Raising an HIV-infected Child:

Associations between parental stress and child functional impairment

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COMPULSORY DECLARATION

This work has not been previously submitted in whole, or in part, for the award of any degree. It is my own work. Each significant contribution to, and quotation in, this dissertation from the work, or works, of other people has been attributed, and has been cited and referenced.

Signature:_____Date:_____

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TABLE OF CONTENTS

LIST OF TABLES

ABSTRACT

This project sought to achieve two major aims. First, I aimed to investigate the differences in functional, behavioural, and emotional impairment of HIV-infected, HAART-naive children compared to HIV-negative controls. Second, I aimed to investigate the levels of parental stress, depression, and quality of life related to caring for an HIV-infected child. Currently, there is limited research focusing on each of these topics. Nineteen HIV-positive (9 HAART-naïve and 10 HAART-treated) parent-child dyads and 10 HIV-negative parent-child dyads were recruited. All participants were from socioeconomically disadvantaged backgrounds. Each parent and child completed measures related to the aims of this study. Parents completed measures related to their child's functional impairment (i.e.: CBCL, CIS, CMS) and questionnaires related to their parental well-being (i.e.: PSI, FRS, FSS, CES-D, WHO QoL). Children completed a comprehensive neuropsychological test battery. Statistical analyses revealed no significant between-group differences in terms of child functional, behavioural, and emotional impairment. These non-significant findings were confirmed by an in-depth qualitative review of three case studies. Statistical analyses also revealed no significant between-group differences with regards to parental stress, depression, and quality of life. The possibility of poor socioeconomic status (SES) explaining the lack of difference is discussed, as well as the possibility of potential protective factors.

Keywords: HAART-naïve, asymptomatic, functional impairment, apathy, parental well-being, quality of life

INTRODUCTION

The Human Immunodeficiency Virus (HIV) poses a great health risk worldwide. Approximately 34 million people worldwide were living with HIV at the end of 2010 (World AIDS Day Report [UNAIDS], 2011). Although this number represents a 17% increase from 2001, it also indicates that more people are living longer with the disease, largely due to the rollout of antiretroviral drugs. Almost 600 000 new HIV infections in children in SSA have been averted since the rollout of ARVs to pregnant mothers and their infants (UNAIDS, 2012).

The United Nations AIDS report (2011) also indicates that, in 2010, 68% of all people living with HIV resided in sub-Saharan Africa, in particular the southernmost regions, including South Africa. The report also estimates that there are more HIV-infected people (approximately 5.6 million) living in South Africa than in any other county, and that women in sub-Saharan African remain the most affected of all people living with the virus globally.

These epidemiological statistics imply, and empirical studies confirm, that HIV is no longer only associated with high-risk groups, but is rather a generalized epidemic in sub-Saharan Africa. Of particular concern here is that, alongside heterosexual sex, the most prominent mode of transmission is that from mother to child (Eisenhut, 2013; Piot, Bartos, Ghys, Walker, & Schwartlander, 2001).

A number of elements influence the risk of *mother-to-child transmission* (MTCT; also known as *vertical transmission*). These include progression of the disease in the mother, gestational age, concordance, birth order, birth weight, route of delivery, and breastfeeding (Dulienge, Amos, Felton, Biggar, & Goedert, 1995). Highly Active Antiretroviral Treatment (HAART) during pregnancy is considered the most successful way to decrease the risk of MTCT (Ciaranello et al., 2008; Moodley, Reddy, Mahungo, & Masha, 2013). Since April 2010, all pregnant women testing positive for HIV in South Africa have been started on HAART treatment, regardless of CD4 count (Van Der Merwe et al., 2011).

Many risk factors affect perinatal outcomes in South Africa (Tomlinson et al., 2013). Hence, to run a successful Prevention of Mother-to-child Transmission (PMTCT) programme, one must adopt a comprehensive approach (Aizire, Fowler, & Coovadia,2013). However, in a low- and middle-income country like South Africa, there are many barriers to creating such comprehensive programmes. These barriers might be at the individual level (e.g., voluntary HIV testing and counselling, ARV adherence) and at the level of health care resources (e.g., adequate hospital facilities, rural populations, amount of GDP designated to healthcare expenditure). All such barriers make running successful PMTCT programmes

difficult (Audureau, Kahn, Besson, Saba, & Ladner, 2013). There is a long way to go before UNAIDS' target to eliminate new HIV infections in children by the year 2015 might be deemed achievable (UNAIDS, 2012).

Effects of HIV on Psychosocial Development and Behavioural Functioning

Compared to typically-developing peers who are not infected with HIV, HIV-positive children are at high risk for experiencing numerous threats to psychosocial development (Smith et al., 2006) and consequent behavioural and emotional dysfunction. Wachsler-Felder and Golden (2001), in a review of the literature to that point, reported that HIV has been consistently shown to have behavioural, cognitive, emotional, developmental, and educational effects on the child infected with this disease.

Whether or not parents disclose their HIV status to children can have a significant impact on psychosocial development, and particularly on the child's interactions with others (e.g., with regard to the likelihood of discrimination and/or stigmatization; Lesch et al., 2007). Furthermore, HIV-positive children are likely to emerge from lower socioeconomic status (SES) backgrounds, and so may not have access to appropriate medical care or to adequate social support. If they are able to access treatment, they have to adhere to complex medication regimes and have to cope with side effects of those medications (Rotheram-Borus, Murphy, Miller, & Draimin, 1997). Perhaps most important among these threats to psychosocial development is the fact that HIV-positive children are more likely to experience the loss of a parent, and so are more likely to spend much of their childhood under the care of members of their extended family or of foster parents (Skinner et al., 2006).

Hegarty, Abrams, Hutchinson, Nicholas, and Heargerty (1989) showed that 20% of the medical care costs of 40 HIV-infected children were related directly to their social circumstances. The relationship implied that the medical cost of caring for a HIV-infected child increased with poorer social circumstances. These social circumstances may include homelessness, poverty, and overcrowding (Kazak, 1989).

As noted above, the higher likelihood of exposure to these threats to psychosocial development is associated with a higher likelihood of behavioural and emotional dysfunction in the HIV-positive child. Numerous studies confirm that these children are much more likely to display symptoms of psychiatric disorders, to experience difficulties with social interactions and relationships, to struggle with adaptive functioning, and to report poorer overall quality of life (Grover, Pensi, & Banerjee, 2007; Li, Lin, Ji, Sun, & Rotheram-Borus, 2009; Mendoza et al., 2007).

Regarding symptoms of psychiatric disorders in HIV-positive children, Mellins, Brackis-Cott, Dolezal, and Abram (2006) found that 26 of the 47 participants in their study of vertically-infected children met criteria for a psychiatric disorder, and that 12 met criteria for multiple disorders. The most prominent disorders present were anxiety-related (e.g., social phobia, separation anxiety disorder, agoraphobia, panic disorder, obsessive-compulsive disorder (OCD), and specific phobias). Behavioural disorders such as conduct disorder, oppositional-defiant disorder (ODD), and attention-deficit/hyperactivity disorder (ADHD) were present in 11 participants.

Nozyce et al. (2006) replicated these findings in a much larger sample (N = 274). More than half of their participants (n = 142) presented with at least one behavioural problem. Specifically, 43 presented with conduct-related problems and 68 with learning-related problems; 76 reported psychosomatic experiences; 52 were classified as being impulsive-hyperactive and 54 as being hyperactive only; and 21 presented with anxiety problems. Although the rank-order of these categories differs somewhat from that reported by Mellins et al. (2006), the fact that behavioural and psychiatric problems were so prevalent in both samples is most concerning from a public health perspective.

