	15	78	0.044**
Elb Ext Left	52.00 (16.35)	15	72	40.31 (15.43)	15	61	0.046**
Elb Ext Right	59.63 (18.92)	15	88	41.00 (14.75)	16	59	0.004**
Hip Flex Left	83.31 (34.29)	23	135	67.69 (24.83)	21	105	0.150
Hip Flex Right	89.06 (35.04)	28	150	68.19 (25.61)	20	104	0.064*
Hip Ext Left	62.31 (20.75)	24	104	54.25 (21.36)	17	91	0.289
Hip Ext Right	66.31 (24.45)	21	105	54.06 (21.36)	18	88	0.142
Knee Flex Left	64.06 (25.34)	27	122	52.19 (24.06)	23	106	0.184
Knee Flex Right	73.69 (29.20)	22	144	57.50 (30.89)	21	118	0.138
Knee Ext Left	87.00 (31.36)	21	140	64.25 (24.76)	19	115	0.030**
Knee Ext Right	97.13 (40.59)	20	177	66.94 (27.48)	22	117	0.020**

* Correlation was significant at the 0.1 level (2-tailed)

** Correlation was significant at the 0.05 level (2-tailed)

Eight muscle groups were tested on both the left and right sides, producing 16 muscle strength values for each group. Table 4.6 indicates 50% of the muscle groups to show significant differences between the group receiving HAART and the group not receiving HAART at a 90% or 95% confidence interval.

4.2.8 Length of time having received HAART

The length of time which the children had been receiving HAART is given in Table 4.7. The mean, standard deviation, minimum and maximum values are included. Values of time are represented in months.

Table 4.7 Length of time having received HAART

	Mean (SD)	Minimum	Maximum
Time (months)	19.06 (10.32)	3	30

4.3 Correlation statistics

Correlation statistics have been adopted in order to examine the research aims and objectives presented in chapter 1 in greater detail.

4.3.1 Length of time having received HAART and CD4 count

Table 4.8 indicates the correlation between CD4 count and length of time having received HAART. Pearson's Product Moment-Correlation Coefficient (r) and probability value (p) are included.

Table 4.8 Correlation between CD4 count and length of time having received HAART

	Pearson's Correlation (r)	Probability Value (p)
Length of Time having received HAART (months)	0.625	0.010

The results in table 4.8 indicate a significant relationship between the length of time the children had received HAART and CD4 count.

4.3.2 Muscle strength and length of time having received HAART

Table 4.9 indicates the correlation between muscle strength and length of time having received HAART. Pearson's Product Moment-Correlation Coefficient (r) and probability value (p) are included.

Table 4.9 Correlation between muscle strength and length of time having received HAART

Muscle Group	Pearson's Correlation (r)	Probability Value (p)
Shoulder Abduction Left	0.279	0.295
Shoulder Abduction Right	0.177	0.513
Shoulder Forward Flexion Left	0.086	0.752
Shoulder Forward Flexion Right	0.100	0.713
Elbow Flexion Left	0.157	0.562
Elbow Flexion Right	0.119	0.662
Elbow Extension Left	0.204	0.449
Elbow Extension Right	0.269	0.315
Hip Flexion Left	0.154	0.569
Hip Flexion Right	0.093	0.731
Hip Extension Left	0.067	0.806
Hip Extension Right	0.116	0.669
Knee Flexion Left	0.096	0.723
Knee Flexion Right	0.208	0.439
Knee Extension Left	-0.102	0.707
Knee Extension Right	-0.035	0.898

The results in Table 4.9 demonstrate no significant relationship between muscle strength and the length of time that the children had been receiving HAART.

4.3.3 Muscle strength and disease status (CD4 count)

Table 4.10 indicates the correlation between muscle strength and disease status, indicated by CD4 count. Pearson's Product Moment-Correlation Coefficient (r) and probability value (p) are included.

Table 4.10 Correlation between muscle strength and CD4 count in the groups not receiving and receiving HAART

	Not receiving HAART n=16		HAART n=16	
Muscle Group	**Pearson's Correlation (r)**	**Probability Value (p)**	**Pearson's Correlation (r)**	**Probability Value (p)**
Shld Abd Left	0.542	0.030*	0.134	0.621
Shld Abd Right	0.345	0.190	0.204	0.449
Shld Fwd Flex Left	0.518	0.040*	-0.032	0.906
Shld Fwd Flex Right	0.413	0.112	0.054	0.844
Elb Flex Left	0.613	0.012*	0.004	0.987
Elb Flex Right	0.538	0.031*	-0.045	0.868
Elb Ext Left	0.741	0.001**	-0.006	0.982
Elb Ext Right	0.651	0.006**	0.078	0.775
Hip Flex Left	0.519	0.039*	-0.088	0.745
Hip Flex Right	0.490	0.054	-0.153	0.571
Hip Ext Left	0.510	0.043*	-0.141	0.603
Hip Ext Right	0.535	0.033*	-0.048	0.858
Knee Flex Left	0.333	0.208	-0.112	0.679
Knee Flex Right	0.501	0.048*	-0.059	0.829
Knee Ext Left	0.540	0.031*	-0.454	0.077
Knee Ext Right	0.441	0.088*	-0.367	0.161

* Correlation was significant at the 0.05 level (2-tailed)

** Correlation was significant at the 0.01 level (2-tailed)

The results in Table 4.10 indicate that there was no significant relationship between the correlations in the group receiving HAART.

