A home-based physical activity programme in combination with massage therapy to improve motor and cognitive development in HIV positive children on antiretroviral therapy: A randomised controlled trial

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Abstract

Introduction: Evidence suggests that physiotherapy interventions, such as physical activity and stimulation can improve neuro-development in children with motor and cognitive developmental delay. However, there is inadequate evidence of its effectiveness in children infected with the human immuno-deficiency virus (HIV). The deficiency of evidence to show the benefits of early intervention programmes for HIV positive children stimulated the researcher to investigate the effects of a specially designed basic home physical activity programme on motor and cognitive development.

Aim: The aim of this study was to prospectively, evaluate the effectiveness of an individually designed home-based physical activity programme in combination with massage therapy, on motor and cognitive development in children infected with HIV.

Methods: This study used a randomized controlled trial design. One hundred and twenty-eight infants and toddlers (children) were recruited between March 2010 and September 2010 and randomly allocated to receive either an individually designed home-based physical activity programme in combination with massage therapy or standard treatment and massage on a 1:1 ratio. Motor and cognitive development was measured using the Bayley Scales of Infant Development third edition (Bayley-III).

Setting: The study was conducted at two hospitals in East London, Eastern Cape Province, South Africa.

Participants: Inclusion criteria was based on an HIV positive status, eligibility to receive antiretroviral treatment, aged 36 months and below, resident in the surrounding areas or availability during the six-month follow-up period and parental or legal guardian signed informed consent. Children with profound
mental, physical, or congenital abnormalities were excluded from the study. Written informed consent was obtained from parents or legal guardians of children who met all the inclusion criteria.

**Interventions:** A home-based physical activity programme in combination with massage therapy was designed in relation to the assessment of the child, the identified long and short-term functional outcomes, the functional abilities and the impairment related goals. Demonstrations of physical activity, stimulation and massage to perform on child at home were shown to caregivers of children in the intervention group. A research assistant taught all caregivers massage techniques for the child and provided with baby oil. The control group received massage only.

**Outcomes:** The primary outcome measures were motor and cognitive development and secondary outcome measures were height and weight. These outcomes were measured at baseline, after three and after six months.

**Results:** One hundred and twenty eight children met the eligibility criteria and were randomized to intervention (n=63) and control (n=65) groups. The prevalence of delay in motor development decreased slightly over the six-month period but no statistically significant differences were observed between the groups. Cognitive development was associated with exposure to alcohol (p<0.04) and employment status (p=0.05). No factors were associated with motor delay. At baseline, 31.7% of the children presented with a delay in motor development in the intervention group and 26.1% in the control group. At the three-month follow-up visit, the prevalence of motor developmental delay was 28.3% in the intervention group and 22% in the control group. The prevalence remained similar at the six-month follow-up.
visit for the intervention group (28%) and decreased slightly more in the control group to 18.4%. None of the differences were statistically significant.

The mean motor development score showed little change from baseline and continued to remain within the normal limits for both groups at the three-month follow-up (91.69 intervention vs 94.31 control) and the six-month follow-up visits (92.80 intervention vs 97.55 control), with no statistically significant difference between the groups.

There was no statistically significant difference between the groups in the prevalence of cognitive delay. The prevalence of cognitive delay decreased slightly over time in the intervention group (baseline, 34.9%; three-month follow-up visit 28.8% and six-month follow-up 32%), but increased over time in the control group (baseline 18.5%; three-month follow-up 27.4% and six-month follow-up 33.3%).

There was a slight decrease in the mean cognitive development index score of both groups at the follow-up visits. The mean cognitive development index scores at baseline were 90.87 for the intervention group vs 95.61 for the control group. At the three-month follow-up, the mean cognitive development index scores were 88.65 for the intervention group vs 90.40 for the control group, and 87.20 for the intervention group vs 87.45 for the control group at the six-month follow-up, with no statistically significant difference between the groups.

**Conclusion:** The author accepts the null hypothesis, that there is no difference in motor and cognitive development between children with HIV infection receiving a home-based intervention and those not receiving the intervention. The results did not show a 15% improvement over six months in either motor or cognitive development. It may be postulated that massage
therapy had a positive effect on both groups as the prevalence of delayed motor development decreased slightly in both groups over time.

It is recommended that further research be conducted to investigate the need for the implementation of specially designed home-based physical activity intervention programmes with massage therapy to improve motor and cognitive development in children infected with HIV.

**Keywords**

Home-based programme  
Physical activity  
Massage  
HIV/AIDS  
Cognitive development  
Motor development  
Infants/Children  
Bayley scale
Declaration
I declare that "A home-based physical activity programme in combination with massage therapy to improve motor and cognitive development in HIV positive children on antiretroviral therapy: A randomised controlled trial" is my own work, that it has not been submitted for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged by means of complete references.

Oswell Khondowe       September 2014

Signed: __________________
Dedication
I dedicate this dissertation to my mother, Loveness Musoka for her support and dedication to provide me with a strong foundation in my quest for knowledge and achievement, and to my siblings, Sylvia, Fred and Happy, whose support and love was and is invaluable.

And to my late father, Watson Sylvester Khondowe, who would have been the happiest person had he been there to witness this achievement. Above all, I dedicate this to all mothers, fathers, caregivers and children who participated on this study.

“If I have been able to see further than others, it was because I stood on the shoulders of giants”

Isaac Newton
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A systematic review on the effect of HIV/AIDS on child motor and cognitive development


Motor and cognitive development in children infected with HIV/AIDS

Chapter One
Introduction to the study

1.1 Introduction
Chapter one introduces the reader to the research study and presents a succinct review of the literature which relates to cognitive and motor development interventions for infants and children who acquired the human immune deficiency virus (HIV) during the gestation period, childbirth or through breastfeeding. Chapter one further describes the rationale that led to the problem statement and the research questions. The aim and objectives of this study are stated to ensure the reader has a good understanding of what the research aimed to achieve. The chapter provides a bird’s eye view of what to expect in the chapters to follow.

1.2 Background literature
Human immuno-deficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) have made a huge global impact, permeating the social, cultural, and economic fabric of almost all nations (Lwin & Melvin, 2001). Approximately 34.2 million people were living with HIV/AIDS in 2011 (United States [US] Global Health Policy, 2012). Sub-Saharan Africa remains the region most heavily affected by HIV/AIDS worldwide, accounting for 23.6 million (69%) of people living with HIV (Joint United Nations Programme on HIV/AIDS [UNAIDS], 2012).

The South African HIV epidemic is one of the largest in the world (Horwood, Voce, Vermaak, Rollins & Qazi, 2010). South Africa had the highest HIV prevalence rate in 2009. Approximately 5.6 million people were living with HIV/AIDS (United States [US] Global Health Policy, 2012).
Vertical transmission of the virus from the mother to her infant, during pregnancy, childbirth or breastfeeding, has reduced drastically through the implementation of treatment to prevent mother-to-child transmission (PMTCT) of HIV. The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that the PMTCT programme will achieve almost 90% coverage in South Africa (UNAIDS, 2012). The UNAIDS (2012) further report that there was a decrease of between 40 and 59% in the number of children newly infected with HIV from 2009-2011.

The South African PMTCT plan was revised in 2010 to extend antiretroviral therapy to HIV positive infants, for the duration of breastfeeding with the hope to further reduce the rate of mother-to-child transmission to less than 5% (Department of Health [DOH], 2010a). Goga, Dinh and Jackson (2012) confirm that the implementation of the programme has been successful as maternal to child transmission has been reduced substantially in South Africa and is at present less than 5%. Despite the prevalence of HIV amongst infants being less than 5%, the incidence of HIV positive children contributes to the increased burden of paediatric HIV consequences such as motor and cognitive delay, which may counteract the success of implementation of PMTCT in reducing child morbidity (Horwood et al., 2010).

Neuro-developmental impairment was identified in children infected with HIV and associated with HIV infection as early as the 1980s (Smith, Malee, Leighty, Brouwers, Mellins, Hittelman, & Blasini, 2006; Van Rie, Harrington, Dow & Robertson, 2007). The virus enters the central nervous system (CNS) early in the course of the disease in children and may persist in the CNS (Tepper et al., 1998; Van Rie et al., 2007). HIV typically develops faster in infants and toddlers than in adults, as their immune systems are underdeveloped at birth.
Clinically and immunologically stable HIV-infected children may develop neurological problems, behavioural problems and delayed physical growth that may be already present at preschool age. This could affect the child’s performance at school (Nozyce, et al., 2005). In a study by Kollár, Jelenik and Hegelsberger (2003), only three in every nine HIV positive children had normal development.

Research findings on motor and cognitive interventions, medical treatments and therapies are essential in enabling early childhood professionals to assist their patients and refer early to appropriate professionals. For the majority of children with motor and cognitive limitations there is little or no referral to professional expertise such as teachers, child health specialists or physiotherapists (Olness, 2003). The use of early interventions by health and rehabilitation personnel may decrease developmental delay.

Interventions that have shown to improve motor and cognitive development include positioning, modification of external stimuli, individualised developmental care interventions and neuro-developmental therapy (NDT) (Gianní, et al., 2006; Symington & Pinelli, 2006). Massage therapy applied by mothers to very preterm newborns has shown to improve neurodevelopment of these infants at two years corrected for age (Procianoy, Mendes & Silveira, 2010).

Children infected with HIV/AIDS struggle to perform on a par with other non-infected children in their age group and it is thus essential that governments and civil society consider expanding high quality, cost-effective early childhood development programmes to achieve the Millennium Development Goal of ensuring successful primary school completion for children (Engle et al., 2007).
Researchers have reported higher levels of stress among caregivers of children with developmental delay than among caregivers of typically developing children (Bailey & Smith, 2000; Banyard, Rozelle, & Englund, 2001; Crnic, Gaze, & Hoffman, 2005). Parental stress may affect mother and child interaction and further reduce child development (Henrichs, 2011). Using mothers as “massage therapists” can enhance mother-child interaction and lower maternal anxiety and depression (Feijo, Hernandez-Reif, Field, Burns, Valley-Gray & Simco, 2006; Field, Diego, & Hernandez-Reif, 2010).

A current problem is a shortage of skilled human resources, lack of validated assessment tools for the South African population, and limited research on neuro-developmental impairment in developing countries even though 90% of infected children live in the developing world. This results in missed opportunities for timely initiation strategies for prevention and care of HIV-associated neuro-developmental impairment (Van Rie et al., 2007).

1.3 Rationale
HIV affects the CNS of HIV infected children, which can cause motor and cognitive delay (Knight, Mellins, Levenson, Arpadi & Kairam, 2000). The researcher observed that developmental delay was hardly identified or assessed in children infected with HIV during routine medical HIV clinic visits. Furthermore, there is limited referral to physiotherapeutic treatment due to shortage of qualified staff (Mars, 2011). This may have repercussions for early motor and cognitive development. Studies have shown that early childhood developmental interventions are helpful for young children (Gianní et al., 2006).

Physiotherapy in the form of exercise or physical activity and stimulation has been used successfully to improve neuro-development in children with motor
and cognitive delay in various conditions such as Down’s syndrome, cerebral palsy and autism (Angulo-Barroso, Burghardt, Lloyd, Ulrich, 2008; Curtain, Bandini, Perrin, Tybor & Must, 2005). Most of these studies have used interventions administered by rehabilitation specialists. The use of home-based physical activity programmes have been evaluated but the results are ambivalent regarding the role of parents when incorporated in physical activity interventions to promote early development (Cameron, Maehle & Reid, 2005; Spittle, Ortom, Doyle & Boyd, 2007). In sub-Saharan Africa, relatives and home-based caregivers offer about 90% of all care and support for HIV/AIDS (Greenburg, 2012).

The inadequate availability of referral, shortage of staff and ambivalent results of parent involvement and the scanty evidence that physical activity may improve motor and cognitive development in preterm and cerebral palsied children, stimulated the researcher to embark on a randomised controlled trial to investigate whether the incorporation of a home-based physical activity programme in combination with massage therapy could improve motor and cognitive development in HIV positive children (Cameron et al., 2005; Gianní et.al., 2006; Melnyk et.al., 2001).

1.4 Uniqueness and significance
The high incidence of HIV and AIDS in many parts of the world, calls for more research pertaining to HIV positive children with developmental delay. Substantial evidence on early screening, detection, and commencement of intervention in HIV infected infants with developmental delay is not currently available. Evidence on neuro-development in HIV infected children may suggest useful points of intervention for improving neuro-developmental outcomes. Mechanisms of paediatric HIV-1 neuro-pathogenesis and factors associated with neuro-developmental abnormalities in peri-natally infected
children are not yet fully understood (Van Rie et al., 2007). The majority of studies reporting on disease specific or other factors associated with development in children have been conducted in the Western world. However, minimal studies have reported on children infected with HIV.

The uniqueness of this study is that at the time of the conceptualisation little evidence was available where a specially designed home-based physical activity programme in combination with massage therapy was used by parents or caregivers to promote motor and cognitive development of HIV positive infants. None of the studies reported on children receiving highly active antiretroviral treatment (HAART).

This study is unique because it is the first study that investigated, through the implementation of a randomised controlled trial, the effect of a home-based physical activity programme given in combination with massage therapy to HIV positive infants and toddlers who were on antiretroviral (ARV) treatment, followed up at predetermined follow-up intervals.

The researcher became aware of Potterton, Stewart, Cooper and Becker’s (2009), findings after the end of the recruitment phase (June 2010). The Potterton, et al. (2009) study used a convenient routine visit scheduled to follow participants up at three, six, nine and 12 months while this study was a medium term intervention, with prospective, directive follow-up at three and six months only. The second differentiation factor between the two studies concerns the issue relating to antiretroviral therapy. Antiretroviral treatment was not freely accessible to participants in the Potterton et al. (2009) study at baseline (15%), whilst all participants in the current study were on antiretroviral treatment. The number of participants that received treatment increased overtime time in Potterton et al. (2009) study and this may have
had an effect on the outcome as the progress of disease maybe exacerbated in the absence of ARV treatment (Corr, 2006).

The third difference was that the current study compared the implementation of a home-based physical activity programme in combination with massage therapy, whilst Potterton, et al (2009) only used physical activity as an intervention. Evidence exists that infant massage improves mother-infant interaction, increases weight gain and infant neurodevelopment and decreases maternal anxiety (Field, Diego, & Hernandez-Reif, 2010; Onozawa, Glover, Adams, Modi & Kumar, 2001; Procianoy, Mendes & Silveira, 2010).

The results of this study may inform interventions directed at health care workers to advocate the implementation of a home-based programme in combination with massage therapy to improve motor and cognitive development in children from an early age.

1.5 Problem statement and research question
The negative effect of HIV on motor and cognitive development in HIV positive children has been established. The problem that arises from the background literature and the rationale is that although several studies have shown that early developmental intervention programmes may improve motor and cognitive development in preterm and cerebral palsy children, the effect of such programmes has not yet been established in children infected with HIV and on antiretroviral treatment. The quadruple burden of disease in South Africa is placing increasing demands on health professionals, leaving little time and resources for comprehensive paediatric HIV care and increasing the use of home-based care. However, there is currently insufficient evidence available to inform policy makers and health care
professionals of the effectiveness of home-based intervention programmes to improve motor and cognitive development in HIV positive children. Further research is thus required to determine whether a home-based intervention can be successful.

Similarly, one can then ask what the effect on motor and cognitive development in HIV positive children is, when they participate in a home-based physical activity programme offered by caregivers.

1.6 Aim and objectives
The overall aim of the study was to prospectively, evaluate the effectiveness of an individually designed home-based physical activity programme in combination with massage therapy, on motor and cognitive development in children infected with HIV.

The specific objectives were:

1. To obtain a description of HIV positive children in relation to socio-demographics, birth history, CD4 count and viral load.
2. To describe motor and cognitive development and anthropometric status of HIV infected children on antiretroviral therapy.
3. To identify factors associated with motor and cognitive development in children with HIV.
4. To measure effectiveness by determining whether a home-base physical activity programme in combination with massage therapy can improve cognitive and motor development composite scores by 15% over a six-month period in HIV infected children on antiretroviral therapy.
1.7 Ethical consideration

Ethical approval was granted by the higher degrees and ethics committee of the University of the Western Cape (Ethical approval number: 05/9/10) and the East London Hospital Complex Ethics Committee prior to commencement of this study. Parents or legal guardians (caregivers) gave written informed consent prior to inclusion into the study. Caregivers were given an opportunity to ask any questions or concerns regarding the study. They were informed of their right to withdraw from the study at any time and that the decision would not affect the care they received from the facilities. Confidentiality was assured at all times. Participation in this study was treated as confidential. Participants were not referred to by their names in any reports of this study. Identities were not disclosed to any person. Documents generated were kept in a secure and locked place. Electronic files were safeguarded using passwords to protect data from unauthorised access, loss or modification.

1.8 Outline of chapters

Chapter one introduces the reader to the research dissertation and describes the rationale that led to the problem statement, the research question and why this study differs from others. The study’s aim, objectives, and ethical considerations are also addressed. Chapter two describes theorist views that led to the conceptual framework. Chapter three presents a systematic review of studies that evaluate the effect of HIV/AIDS on child motor and cognitive development. Chapter four describes the methodology applied in this study including the research purpose, the hypothesis and conceptual framework. Chapter five reports the results of the effect of a home-based physical activity programme in combination with massage therapy on motor and cognitive development in HIV infected children. Chapter six concludes the thesis and elaborates on discussions, conclusions, recommendations and limitations.
Appendices include the ethical approval from University of the Western Cape and East London Hospital Complex, informed consent form; an example of the case report form, link to a massage guide, an example of a home-based physical activity programme, consort statement and a “Turnitin” originality report.

1.9 Summary of chapter one

The background literature, rationale, and problem statement evoked the desire to embark on the research. Theorists view on motor and cognitive development will be discussed in chapter two.
2.1 Introduction to literature review

This chapter addresses literature related to general factors that influence child development and literature addressing the motor and cognitive development and anthropometry of HIV infected children. In addition, different theoretical frameworks and evaluation tools will be critically discussed in the following paragraphs.

2.2 Motor and cognitive delay

Motor and cognitive developmental delay has been reported in children infected with HIV (Gay et al., 1995; Pollack et al., 1996; Blanchette, Smith, King, Fernandes-Penney & Read, 2002; King, Russell, Rosenbaum, Law, & Jaffer, 2004; Baillieu & Potterton, 2008; Koekkoek, de Sonneville, Wolfs, Licht & Geelen, 2008; Ferguson & Jelsma, 2009).

Researchers examined motor and cognitive development in 25 infants with vertically transmitted human immunodeficiency virus infection at a children’s hospital in Canada (Blanchette et al., 2002). They provided evidence that HIV-infected infants obtained significantly lower scores than the uninfected infants on the cognitive and motor standard scores. The Blanchette et al (2002) findings can be endorsed by Van Rie, Dow, Mupuala and Stewart (2009) who conducted a prospective study in the Congo on HIV-infected children accessing care at a paediatric HIV care and treatment facility. Their study found that HIV positive children demonstrated a lower mean level of both motor and cognitive development at entry into care than healthy control children who visited the facility (Van Rie et al., 2009).
Locally, Baillieu and Potterton (2008) reported on a study done in Gauteng, South Africa where they found that 70% of children infected with HIV were significantly delayed in cognitive development and 77.5% in motor development. Thus, the evidence for delayed motor and cognitive development amongst children infected with HIV exists, highlighting the need for understanding the factors that influence it and intervention programmes.

2.3 Pathological effects of HIV on the developing brain

In the mid 1980s, researchers began to investigate the effect of HIV infection on the central nervous system of children documenting neurological involvement clinically, neuro-radiologically and electro-physiologically (Belman et al., 1985; Wachsler-Felder & Golden, 2002). Sharer et al. (1986) investigated brains of HIV infected children at autopsy. The results revealed a unique constellation of findings, including varying degrees of diminished brain weight, inflammatory cell infiltrates, multinucleated cells, vascular calcification, vascular and revascular inflammation and white matter changes. Wachsler-Felder and Golden (2002) reported that children infected with HIV may develop HIV/AIDS progressive encephalopathy. It is further stated that progressive encephalopathy is the most devastating and clearly known symptom of paediatric HIV infection. Features of the disease include motor and cognitive development, poor brain growth as measured by serial head circumference, progressive atrophy, white matter abnormalities and progressive basal ganglia calcification (Wachsler-Felder & Golden, 2002). Progressive encephalopathy manifestations depend on the timing of entry into the CNS in relation to brain development, viral virulence and host factors (Rausch & Stover, 2001; Wachsler-Felder & Golden, 2002).

HIV infection is the primary cause of HIV-associated central nervous system disease, which causes motor and cognitive delay (Wachsler-Felder & Golden,
HIV manifestation in CNS is faster, more common in children than in adults and causes a higher incidence of neurologic abnormalities (Rausch & Stover, 2001; Wachsler-Felder & Golden, 2002). The nervous system is the first organ to be affected by HIV infection (Moulignier, 2009). The virus invades the central nervous system of asymptomatic HIV infected children early after infection and leads to motor and cognitive manifestations (Rausch & Stover, 2001). This may be a result of children having immature neurons and glia, which have different capacity to prevent HIV infection, and replication and the concept that these neurons are exposed to cytotoxins (Ensoli & Cafaro, 2000).

Monocytes infected with HIV passage into the brain and differentiate into macrophages and microglia which are the primary immune cell targets of HIV infection (Koekkoek et al., 2008). The HIV is known to cross the blood-brain barrier and rapidly infects and replicates within macrophages and T lymphocytes upon entering the body and especially the brain (Corr, 2006). The memory CD4 and T lymphocytes may harbour the HIV-1 proviral DNA for many years in its latent form and memory CD4 and T lymphocytes have the ability to reactivate when they come across a cognate antigen, especially in immune-privilege central nervous system (Rausch & Stover, 2001; Corr, 2006; Alexaki, Liu & Wigdahl, 2008). This process is known as the “Trojan Horse” hypothesis (Cholewiska & Szymanska, 2009). The name hails from its stealth in invading the brain (Rausch & Stover, 2001). Neurons are not infected because of their resistance to HIV infection (Corr, 2006). Infected macrophages and microglia secrete pro-inflammatory cytokines and other soluble factors, including HIV proteins, which, over a sustainable period in high concentrations, present a toxic environment for neurons (Rausch & Stover, 2001; Cholewiska & Szymanska, 2009; Lamers, Gray, Salemi, Huysentruyt & McGrath, 2011). Human-immune virus is mostly found in the cerebral spinal fluid (Garcia et al., 1999). The blood brain barrier, which is
located between brain tissue and circulating blood, prevents many damaging substances from reaching the brain, but HIV crosses the barrier (Lowenthal, Cruz & Yin, 2010). Although access to ARVs has increased considerably, neurological complications remain (Corr, 2006). Antiretroviral medication has limited capacity to cross the blood brain barrier to reduce HIV in cerebral vascular fluids to undetectable levels (Winston et al., 2010).