A particular psychiatric symptom that is understudied in children, but that is of particular interest here, is apathy. Gerring et al. (1996, p. 206) define apathy in children as "decreased interest, drive and ability to persist in a course of action" with a "reduced capacity to initiate activity and thus engage in goal-directed behaviours and goal-directed cognition." Skinner et al. (2006) propose that children with apathetic affect appear unhappy, dull, miserable, and demotivated; with specific regard to academic performance, for instance, they may not perform well in class or at school in general, may neglect their schoolwork, or may not attend school regularly. Moss, Wolters, Brouers, Hendricks, and Pizzo (1996) found, after videotaping sessions with HIV-infected nonencephalopathic and encephalopathic children, that those with severe HIV-related CNS damage appeared more apathetic and that, in particular, verbal behaviour was more likely to be absent in them. Furthermore, research on HIV-infected adult populations has shown that apathy is associated with lowered levels of global functioning, decreased response to treatment, poor illness outcomes, caregiver distress, and chronicity (van Reekum, Stuss, & Ostrander, 2005).

Given that HIV-positive children are more likely to experience (a) threats to their psychosocial development and (b) behavioural and emotional difficulties, it is quite likely

that they will also be at higher risk for functional impairment[1] in school, social, and occupational domains. Numerous empirical studies document just such impairment. For instance, Elliot-DeSorbo, Martin, and Wolters (2009) reported that school-related stressful events were the most commonly reported problem by an American sample (N = 55) of HIV-infected children aged 8-18 years. They noted that a drop in grades and behavioural difficulties at school were among the most common problems related to academic functioning.

As is clear from the above review, numerous studies describe the threats to psychosocial development, the behavioural and emotional difficulties, and the functional impairments often experienced by HIV-positive children. Very few studies, however, attempt to describe the associations between those threats, difficulties, and impairments. One possible reason for this lack of relational studies is that behavioural difficulties are probably explained by both environmental and neurological factors. In other words, HIV neuropathology itself may have direct and indirect effects on behavioural, emotional, and cognitive outcomes. Direct effects are related to the degenerative effect the virus has on the brain and its development, and so vary in severity. Indirect effects are related to the psychological stresses associated with living with this chronic disease (Wolters, Brouwers, & Moss, 1995).

Highly Active Antiretroviral Therapy (HAART) and Asymptomatic Children

HAART. HIV-infected children often have to adhere to a complex treatment regime of chronic medication. Treatment with antiretroviral medications (ARVs) helps boost the immune system and CD4 count[2] significantly (Yarchoan et al., 1991). At present, HAART is the most recommended treatment regime for HIV-infected children and adults. HAART usually consists of a combination of three drugs (lamivudine plus, either zidovudine or stavudine, and nevirapine or efavirenz; Koekkoek et al., 2006), and is used to suppress viral replication and progression of the infection.

At present there are five classes of drugs available (1) nucleoside and nucleotide reverse transcriptase inhibitors (NRTI and NtRTI, respectively), (2) non-nucleoside reverse transcriptase inhibitors (NNRTI), (3) protease inhibitors (PI), (4) entry inhibitors, and (5) integrase inhibitors (Merry & Flexnar, 2010). Approved treatment regimens for use in pediatrics are complicated, because the regime and dosages are based on adult efficacy studies (Hazra, Siberry, & Mofenson, 2010). Administering ARVs to children using the adult

[1]Functional impairment is defined here as "specific deficits in multiple domains of functioning developing subsequent to a disorder" (Winters, Collet & Myers, 2005).
[2]CD4 count is defined here as "a standard measure of immunodeficiency in adults and children infected with HIV to initiate and monitor HAART" (Yuming et al., 2011).

guidelines can have serious consequences: For instance, if one administers inappropriate drug dosages, one might thereby affect the efficacy of the treatment and/or increase the risk of side effects. In the United States, the Federal Drug Administration (FDA) has approved 25 different ARV drugs; 16 of these are indicated for use in pediatrics, and 15 of those are available in liquid form for ease of administration in children. An open-label clinical trial by Nahirya-Ntege et al. (2012) found that both caregivers and children preferred tablets over syrup ARV medications. The most common reasons for not choosing syrups were medication transportation problems, the number of bottles needed, the weight of carrying many bottles, and conspicuousness of bottles.

The question of when to start treatment in children is still under debate (Eley et al., 2006). One set of recommendations is as follows: infants younger than 12 months should start ARV treatment immediately after birth, regardless of immunologic, virologic, and clinical symptoms; for children aged 1 year and older, treatment should be considered if the CD4 count is in the range of 350-500 cells p/mm^3, or if the plasma RNA concentration exceeds 1000 copies/ml, regardless of clinical and immunological function (Panel on Antiretroviral Therapy and Medical Management of HIV-infected Children, 2011).

These debates and uncertainties surrounding HAART use in children suggest that more large-scale longitudinal studies of HIV-positive pediatric populations need to be conducted. Also, the progression of the disease for children who have been infected via different modes might vary, and is also in need of study. For instance, the most devastating clinical manifestation of the disease in children who have been vertically infected is HIV encephalopathy,[3] and is mostly a consequence of the pre-HAART era (i.e., prior to the start of the rollout of HAART HIV encephalopathy was highly prevalent (Chiriboga, Fleishman, Champion, Gaye-Robinson, & Abrams, 2005)). HIV encephalopathy may be static or progressive. In most cases of vertically-infected children it is progressive (Little et al., 2007); a handful of studies have shown, however, that sometimes children who survive into adolescence may have more subtle manifestations (Hazra, 2010). These children are referred to as ‘asymptomatic’.

Symptomatic and asymptomatic children. HIV attacks the human immune system. It follows, logically, that degree of disease progression is linked to measures of the level of proper functioning of that system. Following this line of reasoning, HIV-positive individuals

[3]HIV encephalopathy is defined here as “the presence of one or more of the following: progressive neurologic deterioration, loss of developmental milestones, or symmetric motor dysfunction” (Lobato, Caldwell, & Oxtoby, 1995).

are termed either ‘symptomatic’ or ‘asymptomatic’ depending on the progression of the disease and the measures of CD4 count and viral load. CD4 count is the number of T-cells activated in the immune system in response to viral detection, while viral load is amount of copies of the HIV virus in the body (AIDS.gov, 2010). In clinical settings, CD4 count and viral load are used as the gold standard measures to determine progression of the disease (Yuming et al., 2011) and to determine whether the patient is deemed as symptomatic or asymptomatic. CD4 count is also used as a means to determine whether or not HAART treatment should be initiated. High CD4 count and low viral load are an indication that ARV treatment is working in suppressing the virus; asymptomatic individuals have these characteristics. Conversely, a low CD4 count and high viral load are associated with symptomatic individuals and suggest an increase viral replication (AIDS.gov, 2010).

Recent research in this field suggests that being vertically infected with the virus is associated with rapid disease progression (Freguja, 2012), and that vertically-infected children may be slower to reach developmental milestones (AIDS.gov, 2009). These children usually start showing symptoms about 2 years after birth (Eley et al., 2006), but, as Dunckley-Thompson, Figueroa, and Christie (2006) note, there are numerous reports of children only starting to present with symptoms after the age of 8 years. In some cases, initial symptoms only present during adolescence (The European Collaborative Study, 2001; Mandalia et al., 2012; Hoare et al., 2012). Children with such late presentation are termed asymptomatic ‘slow progressors.’ They are also referred to as ‘HAART naïve’ because of their lack of exposure to ARV treatment (Hoare et al., 2012). These children may only present for HIV treatment as adolescents, and may even be unaware of their HIV status until then.

The reason for this slow progression of the disease in some infected children is not yet understood fully. Because these ‘slow progressors’ may go undiagnosed for many years, it presents a problem in that these children are then living with the virus and are untreated. The new HAART treatment guidelines, as described above, should, under ideal conditions, prevent asymptomatic children from being untreated until symptoms present.

HAART for asymptomatic children. In South Africa, the social stigma attached to HIV remains prominent in lower-SES settings (Kalichman & Simbayi, 2004). For this reason, low-SES parents, especially, are reluctant to test for HIV (Kalichman & Simbayi, 2003). Meyers et al. (2007) report that fewer than 50% of women attending antenatal clinics in South Africa opt for voluntary testing and counselling. Hence, an undiagnosed parent-child

dyad could go untreated for many years until symptoms present themselves during adolescence.