The correlations in the group not receiving HAART, however, indicate that there was a significant relationship between all except four correlations.

4.4 Regression analyses

Backward regression analyses were done for both groups together to determine which variable (height, weight, CD4 count, HESSI, family structure, education of caregivers, employment and finance, housing, nutrition, well-being of the caregiver or support from the caregiver) had the greatest impact on muscle strength. Groups were analysed together to ensure more reliability of the dependent variable (muscle strength). Even having taken this into account, the only independent variable to account any significance of the muscle strength was that of the children's weight ($p<0.01$). None of the other independent variables explained a significant portion of the muscle strength seen ($p>0.1$).

4.5 Muscle strength in comparison to available values

Certain differences have been noted when comparing muscle strength of the participants in the present study with respect to those available values.

It was found when comparing one muscle group from the upper limb and one from the lower limb that the mean values were less than half of the available mean value for the groups receiving HAART. The mean value in the lower limb group not receiving HAART was less than half of the available mean value. The mean value in the upper limb group not receiving HAART was 62% of the available mean value. These muscle groups were chosen as all age matched values were available.

Table 4.11 Comparison of a lower limb and upper limb muscle group for the groups not receiving and receiving HAART to available muscle strength values

	Not receiving HAART	HAART	Available Value
	Mean (SD)	**Mean (SD)**	**Mean (SD)**
Shoulder Abduction	47.66 (16.38)	38.44 (12.79)	77.13 (20.50)
Knee Extension	68.88 (36.05)	54.85 (25.77)	146.70 (10.93)

4.6 Summary of results

The findings of this study show the socio-economic status of all participants and their families to be low. Most caregivers had not completed 12 years of formal education and most families relied heavily on government grants or pensions to support the children. Children were shown to be significantly underweight and short in comparison to the norm for their age. The role of primary caregiver was primarily taken on by the mother or grandmother of the child.

The children in the group receiving HAART showed a significantly higher CD4 count than those children not receiving HAART.

The children in the group not receiving HAART were generally significantly stronger than those receiving HAART.

No significant relationship was established between length of time on HAART and muscle strength.

A significant relationship was shown between the length of time on HAART and CD4 count.

The only variable analysed to show any significant impact on muscle strength was that of weight.

For the children receiving HAART, no significant correlation was made between disease progression (CD4 count) and muscle strength. As CD4 count increased in this group, it was not matched by a rise in muscle strength.

A significant correlation was made between disease progression (CD4 count) and muscle strength for the children not receiving HAART. As CD4 count decreased in this group so too did muscle strength.

4.7 Conclusion

The research results presented in this chapter facilitate both a description of the data collected and presentation of the inferential statistics needed to examine the research aims and objectives. Interpretation and discussion of these results will follow in chapter five.

CHAPTER 5
DISCUSSION

5.1 Introduction

In the present chapter the results presented in the previous chapter will be interpreted and discussed in detail. Limitations of the study will be described, clinical implications noted and suggestions for further research put forward. As this is a pilot study the interpretations made cannot be taken as definitive until a representative study has been undertaken. The research question, whether muscle strength of children infected with HIV is different for those receiving HAART compared to those not receiving HAART, is best explained by commencing the discussion with findings of CD4 count and HAART and muscle strength values. The research question and its related findings will be discussed thereafter.

5.2 CD4 count and HAART

The administration of ARV therapy has been found to increase CD4 count in both adults and children (Chakraborty, 2005; Chiriboga et al., 2005; Lwin & Melvin, 2001; McCoig et al., 2002; Mitchell, 2006; Nachman et al., 2002; Raskino et al., 1999; Stein et al., 2005; Tepper et al., 1998; Yarasheski et al., 2001). The present study found a significant correlation between months receiving HAART and CD4 count, indicating that CD4 count increases with a longer length of time having received treatment. It was also shown that the group receiving HAART had a significantly higher CD4 count than the group not receiving HAART. These results are in keeping with goals of ARV therapy that are to reduce plasma viral loads below the limit of detection and maintain good immunological status by repopulation of CD4 and T-cells, to prevent clinical disease progression (Chakraborty, 2005). The efficacy of rapid initiation of ARV therapy has been proven in its restoration and preservation of immune function, promotion of normal growth and development and prolonging of life (WHO, HIV in Children, 2006).

5.3 Muscle strength in comparison to available values

The results show evident weakness of children infected with HIV, especially those receiving HAART, in comparison to available values. The population of this study has been found to be of low socio-economic status and their heights and weights to be below the norm for their age. Literature has shown that a family's social resources have a strong influence on a child's developmental outcome (Barbarin & Khomo, 1997). The present results indicate this developmental outcome to include a child's strength. Social resources include a child's nutritional intake. Not only has the literature shown us that a child infected with HIV has a propensity to protein malabsorption (Arpadi, 2005) but also loss of body protein and abnormal protein metabolism (Hsu et al., 2005). The results of the present study have indicated these children to have a compounded poor nutritional intake. All these factors lead to decreased muscle bulk which has been shown to affect muscle strength (Biancalana et al., 2007; Grinspoon et al., 1999; O'Brien et al., 2008). Not only could all of the above factors discussed be attributed to the weakness of these children, but also to the possibility that undiagnosed, asymptomatic myopathy may be present in children infected with HIV as it has been shown to exist in adults infected with HIV (Biviji et al., 2002; Bower et al., 1990; Otis et al., 2008; Verma et al., 2004). Myopathy, as well as a decline in height and weight, may account for the more severe weakness of the children receiving HAART as it has been shown that ARV therapy may cause myopathy and a decline in growth (Agin et al., 2001; Buchacz et al., 2003; Lewis et al., 1992; Nachman et al., 2002; Panegyres et al., 1990; Sinnwell et al., 1995; White, 2001).