2.4 General factors that influence child development

Winnick (2005) defines development as a continuous process, which begins at conception and ceases at death. In its purest sense, development refers to a progressive series of changes in an individual’s level of functioning over a period. Motor and cognitive development is a gradual but slow and ongoing process and the rate of change happens within the individual. Infancy and toddlerhood refers to the first three years of life and “encompasses the most rapid and contextually transactional period of neuro-developemental change” (Mayes, Gilliam & Sosinsky, 2007; 252). Observed changes in behaviour that take place over time in infants and toddlers are referred to as developmental changes and provide us with guidance to judge whether a child’s behaviour is age appropriate or not (Luiz, Stroud & Jansen, 2005). Of utmost importance in the study of development is the issue of a child reaching developmental milestones within normative limits or whether a pattern of delay can be detected (Li & Rogers, 2006). Children function in a variety of areas, including the motor, social, cognitive and psychological area. As a result, terms such as motor development or cognitive development address the change in particular developmental areas (Haywood & Getchell, 2009).

A range of factors that influence motor and cognitive development were identified during the literature review (Willen, 2006; Blauw-Hospers, de Graaf-Peters, Dirks & Hadders-Algra, 2007; Van Rie et al., 2007; Aubert, 2008;
Sherr, Mueller & Varrall, 2009). These factors are categorized as internal and external factors. External factors include issues such as environmentally unsafe areas with high levels of pollution such as lead from car fumes. Social factors that could influence development include race, ethnicity and poor quality of care during infancy or childhood or lack of opportunity to practice a skill, familial risk factors such as infant or child abuse, presence or absence of quality prenatal care, parental and cultural childrearing practices, social economic level, disease processes and trauma. Some of the internal factors can be classified as genetic inheritance, errors and mutations in genetic transmission, poor maternal/foetal and/or child nutrition, foetal and infant exposure to toxins and other chemical substances, preterm birth, low birth weight and brain damage acquired in the pre or peri-natal period or subsequent (Blauw-Hospers et al., 2007; Aubert, 2008). Evidence of such factors in children infected with HIV is deficient. This study will take note of relevant factors that influence development in the interpretation of results.

2.5 Developmental milestones

Early pioneers in childhood development such as Jean Piaget, Lev Vygosky, Arnold Gessel, Nancy Bayley and Myrtle McGraw have explained and documented the sequences of motor development during infancy and early childhood. Developmental milestones are used to provide a reference framework to observe development and are measured against a set of functional skills or practical tasks which one expects a child to master at a specific chronological age. These are often used in the health profession to help evaluate how a child is developing. Most of the developmental assessments evaluate gross motor (large muscles), fine motor (finger grip), language (verbal and/or non verbal), cognitive (thinking, learning, emotion) and social skills (interacting with others). Other areas of assessment include senses such as visual, hearing, smell, touch and reflexes (French & Sim,
2004; Berk, 2012). It is important to note that infants and toddlers reach developmental milestones in a conventional way. Most will first crawl, then walk, run and then jump. While the sequence may be constant, the rate at which individual children develop can vary a great deal (Piek, 2006). Children who test HIV positive develop in the same sequence as children who are not infected. This allows for assessments and interventions to be aligned with the normal developmental sequence.

2.6 Motor development

Motor development is unique during infancy and early childhood and refers to children’s capability to be in command of their body’s movement, changing from “infants’ first spontaneous waving and kicking movements to the adaptive control of reaching, locomotion, and complex sport skills” (Adolph, Weise & Marin, 2003, p. 134). During this period infants and children display dynamic periods of motor development in a chronological and predictable pattern which is conventionally inherently determined. Motor development is predictable as progress occurs from simple to complex movements, “from cephalic to caudal; from proximal to distal; and from generalized, stimulus-based reflexes to specific, goal-oriented reactions which become increasingly precise” (Haywood & Getchell, 2009; Gerber, Wilks & Erdie-Lalena, 2010, p. 268).

Winnick (2005) provides evidence that motor development can be studied as a process or a product. As a process, when addressing factors that influence early physical activity levels throughout the lifespan and as a product, when referring to normal motor development following a particular sequence. Thus, chronological age consists of different stages during growth and certain key developmental performance is to be achieved at each stage (Winnick, 2005). Infants begin their life with little motor control and as they move towards
becoming toddlers, they gain more control (Piek, 2006; Haywood & Getchell, 2009). Playing with and manipulating objects, self-care, movement and involvement in social activities are major components of motor development (Hersen, 2006).

Motor behaviour refers to all bodily movements, including for example movement of the eyes and can be divided into gross motor and fine motor skill development. Gross motor skill development involves the larger muscle groups to carry out tasks such as crawling, walking and running. Most of the development occur during early childhood and remain unaffected even if not used for many years (i.e. an adult can still crawl even if he has not crawled for many years). Normal child play often assists in the development of gross motor behaviour and is related to the opportunity of children to develop their social skills such as playing outside, kicking and catching a ball. Explorative activity can enhance motor development such as pulling up to stand or climbing on objects to explore (Adolph, 1997).

Smaller muscle groups are used for fine motor skill development and involve conscious and controlled movements of the smaller muscles such as when a child uses her fingers to grasp. The skill to eat with a spoon or to draw and write is some of the development, which can be classified under fine motor development (Adolph, 1997; McCarty, Clifton, Ashmead, Lee & Goubet, 2001).

Researchers with an interest in the field of motor development have put forth several theories to explore and explain practice, which promotes motor development. Selected pertinent theories are discussed next.
2.7 Motor development theories
The influence of the environment on infant and toddler development, and how much is genetically programmed, has been a contentious issue since the philosophers of the 18th century (Piek, 2006). Child developmental theorists posit that there are two broad (maturational versus dynamic) and four central themes related to child motor development. The four broader central themes are: nature (Biological-maturationist theories) versus nurture (environmental-learning theorists), whether development is on a chronological continuum or stage-like fashion, the influence of critical sensitive periods conducive for development and lastly the role of early experience in shaping development (Kessenich & Morrison, 2012).

2.8 Maturational theories
Piek (2006) wrote that a nature perspective holds that human development is genetically governed or predetermined. Biological-maturationist theorists and philosophers such as Plato and Descartes theorised that motor development is due to inborn or genetic heredity factors. Flanagan (2002) confirms that nature (genetics) plays a significant role by pointing out that twins who are separated at birth and raised apart, show many uniformities in developmental processes. Likewise, Flanagan (2002) refers to the absence of similarity in developmental processes when adopted children are compared to their siblings.

Piek (2006) also stated, on the other hand, that purely nurture views argue that experience is the primary determinant of development. The well-known environmental-learning theorists (nurture) such as John B. Watson and Burrhus F. Skinner accentuate the supreme significance of empirical or experiential learning as fundamental to development. An infant’s mind is a blank slate (tabula rasa) and that all the knowledge (motor development) is
predicted by experience, thus external environment (Kessenich & Morrison, 2012). Several studies exist which can confirm that mineral and vitamin supplementation can increase development, which supports nurturing (Schoenthaler, Bier, Young, Nichols & Jansenns, 2000; Dani, Burrill & Demmig-Adams, 2005).

In the early 1900s, theorists, such as Piaget, Gessel, Bayley and McGraw, developed maturational theories (Aubert, 2008). Arnold Gesell contributed the most to the maturationist view and recognized that children need to develop at their own pace (Gesell, 1940; Saracho & Spodek, 2007). This theory is used extensively in measuring instruments for motor development such as the Bayley Scales of Infant and Toddler Development Third Edition (Bayley-III) used in this study to measure motor and cognitive development. It explains development in terms of genetics and biological changes, which occur as the individual ages (Allen & Marotz, 2009). Although the role of environmental factors on motor development is acknowledged by some of the maturational theorists, they emphasize that a child is a product of his or her genetics and that the environment has a minimum influence (Ferrel, 2003; Saracho & Spodek, 2007).

2.9 Dynamical systems theory
Li and Rogers (2006) describe the two perspectives as developmental theories (neuro-maturation theory and dynamical systems theory) (DST). The neuro-maturation theory assumes that movement progresses from primitive reflex patterns to voluntary controlled movements whereby, low-level skills are acquired before more complex skills and that the sequence and rate of development is consistent between all infants and children.
Unlike the maturation theory, which considers the central nervous system (CNS) to be the predominate factor, manager, organizer and regulator of development, the dynamical systems theory suggests that motor behaviour is not prescribed and is the result of many factors, both internal and external (Li & Rogers, 2006; Aubert, 2008). According to Cowden and Torrey (2007) the similarity between DST and the work of Piaget is the emphasis on the interaction of the environment and the organism. However, Piaget’s theoretical concepts of development change relating to cognitive development during the sensori-motor period of an infant are in conflict with DST. Aubert (2008) emphasizes that in the dynamical theory, no one system (such as the CNS in the maturation theory) is the pre-eminent director of development. DST provides an alternative for uncovering the processes that infants and toddlers with delays may utilize to acquire motor skills (Cowden & Torrey, 2007). This is in contrast with physiotherapy interventions, which are conventionally based on maturational theories of motor development, accentuating the function of the CNS in regulating motor performance. However, DST has been used to inform physiotherapy interventions and clinical decision making in the acute stage of revitalisation from acute brain injury (Levac & DeMatteo, 2009).

2.10 Cognitive development
Cognitive or mental development is a field of study in psychology and neuroscience which explores the processes and activities which best describe the emergence of the capability of children to think and to understand, or how thoughts and knowing develop. It also explains, how children become more proficient and successful in their understanding of the environment around them (Oakley, 2004). How they attain knowledge of their environment, how that knowledge is stored, interpreted and how they modify that knowledge are all part of cognitive development.
Cognitive development refers to the changes in the brain related to construction of thought processes, development of intelligence, conscious thought problem-solving and decision-making ability and occurs mainly during infancy and childhood (Li & Rogers, 2006). According to Piaget, cognitive development occurs steadily, in succession and without regression. He hypothesizes that development commences with tangible situations and objects and advances to abstraction - thus moves from uncomplicated to compound (Potts & Mandleco, 2002).

The word cognitive derived from a Latin word “cognoscere” means to know (Oakley, 2004). Cognitive structures in infants, structure and interpret perception, and function in both the presence and absence of perceptual subject matter (Bremner & Fogel, 2004). The frontal lobe is the area of the brain most critically involved in cognitive development and the last brain structure to mature (Li & Rogers, 2006). Taylor (2005) suggests that understanding the nature of cognitive development, the factors, which contribute to it, and the way in which internal and external factors interact and result in changes to the way children think, allows us to develop ways of teaching children so that their development is maximised.

2.11 Cognitive development theories
Over the years, theorists have developed a number of theories with which to explain human development. Theorists in cognitive development exhibit a particular interest in the advancement of how children attain intelligence, speech, thought and reasoning skills in early childhood (Salkind, 2004; Oakley, 2004; Packer, 2008). They studied the “how” and not the “what” of development and speculate that the “how” involves communication processes between the brain and interaction with the brain (Potts & Mandleco, 2002).
The key theorists in cognitive development are Jean Piaget (1896-1980) and Lev Vygotsky (1896-1934).

2.11.1 Jean Piaget’s stages of cognitive development theory

Jean Piaget is known for his research in developmental psychology. Piaget was the first theorist to note that children’s thinking was different from adult thinking and varied at different ages (Oakley, 2004). Piaget stressed that children are naturally inquisitive and are continuously confronted by many new stimuli and actions, which are, not straight away understood (Shaffer & Kipp, 2010). Bremner and Fogel (2004) points out that Piaget’s theory fundamentally subscribes to the concept that development of cognitive behaviour is a process, which involves building blocks in which children move forward from the basic to a more complex thought process, while engaging with their environment. Thus, cognitive development becomes visible through the accomplishment of different tasks while children build and recreate the particulars of the world because of interactions with the surroundings. Piaget claimed that children are born with a limited amount of understanding and therefore cannot execute complex tasks at first. For example, newborns might be able to grasp objects with the whole hand, but they cannot control there thinking to pinch an object. Thus, the grasping, which is merely a reflex at birth, can be seen as a pre-programmed and restricted understanding of using its fingers cognitively (Taylor, 2005).

Potts and Mandleco (2002) state that the process and measures children took as they discovered, reinvented, understood, and acquired knowledge of the world around them, fascinated Piaget. Piaget concluded that children learn through active interaction with the environment (Oakley, 2004). Piaget’s theory suggests that cognitive development is “transactional” and occurs as an outcome of negotiations between the child’s external biological
environment and knowledge gained and the make-up that are inside the child. This constant interaction is responsible for cognitive development (Taylor, 2005). Because of Piaget’s belief that children are from birth formed by the effect of their actions and interplay with their environment, his theory has been criticised that he took little or no cognisance of the role that the social dimension play in cognitive development (French & Sim, 2004; Potts & Mandleco, 2011).

Piaget was of the opinion that there are distinct series of stages in the child’s development of it’s understanding of the world, each qualitatively different from the preceding one and from others (French & Sim, 2004). After studying the reasoning processes of children at various ages, Piaget theorized that cognitive development occurred in four distinct and genetically determined stages and several phases that follow an orderly progression based on the child’s maturation level, experiences with physical objects, interaction with caregivers, other adults and peers, and a self regulating mechanism that responded to environmental stimuli (Potts & Mandleco, 2002). Piaget’s four stages of cognitive development are the sensory-motor stage (0 to 2 years), the pre-operational stage (2 to 7 years), concrete operations (7 to 11 years) and formal operations (12 to adulthood). According to Li and Rogers (2006) Piaget’s stages of cognitive development provide an early look at conceptual models of children’s cognition.

According to Potts and Mandleco (2002) during the sensory stage (0 to 2 years), the foundation of future cognitive functioning is established and sensory and motor capabilities are used to gain a basic understanding of the world. It is further stipulated that infants acquire a primitive sense of who they are and their relation to others and realise objects continue to exist even after they are out of sight. During the pre-operational stage (2 to 7 years) children use language and have a growing understanding of the past, present and
future (Potts & Mandleco, 2002). Their thought is egocentric (unable to take another’s perspective), they are easily fooled, respond to events and objects according to how they appear, are not able to understand the fundamental relationships among and between phenomenon, and inter-mingle fantasy with reality. The concrete operations (7 to 11 years) and formal operations (12 to adulthood) are not discussed in this dissertation as they are beyond the scope of this study.

The Piaget’s stage theory was criticized by theorists such as Donaldson who argued that children can think and reason at a higher level than that suggested by Piaget if asked to undertake activities or problems within a familiar context (Curtis & O’Hagan, 2003). The authors further state that he (Piaget) failed to take account of the effects of the social context upon children’s development. According to his theory, infants are, at birth, devoid of any cognitive structures and are equipped with reflexes and biological mechanisms of assimilation, accommodation and equilibrium (Legerstee, 2005). This implies that infants do not have domain specific knowledge that gives them a head start, but instead, develop cognitive structures that allow for more advanced actions on the environment through exercising their reflexes (Legerstee, 2005).

The Piagetian ideas suggest that children develop by a process of assimilation (taking in information through any and all of the senses), accommodation (taking ones current abilities/understandings and modifying them to adjust to the new circumstance or challenge) and organization of this into a new mental structure or physical action, a schema (Dixon, 2006).

The basic element in Piaget’s theory of the child’s cognitive development is the schema (Oakley, 2004). Shaffer and Kipp (2010) describe schema as an organized pattern of thought or action, which is used to cope with or explain
some aspect of experience. Piaget described schema as units of knowledge (or representations) and he saw development as a gradual increase in both the amount of schema (things which are known and therefore represented) and in the complexity of these schemas (Taylor, 2005). Many three year olds, for example, insist that the sun is alive because it comes up in the morning and goes down at night (Shaffer & Kipp, 2010). These children according to Piaget are operating on a basis of a cognitive scheme that things that move are alive.

Assimilation refers to the process where children incorporate new ideas or information or experiences into existing ideas or patterns (Curtis & O’Hagan, 2003; Nevid, 2009). Oakley (2004) supports Piaget’s concept that children improve their cognitive development through active participation and assimilation processes. During this process, children try to make sense of new activities or events experienced (Curtis & O’Hagan, 2003). Nevid (2009) is of the opinion that assimilation is the ability to adjust when new things fit into existing schemas. For example, an infant will learn to suck on the nipple of a bottle, as he knows how to suck on a breast. Children develop cognitive organization to help them make sense of their worldly experience and when they come across a new experience, they place it into the previous schema, which they have already developed. The process of assimilation may be seen as being subjective, because children may be inclined to alter experience or information somewhat to fit in with their pre-existing schemas. Accommodation on the other hand refers to the process of changing existing ideas or creating new ones to deal with things or experiences that do not fit readily into existing schemas (Nevid, 2009). An example is given that a child may have an idea that all flying objects are birds, but when he or she encounters a helicopter it does not fit readily in the previous concept of flying therefore a new schema need to be constructed. Existing ideas are adapted to fit new requirements (Curtis & O’Hagan, 2003). The more adequate the
understanding of the difference between a bird and a helicopter is, the better is the child able to accommodate the new information (Potts & Mandleco, 2002).

Piaget explained that cognitive development is driven by the process to achieve equilibrium between assimilation and accommodation. To equilibrate their thoughts, cognitive processes reach a state of equilibrium that is then challenged with a new thought that causes disequilibrium. The infant then uses assimilation or accommodation to incorporate the new idea and to reach a new state of equilibrium (Damon & Lerner, 2006; Rathus, 2008). The balanced state of affairs is called equilibrium and the process of achieving it is called equilibration (Shaffer & Kipp, 2010). Thus the child is continuously challenged by new experiences which conflict with their existing understanding and move between a state of equilibrium and disequilibrium constantly (Oakley, 2004; Keenan & Evans, 2009). The processes of assimilation and accommodation allow children to resolve disequilibrium and become accustomed to their environments (Shaffer & Kipp, 2010). States of disequilibrium are important as they require children to adjust their cognitive structures so that they can assimilate changes and get back to a state of equilibrium (Keenan & Evans, 2009). The endeavour to reinstate equilibrium is the foundation of intellectual motivation and is part of the expected inquisitiveness of the child (Rathus, 2008). This theory is thus relevant to physiotherapy interventions in children and understanding how they develop.

### 2.11.2 Vygotsky’s social development theory

Vygotsky’s Social Development Theory is the work of Russian psychologist Lev Vygotsky (1896-1934), who lived during the Russian Revolution and was born in the same year as Piaget (Derry, 2008). Vygotsky’s viewpoint was influenced by the social and political aftermath of the Russian Revolution.
This can be seen through his work. He explained that children’s cognitive development was driven by the notion that cognitive development occurs through relations and activities whilst the child engages with culture and society (Packer, 2008; Salkind, 2004). Vygotsky’s approach is therefore known as the socio-cultural approach, as he emphasized the influence of social interaction and culture on development (Salkind, 2004). Packer (2008) maintains that Vygotsky approached cognitive development as a process that begins with the child as a social human being who only becomes an individual over time.

According to Shaffer (2009), Vygotsky claimed that human cognition is intrinsically socio-cultural, as it is affected by the cultural system of beliefs, values and tools of intellectual adaptation and passed on from society to the individual. Thus, in contrast to Piaget who believed that cognitive development is universal, Vygotsky believed that it is culturally bound. Both of them believed that children are born with an inborn ability to be enquiring and this inquisitiveness drives them to explore and learn from their external environment. Piaget further categorized the developmental stages, but Vygotsky defended his viewpoint and said it was too complex to categorise and that development takes place on a continuum from birth to death (Shaffer, 2009). Piaget further assumed that the child is the most important source of information, where as Vygotsky claimed that the primary force for a child to develop cognitively is his cultural and social environment. Thus in summary, Piaget was of the opinion that development is a natural process whilst Vygotsky believed it is a social, cultural and historical process (Salkind, 2004). Shaffer and Kipp (2010) state that both Vigotsky and Piaget theorized that children as curious and actively involved in activities, which accelerate cognitive development, but Vigotsky claimed that most of the true discoveries made by a child occur within a social context.
Vygotsky’s social development theory has three basic themes. He firstly theorized that “social interaction plays a fundamental role in the process of cognitive development” (Gauvain & Cole, 1997, p. 34). In other words, a child will first learn the function on a social level (between people) before internalising it to the individual level (Gauvain & Cole, 1997). The theory infers that basic capabilities of knowledge are present at birth and grow through interaction with the child’s environment.

The second basic theme is “The More Knowledgeable Other” (MKO), where it is understood that there are other people who have a higher capability than the child with reference to a specific task or concept. This could be an older person, peers or even a younger child and in today’s life even technology such as a computer. The main point here is that the “other” must have more knowledge about the specific task (Gauvain & Cole, 1997).

The third theme addresses the “Zone of Proximal Development” (ZPD), which refers to the zone of learning which occur in the child’s ability to carry out an undertaking under supervision from an adult, younger or peer, and the child’s own ability to do the task without supervision. Thus, the child develops skills that can later be used on their own without supervision. This is a good time where peer-group learning plays a role and children with lower cognitive levels learn from others in a group who have reached higher cognitive levels. Children learn to adapt to instructions from the “supervisors” and supervisors in return adapt to make instructions clear for the child so that the child can respond appropriately. This process where the child is trying to understand the concept whilst under supervision is referred to as “scaffolding’. Thus, even though the environment is required for development, the presence of a “supervisor” is also needed. Through the interaction with the supervisor, the child learns new concepts and internalise the information (Gauvain & Cole, 1997; Derry, 2008; Shaffer & Kipp, 2010; Coon & Mitterer, 2010).
It appears that Vygotsky suffered from tuberculosis and died at the young age of 37 before he fully recorded and developed his theory fully (Kail & Cavanaugh, 2009).

2.12 Interventions for motor and cognitive development

There is little evidence to document that interventions at the impairment level are effective for children with developmental disabilities. The priority goal in children with delayed motor and cognitive development is to enhance the rate of acquiring motor skills and that children function at age appropriate levels (Mahoney, Robinson & Fewell, 2001). Physiotherapists are primarily concerned with motor and cognitive development and much of their treatment is through play (French & Sim, 2004). Motor and cognitive development in children is achieved by working on mental and functional tasks during play. Play is useful in both assessment and intervention in children and is a major tool for learning, early stimulation and training of different developmental functions. Structured play has previously been used to stimulate children to accelerate their motor and cognitive development (Goodway & Branta, 2003; Taneja, Aggarwal, Beri & Puliye, 2005).