What are the consequences for vertically-infected children of only starting HAART treatment well into adolescence? The most obvious consequence is low CD4 count and high mortality rates (Lewden et al., 2012). Furthermore, an established ARV regime in children is associated with enhanced survival, reduction in opportunistic infections, improved growth and neurocognitive function, and better quality of life (Heidari et al., 2012). However, despite these advantages of being on ARVs, HIV-infected children may still lag behind their HIV-negative counterparts with regards to normal growth and development (Heidari et al., 2012; LeDoarè, Bland, & Newell, 2012). LeDoarè and colleagues (2012) also note that motor and cognitive scores are significantly lower (1-2 standard deviations below the population mean) if children are not on HAART.

Krentz and Gill (2012) also note the long-term financial implications of late HAART initiation: They found that late initiation was associated with higher medical costs compared to early initiation.

Research looking specifically at this asymptomatic, HAART-naïve population of HIV-infected children is thus very important. Investigations into their emotional, behavioural, and functional profiles may prove to be a valuable addition to the greater body of knowledge about outcomes in HIV.

Parental Stress Associated with Caring for an HIV-infected Child

Research has demonstrated consistently that chronic pediatric illness is associated with increased family stress and decreased family functioning, and is a strong determinant of subjective quality of life and overall well-being of parents (see, e.g., Herzer et al., 2010). Importantly, however, family and parental functioning may be differentially affected by the specific characteristics of the child's chronic disease (i.e., the varying nature of different chronic diseases in children have different effects on the parents of those children), especially in the case of diseases with a high treatment burden and an unpredictable course. For instance, Ingerski, Shaw, Gray, and Janicke (2010) found that the level of traumatic stress experienced by parents of chronically ill children differed across illness groups (youths who had experienced organ or bone marrow transplantation, HIV-infected youths, and youths with sickle cell disease). The parents of children who had received organ transplants were the most affected, with the parents of HIV-infected children being next; parents of children diagnosed with sickle cell disease were least affected. The same authors stated that a parent's overall view of their child's functioning is affected by their own experience of traumatic stress. This

particular aspect is important to bear in mind when looking at perinatally HIV-infected children, because it means that the parents themselves are also infected with virus and experience its effects as much as their children do.

A few studies have focused specifically on the stress levels of parents with HIV-positive children. Lesar, Gerber, and Semmel (1995) studied a sample of parents (N = 48) who were HIV-positive and who had at least one child also infected with the virus. They found that these parents, all of whom had compromised health, additional care burdens, and a child with developmental delays, experienced more parenting stress than parents of non-infected children. To add to these high parenting stress levels, HIV-infected parents might also have to cope with their own physical health symptoms, complex medication regimens, stigmatization, the fear of an almost certain AIDS-related death, and caring for their living family members (Rotheram-Borus, Lee, Gwadz, & Draimin, 2001). In other words, HIV-infected parents are affected by factors related not only to the health of their HIV-infected child, but also to their own physical and mental health.

HIV infection and its consequent parental stress can also affect the family as a whole. For example, parents who are HIV-infected express fears of disease transmission to their uninfected family members, affecting social aspects of the family functioning like hugging/kissing, showing affection, and using the same bathroom and/or kitchen facilities (Cowgill, Bogart, Corona, Ryan, & Schuster, 2008). Furthermore, parents who are stressed about their parental role exhibit poorer parenting skills than parents who are not as stressed. These poorer skills may result in disorganized family routines, poor parent-child communication, and a relative lack of engagement with the child, and, ultimately, negative behavioural outcomes for the child (Murphy, Marelich, Armistead, Herbeck, & Payne, 2010).

In South Africa, a low-to-middle income country, parental stress may be influenced by many compounding factors, including poor health care systems, ill-equipped schools, high rates of illiteracy, and overall poor economic state (Levin, 2004). Unemployment rates in South Africa are as high as 25.5% (Statistics South Africa, 2012), contributing to the poor economic state. In a national health and stress study, Seedat et al. (2009) found that adults in South Africa were at risk for developing certain lifetime mental disorders (e.g., anxiety and mood disorders) highly correlated to life stressors such as global negative life events, relationship stress, domestic/intimate partner violence, social strain, and early/childhood life stress. The same authors also found that single marital status was the strongest sociodemographic predictor of lifetime mental disorders.

High mortality rates due to HIV and AIDS have resulted in an increase in the number of single caregiver families in South Africa (Smit, 2007). Single-parent families may take many forms (e.g., grandparent-headed families, child-headed families, and families headed by members of the extended family (Smit, 2007). In a study comparing one-parent families to two-parent families of parents with children who had cerebral palsy, McCubbin (2007) found that both types of families had to deal with the same demands and stressors (i.e., resource constraints, family cohesion, family resources of esteem/communication, lack of extended family support, and child health status and improvement), but that one-parent families were significantly poorer in terms of financial well-being. Having to meet and maintain the needs of a family, which has the same demands as a dual-parent family, can indeed be stressful for the single parent.

In a study examining family transitions and parent psychological well-being, Osborne, Berger, and Magnuson (2012) found that parents transitioning into single parenthood reported a decrease in perceived social support and an increase in material hardship, depression, and overall parenting stress. As mentioned earlier, many HIV-affected families in South Africa are dealing with these kinds of family transitions.

Caring for an HIV-infected child is difficult and may be even more so when one has limited resources and social support structures available. In a low-SES setting, as found in many South African communities, family-focused interventions dealing with the various psychosocial impacts of HIV may be valuable. Research has shown that family interventions aimed at both HIV-infected parents and their adolescent children, whether they be infected or not, are beneficial in terms of adolescent emotional and behavioural outcomes (Rotherum-Borus et al., 2001, 2003).

Specific Aims and Hypotheses

The current study is nested within a larger research project examining the integrity of neural pathways, and associated neuropsychological, neuropsychiatric, and behavioural characteristics, of vertically-infected HIV-positive, HAART-naïve children. The study described here focused on investigating differences in functional impairment of HIV-positive HAART-naïve children compared to their HIV-positive HAART-treated and HIV-negative counterparts. I also investigated the parental experience, and overall parental well-being in parents of HIV-positive children (both HAART-naïve and HAART-treated) and parents of HIV-negative children.

The first major aim of this study was to investigate functional and emotional impairment in HIV-positive and HIV-negative children. I examined various aspects of

functioning (e.g., motivation, internalizing and externalizing behaviours, competencies, etc.), as well as symptoms of apathy. The term apathy is used loosely here to suggest a lack of motivation. Motivation is not only an important aspect of daily social and school functioning, but is important for adherence to medication and overall well-being.

In comparing HIV-positive and HIV-negative children, I also sought to determine if there are differences within the HIV-positive group (i.e., between HAART-naïve and HAART-treated subgroups). In so doing, I attempted to answer the question of whether the HAART-naïve participants could truly be viewed as asymptomatic.

Research focusing specifically on the functional, emotional, and behavioral deficits of HIV-infected children has not yet been conducted in sub-Saharan Africa, which bears the largest burden of the HIV epidemic. Even less literature is available on the functioning of asymptomatic HAART-naïve children who are HIV-infected. Research into this specific area can greatly contribute to global knowledge about this specific population. Focusing more specifically on describing or characterizing the asymptomatic HIV-positive children could also, for instance, influence many areas of care for this group (e.g., policy regarding when to start ARVs, behavioural programs, etc.).

The second major aim of this study was to investigate whether caring for an HIV-positive child affects the parental experience. More specifically, I addressed the question of whether levels of child functional impairment and behavioural/emotional difficulties were associated with levels of parental stress and parents' subjective quality of life. Parental stress and functioning has an important effect on the overall functioning of the family, as increased levels of such stress may lead to negative outcomes (e.g., lack of affective involvement and support, and lack of communication) for the child and for the family as a whole (Herzer et al., 2010). I examined whether the parental experience of parents of HIV-positive children is significantly different from that of parents with HIV-negative children.