5.4 Muscle strength and HAART

This study found a significant correlation between disease progression (CD4 count) and muscle strength in the group not receiving HAART. No significant correlation was found between disease progression and muscle strength in the group receiving HAART. A possible explanation is that as CD4 count falls so too does muscle strength (in the group not receiving HAART). Once receiving HAART CD4 count rises, but is not matched by a consummate rise in muscle strength. It would seem that while HAART

stems the fall of muscle strength it does not necessarily facilitate an augmentation of muscle strength. Simply put, the fall in strength is stemmed but not reversed.

Figure 5.1 represents the following scenario. At time nought a child infected with HIV may have a very high CD4 count. This high CD4 count would correspond to high muscle strength in the absence of pathology. As the disease progresses CD4 count drops with a correspondent drop in muscle strength. At a CD4 count of 15% the child becomes eligible for HAART in South Africa and begins to receive treatment. The child's CD4 count increases. No correlation is found between length of time receiving HAART and muscle strength. The child experiences a further drop in strength following commencement of HAART, with no improvement in strength to pre-treatment levels over time. Muscle strength does not correspond to a rise in CD4 count with HAART. It would seem that if any, the effect of HAART on muscle strength would be to halt the decrease after a period of time of approximately three months of receiving HAART, but not improve muscle strength.

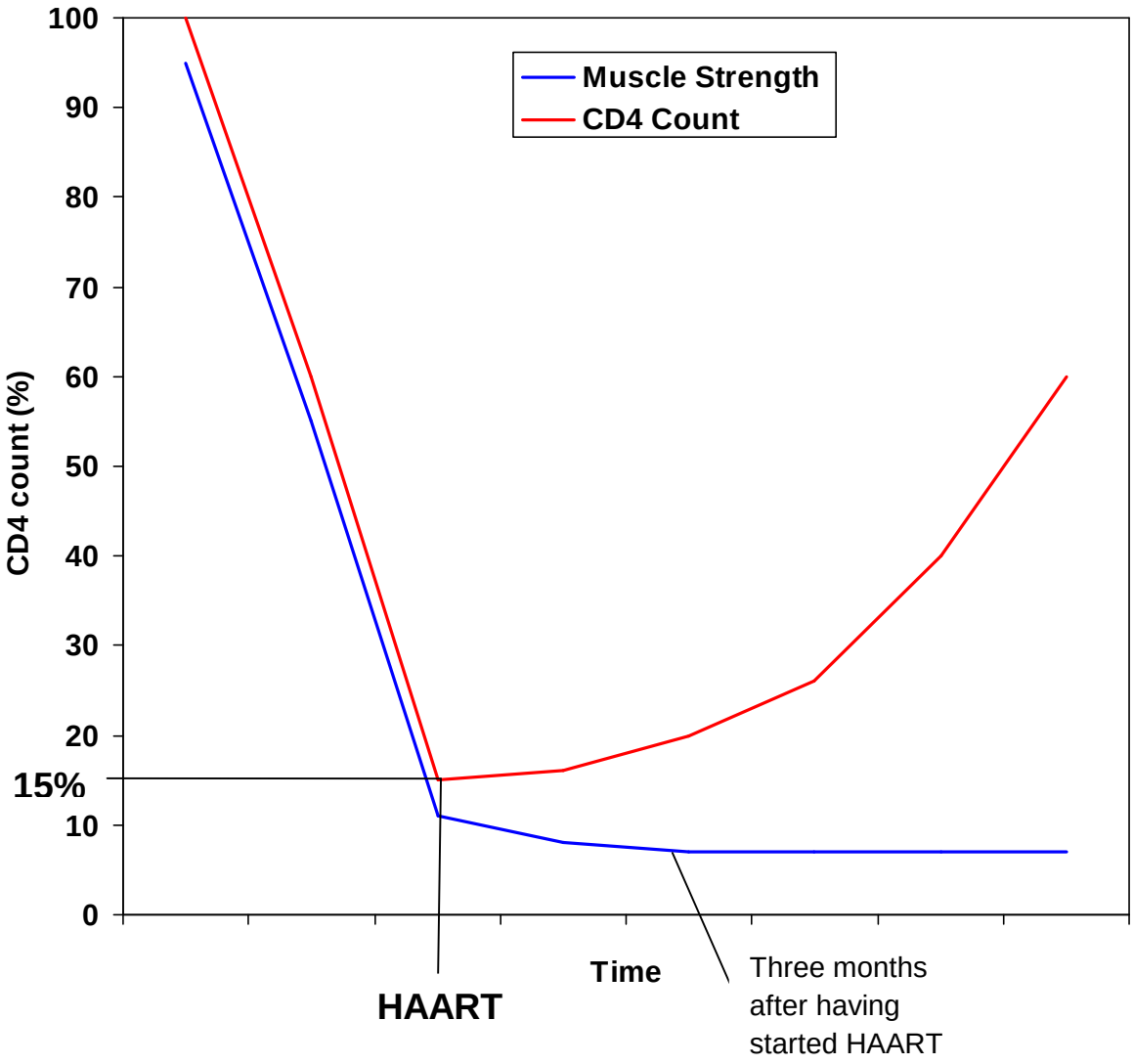

Figure 5.1 Representation of the Relationship between CD4 Count and Muscle Strength