In Kanda, Pidcock, Hayakawa, Yamori and Shikata (2004) four of five children who completed physiotherapy training could either stand still for five seconds or walk at the time of the outcome evaluation 52 months after the beginning of a therapy programme. None of the five subjects with no training or insufficient training could accomplish this task when evaluated 64 months following therapy initiation. Although the sample size was small, the difference was found to be statistically significant (p=0.028). Significant improvement in both motor and object control skills through activity-based intervention has been reported. In another study of twenty-nine children with
meningomyelocele and shunted hydrocephalus, all had motor impairment, but after physiotherapy and training, walking was possible in 23 of them (5 autonomously and 18 with an aid), while six had recourse to a wheelchair (Rendeli, Salvaggio, Sciascia, Bianchi, Caldarelli & Guzzetta, 2002). A statistically significant difference in cognitive level was also found between ambulatory clients (both with and without aids) and those who were dependent on wheelchairs (Intellectual Quotient: 83-85 vs 63).

Two motor intervention models, Developmental Skills (DevS) and neurodevelopmental therapy (NDT) are used routinely in early intervention and physiotherapy programmes which target children with delayed and impaired motor and cognitive development (Mahoney et al., 2001). Neurodevelopmental therapy has been widely used in children with cerebral palsy but also with children exhibiting a wide range of motor impairments, including hypotonia, which is common in HIV positive children (Mahoney et al., 2001). Developmental Skills programmes focus on the learning and mastery of a set of normally sequenced motor milestones, with intervention targets identified from skills at the next higher level. Instructional or treatment strategies tend to be behavioural in nature, i.e. children are encouraged to engage in exercises or structured play activities, which target specific skills and are extrinsically reinforced when they demonstrate greater approximations of the desired behaviour. According to Mahoney et al. (2001) this approach assumes that children will advance to higher levels of motor development and independent functioning through practice and reinforcement.

Albers, Riksen-Walraven and de Weerth (2010) are of the view that physiotherapists use many forms of treatment programmes to enhance development. Some may involve parents or caregivers in the treatment sessions and may instruct them on how to administer a home-based physical activity programme. Treatment sessions include exercises to improve motor function and play to improve and develop cognitive skills. These authors
claim that even small increases in developmental stimulation provided to children may foster children’s development.

A review of literature found a lack of evidence to support the claim of a beneficial effect of physiotherapy programmes used in early intervention such as NDT (Blauw-Hospers et al., 2007). Between 2009 and 2011 a study was conducted which used a new format and alternative to the traditional NDT for early childhood developmental delay (Dirks, Blauw-Hospers, Hulshof & Hadders-Algra, 2011). They found that the early intervention physiotherapeutic programme, Coping with and Caring for infants with neurological dysfunction, a family-centred programme (COPCA), was more beneficial than NDT. However, the findings of the study conducted in the Netherlands are not generalisable to other countries as stipulated by the authors. Furthermore, the study used a small sample size of 46 participants and the intervention sessions varied between the two arms in frequency and duration. The main difference between the two interventions is the main focus. The COPCA programme focuses on encouraging the family’s own capacity of solving problems of daily care and incorporating variation along with trial and error in daily activities whilst in NDT the starting point is the impairment of the child (Dirks, et al., 2011).

Home-based interventions administered by caregivers focussing on improving motor and cognitive development have been reported. Wiart, Ray, Darrah and Magill-Evans (2010) support the use of collaborative family centred service delivery for children with disabilities. Potterton et al. (2009), reported that a basic home-based physical activity programme could significantly improve both motor and cognitive development in young children infected with HIV compared to standard treatment over a one-year period. A parent or primary caregiver driven intervention is critical to successful early intervention (Suchman, Pajulo, DeCoste & Mayes, 2006). Family members, who are
usually primary caregivers, are keen to help in their child’s care with clear guidance (Coyne, 2013). Young children present with different levels of developmental delay and have different family structures. For this reason, interventions to improve cognitive and motor development must be individualized. Newey (2008) states that careful development of individualised interventions can improve quality of life for children and their families. A home-based physical activity programme is tailored according to the child’s needs. Specialists assess the child, identify the level of development, and teach the parent how to stimulate the child.

The role of the rehabilitation specialist in motor and cognitive development is to stimulate the child using play and exploration. Parents and caregivers are encouraged to engage in therapeutic play with the child at home and also allow the child to play with other children. They are also encouraged to provide the child with stimulating and educational age appropriate toys and praise the child when they are doing well. According to Curtis and O’Hagan (2003), Piaget considered that play was a product of assimilation, whereas imitation resulted from accommodation. Play is very important in early childhood as it facilitates motor and cognitive development (Trawick-Smith, 2010). It provides the child with a chance to explore, practice new skills and solve problems.

Physical activity interventions for children with developmental problems seek to develop, maintain and restore maximum movement and functional abilities throughout the lifespan to reach specific milestones. During child assessment, physiotherapists identify the movement potential of the child and develop a specific treatment programme. Families and caregivers are involved throughout the process of assessment, setting up of goals and treatment. Milestones of development are considered in developing treatment strategies. Gessel’s (1940) developmental milestones, which
normal children follow during the development process, are extensively used. Understanding the sequence of development is important for physiotherapists providing interventions to children who are delayed (Ikiugi, 2012). Physical activity through play and stimuli is a major factor in motor and cognitive developmental interventions in children. Common treatment techniques used include Bobath and NDT (Knox & Evans, 2002; Gianní et al., 2006; Dirk, et al., 2011).

Massage therapy has been reported as having a positive effect on motor and cognitive development in preterm and healthy term infants (Procianoy, Mendes & Silveira, 2010; Inal & Yidiz, 2012; Abdallah, Badr & Hawwaric, 2013). Procianoy, Mendes and Silveira (2010) randomly allocated very low birth weight infants to receive massage therapy by their mothers plus skin-to-skin care versus a control group who only received skin-to-skin care. Infants were assessed after two years and motor and neurodevelopment scores were corrected for age. Infants who received massage therapy had significantly higher mental development index scores and slightly higher motor developmental index scores than those who did not receive massage therapy. Similarly, Abdallah et al. (2013) evaluated the effect of massage therapy provided by mothers to their preterm infants. They used the Bayley scale to assess cognitive development and found that infants who received massage therapy had higher cognitive scores at 12 months corrected for age, than those who did not receive massage therapy. Inal and Yidiz (2012) evaluated the effect of infant massage on motor and cognitive development in healthy term infants at three and six months after birth. The Ankara Developmental Screening Inventory (ADSI) was used to assess motor and cognitive development. Infants who received massage therapy provided by their mothers had significantly higher motor and cognitive developmental scores than those who did not receive massage therapy. However, in contrast to these studies a recent meta-analysis concluded that massage
therapy may improve weight gain, but stated that the effect on motor and cognitive development was not conclusive and further evaluation was needed (Wang & Zhang, 2013).

Caregiver driven home-based physical activity interventions have been reported and there is evidence that some result in meaningful improvement in the lives of caregivers and children (Rickards, Walstab, Wright-Ross, Simpson & Reddihough, 2007; Wen, Baur, Simpson, Rissel, Wardie & Flood, 2012). Rickards et al., (2007) reported improvement in a home-based physical activity intervention for children with Autism and developmental delay. A Campbell Collaboration review found no evidence on the effectiveness of home-based child development interventions (Miller, Maguire & Macdonald, 2012). However, studies, which were included in the systematic review, were of poor quality, had small sample sizes and were very old. The most recent study included in the review was published in 1995.

2.13 Measurement for motor and cognitive development
The use of assessment measures can be traced back to old testament times in the Book of Judges Chapter 7 verses 1 to 8 (Foxcroft, Roodt & Abrahams, 2005). It is recorded that in those ancient times “Gideon observed how his soldiers drank water from a river so he could select those who remained on the alert. Ten thousand men were taken to the river and asked to drink water from it in order to select the best men to conquer the Midianites. The best soldiers were selected according to how they drunk the water. Three hundred men lapped the water with their hands to their mouth and were selected. The rest got down to their knees to drink water, lapping with their tongues and were sent back home” (Foxcroft et al., 2005, p. 12).
Measurement is the assignment of numbers to characteristics or the transformation of attributes into numbers (Wolfaardt, & Roodt, 2005). The justification of assessment involves generalizing the sample of behaviour observed in a testing situation to behaviour manifest in other non-test situations (Griessel, 2005). There is benefit in assessing children at an earlier age. The rationale for assessing a child’s development at an early age is that the sooner a child’s difficulties can be identified, the sooner an intervention can be implemented, and hence the sooner a child can be assisted (Luiz et al., 2005). If a problem is detected at an early age and the child is provided with intensive stimulation, the cognitive or motor delay may disappear after a period of time (Luiz et al., 2005). In agreement, Blauw-Hosper et al. (2007) state that early detection of children with developmental disorders offers the opportunity for an intervention at a young age, i.e. during a phase in which the central nervous system is characterized by considerable plasticity.

Diagnostic measures are in-depth, comprehensive, individual, holistic measures used by trained professionals (Luiz et al., 2005). The aim of diagnostic measures is to identify the existence, nature, and severity of the problem (Luiz et al., 2005).

Various scales have been developed to measure motor and cognitive development. The most used scales in motor and cognitive development research are the Bayley Scales of Infant Development - Second Edition (BSID-II), Denver Developmental Screening Test and the Griffiths Scales of Mental Development (Griffiths Scales). According to French and Sim (2004), these norm-referenced scales have been devised to compare individual children with an identified pattern of development common to a supposedly representative population of children of the same age.
Selection of an appropriate measure depends on the purpose of testing and characteristics of participants. Motor and cognitive diagnostic measures for infants and toddlers previously used in South Africa include the Griffiths Scales of Mental Development (Griffiths Scales), the Denver Developmental Screening Test (DDST) and the Bayley-II. There are two types of measures which are relevant to this study, namely, discriminative and evaluative measures.

Discriminative measures are used to identify children with developmental delays and evaluative measures, to evaluate change over time of a child’s score of a specific skill (Tieman, Palisano & Sutlive, 2005). The Bayley-III possesses both types of measures, and is very sensitive to developmental delay, and therefore was used in this study.

2.13.1 The Griffiths Scales of Mental Development
The Griffiths Scales of Mental Development (Griffiths Scales) are British in origin, were developed in 1950 and provide general development quotients in addition to measures of five domains of functioning, each of which is assessed on a separate subscale (Luiz et al., 2005). These subscales are: locomotor, personal–social, hand and eye, hearing and speech, and performance, described as mental development (Allen & Marotz, 2009; Claas et al., 2011). Griffiths Developmental Scales have been demonstrated to show good reliability and validity in four ethnic groups (i.e. White, Mixed Race, Asian and Black) in South Africa, however, item coverage is very limited (Luiz et al., 2005).
2.13.2 Denver developmental screening test

The Denver Developmental Screening Test is a widely used, readily administered screening tool for examining the developmental progress of developmental delays in children from birth to 6 years (Chiu & DiMarco, 2010). The tool measures four aspects of development; personal/social, fine-motor/adaptive, gross motor, and language development. The name "Denver" reflects the fact that this screening test was created at the University of Colorado Medical Center in Denver, United States of America. The scale has 125 items on various areas of development including, personal–social, fine motor, language and gross motor areas and is used to identify developmental delays. The tool is quicker to administer and is inexpensive but does not measure cognitive development.

2.13.3 Bayley scales of infant and toddler development

The Bayley-III is the third edition of the original Bayley Scales of Infant Development (BSID) and is very similar to the BSID-II with some structural additions and publisher-reported improvements (Tylenda, Beckett, & Barrett, 2007). Additions to the scales which are relevant to this study include the growth scores, the growth charts and a scoring assistant. Improvements in BSID-III include easier administration, extended floor and ceiling effects, additional clinical validity studies, new norms, simplified scoring rules and an option for increased input from the caregiver (Tylenda et al., 2007).

The Bayley-III assesses the developmental functioning of infants and young children aged between one month and 42 months (Bayley, 2006). It is a revised edition of the Bayley Scales of Infant Development - Second Edition
(BSID-II), the most widely used instrument and referred to as the “gold standard” for measuring infant and toddler development (Berger, Hopkins, Bae, Hella & Strickland, 2010). The scale is an individually administered instrument, which assesses the developmental functioning of infants and young children aged between one month and 42 months (Bayley, 2006). Elkonin, Foxcroft, Roodt and Astbury (2001) state that individual administration is very time consuming and expensive, but it allows a researcher to work with the individual and identify any problem areas related to its administration.

The BSID-II has previously been used in South African infant populations (Richter & Grieve, 1991; Cooper & Sandler, 1997). The main use of Bayley-III is to identify developmental delay in five domains and to provide information for intervention planning. These domains are: cognitive, language, motor, social-emotional and adaptive. The BSID-III can be used with confidence that the ranges represented indicate on average, typically developing infants and toddlers (Haywood & Getchell, 2009). It takes 30 to 90 minutes to administer, depending on the age of the child.

The Bayley-III has: updated normative data, scales that assess distinct and important domains, high psychometric quality, enhanced administrative features and can be used clinically (Piñon, 2010). The strength of the measure is that it allows for objective assessment, comparable results, yields data, which can statistically be analyzed and provides separate indices for motor and cognitive abilities (Toth & King, 2010). The Bayley-III has maintained the basic qualities of the previous versions. The major limitation of the scale is that it’s full use with children presenting with gross sensory impairments (e.g. blindness, deafness, or hard of hearing), severe spinal cord injuries (apart from cerebral palsy classification), and with other severe
physical conditions may be precluded because the disorder may prevent a
standardized administration (Piñon, 2010). Another limitation is that valid
administration requires considerable experience and practice to avoid under
or overestimating abilities (Toth & King, 2010).

The Bayley-III can be used in a research context as it is well constructed and
the psychometric properties are accessible. Elkonin et al. (2001) favour the
use of an instrument with such properties in research. Normative data have
been previously collected in research on high-risk children such as those with
Down’s syndrome, prematurity, HIV and prenatal drug exposure (Tieman et
al., 2005). Thus, based on the above information and considering the
advantages and disadvantages, the Bayley-III would be considered
appropriate for the current study.

2.14 Summary of chapter two
The pathological effects of HIV, general factors that influence development,
developmental milestones and theories that explain motor and cognitive
development and different instruments used in measuring motor and
cognitive development were addressed in chapter two.
Chapter Three
A systematic review on the effect of HIV/AIDS on child motor and cognitive development

3.1 Introduction

Human immuno-deficiency virus (HIV) infection and acquired immuno-deficiency syndrome (AIDS) continue to be one of the main public health problems, globally, with one in twenty adults living with HIV in Sub-Saharan Africa (World Health Organisation [WHO], 2013). As far as known, the first recorded case of mother-to-child transmission of the HIV is traced back to 1970. Subsequent analyses of stored blood samples of a prostitute and her three children (Shilts, 1987), and that of a sixteen year old, drug user and her baby girl, confirmed HIV positive status (Worobey, Santiago, Keele, Ndjango, Joy, Labama & Hahn, 2004).

Mother-to-child transmission (MTCT) of HIV has risen over the years to 45% in the absence of any intervention (WHO, 2013). It is proposed that successful implementation of the prevention of mother-to-child transmission (PMTCT) programme can prevent transmission to the infant completely. Despite a high coverage of PMTCT programmes and the availability of highly active antiretroviral therapy (HAART) to mothers, the prevalence of HIV in children born to infected mothers in South Africa is still above 5% (Goga et al., 2012; WHO, 2013).

Neuro-developmental delay in HIV-1 infected children has been documented (Ferguson & Jelsma, 2009). Buescher, Gross, Gendelman and Ikezu (2007) confirmed that the pathology of HIV-1 is associated with tissue damage that occurs in the central nervous system. The central nervous system involvement, disease progression, and/or environmental deprivation are critical pathways by which HIV affects early child neuro-development (Baillieu
& Potterton, 2008). The HIV affects children’s cognitive and motor development due to the immaturity of their nervous and immune systems. Inadequate innate viral control mechanisms and adaptive immunity allows active viral replication to occur in the brain (Buescher et al., 2007). Neuro-developmental delay in HIV infected children occurs early in the disease and the main neurological condition related to HIV infection during childhood is HIV-associated progressive encephalopathy, which is the initial presenting condition for AIDS in 18% of cases, affecting 30-60% of sero-positive infants, children and adolescents at any time point of the disease (Millana-Cuevas, Portellano & Martinez-Arias, 2007). It is argued that HIV-associated progressive encephalopathy causes neuro-psychological deficits involving a wide variety of domains, such as speech and language, memory, learning, information processing and motor functioning (Millana-Cuevas et al., 2007). Knight et al. (2000) claim that mental and motor development is significantly reduced in infants infected with HIV compared to sero-reverters. Knight et al. (2000) found that HIV positive infants had significantly lower scores on the Bayley Scales of Infant Development (BSID) at baseline and follow-up (motor development) compared to sero-reverters. The effective use of antiretroviral treatment (ART) fails to show any improvement in developmental impairment in children with HIV (Boivina et al., 2010).

Few studies have been conducted to identify developmental impairments in children who are HIV positive. It is unlikely that a single study can provide a clear picture of the gravity of the problem, especially if it has a small sample size. Small studies usually provide imprecise estimations (Higgins & Green, 2008). Various measures, age groups of children and designs have been used in studies focusing on neurodevelopment in HIV positive participants.
Fowler (2000), Peterson, Drotar, Olness, Guay and Kiziri-Mayengo (2001) and Ferguson and Jelsma (2009) used the Bayley Scales to assess children aged 42 months and below. Some studies used different measuring instruments for older children, including the Griffiths Scales, McCarthy Scales, Denver Scales and the Cognitive Functioning IQ test (Levenson, Mellins, Zawadzki, Kairam & Stein, 1992; Piazza, Astori, Maccabruni, Caselli, Bossi & Lanzi, 1995; Coscia, Christensen, Henry, Wallston, Radcliffe & Rustein, 2001; Tahan, Bruck, Burger & Cruz, 2006). Currently there are no published meta-analyses on the prevalence of motor and cognitive development in children with HIV. Meta-analysis can confirm whether there is enough evidence available that can inform decisions of care for rehabilitation.

The purpose of this systematic meta-analysis was to systematically appraise evidence on the effect of HIV/AIDS on motor and cognitive development in children aged 0 to 42 months.

### 3.2 Methodology used in this systematic review

A systematic review based on the methodology as explained in the Cochrane handbook for systematic reviews was used to identify, and synthesize the information of the studies that were included in this review (Higgins & Green, 2008). A rigorous protocol and unambiguous methods were used to lessen bias in order to ensure that trustworthy findings are produced that can be used to inform decision making.

#### 3.2.1 Search strategy, types of studies, participants and outcomes

The literature search strategy aimed at identifying published and unpublished studies from any country. Electronic searches of journals with articles reporting on motor and cognitive development in children were conducted
through the university library services. The journals that were hand searched were *Pediatrics, Pediatric Physical Therapy* and the *South African Journal of Physiotherapy*. The authors searched several databases from inception to January 2013 including PubMed, CINAHL, Science Direct, CENTRAL, Proquest: Science Journals and PsychINFO. Bibliographies of identified articles and books were reviewed in order to identify more studies. Experts in the field of early childhood development were consulted to assist in identifying other possible studies. No language restrictions were made during the search. The medical search terms (MeSH) that were used in the search included: motor, mental, cognitive, neurolog* development*, encephalopathy, HIV, AIDS neuropsychology*, child*, infants, toddlers and random*.

Published and unpublished articles were evaluated to determine whether they met the following inclusion criteria for selection in this systematic review:

- Primary studies that used randomised, cohort, cross sectional or quasi experimental designs,
- Reporting on motor and/or cognitive development,
- The Bayley Scale (first, second or third edition) used for measuring motor and cognitive development and,
- Participants in the studies being infants and toddlers aged less than 42 months who tested positive for the HIV.

The specific outcome measures of interest were motor and cognitive development of infants and toddlers.

The initial search yielded 319 studies. After reading the titles of the yielded results, 275 were excluded, as they were not relevant to the topic of this review. Forty-four abstracts were then read to identify relevant studies. Only 18 studies were deemed relevant following this process. Twenty-six abstracts were not considered, as they were literature reviews, commentaries or used
other scales to measure motor and cognitive development. Full-texts of the 18 studies were read and the methodological quality was assessed. Eleven studies met the inclusion criteria and were included in the review and meta-analyses and seven were further excluded due to inadequate methodology (Figure 3.1).

Table 3.1 contains studies that were excluded because of methodological reasons. Aylward, Butz, Hutton, Joyner, & Vogelhut, (1992), Pollack et al. (1996), Drotar et al. (1997), Fowlar et al. (2000), Macmillan et al. (2001), Nozyce et al. (2005) and Van Rie et al. (2009) were excluded from the review. Reasons for exclusion are summarised in the table.
Table 3.1  Characteristics of excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aylward 1992</td>
<td>Sample were children exposed to HIV and included children who were not HIV positive</td>
</tr>
<tr>
<td>Pollack 1996</td>
<td>Results were not clear</td>
</tr>
<tr>
<td>Drotar 1997</td>
<td>Delay was wrongly classified as composite score of less than 70 instead of less than 85.</td>
</tr>
<tr>
<td>Fowlar 2000</td>
<td>Only reported raw scores</td>
</tr>
<tr>
<td>Macmillan 2001</td>
<td>Data not clearly presented</td>
</tr>
<tr>
<td>Nozyce 2005</td>
<td>Only reported raw scores</td>
</tr>
<tr>
<td>Van Rie 2009</td>
<td>Reported on children aged 18 to 71 months</td>
</tr>
</tbody>
</table>

Studies were critically appraised using specific criteria to assess the methodological quality of relevant literature as specified in the “critical appraisal tool” developed by Loney, Chambers, Bennett, Roberts and Stratford (1998). This tool was used because it is specific for studies that estimate the prevalence and/or incidence of a health problem. The tool is the most widely used to appraise studies on incidence and prevalence of a health condition (Shamliyan, Kane & Dickinson, 2010). The researcher found no data on validity and reliability on this tool despite its wide use (Loney et al., 1998; Sanderson, Tatt & Higgins, 2007; Shamliyan et al., 2010). The tool consists of eight items grouped in three sections. The first section addresses the validity of the study design and the second, the interpretation of the results. The last section focuses on the applicability of the results. Two items were added to this tool. The items added were: “Was the purpose of the study stated clearly?” and “Was informed consent obtained?” The scoring system of the revised critical appraisal tool therefore consisted of 10 dichotomous questions; a positive answer scored one point (Table 3.2).
Table 3.2  Critical appraisal tool

<table>
<thead>
<tr>
<th>Item no.</th>
<th>Description</th>
<th>Score (1/0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Was the purpose of the study stated clearly?</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Was informed consent obtained?</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Validity of the study design</strong></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Appropriate sampling methods and frame</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Adequate sample size</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Appropriate outcomes measurements</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Appropriate response rates</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Interpretation</strong></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Prevalence given with confidence intervals,</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Adequate subgroup analysis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Applicability of the results</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Study subjects described in detail</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Setting described in detail</td>
<td></td>
</tr>
</tbody>
</table>

(Loney et al., 1998).