Adding to the field of knowledge about the parental experience of caring for an HIV-positive child will be beneficial in terms of developing parental support groups and/or programs. Helping parents cope with the burden of being HIV-positive themselves and caring for their infected child could also be beneficial in terms of patient outcomes (e.g., better coping mechanisms may mean better medication adherence, better attendance at regular clinic appointments, etc.).

Given those two specific aims, I tested the following specific hypotheses:

Hypothesis 1: Overall, HIV-positive children will demonstrate more behavioural and emotional difficulties, and more functional impairment, than HIV-negative controls. Within the HIV-positive group, the HAART-naïve participants will function better than HAART-treated participants. That is to say, the HAART-naïve and control groups are similar in terms of functional, behavioural, and emotional functioning. If the HAART-naïve participants are truly asymptomatic, then this hypothesis will be disconfirmed.

Hypothesis 2: Parents/caregivers of HIV-positive children will report experiencing more stress and depression, and poorer subjective quality of life, than will parents/caregivers of HIV-negative children. Further, caring for a HAART-naïve child will be just as stressful as caring for a HAART-treated child.

Because I was unable to achieve optimum power (see sample sizes and complete discussion of this issue below), this study is a preliminary mixed-methods investigation into the levels of child functional impairment and the association between such impairments and parental stress, depression, and subjective quality of life. Although low power means that direct statistical inferences cannot be made based on my findings, the preliminary results presented here point to future directions for research with children and adolescents affected by HIV.

METHODS

Research Design and Setting

This study used a quasi-experimental design. I compared three sociodemographically-matched groups of parent-child dyads: HIV-positive HAART-naïve children and their parents, HIV-positive HAART-treated children and their parents, and HIV-negative children and their parents. All participants were interviewed and tested at the Red Cross War Memorial Children's Hospital (RXH). This study was nested within a larger research programme, centered at RXH and the University of Cape Town (UCT), investigating neuropsychiatric, neuroimaging, and neuropsychological characteristics of HIV-infected children.

Participants

We recruited 19 vertically infected HIV-positive children (aged 6-12 years) along with one parent/primary caregiver for each. Nine of these children were HAART naïve, and the remaining 10 were on HAART treatment. These children were actively recruited from clinics in the township areas of Khayelitsha (Nolungile Day Hospital, ARV Clinic in Site C) and Mitchell's Plain (Mitchell's Plain Day Hospital, ARV clinic). Representatives of the

research team approached parents in the waiting rooms of these clinics and notified them about the study. If the parents expressed interest, they were later contacted via telephone so that a researcher could give them a more detailed explanation about the study procedures, and could schedule an appointment.

We recruited a matched group of 10 HIV-negative typically developing children, along with one parent/primary caregiver for each, from local township schools and via word-of-mouth in socioeconomically disadvantaged communities in the Cape Town area.

Table 1 presents a summary of the eligibility criteria applied to both HIV-positive and HIV-negative children.

All three groups of children were enrolled into the larger study mentioned above, whereas their parents/caregivers participated in this study only. The only eligibility criterion applied to the latter was that they were either the biological parent or the primary caregiver of a child participating in the larger study. In all instances, the study team attempted to recruit a biological parent if at all possible; if it was not possible, or if neither biological parent was the child's primary caregiver, the team recruited the adult with whom the child lived.

Table 1
Study Eligibility Criteria: Children (N = 29)

	Group		
Variable	HAART-naïve (n = 9)	HAART-treated (n = 10)	HIV-negative (n = 10)
Diagnosis	Known HIV-positive; vertically transmitted	Known HIV-positive; vertically transmitted	Known HIV-negative
Treatment history	HAART naïve[a]	HAART treated	HAART naïve
Age	6-12 years	6-12 years	6-12 years
Developmental status	No known history of disorder	No known history of disorder	No known history of disorder
Functional status	"Normal"/asymptomatic	CD4 count[b] < 500 mm^3	Typically developing
Neurological history	No known other conditions	No known other conditions	No known previous conditions
Psychiatric history	No known history of disorder	No known history of disorder	No known history of disorder

[a]This term refers to individuals who are not currently on HAART, and who have not received it in the past, and who are therefore completely naïve to the medication.
[b]CD4 count is measured in cubic milliliters; one cubic milliliter is equivalent to about one drop of blood (Treatment Training Manual, 2009).

Instruments and Measures

Most instruments used in this study were completed by the parents/caregivers. Some of these instruments pertained to aspects of the child's functioning, while others related to aspects of the parent's functioning and his/her stress levels. The instruments were chosen strategically and specifically to help achieve my research aims.

While the parent/caregiver completed these instruments, the child was administered a comprehensive neuropsychological test battery as part of his/her participation in the larger study referred to above. Because some participants were isiXhosa first-language speakers, all questionnaires, as well as the neuropsychological measures administered to the children, were translated into isiXhosa and back-translated into English by qualified translators at the Stellenbosch University Language Centre. A registered social worker, fluent in English and isiXhosa, administered the measures to all participants in their first language (either English or isiXhosa).

Sociodemographic questionnaire. Researchers involved in the larger study developed this questionnaire. It gathered information about race, language, education, household income, and living conditions (see Appendix A).

Columbia Impairment Scale (CIS). The parent-rated version (Bird et al., 2008) of this instrument (a 13-item Likert-type scale) was used to measure the child's global functioning level. It measures impairment within the following domains: interpersonal relationships, psychopathology, schoolwork, and use of leisure time (see Appendix B).

Parents were asked to rate, by responding to different statements, how much of a problem their child had within different areas of functioning. An example of one such statement is, "How much of a problem would you say he/she has with: his/her behaviour at school". Parents were required to rate their child as having *no problem*, a *very small problem*, *some problem*, a *moderate problem*, or a *very bad problem* with each of the statements/scenarios given. Parents also had the option to answer *not applicable* or *don't know*.

The instrument's developers report that it has a test-retest reliability of 0.89, and that it also has good validity. They also report that the parent-rated version of the questionnaire has better psychometric properties than the child self-rated version; the former is therefore recommended for both clinical and research purposes. This scale has not been used in published South African studies. It is, however, listed on the Mental Health Screening and Assessment Tools for Primary Care toolkit, released by the American Academy of Pediatrics

(2010), as a psychometrically good measure of child global functioning, taking into account cultural considerations.

Children's Motivation Scale (CMS). This 16-item instrument (Gerring et al., 1996) was used to measure the child's motivation levels, or tendency toward apathy (see Appendix C). For each item, the parent was asked to state how often his/her child engaged in self-motived activities. For example, if a statement read "Starts playing (games, activities) on his/her own", the parent would select one of the following options: 0 (*never or rarely occurs*), 1 (*1-3 times during a month*), 2 (*1-3 times per week*), 3 (*4-6 times per week*), or 4 (*1 or more times a day*)

The instrument's developers report that, in their psychometric studies, (a) apathy did not vary as a function of age for both typically developing and clinical samples, and (b) the instrument demonstrated satisfactory test-retest reliability, internal consistency reliability, and validity in both samples (Gerring et al., 1996). This test has not been used in previously-published studies of South African samples.

Child Behaviour Checklist (CBCL). This 113-item instrument (Achenbach & Rescorla, 2001) is one of the most widely used and psychometrically sound measures for assessing child behavioural and emotional problems and psychopathology (Albores-Gallo et al., 2007; Rescorla, 2005). In this study, it was used to measure internalizing and externalizing problems experienced by the child. It was also used to measure total problems experienced by the child, as well as the child's total competence.

Parents were asked to rate items according to how much each given statement applied to their children: 0 (*not true*), 1 (*somewhat or sometimes true*), or 2 (*very true or often true*). Examples of some statements are: "Acts too young for his/her age" and "Can't concentrate, can't pay attention for long."