5.5 Height and weight

Height and weight of all the children in this study was shown to be significantly lower than the norm for their age. There was no significant difference between the height and weight of the children in each group. Three of the children in the group not receiving HAART had persistent diarrhoea or vomiting, while none of the children in the group receiving HAART showed these symptoms. Fifty percent of caregivers could state that the children always had food to eat. Three stated that the children often go hungry, one of whom stated that the children would not have food as often as once every week. Children in this study show factors described as contributors to malnutrition in HIV/AIDS; inadequate intake and malabsorption (Ball, 1998; Hsu et al., 2005).

Although muscle bulk was not measured in this study, these children were at great risk of muscle atrophy. Malnutrition initially results in wasting (Chantry & Moye, 2005). Loss of body protein and abnormal protein metabolism has been documented in HIV infected children (Hsu et al., 2005). These in turn lead to weight reduction and decreased muscle bulk. A decrease in muscle bulk can therefore be and has been described to be associated with poor nutrition in children infected with HIV (Pearson et al., 2000). A child infected with HIV should receive an intake of 10% more protein in their diet in order to maintain body nutrient stores while asymptomatic (Hsu et al., 2005). Suggestion has been made that social welfare address food deficiencies in these children (Hsu et al., 2005). Although children attending the Harriet Shezi Children's HIV Clinic have access to a dietician and are able to receive food supplements free of charge, it seems further assistance is essential. The present study found that the only variable analysed to show any significant impact on muscle strength was that of weight. In a sample of children not infected with HIV it was found that age, height and weight were predictive factors of higher muscle strength (Bäckman et al., 1989; Macfarlane et al., 2008). This study shows that weight reduction and its impact on decreased muscle bulk, has a direct impact on muscle strength in children.

Although no statistically significant difference was found between the heights of the

children in each group, a small difference can be seen in their height. Those receiving HAART are fractionally shorter than those not receiving HAART. It has been shown that protease inhibitor containing antiretroviral therapies have more effect on height than on weight (Buchacz et al., 2003). Children receiving these protease inhibitor containing antiretroviral therapies were found to have stunted growth by as much as 0.7 cm in a year (Buchacz et al., 2003).

5.6 Demographic information

5.6.1 Age

The age range used in the present study was four to eight years of age, with a mean age of 6.22 years of age. The nature of the study was that of a once-off assessment of strength. Gadjosik (2005) found that isometric force of children who are still developing, and as young as two years of age, can be measured with fair to excellent reliability. Using standard testing procedures the researcher was able to produce reliable measures of isometric muscle force in the present study's age group of children.

5.6.2 Gender

The children who participated in this study were consecutively selected from children attending Harriet Shezi Paediatric HIV Clinic on any given clinic day. The population showed a predominance of females over males in both groups. Females made up 75% of the group not receiving HAART and 62.5% of the group receiving HAART, as seen in Figure 4.1. Studies done with a population of HIV infected children of similar ages have accounted female children to make up 49% to 55% of their sample (Buchacz et al., 2003; Coscia et al., 2001; Nachman et al., 2002). Further investigation with a wider age range on a larger sample of children may be needed to determine a pattern in gender predominance of this age group.

5.6.3 Socioeconomic Status

The findings of this study show the socio-economic status of all participants and their families to be low. There were no significant differences found between the two groups. The average HESSI score was 54%. The vulnerability of these families and children to disease and developmental delay has been described (Barbarin & Khomo, 1997; Potterton, 2006). The impact of poverty on a child, their development, their strength and the effect on the family cannot be ignored.

5.6.4 Primary caregivers

The majority of children in this study were cared for by their mothers (31.25%). This average is very low in comparison to other studies done in South Africa which found mothers to account for 85.25% of primary caregivers (Potterton, 2006). The children in that study were, however, an average age of 18.5 months; whereas the children in the present study were between four and eight years of age. The children in the present study had a mean of 6.22 years of age. This shows that mothers are more likely to be deceased in an older population of children. Potterton (2006) found grandmothers to be the next biggest group of caregivers, as was found in the present study. Grandmothers accounted for 21.88% of primary caregivers. One grandmother in the present study was not aware of the whereabouts of her daughter (the child's mother). The remainder of the mothers of these children had passed away. Literature exploring the needs of grandparents raising grandchildren infected with HIV has been conducted in developed countries (Brown & Lourie, 2000; Lwin & Melvin, 2001). In developing countries little research had been conducted to investigate the role of the grandparent as caregiver. The grandmothers in the present study described an uncertainty about their grandchildren's future, being tired and having very little support (financial or emotional) in bringing up the children. In South Africa, it is however common for grandmothers to care for grandchildren while mothers are away earning an income for the family (Potterton, 2006). In this study 15.63% of care giving was conducted in this manner. These grandmothers did not express a need for financial support as mothers of the children provided this. Fathers in this study accounted for 15.63% of primary

caregivers. All of these children's mothers had passed away. A higher percentage of grandmothers than fathers had stepped into the role of primary caregiver if mothers had passed away. Mother and father played a small role in care giving as a couple (9.38%). Where both parents and grandparents had passed away an aunt had taken on the role of primary caregiver (6.25%). These aunts were receiving emotional support from a clinic social worker. Brown and Lourie (2000) describe that when a child has lost both parents a child's caregiver is to be someone with whom the child can make a bond and that bond can be reciprocated.