Two reviewers independently assessed the methodological quality of the studies without being masked to study authors. Following the methodological assessment, articles were excluded if they scored less than five on the critical appraisal tool.

### 3.2.2 Data extraction and analysis

Relevant data were extracted from individual studies using a standardized data extraction form. Information retrieved from the studies included: manuscript authors, year of publication, country, study design, sampling technique, population characteristics, measuring tool and results. Data were then captured into RevMan 5 programme. Meta-analyses were performed
and results presented in tables and graphs, supported by a narrative description of the findings.

The $I^2$ heterogeneity statistic test was used to determine the percentage of variability across the studies which were included in the meta-analysis (Montori, Hatala, Ioannidis, Meade, Wyer & Guyatt, 2008; Deeks, Higgins, & Altman, 2008). The random effects model was used if heterogeneity was observed. An $I^2$ value of 0% to 29% was considered as not important, 30% to 60% as moderate heterogeneity, 61% to 75% as substantial heterogeneity, and 76% to 100% as considerable heterogeneity. Although heterogeneity was undetected in the meta-analysis of mild motor delay, the random effects model was used, as the studies included were heterogeneous in relation to methods used to collect data, sample sizes and age groups of the children. Kontopantelis, Springate and Reeves (2013) support the use of the random effect model as assuming homogeneity often results in a misleading analysis, since heterogeneity is very likely present but undetected.

### 3.3 Description of studies

Eleven studies were included in the systematic review (Table 3.3). Research designs varied across studies. Two studies were randomised controlled trials, five were cohort studies, and three were cross-sectional studies and one study did not report on the design used. Five of the studies used convenient sampling while sampling methods were not mentioned in the other six. The sample size in the studies ranged from 10 participants to 595 participants. Six studies were conducted in Africa, three in the USA, one in Canada and one in Haiti.

Methodological quality ranged from five to eight on a ten-point appraisal tool. Studies by Chase et al. (2000), Llorente et al. (2003), Bailieu and Potterton
(2008), Ferguson and Jelsma (2009) and Potterton et al. (2009) scored eight affirmations for items on the methodological quality tool. Blanchette, Smith, Fernandes-Penney, King and Read (2001) scored the least on the appraisal tool. Blanchette et al. (2001) did not state if informed consent was obtained, the sampling method was not indicated, the sample size was not adequate and prevalence was not provided with confidence intervals (Table 3.3).
Table 3.3  Description of included studies

<table>
<thead>
<tr>
<th>Study author (year)</th>
<th>Design</th>
<th>Sampling</th>
<th>Sample size</th>
<th>Age (months)</th>
<th>Methodological quality (10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baillieu &amp; Potterton (2008) South Africa</td>
<td>Cross-sectional study</td>
<td>Convenience</td>
<td>40</td>
<td>18 -30 (range)</td>
<td>8</td>
</tr>
<tr>
<td>Blanchette (2001) Canada</td>
<td>NR</td>
<td>NR</td>
<td>50</td>
<td>24.7 ± 9.3 (mean, SD)</td>
<td>5</td>
</tr>
<tr>
<td>Chase (2000) USA and Puerto Rico</td>
<td>Prospective, natural history cohort</td>
<td>NR</td>
<td>595</td>
<td>4-30 (Range)</td>
<td>8</td>
</tr>
<tr>
<td>Ferguson (2009) South Africa</td>
<td>Cross-sectional</td>
<td>Convenience</td>
<td>34</td>
<td>15.8 (mean)</td>
<td>8</td>
</tr>
<tr>
<td>Gay (1995) Haiti</td>
<td>Cohort</td>
<td>Convenience</td>
<td>28</td>
<td>24 (mean)</td>
<td>7</td>
</tr>
<tr>
<td>Kigira (2008) Kenya</td>
<td>Observational Cohort</td>
<td>Convenience</td>
<td>36</td>
<td>10.9 (median)</td>
<td>7</td>
</tr>
<tr>
<td>Knight (2000) USA</td>
<td>Observational cohort</td>
<td>NR</td>
<td>45</td>
<td>11.4 (mean)</td>
<td>7</td>
</tr>
<tr>
<td>Ilorente (2003) USA</td>
<td>Longitudinal Cohort</td>
<td>Convenience</td>
<td>157</td>
<td>4 (mean)</td>
<td>8</td>
</tr>
<tr>
<td>McGrath (2006) Tanzania</td>
<td>Randomized double-blinded placebo controlled trial</td>
<td>NR</td>
<td>327</td>
<td>6 (mean)</td>
<td>7</td>
</tr>
<tr>
<td>Peterson (2001) Uganda</td>
<td>Cross-sectional</td>
<td>NR</td>
<td>10</td>
<td>20-30 (Range),</td>
<td>6</td>
</tr>
<tr>
<td>Potterton (2009) South Africa</td>
<td>A pragmatic randomized, controlled clinical trial</td>
<td>NR</td>
<td>122</td>
<td>18.0 (±8.1) in experimental group and 19.0 (±8.2) in control</td>
<td>8</td>
</tr>
</tbody>
</table>

NR: Not reported/not clear
3.4 Results of systematic review

Six studies reported on the prevalence of motor delay. There was substantial heterogeneity among the studies ($I^2 = 68.6\%$, $p = 0.007$). The study by Gay et al. (1995) had the lowest prevalence. The meta-analysis showed that the prevalence of motor delay was 82.78\% (CI 74.98 to 90.57) (Figure 3.2).

Only Baillieu and Potterton (2008) reported on gross motor and fine motor development separately. There was an 85.0% prevalence in gross motor developmental delay and 12.5% in fine motor developmental delay.
Ferguson and Jelsma (2009) did not report on cognitive delay. Meta-analysis of five studies showed that the prevalence of cognitive delay was in general slightly less than motor delay 75.80 (CI 65.89 to 85.72) (Figure 3.3).

**Figure 3.3  Meta-analysis of prevalence of cognitive delay**

<table>
<thead>
<tr>
<th>Study ID</th>
<th>ES (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gay 1995</td>
<td>67.86 (50.56, 85.16)</td>
<td>16.29</td>
</tr>
<tr>
<td>Kigira 2008</td>
<td>61.11 (45.19, 77.04)</td>
<td>17.62</td>
</tr>
<tr>
<td>Potterton 2009</td>
<td>78.69 (71.42, 85.96)</td>
<td>27.52</td>
</tr>
<tr>
<td>Ballieu 2008</td>
<td>90.00 (80.70, 99.30)</td>
<td>25.15</td>
</tr>
<tr>
<td>Blanchette 2001</td>
<td>72.22 (51.53, 92.91)</td>
<td>13.42</td>
</tr>
<tr>
<td>Overall (I² = 67.3%, p = 0.016)</td>
<td>75.80 (65.89, 85.72)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis.
Six studies were meta-analysed for mild motor development. The prevalence of mild motor delay across the studies was 15.26% (95% CI: 11.19 to 19.33). Prevalence ranged from 10.00% (95% CI: 0.70 to 19.30) to 27.78% (95% CI: 7.09 to 48.47). Although the $I^2$ test showed homogeneity amongst the studies, the random effects model was used as the studies used different sampling methods (Figure 3.4).

**Figure 3.4  Meta-analysis of mild motor delay**

<table>
<thead>
<tr>
<th>Study</th>
<th>ES (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferguson 2009</td>
<td>23.53 (11.89, 35.17)</td>
<td>12.23</td>
</tr>
<tr>
<td>Gay 1995</td>
<td>14.29 (1.32, 27.25)</td>
<td>9.87</td>
</tr>
<tr>
<td>Potterton 2009</td>
<td>14.75 (8.46, 21.05)</td>
<td>41.86</td>
</tr>
<tr>
<td>Ballieu 2008</td>
<td>10.00 (0.70, 19.30)</td>
<td>19.18</td>
</tr>
<tr>
<td>Blanchette 2001</td>
<td>27.78 (7.09, 48.47)</td>
<td>3.87</td>
</tr>
<tr>
<td>Overall ($I^2 = 0.0%$, $p = 0.457$)</td>
<td>15.26 (11.19, 19.33)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis
The prevalence of significant motor delay was reported in six studies. Heterogeneity was substantial among the studies ($I^2=70.6\%, \ p<0.004$) and the prevalence ranged from $35.71\% \ (95\% \ CI: \ 17.97 \ to \ 53.46)$ to $77.50\% \ (95\% \ CI: \ 64.56 \ to \ 90.44)$. The meta-analysis produced a combined prevalence of $64.53\% \ (95\%\ CI: \ 54.13 \ to \ 74.94)$ as illustrated in Figure 3.5.

**Figure 3.5  Meta-analysis of significant motor delay**

<table>
<thead>
<tr>
<th>Study</th>
<th>ES (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferguson 2009</td>
<td>66.67 (53.73, 79.60)</td>
<td>18.02</td>
</tr>
<tr>
<td>Gay 1995</td>
<td>35.71 (17.97, 53.46)</td>
<td>14.47</td>
</tr>
<tr>
<td>Kigira 2008</td>
<td>69.44 (54.40, 84.49)</td>
<td>16.41</td>
</tr>
<tr>
<td>Potterton 2009</td>
<td>72.13 (64.18, 80.08)</td>
<td>21.80</td>
</tr>
<tr>
<td>Ballieu 2008</td>
<td>77.50 (64.56, 90.44)</td>
<td>18.02</td>
</tr>
<tr>
<td>Blanchette 2001</td>
<td>55.56 (32.60, 78.51)</td>
<td>11.28</td>
</tr>
<tr>
<td>Overall (I$^2=70.6%, \ p=0.004$)</td>
<td>64.53 (54.13, 74.94)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis
The prevalence of mild cognitive delay was reported in five studies. The combined prevalence of mild cognitive delay was 21.85% (95% CI: 10.40 to 33.30). The $I^2$ test indicated considerable heterogeneity (79.5%) among the included studies (Figure 3.6).

**Figure 3.6  Meta-analysis of mild cognitive delay**

<table>
<thead>
<tr>
<th>Study</th>
<th>ES (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gay 1995</td>
<td>32.14 (14.94, 49.44)</td>
<td>16.83</td>
</tr>
<tr>
<td>Kigira 2008</td>
<td>5.56 (-1.93, 13.04)</td>
<td>24.48</td>
</tr>
<tr>
<td>Potterton 2009</td>
<td>26.23 (18.42, 34.04)</td>
<td>24.25</td>
</tr>
<tr>
<td>Balieu 2008</td>
<td>20.00 (7.60, 32.40)</td>
<td>20.70</td>
</tr>
<tr>
<td>Blanchette 2001</td>
<td>33.33 (11.56, 55.11)</td>
<td>13.74</td>
</tr>
<tr>
<td>Overall ($I^2 = 79.5%, p = 0.001$)</td>
<td>21.85 (10.40, 33.30)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis
The prevalence of significant cognitive delay was reported in five studies (Baillieu & Potterton, 2008; Blanchette et al., 2001; Gay et al. 1995; Kigira. Potterton & Obimbo, 2008; Potterton et al., 2009). It ranged from 35.71% (95% CI: 17.97 to 53.46) to 70.00% (55.80 to 84.20) and had a combined prevalence of 51.94% (95% CI: 40.92 to 62.96). Heterogeneity was substantial across the studies ($I^2=62.8\%$, $p=0.03$) (Figure 3.7).

**Figure 3.7 Meta-analysis of significant cognitive delay**

<table>
<thead>
<tr>
<th>Study</th>
<th>ES (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gay 1995</td>
<td>35.71 (17.97, 53.46)</td>
<td>17.87</td>
</tr>
<tr>
<td>Kigira 2008</td>
<td>55.56 (39.32, 71.79)</td>
<td>19.34</td>
</tr>
<tr>
<td>Potterton 2009</td>
<td>52.46 (43.60, 61.32)</td>
<td>27.41</td>
</tr>
<tr>
<td>Ballieu 2008</td>
<td>70.00 (55.80, 84.20)</td>
<td>21.45</td>
</tr>
<tr>
<td>Blanchette 2001</td>
<td>38.89 (16.37, 61.41)</td>
<td>13.93</td>
</tr>
<tr>
<td>Overall ($I^2=62.8%$, $p=0.029$)</td>
<td>51.94 (40.92, 62.96)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

**NOTE:** Weights are from random effects analysis
Mean composite scores for motor development ranged from 53.67 to 100 and for cognitive development from 65.61 to 97.7 (Table 3.4).

Table 3.4  Mean composite scores for motor and cognitive development

<table>
<thead>
<tr>
<th>ID</th>
<th>Mean composite score for motor development</th>
<th>Mean composite score for cognitive development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petersen 2001</td>
<td>79 (n=10)</td>
<td>79.3 (n=10)</td>
</tr>
<tr>
<td>McGrath 2006</td>
<td>92.2 (n=55)</td>
<td>96.9 (n=550)</td>
</tr>
<tr>
<td>Potterton 2009</td>
<td>53.67 (n=122)</td>
<td>65.61 (n=122)</td>
</tr>
<tr>
<td>Chase 2000</td>
<td>97.7 (n=78)</td>
<td>65.8 (n=80)</td>
</tr>
<tr>
<td>Knight 2000</td>
<td>79.8 (n=20)</td>
<td>76.1 (n=20)</td>
</tr>
<tr>
<td>Llorente 2003</td>
<td>100 (n=127)</td>
<td>97.7 (n=127)</td>
</tr>
</tbody>
</table>

3.5  Discussion

There are few studies documenting motor and cognitive development in young children. The purpose of this systematic meta-analysis was to synthesize research data on motor and cognitive development in children aged 0 to 42 months infected with HIV. By providing more precise estimates of motor and cognitive development in children with HIV, current practice and future research are expected to benefit.

The results of this systematic review showed delay in motor and cognitive development in HIV positive children. Several studies have reported on increased developmental delay in HIV infected children than those without the infection (Nozyce, Hittelman, Muenz, Durako, Fischer & Willoughby, 1994, Gay et al, 1995; Drotar et al, 1999). This study found higher significant delay than mild delay in both motor and cognitive development. One of the shortcomings in the included studies was the wide variability of ages of
subjects. Baillieu and Poterton (2008) assessed children aged between 18 and 30 months whilst in Ferguson and Jelsma (2009) children were aged between 6.2 and 31.7 months. In Gay et al. (1995), all children were assessed at 24 months.

Children develop more rapidly during the early months of life than later. This may create bias in interpretation of results, as age may be a confounding factor. Moreover, the timing of the HIV infection is variable. Only studies that used the BSID tool to measure motor and cognitive development were considered for the purpose of homogeneity. Some studies did not report on sampling methods and three used convenient sampling. This could have been a source of sampling bias. The obvious criticism of convenience sampling is that it is not representative of the population, hence generalisation is not possible. Most of the studies had smaller sample sizes. One of the main limitations to conducting studies focusing on development in children is time constraints and financial demands for assessment. A single assessment may take a long time to complete.

The variability in participants’ ages, the small sample sizes and different sampling methods may have contributed to the high heterogeneity between studies. Limited numbers of participants reduces the power to detect differences between groups. Despite the small sample sizes in individual studies, combining the studies and conducting a meta-analysis increases the power. One of the strengths of the studies included in this review was that they all used the BSID to measure motor and cognitive development.

Birbeck (2007) reported that, children who acquire HIV through vertical transmission have poorer motor development and lower cognitive scores than children born to mothers with HIV who do not become infected. Blanchette et al. (2001) state that, in children with vertically transmitted HIV, infection of the
CNS may occur early in the disease process, while the CNS is still immature. The authors argue that during infancy the brain still experiences a period of rapid myelination, which coincides with the attainment of significant motor and cognitive development.

The prevalence of motor and cognitive developmental delay prevails as life is prolonged with the use of ARVs. There is thus a need to follow the children up and implement relevant interventions that may improve their development. Early delineation of motor and cognitive delay can be helpful in diagnosis and assessment of treatment outcomes and research.

3.6 Conclusion
This study aimed at developing our current understanding of the prevalence of motor and cognitive development in children infected with HIV. Our findings suggest that there is a higher prevalence of motor and cognitive developmental delay in children infected with HIV. Motor and cognitive developmental assessments and interventions based on the outcomes are crucial and should be incorporated in paediatric HIV care. Most of the studies were conducted when HAART was not available to children. Studies to evaluate motor and cognitive development in children on HAART would be beneficial. Despite methodological weaknesses, the literature has shown that paediatric HIV affects children's motor and cognitive development. It is highly recommended that more studies be conducted on motor and cognitive development in infants and toddlers with better research designs to confirm these findings. Such studies should consider larger sample sizes and randomly selected participants from relevant populations.
4.1 Introduction

Chapter four presents the methodological framework of actions that were used to collect, analyse and interpret the information to increase the understanding of the effect of a home-based physical intervention programme in combination with massage therapy on the promotion of motor and cognitive development in HIV positive children. The purpose of the study, hypothesis, definitions, conceptual framework, paradigm, approach, design, intervention, procedure, population and study sample are discussed to ensure that the relationship between the problem statement and the research objectives are addressed using the most appropriate scientific approach. Ethical considerations related to the project are presented.

4.2 Research purpose

The purpose of the prospective, randomised controlled study was to establish whether the implementation of a home-based physical activity programme in combination with massage therapy could enhance the motor and cognitive development of HIV positive children aged 36 months or less who attended the paediatric HIV clinic at Frere and Cecelia Makiwane hospitals. The principle independent outcomes measured were cognitive and motor development as measured on the Bayley-III scale assessment tool.
4.3 Hypothesis

The hypothesis is a tentative testable prediction, which designates the relationship between two or more variables. To allow for statistical hypothesis, testing the null and the alternative hypothesis are considered. It is commonly accepted that the normal sampling distribution mean for a normal population is equal to 1.00. Empirically it can be deduced that about 95% of all samples forming the population will have a sample mean within two standard deviations of the mean. Thus, there is less than a 5% probability that a sample mean beyond two standard deviations of the population mean will be measured. The hypothesis in this study was tested through the implementation of a randomised controlled trial (Fewster, 2013).

The null-hypothesis ($H_0$) tentatively states that there is no difference in motor and cognitive development between HIV positive children up to the age of 36 months who receive a home-based physical activity programme in combination with massage executed at least once a day for six months and those who do only receive massage therapy. The decision to accept or reject the null hypothesis was based on a p-value of less than 0.05.

Using the alternative positive ($H_1$) experimental hypothesis it was postulated that a specifically designed home-based physical activity programme in combination with massage therapy would increase motor and cognitive development in the exposed group by 15% as measured on the Bayley-III assessment scale.
4.4 Conceptual framework

The conceptual framework that served as a guiding principle for the study was based on several theories discussed in chapter two. The theoretical assumption for this study recognises that genetic and social factors may influence motor and cognitive development in infants and toddlers (Gauvain & Cole, 1997; Oakley, 2004). In addition, environmental factors that may influence motor and cognitive development are included in the conceptual framework (Smith et al., 2006).

The conceptual framework of this study is consistent with the Dynamic Systems Theory, Jean Piaget’s stages of cognitive development theory, Vygotsky’s social development theory, the Brain Plasticity Theory, and the conceptual framework of the International Classification of Functioning, Disability and Health (ICF) (Figure 4.1).

Milestones in most infants develop in the same order, at approximately the same age and in stages (French & Sim, 2004; Oakley, 2004). This is in line with Piaget’s Theory, which suggests that development occurs in distinct phases (Potts & Mandleco, 2002). All infants are genetically pre-programmed in these abilities, but will also take cognisance of the fact that the child will develop in a cultural setting (Piek, 2006). Motor and cognitive development takes place in children from primitive skills, to more complex skills, as they engage with their environment (Bremner & Fogel, 2004; Li & Rogers, 2006). Early exposure to physical activity and stimulation may lead to promotion and development of motor and cognitive development.
Brain plasticity theories and early interventions are essential, for stimulating motor and cognitive development and are enriched by approaches increasing the emphasis on human development and social participation (Camden, Tétreault & Swaine, 2013). Plasticity refers to a constantly changing brain in function and structural properties depending on changing inputs and experiences. In Kaas, Merzenich and Killackey's (1983) study, brain activation patterns were noted after abolishing peripheral inputs and
confirmed that plasticity of the brain exists within the neuromotor pathways. The brain can adjust itself in terms of sensory information depending on the information, which is received, and tactile information may directly influence the development of neuromotor pathways (Kaas et al., 1983). Kaas’s work primarily focused on the sensory cortex and his contribution suggests that internal representation can be altered by what transpires externally (Kaas et al., 1983). The research suggests that tactile and sensory information can be used to augment the development of more intact or new pathways and cortical maps (Kaas et al., 1983).

Kaas’s research and the theory of brain plasticity insinuates that external input, such as that arising from sensori-motor stimulation, may change internal representations and create new pathways in the brain which affect both recognition and use of sensori-motor information (Kaas et al., 1983). As a result, stimulation of developmentally delayed children through a specialised physical activity programme may promote development. Besides considering chronological age, people involved in rehabilitation should consider the developmental age of children in each of their life areas (e.g. motor, cognitive and social) in order to identify the most appropriate goals and methods of intervention (Kramer & Hinojosa, 2010).

The goal of paediatric rehabilitation according to the conceptual framework of the International Classification of Functioning, Disability and Health, interventions, is to alleviate the effects of impaired body structures and systems. Furthermore, the goal is to foster the development of children’s capacities and their participation in various activities; and to reinforce environmental facilitators (e.g. education to parents or primary caregivers and adaptation of the physical environment) (WHO, 2011). The clinical picture of children infected with HIV and their needs in terms of motor and cognitive development is diverse. In addition, the survival of infected children is
increasing due to improvement in access to ARVs, medicine and pharmacology. Consequently, the number of children in need of intervention to improve motor and cognitive development is high, and the provision of the required services is likely to extend for a longer term.