The scale developers report test-retest reliability coefficients of 0.95-1.00, and internal consistency reliability of 0.78-0.97. These figures hold for translated versions of the CBCL; the instrument has been translated into more than 70 languages, and is used globally (Albores-Gallo et al., 2007). This scale has been used successfully used to measure child behaviour problems in South African children (Shields, Nasaden, & Pierce, 2004).

Parenting Stress Index (PSI). This instrument is a 120-item scale assessing parental stress as it relates to the child's most prominent functional characteristics and/or problems (Abidin, 1995). In this study, the PSI was used to measure the level of stress experienced by each parent/caregiver.

The scale features a Child domain and a Parent domain, each of which consist of various subscales. The Child domain subscales are *mood*, *distractibility/hyperactivity*, *adaptability*, *demandingness*, *reinforces parent*, and *acceptability*; the Parent domain subscales are *competence*, *isolation*, *attachment*, *health*, *role restriction*, *depression*, and *spouse*. An example of a child-related statement is: "My child is so active it exhausts me." An example of a parent-related statement is: "Being a parent is much harder than I thought." When totalled together, scores from the individual subscales within each of the Parent and Child Domains yield a stress score specific to that domain for each parent. Overall Total Stress scores and Life Stress scores are calculated from those scales. The Life Stress score is based on the amount of stress that the parent reports experiencing outside of the parent-child relationship, whereas the Total Stress score is based on the combined total scores from the Child and Parent domain subscales.

The instrument's developer reports reliability coefficient scores of 0.63 for the Child domain, 0.91 for the Parent domain, and 0.96 for the Total Stress score (Abidin, 1995).

The PSI has been used in a descriptive study examining stress levels in parents of very young HIV-positive babies in Johannesburg, South Africa (Potterton, Steward, & Cooper, 2007) over a period of 12 months. Those authors reported that this scale had good test-retest reliability, and that this was true for the translated (Zulu and Sotho) versions of the scale as well.

Family Resources Scale (FRS). This 30-item scale (Dunst & Leedt, 1986) assesses the adequacy of tangible resources in homes with young children. The specific resources under consideration are those required to be able to meet the needs of the family as a whole (Appendix D). In this study, the FRS was used to measure the access each family had to particular kinds of resources (e.g., money to pay monthly bills, health care for the family, etc.).

The instrument shows good internal consistency (Cronbach's $\alpha = 0.92$) and test-retest reliability ($r = 0.52$; Spratt, Saylor, & Marcias, 2007). The FRS has not been used in previously-published HIV-related studies of South African samples.

Family Support Scale (FSS). The FSS (Dunst & Leet, 1986) is an 18-item scale assessing the perceived level of family and social support to which parents/caregivers have access (Appendix E). The respondent is asked to rate the amount of support he/she receives from various sources (e.g., family, friends, the community, etc.). In this study, the FSS was used to measure the amount of social support the parents/caregivers had available to them.

The scale developers report that the instrument shows good internal consistency (Cronbach's α = 0.77). Hanley et al. (1998) report that test-retest reliability ranges from .35-.76 for the various subscales, and is .80 for the total score. The FSS has not been used in previously-published HIV-related studies of South African samples.

Center for Epidemiologic Studies – Depression Scale (CES-D). This 20-item scale was developed specifically for general use within community populations (Knight, Williams, McGee, & Olaman, 1997; Radloff, 1977). The instrument (see Appendix F) is an amalgamation of the Beck Depression Inventory (Beck, 1996), Zung Self-Rating Depression Scale (Zung, 1965), Raskin scale (Gardner, 1968), and the Minnesota Multiphasic Personality Inventory Depression Scale (Hathaway & McKinley, 1942). In this study, the CES-D was used to measure the level of depression experienced by parents/caregivers over the 2 weeks prior to administration.

Radloff (2000) reports that the CES-D's internal consistency reliability was measured at 0.85 for community populations and at 0.90 for psychiatric samples. This scale has been used successfully to measure depression in HIV-positive South African adults (Singh, Sunpath, John, Eastham, & Gouden, 2008). That study reported a sensitivity of 91% using a cut-off score of 16.

WHO Quality of Life Scale (Brief Version). This instrument is a 26-item version of the WHO QoL 100 assessment scale, which is used to assess life satisfaction. In this study, the instrument was used to measure parents'/caregivers' subjective perception of, and satisfaction with, their quality of life, bearing in mind that they cared for an HIV-infected child. The scale was developed collaboratively, using participants from more than 15 cultural backgrounds, to assess the subjective, rather than objective, quality of life and living conditions as perceived by adults/parents (Gururaj, Math, Reddy, & Chandrashekar, 2008; Li, Young, Xiao, Zhou, & Zhou, 2004).

The psychometric properties of the brief version of the instrument are comparable to those of the full version and, overall, it is regarded as a sound, cross-culturally reliable and valid instrument for measurement of quality of life (Gururaj et al., 2008; Skevington, Lofty, & O'Connell, 2004).

Regarding previous use in South Africa of the aforementioned parental scales (i.e., the PSI, FRS, FSS, CES-D, and WHO QoL), Cheesman (2010) used all, with much success, in a study investigating parental stress and attention-deficit/hyperactivity disorder (ADHD).

Clinical relevance. Regarding the child functional scales, the CBCL and CIS are good at distinguishing between clinically impaired and normal behaviours in children.

Regarding the parental well-being scales, the PSI and CES-D are good at distinguishing between clinically stressed and depressed parents compared to parents who are experiencing a normal amount of stress and/or depression associated with being a parent.

Neuropsychological test battery. Each child participant completed a standardized battery of clinical neuropsychological tests. Each test within the battery is commonly used in pediatric neuropsychological assessment in South Africa. The battery tested cognitive performance in the following domains: general intellectual functioning, hand-eye co-ordination, motor speed, information processing, attention and concentration, working memory, visual memory, verbal memory, visuospatial ability, and executive functioning. Hoare et al. (2012) provide further details on the individual tests within the battery. (See Appendix J for a full list of the neuropsychological test battery).

Procedure

HIV-positive children and their parents/caregivers. As mentioned previously, this study was nested within a larger research programme that aimed to investigate the neural correlates of cognitive, behavioural, and emotional dysfunction in HIV-infected children. HIV-positive participants completed a full medical history screening and laboratory blood tests as part of their routine medical examination at the center/clinic they were attending. Medical doctors affiliated with the larger study, and who had access to participants' medical records, confirmed these participants' HIV-positive status.

Researchers representing the larger project provided the team assigned to this study with the names and contact details of eligible participants. We then contacted the parent/caregiver of each potential child participant telephonically to inform them of their eligibility for voluntary participation and, if they gave verbal consent, to schedule them for a research session. All sessions relevant to this study took place at Red Cross War Memorial Children's Hospital (RXH). Each child participant had to complete three sessions as part of the larger study. The neuropsychological measures were completed at the first session, a brain scan was done at the second session (this session was done at the Cape Universities Brain Imaging Center CUBIC)), and behavioural measures were completed at the third session. The research team provided all participants with transport from their area of residence to the testing sites.

A translator explained the full consent form (Appendix G) to the parents and their children in their first language at the start of the first appointment. If parents/caregivers were willing to sign the informed consent document, we continued with the session. One parent or primary caregiver completed self-report measures about him/herself and his/her child. The

child was not required to participate actively in this aspect of the current study, but he/she completed the neuropsychological test battery as part of participation in the larger study.

Parents completed the instruments listed above while their children were engaged in activities related to the larger study (e.g., while the child was administered a neuropsychological test battery). The total time for filling out the parental measures was approximately 210 minutes per participant. Children took on average 300 minutes to complete the entire neuropsychological test battery. This included a 30-min break, during which we provided them with light refreshments. Children who were unable to complete all the tests due to fatigue were scheduled for another appointment. About one-third of the current sample of children returned for an extra session to complete the neuropsychological measures.

HIV-negative children and their parents/caregivers. Controls were recruited mainly via word-of-mouth. Individuals who had completed their participation would provide us with the names and contact details of friends who were also interested in participating. We contacted these parents and provided them with a brief explanation of what the study entailed, obtained verbal telephonic consent, and made an appointment.