5.6.5 Family structure, housing and wellbeing

The results show a strong tendency of extended families coming together to live in the same house. In a family structure such as these, caregivers described a strong support from family. Eight subjects shared a house with other families. Eight subjects lived in shacks and one subject lived in a room. Three families living in shacks had more than seven people living in the dwelling. One father and three mothers lived in a room or shack alone with one or two children, living on a child support grant and having no support from any family. These single caregivers described hopelessness as they wanted to provide their children with more but did not know how or where to access provision or gain the emotional support needed for effective parenting. The importance of providing holistic care for these families is highlighted in these findings. Psychosocial support is essential for these children and their families (Potterton, 2006).

5.6.6 Education

Seven of the 32 primary caregivers had passed matriculation examinations, one a university degree and one a technical diploma. Two caregivers had never received any formal education and the majority of caregivers had completed only a grade seven to nine level of schooling. Although these caregivers should have acquired basic literacy and mathematical skills, vocational options would be limited (Barbarin & Khomo, 1997). Villamor et al. (2005) found that level of maternal education was an important predictor of growth in HIV infected children; children of mothers who did not complete grade school had decreased annual growth.

5.6.7 Occupation and finance

Fifty percent of primary caregivers were unemployed, and 31.25% of primary caregivers had formal employment. Two families relied solely on a grandparent's pension as a monthly income. The remainder supplemented grants with that earned from "piece jobs" (sporadic work). Child support grants were received by 56.25% of families. Throughout the world low income and an impoverished social environment have been described as risk factors of childhood diseases (Lwin & Melvin, 2001). Both families with HIV infected parents and children in Australia and the USA have reported severe financial pressure and fewer support services (Brown & Lourie, 2000).

5.7 Limitations of the study

Children not receiving HAART were consecutively allocated to this group when inclusion criteria were met. As a result four of the children allocated to this group were not eligible for HAART, while the remaining 12 children were eligible for HAART. Had the entire group been Pre-HAART further research implications could be deduced from the results of the study.

The sample size of 32 children in this study is relatively small as these children were divided into two groups, making the number of children in each group 16. This small sample size is a possible reason that in the regression analyses done, none of the socioeconomic or anthropometric factors showed any significant impact on muscle

strength. Had each group comprised 32 children, a complete sample size of 64 children, significance of the results would be improved. As it stands, the results of the study are significant at high confidence intervals yielding reliability. Statistical analyses done have thus been analysed and tendencies of the results used to draw up statements. A full study, as opposed to a pilot study, is needed to substantiate the findings of this study.

Although the hand held dynamometer has been found valid and reliable, the non-conduct of an intra-rater reliability test may influence the reliability of the muscle strength scores.

Due to the specific inclusion criteria and homogenous background of the children in this study, the results of the study may not be generalisable to other populations.

A subsequent study on the topic of muscle strength of children infected with HIV can be improved by including an analysis of the level of activity of the children. A control group of children not infected with HIV would be a sensible way to compare the muscle strength of children infected and not infected with HIV.

5.8 Clinical implications of the study

- HAART should be initiated before CD4 count drops below that of 25% as this could halt irreversible loss of muscle strength in children.
- Strength decrease in children is not halted and does not increase in response to HAART in the same way that CD4 count responds to HAART.
- All South African healthcare professionals need to be aware of criteria for initiating HAART in children. Children infected with HIV should be referred to specialist clinics where they can be managed holistically and appropriately.
- The diversity of families caring for children infected with HIV needs to be recognized and individual family centred programmes need to be introduced.
- Mothers and fathers should have access to counselling to plan for the care of

their children after their own death.

- Grandmothers need support in their parenting roles. Methods of meeting their unique needs need to be investigated.
- Poverty alleviation should be a national priority in South Africa and healthcare workers should advocate for programmes that can improve the wellbeing of the patients in their care.
- All children infected with HIV should have their height and weight monitored at regular intervals, even if they are asymptomatic.
- Nutritional support and dietary advice should be available to all HIV infected children as soon as their diagnosis is known.
- The prescription of an exercise program should be made in order to maintain and improve muscle strength among children infected with HIV.

5.9 Research implications of the study

- International normative muscle strength values need to be established. A collaboration study of the existing normative samples may be a solution.
- The impact on muscle strength of starting HAART when CD4 counts are that of 25% needs to be investigated.
- Further research is needed to establish whether or not any increase in muscle strength is made over time in response to HAART.
- In the present study, proximal joint muscle groups were chosen to test as the available muscle strength values did not allow for testing of distal joint muscles. It is recommended that further studies include the testing of the muscle groups of distal joints.
- Further investigation of muscle strength and its impact on development needs to be made.
- Further investigation on a wide age range and large sample size of children is needed to determine a pattern in gender predominance in HIV infected children in the developing world.
- Family structure and support mechanisms for families or single caregivers need

to be explored.