The development of newer technology contributes to increasing pressure on health care. Early intervention and enhanced services when children are very young are based on brain plasticity theories (Camden et al., 2013). The planning of physical activity interventions for infected children with developmental delay is thus set within a long-term perspective. However, waiting lists often compromise access to services, and as a result, are most likely to affect the well-being of children (Grilli et al., 2007; Freeman, 2008). Accessing such health care at health facilities can cause tremendous financial burdens on the family especially in the resource-limited context. Primary caregivers of children form early bonds with health facilities and have the potential to be rehabilitation agents. Besides the HIV diagnosis, the uncertainty of the prognosis may contribute to increased level of stress in parents and primary caregivers. However, these individuals often wish to provide children the opportunity to achieve their full potential (Camden et al., 2013).

The conceptual framework therefore supports incorporating parents and primary caregivers for optimal functioning and social participation in the short term and setting within a long-term perspective of prevention as these domains are determining factors of the child's future health status (Camden et al., 2013).
4.5 Research methodology

A systematic and logical methodology was used to underpin the research methodology for this study.

4.5.1 Research paradigm

The researcher as a scientist strived to obtain purposeful knowledge, without being involved in the decisions that could influence the outcomes. He took an etic (outsider’s) view to try and understand the effect of a home-based physical activity programme in combination with massage therapy intervention on the promotion of motor and cognitive development in HIV positive children. A positivistic paradigm was thus followed to direct the research. The positivist paradigm asserts that real events can be observed empirically and explained with logical analysis. The criterion for evaluating the validity of a scientific theory is whether our knowledge claims (i.e., theory-based predictions) are consistent with the information we are able to obtain using our senses. Positivist research methodology (methodological individualism) emphasizes micro-level experimentation in a laboratory-like environment that eliminates the complexity of the external world (e.g., social, psychological, and economic linkages between unemployment, and crime or suicide). Epistemologically this paradigm ensured that the researcher and the participants were independent while testing the hypothesis through objective measurements, which can be replicated in the future. The viewpoint enforces the value that the findings would be considered as a true reflection of the reality so that the hypothesis could be accepted or rejected after the results have been made known. A randomised controlled trial was used to ensure that the researcher’s axiology was controlled, thus not to influence the results. Ontologically this paradigm and the chosen research methodology were chosen to ensure that the findings could be generalised if the statistical relationships are shown to be significant. Procedural objectivity was ensured
by following a detailed procedure, whilst, limitations and protocol violations are acknowledged (Creswell, 2012).

4.5.2 Research approach and study design

A quantitative research approach was used as the aim of this study was to conduct a systematic, experimental investigation to test a hypothesis, using a predetermined calculated sample size and predetermined statistical analysis procedures to ensure that the results are unbiased and applicable to the greater population. The quantitative approach supports the principle that findings are presented in numerical formats. The strength of a quantitative approach is the fact that precision is enhanced through reliable instruments, causal statements can be tested through controlled experiments, the study is replicable and can be generalised to the greater population (Creswell, 2012; Hughes, 2012). A limitation of a quantitative approach is that the strict implementation of randomisation, manipulation and control exclude notions of freedom and do not allow people to interpret their own experiences.

This study embarked on an experimental design (pre-test - post-test controlled design). Experimental or intervention studies, as explained by Bonita Beaglehole and Kjellström (2006) involve an active attempt to change a disease determinant such as an exposure, behaviour or the progress of a disease through treatment. Alternatively stated, the study sought to establish whether the intervention (home-based physical activity programme in combination with massage therapy) had the planned causal effect on the participants who received the treatment (improved motor and cognitive development). Three components have been described as key concepts of an experimental study design, namely, randomisation, manipulation and control. These key components ensure strong internal validity, which enhances the probability of deciding whether the home-based physical
activity programme in combination with massage therapy had a causal effect on the exposed participants. Experimental methods allow researchers not only to describe and predict but also to determine whether a cause-and-effect relationship exists between the variables of interest and can lead to some firm conclusions (Oakley, 2004; Jackson, 2009). Moreover, the findings of an experimental study can be applied to the greater population with similar characteristics and the use of experiments therefore makes for reliable and valid research and results (Oakley, 2004).

Experimental designs also have limitations, as a time frame is often set for completion (Oakley, 2004). Often experimental conditions are unnatural, restrictive and outside the experience of many children and results can be obtained which may not be a representation of the child’s natural behaviour (Oakley, 2004). A child may perform below his/her level on the measuring instruments as a result of being exposed to an unfamiliar environment. This is obviously important if decisions about development are made based on the findings (Oakley, 2004). While no experimental design is perfect and entirely free from validity threats, the goal of scientific research is to minimize threats to the validity of one’s study in order to provide as adequate a test of the hypothesis as possible (Keenan & Evans, 2009).

Randomisation can be achieved by using an electronic or manual random calculator to randomly assign participants to a treatment (receiving the home-based physical activity and massage therapy programme) or control group (massage therapy alone). Of utmost importance is that participants should have an equal chance to be assigned to either of the groups. The use of randomisation is to reduce bias by spreading variation to extraneous variables equally between the groups in the study (Jackson, 2009). Although it does not guarantee that the groups will be similar at baseline, it reduces the risk that a significant difference may occur at baseline. It is also important
that the sample size is large enough and correctly calculated to ensure that the baseline data are similar and that the differences between the groups after the intervention are caused by the intervention and not by chance (Creswell, 2012).

Jackson (2009) states that the researcher manipulates the independent variable (implementation of a home-based physical programme combined with massage therapy), and measures the dependent variable (motor and cognitive development) in order to establish the cause-and-effect relationship. It is important that the control group receive similar treatment as the intervention group except for the independent variable. Thus, the routine care that the groups receive, for example, follow-up calls or visits should be the same and the only difference between the control group and the intervention group should be the intervention (Bonita et al., 2006).

Shadish, Cook and Campbell (2001) assert that in order to validate inference, threads should be eliminated through control over the research environment, the intervention and the extraneous variables. Control strengthens the internal validity of experimental designs and manages unwanted variables that may cause a difference in the dependant variable (outcome).

Randomised controlled clinical trials are often referred to as the "gold standard" of experimental designs as they provide the most effective way to control for extraneous variables when an intervention is tested. A randomised controlled trial (RCT) is the best design to follow in order to answer the primary objective of the study, which seeks to investigate whether a home-based physical activity programme combined with massage therapy can enhance motor and cognitive development in HIV positive children. In a randomised controlled trial design, participants have an equal chance to be assigned to the control or the treatment group (West et al., 2008).
A strict procedure was followed to ascertain that participants in both groups were treated the same except for the intervention that was given to the treatment group. Advantages of an RCT included the random assignment of participants to make sure those environmental factors that may affect the outcome are uniformly distributed across conditions. Since random assignment balances the two groups for extraneous variables, there is some guarantee that the difference in the outcome is actually caused by the intervention. The use of an RCT design further eliminates bias and confounding variables whilst it facilitates blinding if correctly applied (Spring, 2007).

A disadvantage of an RCT is that some may claim that it is not generalisable as the study was done under optimal and controlled settings (efficacy or explanatory trial) to produce the expected therapeutic effect and therefore, may exclude children in the general population with characteristics other than the target population (real world -effectiveness or pragmatic trials). Thus, external validity is limited and findings cannot be applied to, for instance, populations in other countries or study procedures maybe difficult to apply in the real world (Van Spall, Toren, Kiss & Fowler, 2007). However, it is known that once an intervention has shown to have efficacy, its effectiveness can be tested at a later stage in community settings or the real world. This study falls on a continuum between an efficacy and effective study as the researcher aimed to address the internal validity in that he proposed the intervention would enhance motor and cognitive development in HIV positive children, but also wished to ensure that the results had external validity to the greater population of HIV positive children.

Concerns about RCTs are also raised in relation to withholding treatment to the control group in placebo trials. This was a challenge to this study, as the University of the Western Cape Ethical committee did not accept the original
proposal when it was proposed that the home-based physical therapy programme be the only intervention and that the control group receive only standard care. The ethical committee approved the proposal on condition that the control group receive a “dummy” intervention. The reason given by them was that it might reduce group contamination. The researcher contested the recommendation but it was not accepted and had to revert by including massage to both groups.

Other significant disadvantages of RCTs are that they are costly, time consuming and need to be executed strictly according to protocol (Johnston, Rootenberg, Katrak, Smith & Elkins, 2006). The effectiveness of an RCT depends on the extent of how logically the researcher deduced that the home-based physical activity programme combined with the massage therapy indeed caused the difference in motor and cognitive development. The ability to make valid conclusions depends on how well the researcher planned, conducted and reported on measures to minimize bias (Sanson-Fisher, Bonevski, Green & D’Este, 2007).

Critical aspects such as, bias, randomisation, blinding, sample and intervention, to mention a few, were addressed to ensure that this study met the criteria of a randomized controlled trial. These critical aspects together with how it was applied in the study are discussed in the following paragraphs.

### 4.5.3 Intervention

The early developmental intervention method was used with the aim of improving the overall motor and cognitive functional outcomes of the infants in the intervention group.
4.5.3.1 Intervention group

The intervention consisted of a specific therapeutic exercise programme specially designed to meet the needs of each individual participant as identified following the Bayley-III scale assessment. The caregiver also received specific verbal information on child development, related to the identified problems (Blauw-Hosper et al., 2007).

The needs were identified for long and short-term functional outcomes, the functional abilities and the impairment specific goals. The neuro-developmental treatment approach was used to achieve the specific outcomes as NDT is aimed at improving motor and cognitive development and to promote the most independent function possible according to the child's age and abilities. Although traditionally NDT is targeted at motor development, it allows more opportunities for the child to interact with the environment. Blauw-Hospers et al. (2007) reported that early childhood developmental programmes often do not only aim at the improvement of motor outcome but also at the facilitation of cognitive development.

Caregivers of children in the intervention group were given individual demonstrations of physical and educational activities to administer at home. The techniques were demonstrated while the caregiver observed the researcher. The caregiver was then asked to demonstrate the activities back to the researcher to ensure the instructions were understood. Caregivers continued to demonstrate until the researcher was satisfied that the instructions were understood. Caregivers were advised to perform the exercise routine with the child every day and as often as possible until the next clinic visit (three or six months visits). The number of repetitions per activity was determined individually. Caregivers were also provided with toys, books and pictorials appropriate to the child's age to incorporate when
applying physical activity. Short term and long term goals were determined together with the caregiver.

4.5.3.2 Massage therapy
Caregivers in both groups were given demonstrations on how to massage their infants or toddlers. The research assistant demonstrated the stroking techniques to the caregiver and the caregiver was given an opportunity to demonstrate back to the research assistant. A sufficient supply of baby oil, sponsored by Johnson and Johnson (Pty) Ltd., was provided to all caregivers, including a pictorial guide, depicting the instructions on how to effectively massage their children. The guides were sponsored by Johnson and Johnson (Pty) Ltd. and available online at: http://www.babycenter.com.au/i/advertorials/Massage_Poster.pdf.

4.5.3.3 Control group
Caregivers, infants, and toddlers in the control group were only exposed to the demonstration of massage therapy and provided with oil and massage guides as described above. Thus, the only difference between the control group and the intervention group was the home-based physical activity programme.

4.6 Research setting
The study was conducted at two hospitals in East London, Eastern Cape in the Republic of South Africa. East London is located in the Amatole District. The institutions are known as the East London Hospital Complex. Cecilia Makiwane Hospital and Frere Hospitals form this hospital complex. The facilities have dedicated clinics for HIV-infected children. The services
offered include the provision of anti-retroviral drugs for children who meet the criteria. Mothers or caregivers bring their children for assessment and to collect medication at least once a month. The hospitals provide services to patients in the city and villages in the outskirts of East London. Both hospitals have physiotherapy departments. There were four physiotherapists working at Frere Hospital and three at Cecilia Makiwane Hospital during data collection. Nevertheless, the children attending the clinics were hardly referred for physiotherapy. The HIV clinic staff did not include any rehabilitation staff and children displaying severe motor and cognitive development are hardly ever referred to rehabilitation services.

4.7 Population, study sample and inclusion criteria
The study population consisted of all children who were HIV positive, attending HIV clinics at Frere and Cecilia Makiwane Hospitals in East London in the Amatole District of the Eastern Cape Province. HIV prevalence (27.2%) in the Amatole District was the third highest in the Eastern Province in 2009 and the highest (31.6%) in 2010 (DOH, 2010b). Approximately, 400 children attend HIV clinics at each of the hospitals every three months. About 20% of these are aged between 0 and 36 months. Each hospital has about a thousand HIV positive children in the registry, although not all are seen every month. The majority of the children are from disadvantaged communities and are brought to the clinic mostly by the mother or primary caregiver.

4.7.1 Inclusion and exclusion criteria
All HIV positive children attending the HIV clinics at the two hospitals at the time of data collection were eligible to enter the study. The inclusion criteria were based on the following;

Confirmed HIV positive status
Eligible to receive antiretroviral treatment or HAART
Aged between one and 36 months
Signed informed consent form by parent or legal guardian
Resident in the Eastern Cape Province and available during the period of intervention and data collection

Infants with the following conditions were excluded from the study:
- Profound mental or physical disabilities
- Congenital abnormalities
- Participating in any other clinical trial

Profound mental disability was defined as a disorder characterized by significantly impaired cognitive functioning and deficits in adaptive skills (Belva & Matson, 2013). Physical disability was defined as any disability which limits the physical functioning or requires supervision to perform at least one activity of daily living (Pumkam, Probst, Bennett, Hardin, & Xirasagar, 2013). Profound mental and physical disabilities require pervasive support and such children may have difficulties with communication, self care and problem solving.

4.8 Sample size calculation
A computer programme was used to determine the sample size. The sample size was calculated based on a 5% level of statistical significance (p < 0.05) and a power of 80% (β=0.20). The primary hypothesis to be tested in the trial was based on a repeated measures design with a single between-subjects factor (i.e massage and physical activity vs massage only). The measurement was based on whether the use of home-based physical activity programme in combination with massage therapy could result in a 15% difference (improvement) in motor and cognitive development between the
two groups at the end of the six months intervention period using the Bayley-III scale. The 15% is based on a study by Trahan and Molouin (2002), who reported an increase of 3 to 15% in motor development following a six-month physical activity intervention. Trahan and Molouin (2002) claimed that differences at this level are deemed to be clinically significant. Input parameters for the calculation of the sample size were based on mean Psychomotor Development Index (PDI) values obtained by Bayley (2006) in a validation sample. The software used was the EpilInfo version 7. The software requires the following: the "known" mean value for the population, the "expected" mean value from the sample (to be considered as a significant difference), the chosen value for alpha (α) and power of the test. The following values were entered:

- The "known" mean value for your population: 83 (Blanchette, 2000)
- The "expected" mean value from the sample: 98 (15% increase in mean)
- The value for alpha (α): 0.05
- Power of the test: 0.80

Using above calculations a sample size of 118 participants, 59 in each group, were required. Considering a possible 10% dropout rate, a sample size of 130 participants was determined.

4.9 Data collection
Baseline information including socio-demographic information, birth history data and birth anthropometric data were captured from the participants' clinic card. A case report form (CRF) was used to collect basic information on socio-demographic indices including: maternal age, parity, marital status, education, employment, gestational age at delivery and mode of delivery, the child's age and gender, viral load and CD4 count and pregnancy history. Anthropometric measurements were done using an infantometer, stadiometer
and a digital weighing scale by the researcher who was assisted by the research assistant. The Bayley-III assessment was done by the researcher and the scores were recorded on the CRF and the Bayley-III record form. The variables recorded were developed with reference to literature (Nozyce et al., 1994; Smith et al., 2006).

### 4.9.1 Bayley scale of infant and toddler development

The Bayley Scales of Infant Development third edition (Bayley-III) assesses the developmental functioning of infants and young children aged between 1 month and 42 months (Bayley, 2006). The third version was produced to improve the quality and enhance the utility of the instrument (Bayley, 2006). The Bayley-III normative data were generated from a standardization sample of 1700 children aged 1–42 months. The standardization sample was stratified on: parent education, race/ethnicity and geographic region to represent the 2000 United States of America (USA) Census data for children aged 1–42 months (Bayley, 2006). Bayley-II was validated in a South African population in the 1980s (Richter & Griesel, 1988; Richter, Griesel & Rose, 1992). The Bayley-III indices and subscales have good internal consistency; coefficient alphas of ≤ 0.86 (Bayley, 2006). The main use of Bayley-III is to identify developmental delay in five domains and to provide information for intervention planning. These domains are: cognitive, language, motor, social-emotional and adaptive. It takes 30 to 90 minutes to administer, depending on the age of the child.

The Bayley-III scale was used in this study to assess the participants’ cognitive, gross and fine motor development. The full kit includes the following materials: an administration manual, a technical manual, a stimulus book, record forms, a social-emotional and adaptive behaviour questionnaire, a caregiver report used to interpret results to the caregiver, a scoring
assistant with a personal digital assistant (PDA) administration, an accompanying user’s guide and a large kit of administrative toys. The variety of toys is of interest to infants and young children and facilitates their involvement in the tasks (Bradley-Johnson & Johnson, 2007). The researcher purchased the Bayley-III Scale of Infant Development. His qualifications and experience (user level) in testing methods of the Bayley-III were assessed and approved (NINDS CDE, n.d.). Pearson Education, Inc owns the instrument and all written information is copyright protected (NINDS CDE, n.d.). Duplications of the instrument are therefore not attached as an appendix to this thesis (NINDS CDE, n.d.).

4.9.1.1 Mental Developmental Index (MDI)
The MDI (cognitive development) contains 91 items which assess a variety of skills including sensori-motor development, exploration and manipulation, object relatedness, concept formation, memory and other aspects of cognitive processing (Bayley, 2006; Bradley-Johnson & Johnson, 2007). The strength of this scale is that 21 items are timed, no vocalization is required on any of the items, and, therefore, can be used with children who cannot or will not vocalize during testing, or those whose speech cannot be understood (Bradley-Johnson & Johnson, 2007). The Bayley-III provides scaled scores, composite scores, growth scores, percentile ranks, confidence intervals and developmental age equivalents for the cognitive scale (Bayley, 2006).

4.9.1.2 Psychomotor Developmental Index (PDI)
The Psychomotor Development Index (motor development) is divided into two subtests, one to test fine motor and the other gross motor development. Individual scaled scores, growth scores and developmental age equivalents are provided for fine and gross motor subtests. Composite scores, percentile
ranks and confidence intervals are provided for the general motor scale which is a combination of both the fine and gross motor subtests (Bayley, 2006).

4.9.1.3 Fine motor subtest
The fine motor subtest consists of 66 items which contain perceptual-motor integration, motor planning and motor speed and assesses skills in infants and toddlers related to visual tracking, reaching, object manipulation, grasping and responses to tactile information (Bayley, 2006).

4.9.1.4 Gross motor subtest
The 72 items in the gross motor subtest measures movements of the upper and lower limbs and torso and assess static positioning such as sitting and standing; dynamic movement, including locomotion and coordination; balance and motor planning (Bayley, 2006).

Raw scores obtained by participants on measures have little or no meaning. In order to make the interpretation more meaningful, these raw scores are converted to normal scores through statistical transformation. Individual raw scores on the Bayley-III are measured against norms whereby an individuals’ position is related to that of the normative samples. Performance on Bayley-III is represented in the form of scaled scores, composite scores, percentile ranks and growth scores (Salvia, Ysseldyke & Bolt, 2010). The growth scores can be plotted for an individual child to determine relative growth over time (Bayley, 2006). The degree of neuro-developmental disability are classified as normal or not delayed (scores of $\geq 85$), and delayed (scores of $< 85$).
4.9.2 Anthropometry

Length of infants was measured in centimetres (cm). A Seca 416 infantometer was used to measure length. Its measuring range is 33 to 100cm and is used for children aged 0 to 2 years. The equipment was placed on a firm flat surface on the floor. Before beginning the procedure, the researcher or research assistant politely explained to the caregiver what they were going to do. The caregiver was requested to undress the baby before he/she was placed on the board. This was done to reduce errors in measuring. A light piece of cloth was placed on the surface of the board to avoid soiling. The child was gently placed in a supine position on the board. The person taking the measurement knelt on the right side of the infant and held the foot piece with his right hand. The assistant supported the infant’s crown of the head against the headboard by cupping both hands over the infant’s ears so that he/she was looking straight up. The infant’s line of sight was perpendicular to the ground. The researcher straightened the infant’s lower limbs by gently pressing on the shins or knees. Extra care was taken not to use excessive pressure, which may cause discomfort or trauma to the child. The foot piece was pushed until it touched the infant’s heels, which were perpendicular to the board and flat against the foot piece. The researcher then read the measurement on the scale and recorded the length to the nearest 0.1 cm in an anthropometry log section of the CRF. The measurement was repeated to ensure reliability. The caregiver was informed of the baby’s length, requested to gently lift the baby off the measuring board and thanked.
A wall mounted stadiometer was used to measure height for children older than 2 years. The research assistant assisted the researcher in measuring the height. The following guidelines were followed during the measuring of height. Shoes and socks were removed from the children prior to measuring the height. The head plate was raised to allow sufficient room for the child to stand underneath it. The children were made to stand with their feet flat on the centre of the base plate, feet together and heels against the rod. The child's back was placed as straight as possible, preferably against the rod, and they were asked to have their arms hanging loosely by their sides facing forwards. The measuring arms were placed just above the child's head. The child's head was moved so that the Frankfort Plane was in a horizontal position.

The procedure was explained to the child and their parent(s) or guardian so that they could understand that the child's head needed to be supported.
when taking the measurement. The child’s head was cupped in the researcher’s hands by placing the heels of his palms either side of the chin, with his thumbs just in front of the ears, and his fingers going round towards the back of the neck. Firmly but gently, upward pressure were applied to lift the child’s head upwards towards the stadiometer headplate and thus stretching the child to their maximum height. Jerky movements were avoided. The research assistant helped to lower the headplate down gently onto the child’s head to ensure that the plate touched the skull softly. While holding the child’s head, the traction was relieved and the child was allowed to stand relaxed. Care was taken that the children did not knock the head plate as they stepped off. The height measurement was read in metric units to the nearest millimetre and the reading was entered. The procedure was repeated once to ensure reliability of the reading.