Researchers involved with the larger project created a separate consent form for controls (see Appendix H), which was explained to them at their first appointment. Also at the first appointment, parents were required to report the results of their child's, as well as their own, most recent HIV test. If parents were not comfortable disclosing this information to the study team, they were excluded from participation. Participants attended two sessions as part of the larger study. The first session involved the child completing the neuropsychological testing, and the second session involved the child having a MRI scan.

We followed the same questionnaire administration procedure as described above for the HIV-positive parent-child dyads. Parents in the control group completed all of the above-mentioned parental measures, and their children completed the neuropsychological test battery as part of their participation in the larger study.

Ethical Considerations

The Human Research Ethics Committee (HREC) of UCT's Faculty of Health Sciences granted ethical approval for the larger research programme within which this one was nested (HREC REF: 406/2010). Use of the instruments, measures, and procedures detailed above was covered by the ethical protocols of the larger programme.

All demographic information, test scores, and any other data collected were kept strictly confidential. Adult participants were required to give their full informed consent

before they could enroll in this study. Parents/caregivers gave consent for themselves and for their children. Children gave assent for their participation in the larger study. We provided consent forms in English and isiXhosa. The research team made every effort to ensure the integrity and confidentiality of the children and their parents.

All of the parents/caregivers received feedback regarding the summary scores on the questionnaires they had completed. Parents/caregivers had the option to request a written summary of questionnaire results. That summary contained general interpretive statements about what scores on each subscale meant. If requested by the parent, these results were also communicated via telephone instead of a written report. Where needed, parents and/or their children were referred for further psychological help or counseling at an appropriate institution.

There were no psychological or physical risks involved in participation. Because of the sensitive nature of the research topic, however, some participants may have experienced some social or emotional fear. Social and emotional fear may include experiences of worry about social situations and interactions with people, fear of discrimination and rejection, and anxiety about negativity one might experience social situations. The research team approached these situations with empathy and understanding. Specifically, throughout administration of the study protocols we gave verbal encouragement and reassurance continually to each of the participants. We tried to limit, as far as possible, any discomfort parents/caregivers may have experienced, as most of the study tests questionnaires dealt with very sensitive information about themselves and their children.

Adult participants were compensated with a ZAR50 travel reimbursement and a ZAR50 Pick n Pay food voucher. Children were given a certificate (see Appendix I) and a T-shirt as an incentive upon completion of their tasks.

Data Management and Statistical Analysis

Data Entry. After data collection was completed, I captured the data into MSExcel spreadsheets, cleaned them, and calculated summary scores for each outcome variable. To get a global cognitive performance score for each child, I converted all neuropsychological test scores into *Z*-scores, added them together and averaged them for each child. These Z-scores were calculated in Excel using the mean and standard deviation for the control group of current sample.

Outcome variables. For this particular study I had two sets of outcome variables, one set to test each hypothesis. For hypothesis 1, the outcome variables all pertained to child functional, emotional and behavioural impairment and included the following: CIS, CMS,

CBCL Internalizing, CBCL Externalizing, CBCL Total Problems, and CBCL Total Competence. Hypothesis 2 consisted of outcome variables related to parental stress, depression and quality of life, and included the following: PSI Parent domain, PSI Child domain, PSI Total Stress, PSI Life Stress, FRS, FSS, CES-D, and WHO QoL.

Descriptive Statistics. I entered all summary scores into SPSS 20, which I used to complete all descriptive and inferential statistical analyses. For the latter, I set alpha at .05 for all decisions regarding statistical significance. I tested all data sets for normality using the Shapiro-Wilk test; this test was appropriate here because the current sample size is smaller than 50.

For each ANOVA described below, I used Levene's test to assess between-group homogeneity of variance. If Levene's test was not violated, ANOVAs would proceed normally. If, however, Levene's test is violated then an alternative analysis which does not assume equality of variance will be considered.

I also calculated, for each of these analyses, statistical power to detect significant between-group differences (Faul, 2012). A power statistic ranges between 0 and 1, with a score of 1 being excellent power. A power statistic of at least .80 is acceptable to accept or reject hypotheses confidently.

Sample Characteristics. Prior to carrying out inferential analyses specific to the hypotheses under consideration, I ran a series of one-way ANOVAs to confirm that the three groups were matched in terms of parent demographic characteristics (age, education, household income, and marital status) and child demographic characteristics (gender, age, and education).

Hypotheses Testing. Subsequent data analysis proceeded across several steps. First, I performed a series of one-way ANOVAs, with group (HAART-naïve, HAART-treated, Control) as the predictor variable in each, and a different outcome variable (CIS, CMS, CBCL Internalizing, CBCL Externalizing, CBCL Total Problems, CBCL Total Competence, PSI Parent domain, PSI Child domain, PSI Total Stress, PSI Life Stress, FRS, FSS, CES-D, and WHO QoL) as the outcome variable in each. For each between-group analysis, I calculated an effect size estimate. I used a confidence interval of 95% to determine the range within which the true effect is likely to occur and reported both lower and upper bounds. I used the mean score for each group, the mean square within-groups value and the *F*-value to calculate the effect sizes (*r*). If the value of *r* is between 0.10 and 0.30, the effect is small. Values between 0.30 and 0.50 indicate medium effects and values 0.50 or more indicate a large effect (Cohen, 1988).

Second, I performed chi-square tests to determine whether scores on the outcome variables were contingent upon group status. To facilitate these analyses, I classified each participant as either 'clinical' or 'normal' based on their scores on each the following scales/subscales: CIS, CBCL Internalizing Problems, CBCL Externalizing Problems, CBCL Total Problems, CBCL Total Competence, PSI Parent domain, PSI Child domain, PSI Total stress, PSI Life stress, and CES-D. Each outcome variable was analysed separately. I used Cramer's *V* to determine the strength of the relationship between group status and number of clinical cases within the groups.

Third, I constructed a series of general linear models to test for significant main and interaction effects in predicting scores on each outcome variable (CIS, CMS, CBCL Internalizing, CBCL Externalizing, CBCL Total Problems, CBCL Total Competence, PSI Parent domain, PSI Child domain, PSI Total Stress, PSI Life Stress, FRS, FSS, CES-D, and WHO QoL). For each model, the predictors were (in this order): group status, global neuropsychological performance, and the interaction between the two.

Finally, I selected three cases (one from each group) based on their cognitive performance, and wrote up their data as qualitative case studies. From the HAART-naïve group I selected the lowest-functioning child and from the HAART-treated and control groups I selected the highest-functioning child for each. This analytic step sought to make between-group comparisons on a more individual and in-depth clinical level. In so doing, I hoped to find trends or evidence to support inferential statistical findings.

RESULTS

Sample Characteristics

Tables 2 and 3 summarize the sociodemographic characteristics of the parent/caregiver and child participants, respectively.

In the sample of parents/caregivers, all participants were female. Most had a home language of isiXhosa. One-way ANOVAs revealed that there were no significant between-group differences in terms of age, $F(2) = 0.63$, $p = 0.54$, $R^2 = 0.14$, or years of education, $F(2) = 0.18$, $p = 0.84$, $R^2 = 0.14$. Regarding SES, all families were from low-income brackets. Regarding marital status, most participants were unmarried, and one-way ANOVAs revealed that there were no significant between-group differences, $F(2) = 0.49$, $p = 0.62$, $R^2 = 0.22$. Most participants ($n = 24$) were the biological mother of the child participant. Only 3 child participants were cared for by foster parents. Regarding race, 93% ($n = 27$) of participants were black African, with the rest being coloured.

In the sample of children, one-way ANOVAs revealed no significant between-group differences with regards to gender, $F(2) = 2.89$, $p = 0.07$, $R^2 = 0.45$.One-way ANOVAs revealed no significant between-group differences in terms of age, $F(2) = 1.46$, $p = .25$, $R^2 = .28$, or education, $F(2) = 1.61$, $p = .22$, $R^2 = .35$.