- Provision of scientifically sound nutritional support for children infected with HIV needs to be investigated.
- Long term studies are needed to determine the impact of nutritional intake and protein intake on muscle bulk.
- Long term studies are needed to determine the impact of nutritional intake and protein intake on muscle strength.
- Further investigation is needed to determine the impact of ARV therapy on muscle bulk.
- Further investigation is needed to determine the impact of ARV therapy on muscle strength.
- It is recommended that the level of activity of children be established in further studies on the topic of muscle strength in children infected with HIV.
- The implication of exercise on muscle strength and quality of life of children infected with HIV needs to be investigated.

5.10 Conclusion

The results discussed in this chapter have brought to light many original findings with regards muscle strength in children infected with HIV. Many clinical and research implications have been put forward. It is, thus, essential that a full study be undertaken.

The following chapter will summarise the main conclusions of the present study.

CHAPTER 6
CONCLUSIONS

This chapter will summarise the main conclusions drawn from this study.

A representative study of the muscle strength of children infected with HIV is feasible and required.

Children receiving HAART are weaker than aged-matched children who are not receiving HAART.

HAART, once initiated, was found to stem but not reverse the decrease in muscle strength found. No significant correlation was found between length of time receiving HAART and muscle strength.

CD4 count of the group receiving HAART was found to be significantly higher than those not receiving HAART. CD4 count was found to increase with the length of time that the children received treatment.

No significant differences of socio-economic and anthropometric results in the present study were found between groups receiving and not receiving HAART. Children and caregivers who participated in the present study were faced with adversities such as poor socioeconomic status, limited access to medication and ARV treatment and inadequate nutritional intake, most of which were largely beyond their immediate control. Such poverty alleviation should be a matter of South African national priority.

It is essential that the impact of initiating HAART at various stages of the disease process be investigated in order to establish a protocol that allows for children's best long term outcomes. These outcomes are potentially those of alleviation of malnutrition and wasting, maintenance of higher muscle strength, limiting of developmental

impairments and improvement in quality of life.

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APPENDICES

Appendix I

WHO Clinical Staging of HIV/AIDS for Children with Confirmed HIV Infection

ANNEX B

PART A: WHO CLINICAL STAGING OF HIV/AIDS FOR CHILDREN WITH CONFIRMED HIV INFECTION

Clinical Stage 1

Asymptomatic
Persistent generalized lymphadenopathy

Clinical Stage 2

Unexplained [a] persistent hepatosplenomegaly
Papular pruritic eruptions
Fungal nail infection
Angular cheilitis
Lineal gingival erythema
Extensive wart virus infection
Extensive molluscum contagiosum
Recurrent oral ulceration
Unexplained [a] persistent parotid enlargement
Herpes zoster
Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)

Clinical Stage 3

Unexplained [a] moderate malnutrition or wasting not adequately responding to standard therapy
Unexplained [a] persistent diarrhoea (14 days or more)
Unexplained [a] persistent fever (above 37.5° C intermittent or constant, for longer than one month)
Persistent oral candidiasis (after the first 6–8 weeks of life)
Oral hairy leukoplakia
Acute necrotizing ulcerative gingivitis/periodontitis
Lymph node TB
Pulmonary TB
Severe recurrent bacterial pneumonia
Symptomatic lymphoid interstitial pneumonitis
Chronic HIV-associated lung disease including bronchiectasis
Unexplained anaemia (<8 g/dl), neutropenia ($<0.5 \times 10^9/L^3$) or chronic thrombocytopenia ($<50 \times 10^9/L^3$)

Clinical Stage 4 [b]

Unexplained [a] severe wasting, stunting or severe malnutrition not responding to standard therapy
Pneumocystis pneumonia
Recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration or visceral at any site)
Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
Extrapulmonary/disseminated TB
Kaposi sarcoma
Cytomegalovirus infection: retinitis or CMV infection affecting another organ, with onset at age >1 month
Central nervous system toxoplasmosis (after one month of life)
Extrapulmonary cryptococcosis (including meningitis)
HIV encephalopathy
Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis)
Disseminated non-tuberculous mycobacterial infection
Chronic cryptosporidiosis (with diarrhoea)
Chronic isosporiasis
Cerebral or B cell non-Hodgkin lymphoma
Progressive multifocal leukoencephalopathy
Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

[a] Unexplained refers to where the condition is not explained by other causes.
[b] Some additional specific conditions can also be included in regional classifications (e.g. reactivation of American trypanosomiasis [meningoencephalitis and/or myocarditis] in Americas region, penicilliosis in Asia and HIV-associated rectovaginal fistula in Africa).