Weight of infants was measured in kilograms (kg) to one decimal point. A Seca 872 flat digital weighing scale was used to measure weight. The scale is set to measure weight in kilograms. The ‘mother-baby-function’ allows for the mother’s and baby’s weight to be measured simultaneously with the baby’s weight being automatically computed as the difference between the mother and baby’s weight and the mother’s weight alone. The scale was placed on flat ground. Before beginning the procedure, the researcher or research assistant politely explained to the caregiver what they were going to do.

The caregiver was requested to completely undress the baby. She could use a light sheet to temporarily cover the baby until when the baby is handed to her during weight measurement. The researcher briefly and gently stepped on the weighing platform to switch the scale on and waited until ‘0.0’ appears on the digital display. The caregivers were requested to stand on the scale, making sure her feet were placed along the imprinted foot marks on the weighing platform and asked to look straight ahead and stand still.
Once the value was stable, the caregiver’s weight appeared on the digital display. The weight was recorded to the nearest 0.1kg on the CRF. After the reading was recorded the mother-and-baby key was activated. The scale stores the weight of the mother and ‘0.0’ appears on the display. The infant was then handed without any clothing to the caregiver. Once the value was stable, the baby’s weight appeared on the display. The weight was recorded to the nearest 0.1kg on the anthropometry log section of the CRF. The caregiver was asked to step off the scale and to dress the baby. The infant’s weight was plotted on the health card to provide a reference point for growth monitoring. The caregiver was informed of her/his weight and her/his baby’s weight and thanked her for her cooperation. The procedure was repeated to ensure reliability of the measurements.

4.10 Pilot study
The research design, assessment tools and interventions were tested on 13 participants aged less than 36 months prior to commencement of the main study. The aim of the pilot study was to estimate the duration of assessment of participants, familiarise with measuring instruments, to identify any training needs of the assessor and research assistant and to determine the likely success of the recruitment strategy and willingness of clinicians and nurses to support the recruitment process. Thirteen mothers attending HIV baby clinics at Cecilia Makiwane Hospital were approached to participate in the pilot study. Time taken for each assessment was approximately 45 minutes. Measurements for motor development, cognitive development, height and weight were performed twice on each child and intra-rater reliability measured. The assessor read all the material provided for carrying out assessments using the Bayley-III scales for motor and cognitive development. A digital versatile disc (DVD) was viewed several times to observe how the assessments were done. Time taken to complete and individual assessment
was observed on infants and toddlers at various ages. No additional information was added to the CRF. Nursing staff and clinicians assisted in identifying potential participants for the pilot study. The children in the pilot study were aged between 3 and 36 months (average age was 19 months). The average height and weight were 74.4 cm and 9.4 kg respectively. There were five females and eight males. The average motor and cognitive composite scores were 85 and 90 respectively. Three children had cognitive delay and six were delayed in motor development. Results of the pilot study were excluded from the main study.

The researcher evaluated the convenient sample of 13 participants in the morning and after a minimum of two hours. The intra-rater reliability was calculated using the Pearson correlation coefficient and was high for the two measurements for height, weight, cognitive and motor scaled scores (Table 4.1). The table indicates the Pearson correlation coefficients of the sets of scores. The Pearson correlation coefficient has values ranging from −1 to 1. If the Pearson correlation coefficient has a value of 1, it means that a linear equation describes the relationship between x and y perfectly, and all data values lie on a line for which y increases as x increases. The Pearson correlation coefficients for height, weight, gross motor scaled score, fine motor scaled score, and cognitive scaled score showed good correlation.

Differences between first and second measurements on the Seca 872 flat digital weighing scale were not wide. The difference ranged between 0 and 0.6 and 0 to 0.8 for the stadiometer.
### Table 4.1  Pilot study results

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pearson r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>0.99</td>
</tr>
<tr>
<td>Weight (g)</td>
<td>0.99</td>
</tr>
<tr>
<td>Gross motor scaled score</td>
<td>0.99</td>
</tr>
<tr>
<td>Fine motor scaled score</td>
<td>0.98</td>
</tr>
<tr>
<td>Cognitive scaled score</td>
<td>0.99</td>
</tr>
</tbody>
</table>

### 4.11 Reliability and validity

A general distinction between internal and external validity is that the later relates to conditions internal to the study design such as selecting study participants from only one kind of background and the former focuses on whether the study findings can be generalised to other settings and participants (Keenan & Evans, 2009). As in any other kind of assessment, errors can occur during the assessment of motor and cognitive development in infants and toddlers. Sources of error include effects of the participant characteristics, characteristics of the assessor and the testing situation (Griessel, 2005). Fluctuations in test results in infants/toddlers that are affected by HIV/AIDS may occur because of their health status at the time of assessment (Luiz et al., 2005).

Pannucci and Wilkens (2010) are of the opinion that bias is a systematic error that occurs when scientists influence the true effects of a study in order to depict a certain outcome, leading to invalid conclusions. Random bias such as chance and confounding can be avoided by using an appropriate study design, study sample and statistical methods. “Systematic Biases are reproducible inaccuracies that produce a consistently false pattern of
differences between the observed and the true values” (Krishna, Maithreyi & Supapaneni, 2010, pp. 2321).

Bias can be introduced during any of the following phases of research: planning, design, data collection, analysis, interpretation or publication of the results (Pannucci & Wilkens, 2010). The most frequent types of bias that influence the validity are: selection bias, measurement bias and intervention bias (Krishna et al., 2010). The researcher used specific strategic measures to maximize internal validity, minimize bias and minimize threads to external validity during the planning, design, data collection, and analysis and interpretation phases of the study.

Random allocation occurred after inclusion and exclusion criteria were verified and the baseline data were collected to ensure that selection bias could not interfere, participants had an equal chance to be assigned to either of the groups and baseline data did not differ between the two groups. Measurement bias was addressed in this study by ensuring that the equipment that was used, such as the scale was calibrated at regular intervals. The Bayley-III scale was used as it is validated for use in the South African population and is sensitive enough to measure motor and cognitive development in the sample and detect delays in development (Krishna et al., 2010).

Expectation bias was a limitation in this study in that the participants knew the researcher and the assistant at the follow up visits. The researcher relied on the concept that time would reduce the possibility that he would remember what group the participant was allocated to. During the follow-up visits, the Bayley scale assessment test was done before the researcher reminded himself to which group the participant belonged. Cognisance is given that this knowledge may have favoured the treatment group.
Individual appointments were given but, contamination of the control group was possible in that the caregivers may have sat in a waiting room where they could have exchanged discussions about the intervention with other caregivers. Special caution was taken to ensure that none of the participants in the control group inadvertently received the intervention.

Exclusion criteria ensured that the participants did not participate in any other research project that could have introduced co-intervention bias. The duration of the intervention was only for six months and there is no reason to believe that time bias could have been introduced through maturation.

As with any follow-up study, withdrawal bias, due to loss to follow up is always a concern. To try to prevent loss to follow up or attrition, several contact numbers and addresses were recorded. The researcher and the research assistant were the only people who explained the intervention to the caregivers, both were proficient in applying the massage technique and the researcher alone instructed the caregiver on the home-based physical activity programme (Krishna et al., 2010).

The main purpose of randomising participants into treatment and control arms is to prevent researchers from predicting, and thus influencing, which participants receive which treatments until they are unambiguously enrolled onto the trial (Doig & Simpson, 2005). For the purpose of this trial the randomisation process entailed two methods; the first was to use a computer generated table which produces an unpredictable series of allocations (sequence generation). The sequence generation was performed by a person independent from the study using a computer generated randomisation table. Permutated block randomisation in groups of four was used to balance the group sizes and reduce variability (Schulz & Grimes, 2002) as equal group sizes normally maximize statistical power (Avins, 1998).
The second process was to enhance allocation concealment by ensuring that all baseline data were collected before the randomisation envelope was opened. Sequentially numbered, sealed, opaque envelopes were used to ensure allocation concealment. The researcher and research assistant could not predict which group participants would be allocated to. Selection bias was thus minimised, as the researcher could not predict which participant would receive the intervention.

Randomisation was stratified based on the scaled scores of cognitive, fine motor and gross motor subtests before randomisation. Criteria for stratification depended on two or three scaled scores of subtests were at or above the 75th Percentile on the Bayley Scales growth chart. The rationale was to ensure that the level of development would not be viewed as a confounder. Group allocation was concealed in the two sets of sequentially numbered, opaque, sealed, identical sized envelopes (SNOSE) to minimize allocation bias and to ascertain that the treatment allocated to the participant was not known until all baseline data were collected (Schulz & Grimes, 2002).

Participants were assigned to the study by opening the next consequential envelope after baseline data were recorded, baseline measurements and the baseline Bayley scale assessment was done. The research assistant took the next consequentially marked envelope to randomly allocate the participant either to the control or the intervention group. The participant’s name and date were entered on the envelope before the envelope was opened (Figure 4.3).
Figure 4.3  Randomisation allocation

All baseline data including the first Bayley-III test were performed before assignment of participants to ensure that participants, caregivers and researchers did not know which intervention the participant would receive. Due to the nature of the intervention, it was impossible to keep the researcher, participant and caregiver blinded to the intervention as the intervention required active participation from the caregiver in administering the home-based physical activity programme and massage. This study thus used an open-label blinding method (Haas, Aickin & Vavrek, 2010).

The researcher himself explained the intervention (home-based physical activity programme) to each participant allocated to the treatment group, as the programme was very specific to the participants needs. Massage was illustrated to all participants in both groups by the research assistant. The researcher was the only trained and qualified person to use the Bayley-III scale for assessment at the study sites. Thus, it is acknowledged that
participants, the researcher and the research assistant were not blinded after randomisation.

The Bayley assessment was scored using set criteria. According to Elkonin et al. (2001) a measure, which is administered and scored using set criteria, ensures objectivity. A detailed trial procedure was used to achieve external validity with specific inclusion and exclusion criteria as well as a calculated sample size to give results that would be reliable. Statistical tests were conducted and conclusions made according to the differences between the two groups. The same standard tools were used on all subjects to ensure measurement reliability during screening and reassessments. All children were assessed by one assessor using the same instruments.

Questionnaires were checked for completeness at the end of each interview. Participants who did not turn up for a follow-up visit were contacted telephonically and an alternative date arranged. The research assistant and researcher underwent a “good clinical practice” course and were trained on how to obtain written informed consent and conduct a basic interview to obtain the information required.

4.12 Procedure

Participants were recruited when they reported for routine visits at the HIV paediatric clinics. The research assistant identified potential participants and approached the caregivers to inform them about the study and invited them to participate. The children of caregivers, who were willing to participate were screened for eligibility. Written informed consent was obtained from those that met all the inclusion criteria. Required information was transcribed from the hospital and clinic card onto a CRF. The caregiver was then interviewed by the research assistant to obtain socio-demographic data that were not
recorded on the hospital or clinic card. If the child had been sleeping the mother and the assistant spent some time with the child and toys until the child was alert. Pertinent demographic information available of the child were entered onto the CRF. Anthropometric measurements for height and weight were taken by the researcher and the research assistant assisted with the process. The assessor was very familiar with the general administration of the Bailey-III instrument and specific instructions for the various sections of the measure.

Exact verbal instructions were memorized to ensure that all participants were exposed to similar testing. The caregivers were asked not to tell the child what to do unless asked to. The majority of the children were from Xhosa speaking families. The researcher did a beginners and intermediate course in Xhosa speaking during the year that preceded data collection. All instructions were transcribed from English to Xhosa and the researcher spent enough time learning and mastering the instructions. The venues used for the assessments were spacious, well ventilated, had adequate lighting, little noise and free from disturbances. After the caregiver and the child entered the assessment room, the researcher introduced himself to the caregiver and the child to create rapport. Assessments were conducted on a mat.

Motor and cognitive assessments were conducted using the Bayley-III. The cognitive assessment was conducted first followed by fine motor and gross motor development. The primary purpose of the scale is to identify developmental delay and provide information for intervention planning. The child’s chronological age was calculated adjusting for prematurity as necessary. The chronological age was calculated to designate the start point for administration of subtests. The researcher recorded the date of testing, the child’s date of birth, the child’s age and converted years, months and days to months and days. Using the chart on the cover page of the record
form the researcher then located the letter in the start point column that corresponded with the child’s age in months and days. Each item was scored as one (credit) for a successful attempt by the child and 0 (no credit) for failure.

To start scoring, the reversal rule was applied. To proceed, the first three consecutive items needed to have a score of one. If one of the first three items had a score of 0, the assessor went back to the start point of the previous age. The reversal rule was continuously applied until the child passed the first three items at the start point of any age. After establishing a starting point with three consecutive scores of one, items were administered in a forward direction until a child received scores of 0 for five consecutive items. This is called the discontinuity rule (Bayley, 2006). Previously administered items where the child scored 0 apply towards the discontinuity rule.

After completion of administering of all the subtests, the raw, scaled and composite scales were calculated. The raw scores were calculated by counting the total number of items for which the child received credits together with the number of unadministered items preceding the basal. Total raw scores for cognitive, fine motor and gross motor subtests were entered in the summary scores table on the cover page of the record form. The Bayley-III was used to determine scaled scores. Scaled scores ranged from one to 19 with a mean of 10 and a standard deviation of three. Composite score equivalents for cognitive scaled scores were recorded and the scaled scores for fine and gross motor were summed and the total recorded. The score chart was used to look up the composite score that matched the sum of scaled scores for motor scales. The child was then randomised to intervention or control using the computer-generated random numbers. The intervention and control were then instituted based on procedures.
Randomisation was performed after completing the assessment. The control or treatment was provided depending on allocation of the child. Anthropometry and Bayley-III assessments were conducted at three-month and six-month follow-up. After the intervention, caregivers were encouraged to report for the follow-up assessments at three-month and six-month follow-up. Their next appointment at the clinic with the physician was noted and recorded in a field notebook. The aim was that the trial follow-up date would be the same date that the infant had to see the physician.

Directions to execute the Bayley-III scale were given in the precise way that they are presented in the Bayley-III manual. No deviations from the instructions were made. Where necessary the mother was asked to give an instruction to the child. Timing of particular activities as prescribed by the manual was strictly adhered to. A stop watch was used to comply with the time limits. Following assessments, all materials were secured. The assessment booklets were counted and collated and checked to make sure that no information was missing. The assessment booklets and questionnaires were kept confidential and stored in a safe and locked place. Any important observations made during the assessments were recorded. Assessment results were communicated to the caregiver using general, understandable terms. Where necessary the child was referred to a specialist (physiotherapist, occupational therapist or orthopaedic consultation). A booking was made for the next appointment. Caregivers were telephonically contacted to remind them to return for subsequent assessments after three months and six months.

Everyday, before consultation, instruments were calibrated and assessment booklets checked to ensure that they were complete and enough in number for the day. The assessment toolkit was also checked to ensure that none of the assessment materials were missing. The tools used during a session
were cleaned with a sanitizer after every session. The research assistant, who was from the local community, was Xhosa speaking and available at all times to assist when necessary. All cell phones were switched off during the assessment.

Caregivers were contacted a week before the scheduled visit to be reminded of the appointments. At three and six-month follow-up, the children were reassessed for motor and cognitive development using the Bayley-III scale, height and weight and the exercise programme were adjusted according to milestones achieved. Where possible, the follow-up visits at three and six months coincided with the next clinic visits. Arrangements were made with caregivers for a child to be assessed at home in cases where the participants could not report at the two hospitals. Assessments were done at least two weeks before or after the scheduled date.

4.13 Data capturing and analysis
Data were captured onto Microsoft Excel by a research assistant. The researcher double checked data entered in excel for consistencies using source documents. The data were then imported into Epi Info version 7 (a statistical package) for analysis.

General descriptive and inferential analyses were used to analyse the data and to test the hypothesis. Means, frequencies, 95% confidence intervals, standard deviations and maximum and minimum values were used to compute descriptive statistics for continuous and categorical data respectively. Statistical comparisons of nominal, ordinal and continuous variables were done by using Epi Info version 7 and Revman 5 software. Bartlett’s test for homogeneity of variance was applied to continuous variables. If homogenous, the ANOVA test was used. If differences between
the samples were detected, the Kruskall Wallis H test were applied. The chi-
square test was used for categorical data and the Fisher exact test if any
number was less than five. The Taylor series 95% confidence intervals were
used for relative risks. The statistical test for significance was the two-tailed
Yates Corrected. If there was a value of less than 5 (n=< 5 in a group), the
Fischer Exact Test was used. Differences between treatment groups were
taken to be significant if the type 1 error was less than 0.05. Analysis of
Variance (ANOVA) was used to compare cognitive and motor development at
baseline, after three and six months for normally distributed data and the
Kruskal Wallis Test for skewed data.

All factors that may potentially affect MDI or PDI were added to linear
regression models with the MDI and PDI of the children as outcome
measures. Categorical factors were transformed into binary variables for this
purpose. The potential confounding variables in the regression model were:
prematurity, prenatal exposure to alcohol and drugs, breastfeeding option,
use of ARVs, maternal education attainment, employment status and gender
of the child. The forward stepwise regression was utilized to identify the
predictors of cognitive and motor development. The p-value was set at 0.1.

4.14 Data interpretation
To ensure adequate reporting of the methodology and results of this study,
we used the Consolidated Standards of Reporting Trials (CONSORT)
statement (Schulz, Altman & Moher, 2010). It consists of 25 items (see
appendices) and provides guidance to authors for reporting all randomised
controlled trials, editors and peer reviewers in reviewing manuscripts for
publication, and readers in critically appraising published articles (Schulz et
al., 2010).
Graphical depictions, descriptive tables and discussion of findings were used for the presentation of the results. Concise summary statements of the findings were formulated from the analysis and accompany the displays. For uniformity, the results were expressed in terms of the incidence of the less favourable outcome in each case. A relative risk (RR) of less than one indicates a better outcome in the treatment group. If the 95% confidence interval does not include one, then the result is statistically significant at \( p<0.05 \). Variables were analysed using “intention to treat” analysis.

4.15 Dissemination of findings

Scholarly findings of this study will be disseminated in accredited paediatric and HIV journals and conferences. Relevant findings will be distributed to organizations with interest in motor and cognitive development in HIV positive children including policy makers. Caregivers of participants will be informed of the results and where possible advice will be provided through, fliers, posters and presentations at the HIV clinics.

4.16 Summary

The methodology that guided the researcher in his quest for knowledge generation was presented in chapter four. Chapter five engage with the results of the study.
5.1 Introduction
Chapter five presents an interpretation of the results. The results are presented in order to address the objectives of the study. The CONSORT flow diagram is presented followed by a description of the socio-demographics, birth history, CD4 count and viral load of the participants. Motor and cognitive development and anthropometric status of HIV positive children on antiretroviral therapy as a whole are discussed and factors associated with motor and cognitive development in children infected with HIV are presented. Finally the main outcome of the study is presented which entails results related to the effectiveness of a home-based physical activity programme in combination with massage therapy on cognitive and motor development composite scores.

5.2 Randomisation
Between March and September 2010, 140 participants were invited to participate in the study. One hundred and twenty-eight met the eligibility criteria. Nine did not meet the eligibility criteria as they had severe cerebral palsy, informed consent was refused in two cases and one child was brought to the clinic by a non-legal guardian (Figure 5.1). Similar numbers of participants were lost to follow-up in both groups. At the three-month follow-up, 24 children were not assessed, 10 in the intervention and 14 in the control group (Figure 5.1). At the six-month follow-up another two in the intervention group were lost to follow-up. Thus a total of 12 in the intervention group were lost to follow-up and a total of 14 in the control group (Figure 5.1).
Chapter five: Results

Loss to follow-up was accounted for as follows; one participant in the intervention group was excluded from the study at three months post recruitment when it was discovered that the initial age provided was incorrect and fell outside the inclusion criteria. Six participants migrated to locations outside East London (2 intervention and 4 control). Seven children could not be assessed as they were too ill and hospitalised (2 Intervention and 5 Control). Nine participants could not be traced and were not contactable at the time that the assessment took place (6 Intervention and 3 Control). The total attrition rate at six-month follow-up was 20%, which is an acceptable loss to follow-up rate in clinical trials (Stinner & Tennent, 2012; Tyrer et al., 2001) (Figure 5.1).

Figure 5.1 CONSORT randomization flow diagram
5.3 Baseline information

The intervention and control groups were well matched for socio-demographic data at baseline with no statistically significant differences between the two groups. The mean age of the two groups at randomisation was similar (Table 5.1).

The Department of Health (2010c) antiretroviral treatment guidelines required that all children younger than 12 months of age, children aged one to five years with clinical stage 3 or 4 or with a CD\(_4\) percentage of \(\leq 25\%\) or an absolute CD\(_4\) count < 750 cells/μl commence with antiretroviral therapy. The blood CD\(_4\) percentage of the children in the study was obtained from the medical records. Consent was not obtained to do any blood tests on the participants. Routine blood tests are usually done annually and therefore three and six-month blood results were not available.

CD\(_4\) percentage at baseline was low in both groups with no statistically significant difference between the groups (Table 5.1).

<table>
<thead>
<tr>
<th></th>
<th>Intervention n (Mean) SD (Range)</th>
<th>Control n (Mean) SD (Range)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at randomisation</td>
<td>63 (19.94) 9.83 (3.29-35.36)</td>
<td>65 (19.98) 8.68 (3.20-35.21)</td>
<td>0.98</td>
</tr>
<tr>
<td>CD4 % at baseline*</td>
<td>55 (22.10) 9.73 (3.00-.41.80)</td>
<td>57 (23.82) 9.60 (8.90-44.00)</td>
<td>0.35</td>
</tr>
</tbody>
</table>

*CD4% was not available for 16 children
There were slightly more male participants in the control group (58.5%) than the intervention group (44.5%). Very few of the infants were born prematurely and the majority of the participants were on anti-retroviral drugs during the study (Table 5.2).

### Table 5.2  Categorical infant baseline demographic information of children

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>95% CI RR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>28/63 (44.5%)</td>
<td>38/65 (58.5%)</td>
<td>0.75(0.52-1.07)</td>
<td>0.16</td>
</tr>
<tr>
<td>Female</td>
<td>35/63 (55.5%)</td>
<td>27/65 (41.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Premature at birth</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>8/63 (12.7%)</td>
<td>8/64 (12.5%)</td>
<td>1.01(0.41-2.54)</td>
<td>0.82</td>
</tr>
<tr>
<td>No</td>
<td>55/63 (87.3%)</td>
<td>56/64 (87.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>On ARV’s</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>62/63 (98.4%)</td>
<td>63/65 (96.9%)</td>
<td>0.99(0.93-1.04)</td>
<td>0.98</td>
</tr>
<tr>
<td>No</td>
<td>1/63 (1.6%)</td>
<td>2/65 (3.1%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Most of the caregivers were unemployed and had only completed primary school education. Slightly more mothers in the control group were unemployed and completed primary school only, but the difference was not statistically significant between the groups. Biological mothers were the majority caregivers in both groups. (Table 5.3).