Tests of Normality

I planned to use one-way ANOVAs to test my hypotheses. Although this particular technique is robust enough to be used for data that are not normally distributed, it is important to know the characteristics of the distributions under consideration because they might inform one about, for instance, potential outliers which could obscure statistically significant trends findings. Hence, before beginning any inferential statistical analyses, I assessed the outcome variable data, using the Shapiro-Wilk statistic, to determine if the distributions were normal. Table 4 presents the results of those analyses. As the Table shows, only the following sets of data were normally distributed: CIS, CBCL Internalizing Scale, CBCL Externalizing Scale, CBCL Competence, CBCL Total Problems, and FRS.

Table 2
Sociodemographic Characteristics: Parents/caregivers (N = 29)

	Group		
Variable	HAART-naïve (*n* = 9)	HAART-treated (*n* = 10)	Control (*n* = 10)
Gender (F : M)	9:0	10:0	10:0
Home language			
isiXhosa : English : Other	8:1:0	9:1:0	10:0:0
Age (in years)			
M (*SD*)	43.90 (12.19)	41.50 (6.93)	39.50 (5.44)
Range	23-65	33-51	33-49
Education[a] (years completed)			
M (*SD*)	11.22 (2.91)	10.50 (3.03)	10.80 (1.93)
Range	8-17	8-17	8-12
Household income[b]	Low	Low	Low
Marital status			
Married : Single : Divorced : Widowed	2:6:0:1	4:5:1:0	2:8:0:0
Biological parent : Non-biological caregiver	6:3	9:1	9:1
Race			
Black : Coloured : White : Other	8:1:0:0	9:1:0:0	10:0:0:0

Note. [a]Education was categorized as follows: 1-8 years = some primary school; 9-12 years = some secondary(high) school; 13-15 years = some college or tertiary; more than 15 years = college or tertiary graduate. The education categorization was taken from the Parental Stress Index scale (item 59). Number of years completed taken according to upper limit. [b]Household income was categorized following the taxonomy used by researchers leading the larger

research programme within which this one was nested: Low = ZAR0-80 000; Medium = ZAR81 000-120 000; High = ZAR121 000-150 000 and more.

Table 3
Sociodemographic Characteristics: Children (N = 29)

Variable	Group		
	HAART-naïve (n = 9)	HAART-treated (n = 10)	Control (n = 10)
Gender (F : M)	7:2	5:5	6:4
Age[a] (in years)			
M (*SD*)	9.90 (2.01)	11.00 (1.09)	9.80 (1.06)
Range	6-12	7-12	8-11
Education[a] (years completed)			
M (*SD*)	2.44 (1.42)	3.50 (1.58)	2.60 (1.17)
Range	0-5	1-5	1-4

Note. [a]Data about child age and education were gathered from the parent report on the Child Behaviours Check List. For education, the number of years completed, not current grade at the time of testing, is shown.

Table 4
Study Outcome Variables: Data from Shapiro-Wilk test of normality (N = 29)

Scale	Statistic	*p*
CIS	.77	< .001***
CMS	.98	.82
CBCL		
Internalizing	.83	< .05*
Externalizing	.84	< .05**
Total Problems	.81	< .05***
Total Competence	.82	< .001***
PSI		
Child domain	.95	.21
Parent domain	.96	.41
Total Stress	.95	.23
Life Stress	.93	.07
FRS	.90	.01*
FSS	.94	.08
CES-D	.94	.10
WHO QoL	.95	.19
Global Cognitive *z*-score	.93	.05

Note. A p value of < 0.05 indicates that the data are distributed normally. CIS = Columbia Impairment Scale; CMS = Children's Motivation Scale; CBCL = Child Behaviour Checklist; PSI = Parental Stress Index; FRS = Family Resources Scale; FSS = Family Support Scale; CES-D = Center for Epidemiological Studies – Depression scale; WHO QoL = World Health Organization Quality of Life scale.
*p < .05. **p < .01. ***p < .001.

Hypothesis Testing: Analyses of variance

For all of the between-group comparisons described in this section, Levene's test was not significant (i.e., the assumption of homogeneity of variance between the groups was not violated). Hence, all ANOVAs proceeded in the conventional manner.

Hypothesis 1. This hypothesis stated that HIV-positive children would demonstrate more behavioural and emotional difficulties, and more functional impairment, than HIV-negative controls. Furthermore, I predicted that HIV-positive HAART-naïve participants would demonstrate better functioning than their HAART-treated counterparts. The relevant outcome variables here were scores on the following instruments/scales: CIS, CMS, CBCL Internalizing, CBCL Externalizing, CBCL Total Problems, and CBCL Total Competence. Child performance on the neuropsychological test battery, as capture by the global performance *z*-score, was also of interest here.

As Table 5 shows, there were no significant between-group differences on any of the outcome variables listed in the paragraph above. It appears, then, that group status (i.e., being HIV-positive and HAART naïve, or HIV-positive and HAART treated, or HIV-negative) had no significant effect on how the parent/caregiver reported the child was functioning in terms of general functional, emotional, and behavioural characteristics. Group status was also not related to general cognitive functioning, as measured by standardized neuropsychological testing.

None of the analyses reported here achieved the minimum ideal power of .80. Otherwise stated, given the observed effect sizes, and with alpha set at .05, the sample size was too small to generate enough power to detect between-group differences. To achieve optimum power I would have need to recruit a total of 339 participants.

Hypothesis 2. This hypothesis stated that parents/caregivers of HIV-positive children would report experiencing more stress and depression, and poorer subjective quality of life, than would parents/caregivers of HIV-negative children. The relevant outcome variables here were scores on the following instruments/scales: PSI Parent domain, PSI Child domain, PSI Total Stress, PSI Life Stress, FRS, FSS, CES-D, and WHO QoL.

As Table 5 shows, there were no significant between-group differences on any of the outcome variables listed in the paragraph above. It appears, then, that raising a HIV-positive child, regardless of whether that child is HAART naïve or HAART treated, had no significant effect on the parental experience and overall parental well-being compared to raising a HIV-

negative child. Otherwise stated, parents from all three groups reported experience parenting in similar ways.

Again, none of the analyses reported here achieved the minimum ideal power of .80. Otherwise stated, given the observed effect sizes, and with alpha set at .05, the sample size was too small to generate enough power to detect between-group differences. Again, to achieve optimum power I would have need to recruit a total of 339 participants.

Table 5

Between-group Comparisons: Child behavioural, emotional, and cognitive functioning, and parental well-being (N = 29)

	Group							
Outcome variable	HAART-naïve (*n* = 9)	HAART-treated (*n* = 10)	Control (*n* = 10)	*F*	*p*	95% *CI*	*r*	*β*
CIS								
M (*SD*)	11.11 (6.68)	22.10 (27.40)	20.30 (18.07)	0.76	.48	10.30-25.84	.27	.23
Range	1-20	0-92	0-65					
CMS								
M (*SD*)	32.11 (10.22)	26.90 (6.23)	34.40 (15.38)	1.13	.34	26.76-35.38	.23	.17
Range	15-50	16-38	4-59					
CBCL								
Internalizing								
M (*SD*)	54.44 (24.27)	60.10 (8.06)	60.20 (12.81)	0.39	.68	52.38-64.38	.17	.12
Range	0-83	50-76	33-83					
Externalizing								
M (*SD*)	56.44 (23.91)	60.90 (6.49)	58.70 (14.56)	0.18	.84	52.76-64.75	.14	.09
Range	0-78	49-71	34-78					
Total Problems								
M (*SD*)	58.67 (23.18)	61.10 (7.77)	58.90 (16.33)	0.06	.94	53.45-65.72	.07	.06
Range	0-79	49-76	25-77					
Total Competence								
M (*SD*)	37.56 (15.93)	36.80 (7.47)	37.10 (13.99)	0.01	.99	32.43-41.85	.03	.05
Range	0-56	25-48	0-49					
PSI								
Parent domain								
M (*SD*)	152.44 (24.29)	162.40 (28.76)	158.00 (35.89)	0.26	.78	146.60-168.98	.16	.11
Range	124-191	122-213	109-212					
Child domain								
M (*SD*)	135.44 (15.79)	123.70 (18.79)	128.90 (24.36)	0.81	.46	121.54-136.73	.28	.25
Range	104-155	91-154	94-161					