Appendix II

Ethical Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Zeijlstra

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER M070235**
PROJECT	A Pilot Study to Investigate the Muscle Strength of Children Infected with HIV, Compared to those Not Infected
INVESTIGATORS	Miss C Zeijlstra
DEPARTMENT	Department of Physiotherapy
DATE CONSIDERED	07.03.02
DECISION OF THE COMMITTEE*	APPROVED UNCONDITIONALLY

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

DATE 07.05.07 **CHAIRPERSON** .....
(Professors PE Cleaton-Jones, A Dhai, M Vorster, C Feldman, A Woodiwiss)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : J Potterton

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 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 III

Letter of permission from Chris Hani Baragwanath Hospital

Gauteng Health
Physiotherapy Department
Chris Hani Baragwanath Hospital
Post Office Bertsham 2013
Tel: (011)933 8309

Dr J. Gavanescu

Research Project to Investigate Muscle Strength in Children Infected with HIV, compared to those not infected

Carolyn Zeijlstra, a Physiotherapist employed at Chris Hani Baragwanath Hospital wishes to conduct a study to compare the muscle strength of children infected with HIV compared to those who are not infected. The purpose is that it will form part of the completion of a Masters degree in Paediatric Physiotherapy.

Twenty children would be recruited from Harriet Shezi Clinic, following a doctor's examination. A control group of twenty children would be recruited following a doctor's examination from Ward 31. All children would have a once-off test of muscle strength done using a hand-held dynamometer. This instrument will cause no harm or discomfort to the children. A questionnaire (the Household Economic and Social Status Index) would be administered to caregivers to ascertain socio-economic status. Participation in the study would have no impact on medical or Physiotherapy care received at the hospital. Children between three and eight years of age would be selected.

Consent and assent would be obtained from caregivers and children of age. The study would be explained to caregivers and children in the language of their choice.

Please see the attached research proposal for further information.

Permission is requested to begin this study in April 2007 and once ethical approval has been obtained.

Carolyn Zeijlstra
Physiotherapist (Investigator)

Tracey Bulmer
Chief Physiotherapist, Paediatrics

Naumi Mashalane
Physiotherapy Head of Department

DR. J.M. GAVANESCU
M.D., M.B.A.
SENIOR CLINICAL EXECUTIVE

Appendix IV

Information Sheet (Caregiver)

Dear Parent/ Caregiver

Thank you for taking time to read this information. I am a Physiotherapist working at Chris Hani Baragwanath Hospital. As part of a Masters Degree in Physiotherapy I am studying muscle strength in children.

I aim to find out how strong your child is by using an instrument called a dynamometer. Should your child participate in the study, they will be asked to lie down in order to push this dynamometer as hard as they can with their arm or leg and a reading will be taken from the instrument. This will not hurt your child in any way. It will take about fifteen minutes to explain and perform the test of your child's muscle strength.

I will also ask that you (the parent/caregiver) to fill in a questionnaire about your home and family. This questionnaire is available in English, Zulu and Sotho. It will take about 20 minutes to fill in the questionnaire.

If you are willing to allow your child to participate we would need you to sign a CONSENT FORM. If your child is 6 years of age we will also ask his or her permission and they will be asked to sign an ASSENT FORM. Your child will receive the same treatment at the hospital if they participate in the study or not. No names will be put on any of the study sheets or results.

Before giving permission please be sure that you understand what we are

testing and the questions that will be asked of you. If you are unsure we will make sure that someone is available to answer your questions in your home language.

Thank You.

Carolyn Zeijlstra

(Physiotherapist)

Appendix V

Information Sheet (Child)

Hello,

Thank you for taking time to read this information. I am a Physiotherapist working at Chris Hani Baragwanath Hospital. As part of a Masters Degree in Physiotherapy I am studying muscle strength in children.

I aim to find out how strong you are by using an instrument called a dynamometer. You will be asked to push this dynamometer as hard as you can with your arm or leg and it will show me how strong you are. This will not be sore. It will take about fifteen minutes to do this.

If you are willing to let me test how strong you are you will be asked to sign an ASSENT FORM. You will get the same treatment at the hospital if you join in the study or not. Your name will be put on any of the study sheets or results.

Before giving permission you understand what we are testing. If you have any questions we will make sure that someone is available to answer them in your home language.

Thank You.

Carolyn Zeijlstra

(Physiotherapist)

Appendix VI

Consent Form

Research Title: A Pilot Study to Investigate the Muscle Strength of Children infected with HIV.

I _____ understand the purpose of this study and give consent of my child/the child I care for to participate in this research. I have read and understand the information sheet and my questions have been answered. I am aware that the procedures will not harm the child in any way. I am aware that the child may withdraw from the study without any prejudice toward the child or me.

_____

Parent/Caregiver

_____

Date

_____

Researcher

_____

Date

Appendix VII

Assent Form

Research Title: A Pilot Study to Investigate the Muscle Strength of Children infected with HIV.

I _____ am happy to participate in this study. I understand how my muscle strength will be tested and know that this will not hurt me. I understand what the study is about and my questions have been answered. I know that if I can say that I don't want to be part of this study.