**Table 5.3  Categorical information of caregivers**

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>95% CI RR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Employment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>9/63 (14.3%)</td>
<td>7/65 (10.8%)</td>
<td>1.04 (0.91-1.19)</td>
<td>0.74</td>
</tr>
<tr>
<td>Unemployed</td>
<td>54/63 (85.7%)</td>
<td>58/65 (89.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tertiary</td>
<td>1/62 (1.6%)</td>
<td>2/65 (3.1%)</td>
<td>Undefined</td>
<td>0.26*</td>
</tr>
<tr>
<td>Secondary</td>
<td>14/62 (23.0%)</td>
<td>8/65 (12.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>47/62 (75.4%)</td>
<td>55/65 (84.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Caregiver</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>45/63 (71.0%)</td>
<td>45/65 (69.2%)</td>
<td>Undefined</td>
<td>0.41*</td>
</tr>
<tr>
<td>Grand mother</td>
<td>14/63 (22.6%)</td>
<td>13/65 (20%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foster mother</td>
<td>2/63 (3.2%)</td>
<td>1/65 (1.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father</td>
<td>1/63 (1.6%)</td>
<td>4/65 (6.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cousin</td>
<td>1/63 (1.6%)</td>
<td>0/65 (0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aunt</td>
<td>0/63 (0%)</td>
<td>2/65 (3.1%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Fisher exact
The use of alcohol, cigarettes, and habit-forming drugs by mothers of participants were similar between the two groups (Table 5.4).

### Table 5.4 Social habits of biological mother

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>95% CI RR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prenatal alcohol use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11/63 (17.5%)</td>
<td>12/64 (18.7%)</td>
<td>1.07(0.51-2.25)</td>
<td>0.97</td>
</tr>
<tr>
<td>No</td>
<td>52/63 (82.5%)</td>
<td>52/64 (81.3%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **Smoke cigarettes** |         |         |           |         |
| Yes                  | 5/63 (8.0%) | 3/64 (4.7%) | 0.59(0.14-2.36) | 0.49*   |
| No                   | 58/63 (92.0%) | 61/64 (95.3%) |           |         |

| **Habit-forming drugs** |         |         |           |         |
| Yes                  | 0/63 (0%) | 2/64 (3.1%) | Undefined | 0.50*   |
| No                   | 63/63 (100%) | 62/64 (96.9%) |           |         |

* Fisher exact

*Social habits were not available for a mother

### 5.4 Anthropometry and age

The baseline anthropometric measurements and age of the participants in both the intervention and the control groups were similar. The growth pattern did not show any statistically significant differences between the two groups after three and six months (Table 5.5).
## Table 5.5 Anthropometry of children at baseline and follow-up

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weight (kg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At baseline</td>
<td>63 (10.15)</td>
<td>61* (10.13) 2.45</td>
<td>0.97</td>
</tr>
<tr>
<td></td>
<td>(4.30-15.55)</td>
<td>(4.46-14.85)</td>
<td></td>
</tr>
<tr>
<td>Follow-up visit after 3 months</td>
<td>50 (11.34)</td>
<td>51 (11.18) 2.22</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>(5.41-16.25)</td>
<td>(7.25-16.25)</td>
<td></td>
</tr>
<tr>
<td>Follow-up visit after 6 months</td>
<td>47 (11.80)</td>
<td>47 (11.61) 2.16</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>(6.13-16.60)</td>
<td>(7.10-17.00)</td>
<td></td>
</tr>
<tr>
<td><strong>Length (cm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At baseline</td>
<td>61 (75.62)</td>
<td>58* (76.01) 9.15</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>(56.60-101.30)</td>
<td>(55.30-91.20)</td>
<td></td>
</tr>
<tr>
<td>Follow-up visit after 3 months</td>
<td>51 (79.22)</td>
<td>51 (79.81) 7.81</td>
<td>0.72</td>
</tr>
<tr>
<td></td>
<td>(62.30-103.70)</td>
<td>(63.00-94.50)</td>
<td></td>
</tr>
<tr>
<td>Follow-up visit after 6 months</td>
<td>48 (82.41)</td>
<td>48 (81.36) 7.94</td>
<td>0.51</td>
</tr>
<tr>
<td></td>
<td>(66.50-105.20)</td>
<td>(63.60-95.20)</td>
<td></td>
</tr>
<tr>
<td><strong>Age (months)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At baseline</td>
<td>63 (19.94)</td>
<td>65 (19.96) 8.68</td>
<td>0.98</td>
</tr>
<tr>
<td></td>
<td>(3.29-35.36)</td>
<td>(3.20-35.21)</td>
<td></td>
</tr>
<tr>
<td>Follow-up visit after 3 months</td>
<td>53 (23.00)</td>
<td>51 (23.37) 8.58</td>
<td>0.84</td>
</tr>
<tr>
<td></td>
<td>(6.22 -38.19)</td>
<td>(7.02-38.05)</td>
<td></td>
</tr>
<tr>
<td>Follow-up visit after 6 months</td>
<td>51 (27.97)</td>
<td>51 (25.41) 8.80</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>(8.19-43.06)</td>
<td>(8.20-42.07)</td>
<td></td>
</tr>
</tbody>
</table>

*Data on weight and length were missing for four and seven children respectively
The data were analysed as one group and stratified according to gender to compare the anthropometry of the sample with that of the greater population. The Centers for Disease Control and Prevention [CDC] (2004) growth charts were used to compare the mean height-for-age and weight-for-age. The mean weight-for-age for both the males and the females was below the 10th percentile. Estimated 50th percentile weight-for-age in the normal population is 11.6 kg and the children in the study were 10.11kg and 10.14kg respectively for males and females. The mean height-for-age for males (74.65 cm) and females (76.60 cm) was below the 5th percentile with an expected 50th percentile height-for-age of at least 83 cm (Table 5.6).

**Table 5.6   Anthropometry of children according to gender**

<table>
<thead>
<tr>
<th></th>
<th>Male (Males)</th>
<th>Female (Females)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (Mean) SD</td>
<td>n (Mean) SD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Range)</td>
<td>(Range)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At baseline</td>
<td>59*(10.13)</td>
<td>65 (10.15)</td>
<td>0.97</td>
</tr>
<tr>
<td></td>
<td>(4.46-15.55)</td>
<td>(4.30-14.85)</td>
<td></td>
</tr>
<tr>
<td>Length (cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At baseline</td>
<td>57*(74.73)</td>
<td>62*(76.81)</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>(55.30-101.3)</td>
<td>(56.60-91.20)</td>
<td></td>
</tr>
<tr>
<td>Age (months)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At baseline</td>
<td>62 (18.45)</td>
<td>66 (21.38)</td>
<td>0.21</td>
</tr>
<tr>
<td></td>
<td>(3.20-35.07)</td>
<td>(4.12-35.36)</td>
<td></td>
</tr>
</tbody>
</table>

*missing data
Weight of children in the intervention and control groups remained statistically insignificant at three and six-month follow-up for both males and females. Physical activity and massage did not have any effect on weight (Table 5.7).

**Table 5.7 Anthropometry (weight) of children according to gender**

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (Mean) SD (Range)</td>
<td>n (Mean) SD (Range)</td>
<td></td>
</tr>
<tr>
<td><strong>Weight at baseline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>35 (10.61) 2.80 (5.70-15.55)</td>
<td>24 (9.42) 3.00 (4.46-14.80)</td>
<td>0.13</td>
</tr>
<tr>
<td>Females</td>
<td>28 (9.57) 2.72 (4.30-14.00)</td>
<td>37 (10.58) 1.92 (6.33-14.85)</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Weight 3 months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>27 (12.35) 2.28 (6.50-16.60)</td>
<td>21 (11.67) 2.75 (7.10-17.00)</td>
<td>0.35</td>
</tr>
<tr>
<td>Females</td>
<td>20 (11.06) 2.33 (6.13-15.00)</td>
<td>26 (11.55) 1.58 (8.00-15.00)</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>Weight 6 months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>27 (12.36) 2.28 (6.50-16.60)</td>
<td>21 (11.67) 2.75 (7.10-17.00)</td>
<td>0.35</td>
</tr>
<tr>
<td>Females</td>
<td>20 (11.06) 2.33 (6.13-15.00)</td>
<td>26 (11.55) 1.58 (8.00-15.00)</td>
<td>0.39</td>
</tr>
</tbody>
</table>
There was a statistically significant difference in the mean length between the two groups for both males and females at baseline. This significant difference could be due to chance. The difference was no longer statistically different at the three-month and six-month follow-up visits for females. At the three-month follow-up there was also no significant difference between the males in the two groups, but males in the intervention group were significantly taller than the males in the control group at the six-month follow-up visit (Table 5.8).

### Table 5.8 Anthropometry (length) of children according to gender

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (Mean) SD (Range)</td>
<td>n (Mean) SD (Range)</td>
<td></td>
</tr>
<tr>
<td><strong>Length at baseline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>34 (76.85) 8.93 (62.5-101.3)</td>
<td>23 (71.58) 9.56 (55.3-90.00)</td>
<td>0.04</td>
</tr>
<tr>
<td>Females</td>
<td>27 (74.07) 9.30 (56.60-89.70)</td>
<td>35 (78.93) 7.69 (60.90-91.20)</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Length 3 months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>28 (80.96) 8.48 (64.50-103.70)</td>
<td>20 (77.62) 8.93 (63.00-91.40)</td>
<td>0.20</td>
</tr>
<tr>
<td>Females</td>
<td>23 (77.10) 9.02 (62.30-90.10)</td>
<td>31 (81.23) 6.78 (65.40-94.50)</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>Length 6 months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>28 (83.45) 7.48 (69.40-105.20)</td>
<td>21 (78.61) 8.61 (63.60-93.80)</td>
<td>0.04</td>
</tr>
<tr>
<td>Females</td>
<td>20 (80.96) 7.85 (66.50-90.90)</td>
<td>27 (83.49) 6.79 (67.80-95.20)</td>
<td>0.24</td>
</tr>
</tbody>
</table>
5.5 Association between composite factors and development

Although only a few individuals (n=23) abused alcohol during pregnancy, there was a statistical significant association between cognitive delay and the use of alcohol (p=0.04). There was positive inclination between prematurity and cognitive delay, as well as employment and cognitive delay. None of the other factors showed a correlation (Table 5.9).

Table 5.9 Composite factors and cognitive delay at baseline

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Coefficient</th>
<th>Std Error</th>
<th>P-value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>-1.87</td>
<td>1.94</td>
<td>0.336</td>
<td>-5.69 to 1.94</td>
</tr>
<tr>
<td>ARVs</td>
<td>-3.22</td>
<td>2.87</td>
<td>0.263</td>
<td>-8.88 to 2.43</td>
</tr>
<tr>
<td>Gestation</td>
<td>-2.47</td>
<td>1.30</td>
<td>0.057</td>
<td>-5.02 to 0.08</td>
</tr>
<tr>
<td>Exposure to alcohol</td>
<td>-5.36</td>
<td>2.54</td>
<td>0.036</td>
<td>-10.37 to -0.36</td>
</tr>
<tr>
<td>Exposure to drugs</td>
<td>-2.81</td>
<td>7.04</td>
<td>0.691</td>
<td>-16.66 to 11.05</td>
</tr>
<tr>
<td>Currently breastfeeding</td>
<td>2.13</td>
<td>2.26</td>
<td>0.348</td>
<td>-2.32 to 6.58</td>
</tr>
<tr>
<td>Education*</td>
<td>3.34</td>
<td>2.25</td>
<td>0.139</td>
<td>-1.09 to 7.77</td>
</tr>
<tr>
<td>Employment*</td>
<td>-5.49</td>
<td>2.79</td>
<td>0.050</td>
<td>-10.97 to -0.003</td>
</tr>
</tbody>
</table>

* Caregiver
No factors could be associated with motor delay

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Coefficient</th>
<th>Std Error</th>
<th>P-value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>-0.66</td>
<td>4.48</td>
<td>0.883</td>
<td>-9.55 to 8.23</td>
</tr>
<tr>
<td>Gestation</td>
<td>-4.23</td>
<td>3.09</td>
<td>0.174</td>
<td>-10.38 to 1.90</td>
</tr>
<tr>
<td>Exposure to alcohol</td>
<td>-5.08</td>
<td>5.68</td>
<td>0.374</td>
<td>-16.35 to 6.20</td>
</tr>
<tr>
<td>Currently breastfeeding</td>
<td>21.54</td>
<td>17.42</td>
<td>0.219</td>
<td>-13.01 to 56.10</td>
</tr>
<tr>
<td>Education*</td>
<td>0.72</td>
<td>6.91</td>
<td>0.219</td>
<td>-13.01 to 56.10</td>
</tr>
<tr>
<td>Employment*</td>
<td>-5.49</td>
<td>2.79</td>
<td>0.918</td>
<td>-12.99 to 14.42</td>
</tr>
</tbody>
</table>

*Caregiver
5.6 Motor development index

The baseline mean motor development index was similar and within normal limits (94.07 intervention; 94.66 control) for both groups with no significant difference between the groups. The mean motor development index continued to stay within the normal limits for both groups at the three and six-month follow-up visits, with no difference between the groups. The intervention thus had no effect on the motor development index (Table 5.11).

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor development</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>composite score (PDI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at baseline</td>
<td>63 (94.05)</td>
<td>65 (94.66)</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>22.59</td>
<td>20.86</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(46-139)</td>
<td>(46-151)</td>
<td></td>
</tr>
<tr>
<td>Motor development</td>
<td>52 (91.69)</td>
<td>48 (94.31)</td>
<td>0.50</td>
</tr>
<tr>
<td>composite score (PDI)</td>
<td>19.95</td>
<td>18.70</td>
<td></td>
</tr>
<tr>
<td>Follow-up visit after 3</td>
<td>19.95</td>
<td>18.70</td>
<td></td>
</tr>
<tr>
<td>Months</td>
<td>(46-127)</td>
<td>(46-124)</td>
<td></td>
</tr>
<tr>
<td>Motor development</td>
<td>50 (92.80)</td>
<td>49 (97.55)</td>
<td>0.23</td>
</tr>
<tr>
<td>composite score (PDI)</td>
<td>20.92</td>
<td>17.82</td>
<td></td>
</tr>
<tr>
<td>Follow-up visit after 6</td>
<td>20.92</td>
<td>17.82</td>
<td></td>
</tr>
<tr>
<td>Months</td>
<td>(46-133)</td>
<td>(46-136)</td>
<td></td>
</tr>
</tbody>
</table>

PDI = Psychomotor Development Index = Composite motor development score
Prevalence of delay in motor development at baseline was 31.7% in the intervention group and 26.1% in the control group, with no statistically significant difference between the groups (p=0.62). There were no statistically significant differences between the prevalence at the follow-up visits. Both groups showed a slight decrease in the number of children that presented with a delay in motor development at three and six-month follow-up. The intervention thus did not improve the motor development of the children (Table 5.12).

**Table 5.12  Proportions of motor developmental delay**

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>95% CI RR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Motor development At baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>43/63 (68.2%)</td>
<td>48/65 (73.8%)</td>
<td>1.21 (0.70-2.09)</td>
<td>0.62</td>
</tr>
<tr>
<td>Delayed</td>
<td>20/63 (31.7%)</td>
<td>17/65 (26.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Motor development Follow-up visit after 3 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>37/52 (71.2%)</td>
<td>37/48 (78.0%)</td>
<td>1.26 (0.64-2.46)</td>
<td>0.65</td>
</tr>
<tr>
<td>Delayed</td>
<td>15/52 (28.8%)</td>
<td>11/48 (22.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Motor development Follow-up visit after 6 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>36/50 (72.0%)</td>
<td>40/49 (81.6%)</td>
<td>1.52 (0.73-3.19)</td>
<td>0.37</td>
</tr>
<tr>
<td>Delayed</td>
<td>14/50 (28.0%)</td>
<td>9/49 (18.4%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5.7 Cognitive development index

The baseline mean cognitive development index score was similar and within normal limits (90.87 Intervention; 95.61 Control) for both groups with no statistically significant difference between the groups at baseline. There was a slight decrease in the mean cognitive development score for both groups at the follow-up visits, with no statistically significant difference between the groups (Table 5.13).

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive development</td>
<td></td>
<td></td>
</tr>
<tr>
<td>composite score (MDI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>at baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>63</td>
<td>65</td>
</tr>
<tr>
<td>(Mean)</td>
<td>(90.87)</td>
<td>(95.62)</td>
</tr>
<tr>
<td>SD</td>
<td>19.36</td>
<td>16.67</td>
</tr>
<tr>
<td>(Range)</td>
<td>(55-140)</td>
<td>(55-145)</td>
</tr>
<tr>
<td>P value</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>Cognitive development</td>
<td></td>
<td></td>
</tr>
<tr>
<td>composite score (MDI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up visit after 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>52</td>
<td>50</td>
</tr>
<tr>
<td>(Mean)</td>
<td>(88.65)</td>
<td>(90.40)</td>
</tr>
<tr>
<td>SD</td>
<td>14.92</td>
<td>14.91</td>
</tr>
<tr>
<td>(Range)</td>
<td>(55-120)</td>
<td>(55-120)</td>
</tr>
<tr>
<td>P value</td>
<td>0.55</td>
<td></td>
</tr>
<tr>
<td>Cognitive development</td>
<td></td>
<td></td>
</tr>
<tr>
<td>composite score (MDI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up visit after 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>50</td>
<td>51</td>
</tr>
<tr>
<td>(Mean)</td>
<td>(87.20)</td>
<td>(87.45)</td>
</tr>
<tr>
<td>SD</td>
<td>14.71</td>
<td>12.50</td>
</tr>
<tr>
<td>(Range)</td>
<td>(55-115)</td>
<td>(55-110)</td>
</tr>
<tr>
<td>P value</td>
<td>0.93</td>
<td></td>
</tr>
</tbody>
</table>

MDI = Mental Development Index = Composite cognitive development score
There was no statistically significant difference in cognitive development at baseline, three or six-month follow-up between the two groups. Nearly twice as many participants presented with cognitive developmental delay at baseline in the intervention group (22/63 Intervention; 12/65 Control), but the difference was not statistical significant (p=0.06). Although the proportion of children with cognitive delay decreased by 2% in the intervention group and increased by 15% in the control group between baseline and six months, there were no statistically significant differences between the groups, inferring that the intervention did not increase cognitive development (Table 5.14).

**Table 5.14  Proportions of cognitive developmental delay**

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>95% CI</th>
<th>RR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cognitive development at baseline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>41/63 (65.1%)</td>
<td>53/65 (81.5%)</td>
<td>1.89 (1.02-3.49)</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Delayed</td>
<td>22/63 (34.9%)</td>
<td>12/65 (18.5%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cognitive development follow-up visit after 3 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>36/52 (69.3%)</td>
<td>36/50 (72.0%)</td>
<td>1.10 (0.60-2.01)</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>Delayed</td>
<td>16/52 (30.7%)</td>
<td>14/50 (28.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cognitive development follow-up visit after 6 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>34/50 (68.0%)</td>
<td>34/51 (66.7%)</td>
<td>0.96 (0.58-1.68)</td>
<td>0.94</td>
<td></td>
</tr>
<tr>
<td>Delayed</td>
<td>16/50 (32.0%)</td>
<td>17/51 (33.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
We accept the null-hypothesis that there is no difference in motor and cognitive development between children with HIV infection receiving a home-based intervention and those not receiving the intervention. The results did not show a 15% improvement over six months in neither motor nor cognitive development. It may be postulated that massage therapy had a positive effect on both groups as the prevalence of delayed motor development decreased slightly in both groups over time.

5.8 Summary
This chapter presented findings addressing the objectives of the study. The study illuminated motor and cognitive development in infants and toddlers infected with HIV. Children were either on HAART or eligible for HAART. It was revealed that motor and cognitive developmental delay was present in the sample. Abuse of alcohol by the mother was associated with cognitive delay in children. The main findings presented in this chapter were the effect of a home-based physical activity programme and massage versus massage only on motor and cognitive development in infants and toddlers. The increase in the proportion of motor developmental delay, between baseline and six-month follow-up in the control and intervention groups were not statistically significant.
Chapter six: Discussions

Discussions, implications for practice and research recommendations

6.1 Introduction
This chapter highlights the findings of the study and serves as a framework for the discussion. The comparisons with similar literature are incorporated to relate salient points observed in this study. Limitations are acknowledged and implications to practice and research highlighted. Recommendations for further research are made.

6.2 Discussion
As far as is known, this is the first study to investigate the possible effect of a home-based physical activity programme and massage versus massage only on motor and cognitive development in children receiving HAART. The first and third objectives of the study were to describe the socio-demographics, birth history, CD4 count and viral load of HIV positive children and to determine if the factors have any association with motor and cognitive development. Koekkoek et al. (2008), Chowdhury, Wrotniak and Ghosh (2010) and Pearson et al. (2013) attest that socioeconomic status, prematurity, age and gender can affect motor and cognitive development in children infected with HIV. The results of this study showed that there was an inclination of employment status of the caregiver towards predicting cognitive development in HIV positive children, whilst no predictive value could be confirmed for prematurity and gender.

Alcohol was used by 18% of women during pregnancy in this study. Alcohol and employment status were shown to be a significant predictive indicators for cognitive development. These findings, related to prenatal exposure to
alcohol and employment status of the caregiver are unique findings of the current study. Kelly et al. (2013) argued that infants of pregnant women who drank less than two units of alcohol per week, were not at risk of experiencing cognitive developmental problems. Falgreen-Eriksen et al. (2012) further express caution that alcohol is a known teratogen and high daily alcohol intake levels during pregnancy can cause cognitive development impairment.

Pearson et al. (2013) affirmed that low CD4 count and high HIV RNA viral load are significant predictors of disease progression in children and often associated with disease progression in infants. Current results are ambivalent in respect of cognitive development in children on HAART with higher CD4 counts. Le Doaré, Bland and Newell (2012) report that HIV positive children on HAART in developed countries may display normal cognitive development scores, whilst Koekkoek et al. (2008) claim that HIV positive children on HAART in under resourced countries may present with a higher mean cognitive development score than those not on HAART, although the mean score may still be one to two standard deviations lower than the average population mean score.