_____

Subject

_____

Date

_____

Researcher

_____

Date

Appendix VIII

Household Economic and Social Status Index (HESSI)

Household Economic and Social Status Index (HESSI)

(Barbarin, et al, 1995)
Who provided the information below_____)

I. **Family Structure/Household Composition** (Score 1-10)
Ia. Marital Status of Mother
1. Never married, not now living with a partner
2. Married, but not living now with a partner (e.g. divorced, separated)
3. Widowed
4. Never married, but now living with partner
8. Married and currently living with partner

Ib. Household Membership. How many people currently reside in the household?_____
Number 18 and older_____
Number 6–18 yrs old _____
Number under 6 yrs old _____

Ic. Are there adult relative now residing in the household? 0. No 2. Yes.
If yes who are they in relationship to the child?_____

II. **Social Status**- (Education, Occupation, [2–18])
A. Mother's Education: What is the highest level of education attained by mother?
1. Less than Standard 3
2. Primary School (Standard 3–4)
3. Junior Secondary (Standard 5–7)
4. Senior Secondary (Standard 8–9)
5 Matric/High School graduate/vocational training diploma
6. 1–2 yr College, Technikon
7. 3–4 yrs of University
8. Ph.D., M.D., J.D., D.D.S., or other doctoral degree

B. Education of Mother's Partner: What is the highest level of education attained?
1. Less than Standard 3
2. Primary School (Standard 3–4)
3. Junior Secondary (Standard 5–7)
4. Senior Secondary (Standard 8–9)
5. Matric/High School graduate/vocational training diploma
6. 1–2yr College, Technikon
7. 3–4 yrs of University
8. Ph.D., M.D., J.D., D.D.S., or other doctoral degree

What are the names, occupation and industry of the primary wage earners in the house?

	Name	Occupation	Industry
1.			
2.			
3.			

Access to Finances Who in the family earns money? Check all that apply.

___BTT mother
___Partner
___Parent
___Parent Pension
___Sibling/Aunt/Uncle

III. Housing Accommodation. In what type of housing do you live?

0. None, homeless
1. Shack
2. Hostel
3. Room, garage
4. Flat, cottage
5. Home shared with other family(ies).
6. Home that is not shared with other families.

B. Does your home have

1) A **Separate Kitchen?** 0. No 1. Yes
2) A **Separate Bathroom?** 0. No 1. Yes

a) In your home how many separate rooms are there just for sleeping?
(circle one number) **0** **1** **2** **3** **4** or more.

b) What type of toilet facilities does your home have:

0. None
1. Pit or Bucket
2. Outside flush toilet
3. Inside flush

c) Do you own or rent a home.

0. Neither
1. Rent
2. Purchasing on Bond
3. Own

d) How much do you pay monthly for rent or bond? R_____.
For Service Charges R____

e) For Electricity:
(highest in the last year) R_____
(the lowest) R_____

Does the place you live in have a . . . ?

a)	Refrigerator	0. No	1. Yes
b)	Television	0. No	1. Yes
c)	Telephone	0. No	1. Yes
d)	Car	0. No	1. Yes
e)	Video recorder	0. No	1. Yes
f)	Washing machine	0. No	1. Yes
g)	Microwave oven	0. No	1. Yes

h) In the past, have your children gone hungry because you did not have food?:

3. No, never
2. Rarely
1. Often
0. All the time

Factor VI. **Savings:** (Score 0-3)

a) Do you have savings or participate in a savings plan?	0. No	1. Yes
b) Do you have life insurance	0. No	1. Yes

(version 1/25/96)

Maternal Well-being

Do you have any problems you might like to talk over with a doctor?

0. No
1. Yes (specify)

During the past 3 months have you had any physical or emotional condition for which you have been receiving treatment or taking medication?

0. No
1. Yes (specify)

During the past 3 months Have you been anxious,worried or upset?

Extremely so—to the point of being sick or almost sick
Very much so
Quite a bit
Some—enough to bother me
A little bit
at all

During the past 3 months, have you felt so sad, discouraged, hopeless or had so many problems that you wondered if anything was worthwhile?

Extremely so—to the point that I have just about given up
Very much so
Quite a bit
Some—enough to bother me
A little bit
Not at all

In **any one year** have you had at least 12 drinks of any kind of alcoholic beverage? Yes No

Have you ever had any serious physical handicap? 0. No 1. Yes

Have you ever been a patient (or outpatient) at a mental hospital, mental health ward of a hospital, or a mental health clinic for any personal emotional, behavior, or mental problem?:

Yes, during the past year
Yes, more than a year ago
No

Neighborhood Safety

A. In general how safe is the area in which you live?

1. Extremely dangerous
2. Dangerous
3. Safe
4. Extremely Safe

B. How much do you worry about your child getting hurt when s/he is outside of your home?

1. Never
2. Sometimes
3. Often
4. All the time

Satisfaction with Family Life (Support)

My family has a lot of problems:

1. Not True 2. Sometimes True 3. Often True 4. Always True

My family is always there for me when I need them.

1. Not True 2. Sometimes True 3. Often True 4. Always True

Appendix IX

Data Collection Sheet

1. Subject Number: _____2. Subject Age: _____

3. Subject Height (cm): _____4. Subject Weight (kg): _____

5. CD4 Count: _____

6. ARV treatment:

_____

7. Date on which ARV treatment started:

_____

8. Other Medication:

_____

9. Has the child had diarrhoea or been vomiting in the past week? Yes No

10. Has the child seen a traditional healer in the past week? Yes No

11. Muscle Strength Results:

- Shoulder abduction strength _____
- Shoulder forward flexion strength _____
- Elbow flexion strength _____

- Elbow extension strength _____
- Hip flexion strength _____
- Hip extension strength _____
- Knee flexion strength _____
- Knee extension strength _____

11. HESSI Questionnaire (attached)