The second objective was to establish the prevalence of motor and cognitive development and to describe the anthropometric status of HIV positive children on antiretroviral therapy. A meta-analysis of five studies revealed that the prevalence of motor delay was 82.78% (Figure 3.2) in contrast to the 28.9% prevalence of motor delay found in this study. Meta-analysis of cognitive development confirms that development is delayed in HIV positive children with a prevalence of 75.80% (Figure 3.3), which is slightly less than the prevalence of motor development.

The result of this study support the finding that cognitive delay is less prevalent than motor delay although the overall prevalence was much lower
(26.7%) than that demonstrated in the results of the meta-analysis (Gay et al., 1995; Blanchette et al., 2001; Baillieu & Potterton, 2008; Kigira et al., 2008; Ferguson & Jelsma, 2009; Potterton et al., 2009). In the Fergusson and Jelsma (2009) study, 90% of infected children were delayed in motor development whilst Baillieu and Potterton (2008) reported 90% and 87.5% delay in cognitive and motor development respectively. The low prevalence may have been as a result of the children being on ART.

The failure to grow is a frequent attribute of HIV positive children especially when HIV RNA viral loads are high (Lowenthal, & Phelps, 2010; Feinstein, Yotebieng, Moultrie, Meyers & Van Rie, 2012). The use of HAART has been documented to improve length and weight of HIV positive children (Verweel, van Rossum, Hartwig, Wolfs, Scherpber & de Groot, 2002). HAART had newly been implemented to HIV children at the time of data collection. The high viral loads and low CD4 counts, could have been as a result of not being long enough on treatment at the time of the baseline measurements. The results of this study concur with Feinstein et al. (2012) in that stunting and underweight was present at baseline.

The primary outcome of the study on which the hypothesis was based was to determine whether a home-base physical activity programme in combination with massage therapy could improve cognitive and motor development composite scores by 15% over a six month period in HIV infected children on antiretroviral therapy. Chapter three discussed the results of a systematic review of literature that used Bayley scale to assess motor and cognitive development in HIV positive children (Table 3.4). The mean composite score for motor development of six studies was 83.73, with the lowest mean score (53.67) reported by Potterton et al. (2009) and the highest (100) by Llorente et al. (2003). The baseline mean motor development composite score, in both the intervention (94.07) and the control (94.66) group, was within normal
limits and higher than the mean of the studies in the systematic review (83.73).

Similar to the results of the systematic review, the mean composite score for cognitive development (93.24) was slightly lower than the mean composite score for motor development (94.37), but not as low as the mean score of the systematic review. The mean composite score for cognitive development of six studies was 80.24 with the lowest mean score (65.61) reported by Potterton et al. (2009) and the highest (97.7) by Llorente et al. (2003). There was a slight decrease in the mean cognitive development score for both the intervention and the control groups at the follow-up visits, but not as low as the mean score reported in the systematic review.

There was a 2% decrease in the proportion of children with cognitive developmental delay between baseline and six months whilst the proportion increased by 15% in the control group. This was likely a result of the intervention. However, this change was not statistically significant. The difference may have been statistically significant if the intervention duration was longer. Increasing the follow-up time would have considered fewer participants as the Bayley-III measures children aged 42 months and below. Eighteen percent would have been older than 42 months beyond six months.

In conclusion, it is evident from the results of this study that the use of a home-based physical activity programme in combination with massage therapy did not improve neither motor nor cognitive development. It may be postulated that massage therapy had a positive effect on both groups as the prevalence of delayed motor development decreased slightly in both groups over time.
6.3 Limitations

One of the limitations of this study is the fact that the researcher was not blinded to group allocation at follow-up visits. Furthermore, the study did not include an additional arm of HIV negative children. Inclusion of such a group could have made it possible to assess more carefully the risk of milder neurodevelopmental deficits. The study also did not evaluate adherence or duration of HAART before randomisation, this may have influenced the anthropometry results of the study, as growth occurs over time and the children may have been on HAART for only a short period at commencement of baseline data collection. The researcher conducted all the Bayley-III and anthropometry assessments. The use of an independent assessor could have reduced any possible detection bias.

6.4 Implication to practice and research

In South Africa and many other countries, access to ART for children has increased. This in turn has increased the lifespan of children. HIV clinics need to consider monitoring of developmental delay in children infected with HIV. Where feasible, children should be referred for physiotherapy and other rehabilitation services in order to address identified motor and cognitive development. There is great potential for knowledge translation into paediatric HIV care. HIV clinics should include physiotherapists or psychologists to assess HIV positive children regularly for early diagnosis of developmental delay and to ensure that interventions are initiated during the early stage to assist children who are delayed in development. Caregivers may be a valuable resource to assist children at home with acquiring developmental milestones through provision of massage.

A simple massage technique may be implemented to all children until further evidence become available of whether a structured home-based physical
activity programme can significantly improve motor and cognitive development (Ulrich, Ulrich, Angulo-Kinzler, & Yun, 2001; Day, Fox, Lowe, Swales & Behrman, 2004; Begnoche, Sanders & Pitetti, 2005; Angulo-Barroso et al., 2008).

Due to the ambivalent data between studies, it is suggested that larger multicentre, randomised controlled trials be implemented to evaluate the efficacy and the efficiency of a home-based physical activity program to improve motor and cognitive development. Studies should also include a control arm of HIV negative children. The duration of the intervention could be increased and more focus is needed on the intensity of home programmes, materials and more appealing activities for caregivers and children. Services for these children should include collaboration among schools, the community and health care professionals (Wachsler-Felder & Golden, 2002).

6.5 Recommendations
Currently there is no policy in South Africa that addresses the motor and cognitive developmental needs of children, especially children infected with HIV. An urgent agenda for evidence and provision of neuro-developmental support for children infected with HIV needs to be established.


Hughes, C. (2012). Qualitative and quantitative approaches to social research. Retrieved 12/02/2012 from http://www2.warwick.ac.uk/fac/soc/sociology/staff/academicstaff/chughes/hughesc_index/teachingresearchprocess/quantitativequalitative/quantitativequalitative


Appendix A: Care report form

Social demographic and BIRTH HISTORY, WEIGHT AND RECUMBENT LENGTH QUESTIONNAIRE

1. Name of the health centre : __________________________
2. Today’s Date ___ ___ / ___ ___ / ___ ___ ___ ___
   (day)      (month)          (year)
3. Study visit number: _____
   (1 = 1st assessment, 2 = 2nd Assessment, 3 = 3rd Assessment)
4. Child’s ID : ______
5. Date of birth of child : ___ ___ / ___ ___ / ___ ___ ___ ___
   (day)     (month)          (year)
6. Gender of child : ______
   □ Male
   □ Female
7. Child on ART
   □ NO
   □ YES
8. Viral Load and CD4 count (please record the latest if the tests have been done)

<table>
<thead>
<tr>
<th>Test</th>
<th>Measurement</th>
<th>Date taken</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral Load</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 Count</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
9. Date of birth of mother : ___ ___ / ___ ___ / ___ ___ ___ ___
   (day)     (month)          (year)
10. Residential address :
    ________________________________________________________________
    ________________________________________________________________
    ________________________________________________________________
11. Contact number of mother : __________________________
12. Person caring for the child

☐ Mother
☐ Father
☐ Other _____________________ (please specify)

13. Mother's Educational status

☐ Did not complete high school
☐ Completed high school
☐ At college/university
☐ Completed college/university

14. Employment status

☐ Employed
☐ Unemployed

Pregnancy History

15. How many times had the birth mother been pregnant before giving birth to the child being evaluated in this study (including that pregnancy)?

___________ times

16. How many children does the mother currently have (including that child)?

___________ babies

17. Was this child part of a multiple pregnancy?........

☐ NO
☐ YES

(If yes):
How many babies?

___________ babies

18. Labour and delivery

☐ Fine
☐ Problems

19. If with problems describe

___________________________________________________________
___________________________________________________________
___________________________________________________________
_________________________________________________________

20. What was the gestational age at delivery? : _______________

21. In this pregnancy, did the birth mother do any of the following activities? If so, did she do so before or after she knew she was pregnant or both (i.e., before AND after she knew she was pregnant)? (circle one for each item)

Drink alcohol..................................................

☐ Yes
☐ No
22. Smoke cigarettes or other tobacco products.................................................................

☐ Yes
☐ No

23. Used recreational drugs during pregnancy (e.g. marijuana, cocaine, Tik, etc)

☐ Yes
☐ No

24. Anthropometric status of the infants (IN CENTIMETRES)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Baseline (6 weeks)</th>
<th>(14 weeks)</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Appendix B: Developmental score capturing form

Child’s Research ID..............................................

**Scaled Scores**

<table>
<thead>
<tr>
<th></th>
<th>Base line</th>
<th>After 3 months</th>
<th>After 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive development</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fine Motor development</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gross Motor development</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Scaled scores range from 1 to 19

**Composite score**

<table>
<thead>
<tr>
<th></th>
<th>Base line</th>
<th>After 3 months</th>
<th>After 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive development</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor development</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Composite scores range from 45 to 155
Appendix C: University of the Western Cape ethical clearance

27 January 2010

To Whom It May Concern

I hereby certify that the Senate Research Committee of the University of the Western Cape has approved the methodology and the ethics of the following research project by: Mr. O Khondowe (Dept. of Physiotherapy)

Research Project: A randomized controlled trial of physiotherapy as an intervention for motor and cognitive development in children with vertically transmitted HIV infection at selected hospitals in the Western Cape

Registration no. 05/9/10

[Signature]

Peter Stryer
Manager: Research Development Office
University of the Western Cape
Appendix D: East London complex ethical clearance

Ethics Committee: E. L Hospital Complex

Postal Address:
C/o East London Health Resource Centre
PO Box 12882
Amalinda
5252

Physical Address:
Cheltenham Road
East London
5201 South Africa

Telephone: 043 - 709 2401
Fax no.: 043 - 7092386

14 April 2010

Mr Oswell Khondowe
East London Health Complex
East London
5200

Dear Mr Oswell Khondowe

RE: Research Project: A randomized controlled trial of Physiotherapy as an intervention for motor and cognitive development in children with vertically transmitted HIV infection at selected hospitals in the Western Cape

We acknowledge receipt of the above mentioned proposal.

Having gone through your proposal, the committee has no ethical problems noted.

Please be advised that the committee has granted you the consent to do the research.

Yours sincerely

[Signature]
Appendix E: Informed consent

Informed consent Infant Development Study. Version IDS-OK 1

UNIVERSITY OF THE WESTERN CAPE
in collaboration with Frere Hospital.
Tel 021 995 3024 email okhondowe@uwc.ac.za
School of Nursing.

A place of quality, a place to grow, from hope to action through knowledge

Informed consent form and statement
(To be explained by the Investigator or dedicated research assistant).

TITLE OF THE RESEARCH PROJECT:

A RANDOMISED TRIAL OF PHYSIOTHERAPY AS AN INTERVENTION FOR MOTOR AND COGNITIVE DEVELOPMENTMENT IN CHILDREN WITH VERTICALLY TRANSMITTED HIV INFECTION

REFERENCE NUMBER: 05/9/10

INVESTIGATOR: Oswell Khondowe
CLINICAL SUPERVISORS: Professor José Frantz, Professor Cheryl Nikodem and Dr Kim Harper

ADDRESS: University of Western Cape, School of Nursing, private X17, Bellville, Cape Town
You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is entirely voluntary and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part.

This study has been approved by the Higher Degrees and Ethics Committee at the University of the Western Cape and will be conducted according to the ethical guidelines and principles of the international Declaration of Helsinki, South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is this research study all about?
The purpose of this study is to evaluate the effect of an intensive exercise programme on HIV positive children in enhancing their motor and cognitive function. We would like to know if you would be willing to have your child participate in the above explained research.

A developmental scale will be used to assess your child’s neuro-developmental status after consent has been attained. The children will be assessed again after three and six months. Additional information will be obtained from patient files. A research staff will ask questions and the answers will be written down on your specific question paper. If your child fits...
the inclusion criteria, it will be allocated to either the intervention or control group. In the intervention group, mothers will be taught an intensive daily exercise programme to carry out while at home. These exercises will be designed according to the child’s developmental level. They will be modified monthly according to the level the child would have attained during your visits to the hospital.

**Why have you been invited to participate?**
The study involves an intervention on children’s neuro-development.

**What will your responsibilities be?**
Your responsibility is to the child to ensure you are comfortable with the study and obtain a signed consent before the study and follow advice from the research staff.

**Will you benefit from taking part in this research?**
We believe that this investigation will help to identify delays in motor and cognitive development and help develop a programme to provide appropriate early intervention so that the infants can catch up with their normal peers in development and growth. Also to ensure that health personnel are informed and engage in better practices. The analysis of the study will help further research and benefit children in the future.

**Are there any risks involved in your taking part in this research?**
This study has no risks involved.

**If you do not agree to take part, what alternatives do you have?**
Participation in this study is entirely voluntary. If you decide not to allow your baby or you to participate, either now or at a later stage, you are free to do so and this will not in any way affect your current or future care or other benefits.
Who will have access to your medical records?
Information about you obtained because of your participation in this survey will be kept confidential and any reports from this study will be confidential. Auditors will review the records to ensure that all ethical and protocol conditions have been applied. If you have any questions, please do not hesitate to ask the research staff.

Will you be paid to take part in this study and are there any costs involved?

Transport money will be available to you for the monthly visits to the hospital.

Is there any thing else that you should know or do?
For the duration of the survey, your child will be under the care of Dr. Kim Harper. If at any time you have questions during the study, please do not hesitate to contact him. The telephone number where you can reach him or another authorized person is 021 558 5018.
You may also contact the study supervisor, Professor Cheryl Nikodem on 021 959 3024.

- You will receive a copy of this information and consent form for your own records.

Declaration by participant

By signing below, I ......................................................... agree to take part in a research study entitled; A randomised trial of physiotherapy as an
intervention for motor and cognitive development in children with vertically transmitted HIV infection

I declare that:

- I have read or had read to me this information and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is voluntary and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.
- I may be asked to leave the study before it has finished, if the study doctor or researcher feels it is in my best interests, or if I do not follow the study plan, as agreed to.

Signed at (place) ........................................ on (date) .......................... 20 .

____________________________________________________________________________________

Signature of participant Signature of witness

Declaration by investigator

I (name) ................................................................. declare that:

- I explained the information in this document to ..........................................................
- I encouraged him/her to ask questions and took adequate time to answer them.
• I am satisfied that he/she adequately understands all aspects of the research, as discussed above

• I did/did not use an interpreter. (If an interpreter is used then the interpreter must sign the declaration below.)

Signed at (place) ................................ on (date) .......................... 20.

................................................................................
Signature of investigator  Signature of witness

Declaration by interpreter

I (name) .......................................................... declare that:

• I assisted the investigator (name) .......................... to explain the information in this document to (name of participant) ........................................... using the language medium of Afrikaans/Xhosa.

• We encouraged him/her to ask questions and took adequate time to answer them.

• I conveyed a factually correct version of what was related to me.

• I am satisfied that the participant fully understands the content of this informed consent document and has had all his/her question satisfactorily answered.

Signed at (place) .........................  on (date) ......................... 20.

................................................................................
Signature of interpreter
Appendix F: Baby massage guide

Link to download baby massage guide:
Appendix G: Example of stimulation programme

Engaging in play
Select an activity, which the child enjoys such as throwing a ball/toy, banging an object or holding a toy.
Find a way of making the activity a two person game in which you participate with the child.
Your intervention into the child’s activity should be pleasurable. Do not persist if the child becomes frustrated or annoyed.
Teach the child to play games such as hiding an object and letting the child find it.
Impose yourself and your game on the child. Try your best to have the child attend to the game and respond to it. Stimulate the child by making vocalizations and laughing. Reward the child for any participation in or response to the game.
The gross motor tasks are developed to address the following skills

Head and neck control
While lying supine tickle the child at one corner of the mouth with a feather or your finger so that the child will turn the head to the side of the face that is being stimulated. Repeat on the other side. Hold a squeaky toy or some type of stimulating toy in front of the child about 30cm and at eye level. Encourage the child to raise the head by squeaking the object. Place the child in a sitting position and hold the child with one arm. If the child’s head sags forward, return it to an erect position by tipping the body backward. Repeat whenever the child’s head begins to sag. Perform this exercise for a few minutes, several times a day.
Sitting with support
Hold the child in a sitting position on your lap. Support the child’s weight by holding the child under the armpits. If the child can maintain the upper body in an upright position without your assistance, merely provide the child with balance. The child should practice sitting in this manner several times a day for several minutes at a time.

Rolling over
Place the child on his or her back. Kneel besides the child’s right side; reach across the child’s body and place one hand on the left shoulder and one hand on the left knee. Gently pull the child toward you so that the child rolls to the right from the back to the stomach. Return the child to the back; kneel at the child's left side and repeat by pulling on her or his right shoulder and right knee. Gradually provide less assistance and require the child to expend an increasing amount of energy to pull him or herself over.

Raising upper body when prone
Place the child in prone position. Kneel or stand in front of the child. Hold a squeaky toy or a stimulating object about 30 cm and about 10 cm over the child’s head. Encourage the child to support his or her body weight on the forearms and the lower portion of the body by squeaking a toy so that the child rises up toward it.

Sitting without support
Place the child in a sitting position on the floor. If necessary hold the child gently for balance. Gradually withdraw your assistance until the child is able to maintain balance in a sitting position.
Pulling to sitting position
Place the child on the back on a mat. Hold the child’s hands with yours and pull the child into the sitting position. Encourage the child to pull with his or her arms by pulling slowly and keeping the child in a bent-arm position. Gradually require the child to pull more while you do less of the pulling.

Creeping
Place the child on a mat on hands and knees. Move a few meters away and call, wave a toy or hold food out to the child. If the child makes any attempt to move toward you, provide a reward. The objective should be for the child to crawl across the mat using a left arm-right arm pattern.

Pull to standing
Sit the child on a child’s seat. Stand in front and hold the child’s hands. Gradually raise his or her hands so that the child attains a standing position. Reward. Return the child to the sitting position and repeat. Gradually withdraw the amount of impetus you provide and require the child to use the arms to pull him or herself into a standing position.

Standing with support
Place the child in an upright position with feet on the floor. Hold the child under the armpits and provide support as necessary. Have the child support as much of his or her own weight as possible without the knees or ankles buckling. Talk to and praise the child. Maintain the child in the standing position for 3 to 5 minutes per session and repeat the exercise several times a day. When the child can support most of his or her weight while standing, move your means of supporting the child from the armpits to holding the child by the arms. To stand independently by holding a stationary object, place the child’s hands on a stationary object. A desk, table, chair or walker could be
used. When the child is able to support body weight while standing, remove all sources of support.

**Walking**

Have the child stand. Stand behind and hold the child under the armpits. Place one of your feet behind each of the child’s feet. Use your arms and feet as necessary to walk the child. Push alternate feet forward with your feet. Talk to and praise the child as he or she walks. Continue with this until the child can make steps without your support. Progress by allowing the child to walk while you provide support from the sides. Stand beside the child facing the same direction. Hold the arm nearest to you just above the elbow. Walk the child, providing support and balance as necessary. To walk with minimal support, stand besides the child. Hold the hand and walk the child. Allow the child to use your hand for balance but do not support or balance the child yourself. Set a goal and reward the child when it is reached. To walk independently using stationary support, have the child stand next to a wall for balance. Stand in front of and face the child; call the child to you. When the child walks to a designated place reward him or her. To walk without support or assistance, place the child in the middle of the room where there are no walls or objects to use for balance. Stand away from the child and call the child to you. Reward the child for reaching you. Gradually increase the distance.

**Reaching for an object**

Hold a toy which the child is attracted to in front of the child. When the child reaches with one hand, take the other hand in yours and place it on the object. To reach for and grasp an object with one hand, place the child’s favourite toy or food within reach. When the child reaches for the object and makes an effort to pick it up, place your hand over the child’s, bend the fingers into the grasp position and assist the child in picking it up. Gradually
reduce the amount of assistance you provide. For eye hand coordination let the child place coins into a slot. Ensure that the child does not put the coins in the mouth. Child can also place solid objects such as blocks into a cup.

**Puzzles**

Puzzles are an excellent means by which to teach a child order and assembly. Begin using them as soon as the child is able to put one piece in a simple two or three-piece puzzle. Progress to puzzles with more pieces
Appendix H: Consort statement

CONSORT 2010 checklist of information to include when reporting a randomised trial

<table>
<thead>
<tr>
<th>Section/Topic</th>
<th>Item No</th>
<th>Checklist Item</th>
<th>Reported on page No</th>
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<tbody>
<tr>
<td>Title and abstract</td>
<td>1a</td>
<td>Identification as a randomised trial in the title</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1b</td>
<td>Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)</td>
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<tr>
<td>Introduction</td>
<td>2a</td>
<td>Scientific background and explanation of rationale</td>
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<td>Specific objectives or hypotheses</td>
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<td>Methods</td>
<td>3a</td>
<td>Description of trial design (such as parallel, factorial) including allocation ratio</td>
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<td></td>
<td>3b</td>
<td>Important changes to methods after trial commencement (such as eligibility criteria), with reasons</td>
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<td>Participants</td>
<td>4a</td>
<td>Eligibility criteria for participants</td>
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<td>Sources and locations where the data were collected</td>
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<tr>
<td>Interventions</td>
<td>5</td>
<td>The interventions for each group with sufficient details to allow replication, including how and when they were actually administered</td>
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<td>Outcomes</td>
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Turnitin Originality Report
PhD Submission by Oswell Khondowe
From Oswell Khondowe PhD Submission (PhD submission)

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2. < 1% match (publications)
Appendix I: Proof from editor

To whom it may concern

RE: Professional Editing of PhD Dissertation (OSWELL KHONDOWE)

This serves to confirm that the dissertation entitled “A HOME-BASED PHYSICAL ACTIVITY PROGRAMME IN COMBINATION WITH MASSAGE THERAPY TO IMPROVE MOTOR AND COGNITIVE DEVELOPMENT IN HIV positive CHILDREN ON ANTIRETROVIRAL THERAPY: A RANDOMISED CONTROLLED TRIAL authored by Oswell Khondowe was edited and proof read by S.A.S Transcribers and Editors in December 2013.

Sinikiwe Simakani
Chief Editor

sas.transcribers@gmail.com