Outcome variable	Group: HAART-naïve (n = 9)	Group: HAART-treated (n = 10)	Group: Control (n = 10)	F	p	95% CI	r	β
PSI								
Total Stress								
M (*SD*)	287.89 (30.71)	286.10 (33.53)	286.90 (55.29)	0.04	.99	271.65-302.21	.02	.05
Range	238-346	243-357	218-362					
Life Stress								
M (*SD*)	15.67 (10.28)	15.80 (12.92)	19.90 (14.01)	0.36	.70	12.50-21.84	.01	.05
Range	2-32	0-32	0-40					
FRS								
M (*SD*)	67.11 (19.82)	75.20 (27.48)	63.10 (16.01)	0.81	.46	60.32-76.71	.18	.12
Range	49-114	44-134	39-83					
FSS								
M (*SD*)	33.56 (23.79)	44.40 (14.86)	35.20 (17.38)	0.94	.41	30.71-45.01	.28	.24
Range	14-86	23-70	16-60					
CES-D								
M (*SD*)	23.11 (16.37)	21.00 (13.94)	22.40 (14.76)	0.05	.95	16.63-27.65	.07	.06
Range	0-50	3-45	4-47					
WHO QoL								
M (*SD*)	78.11 (12.99)	72.10 (15.83)	66.20 (11.99)	1.79	.19	66.77-77.51	.19	.13
Range	56-92	54-95	41-88					
Global cognition								
M (*SD*)	0.05 (1.13)	.39 (.35)	.12 (.44)	0.61	.55	-.07-.92	.23	.18
Range	-1.63–2.23	.021–1.02	-.69-.79					

Note. CIS = Columbia Impairment Scale; CMS = Children's Motivation Scale;CBCL = Child Behaviour Checklist; PSI = Parental Stress Index; FRS = Family Resources Scale; FSS = Family Support Scale; CES-D = Center for Epidemiological Studies – Depression scale; WHO QoL = World Health Organization Quality of Life scale.

Hypothesis Testing: Chi-squared tests of contingency

The ANOVAs reported above indicate that there were no significant between-group differences in terms of child functional impairment and parental well-being. On clinical observation of individual data, however, there appeared to be notable between-group differences. These differences appeared particularly noteworthy when examining whether each case could be classified as 'normal' or 'clinical,' and when looking at the group mean scores.

The CIS, CBCL, PSI, and CES-D instruments each have cut-off scores that mark where the boundary lies between clinical cases and healthy normal cases. When looking at group mean scores, it appears there might be between-group differences in terms of whether the average score for participants in a group fall into the clinical range or the normal range on some of those measures. For instance, on the CIS, the mean scores for the HAART-treated and Control groups fell within the clinical range, whereas the mean score for the HAART-naïve group fell within the normal range. Naturally, these mean scores might be misleading: There might be outliers within a group that affect the average disproportionately, particularly when sample sizes are so small. Nonetheless, if one separates, within each group, the clinical cases from the normal cases, some interesting questions might be: Are there significantly more clinical cases than normal cases in each group? Is there an association between group status and the likelihood of scoring in the clinical range on any one of those scales?

To answer these questions, I performed a series of chi-squared analyses for the following outcome variables, all of which have cut-off scores separating clinical or diagnostic scores from normal or non-diagnostic scores: CIS, CBCL Internalizing, CBCL Externalizing, CBCL Total Problems, CBCL Total Competence, PSI Parent domain, PSI Child domain, PSI Total Stress, PSI Life Stress, and CES-D. Table 6 presents the results of these analyses.

The data presented in the Table suggest that there were no between-group differences in terms of distribution of clinical cases to non-clinical cases. Otherwise stated, on each of the outcome variables listed in the paragraph above, the number of clinical and normal cases was more or less equally distributed across groups. These data confirm the lack of detectable between-group differences described above for the ANOVAs.

Table 6

Chi-squared analyses: Number of normal versus clinical cases in each group (N = 29)

	Group					
Outcome variable	HAART-naïve (*n* = 9)	HAART-treated (*n* = 10)	Control (*n* = 10)	*F*	*p*	Cramer's *V*
CIS	2	4	4	0.87	.65	.17
CBCL						
Internalizing	5	5	6	0.20	.90	.08
Externalizing	3	7	4	2.97	.23	.32
Total Problems	5	4	5	0.48	.79	.13
Total Competence	5	7	7	0.57	.75	.14
PSI						
Parent domain	5	6	6	0.05	.98	.04
Child domain	8	7	7	1.21	.55	.20
Total Stress	8	8	6	2.30	.32	.28
Life Stress	6	6	6	0.12	.94	.06
CES-D	5	5	7	0.88	.65	.17

Note. The numbers in each of the second, third, and fourth columns reflect the number of clinical cases in the relevant group. Degrees of freedom = 2 for all of the contingency tests. CIS = Columbia Impairment Scale; CBCL = Child Behaviour Checklist; PSI = Parental Stress Index; CES-D = Center for Epidemiological Studies – Depression scale.

Univariate Analyses of Variance

Because the ANOVAs and chi-square tests revealed no significant between-group differences, I tested the contribution that group status, child cognitive function, and the interaction between the two contributed to the variance in outcomes on measures of (a) child behavioural and emotional functioning and (b) parental stress and well-being. To do so, I created a series of general linear models, one for each of the outcome variables of interest. For each model, I entered group status first, global cognitive *z*-score second, and the interaction between the two third. Table 7 presents the results of these analyses.

Regarding child behavioural and emotional functioning, the relevant outcome variables here were scores on the following scales/subscales: CIS, CMS, CBCL Internalizing, CBCL Externalizing, CBCL Total Problems, and CBCL Total Competence. As shown in Table 7, none of the main effects or interaction effects were statistically significant predictors of any of the outcomes. For each model, however, the observed power fell some way short of the .80 standard. Looking at the trends in these data sets, the only predictor that approached statistical significance was global cognitive performance, for scores on the CBCL Internalizing subscale ($p = .06$). This piece of data suggests that larger studies might test whether, in HIV-positive samples, a child's cognitive performance might influence their degree of internalizing problems.

Regarding parental stress and well-being, the relevant outcome variables here were scores on the following scales/subscales: PSI Parent domain, PSI Child domain, PSI Total Stress, PSI Life Stress, FRS, FSS, CES-D, and WHO QoL. As shown in Table 7, none of the main effects or interaction effects were statistically significant predictors of any of the outcomes. Again, however, for each model the observed power fell some way short of the .80 standard. Looking at the trends in these data sets, the only predictor that approached statistical significance was group status, for quality of life ($p = .07$). This piece of data suggests that larger studies might test whether a child being HIV-positive and HAART naïve, or HIV-positive and HAART-treated, or HIV-negative, might influence a parent's subjective quality of life.

Table 7
General Linear Models: Is child cognitive performance a significant factor? (N = 29)

Outcome variable	*F*	*p*	R^2	Observed power
CIS				
Group	0.66	.43		
Global cognition	0.07	.80		
Group x Global cognition	0.24	.63	.05	.08
CMS				
Group	0.43	.52		
Global cognition	0.01	.91		
Group x Global cognition	0.58	.45	.13	.11
CBCL				
Internalizing				
Group	0.54	.47		
Global cognition	3.78	.06		
Group x Global cognition	0.93	.35	.23	.15
Externalizing				
Group	0.23	.64		
Global cognition	0.13	.72		
Group x Global cognition	0.82	.37	.07	.14
Total Problems				
Group	0.02	.89		
Global cognition	0.02	.89		
Group x Global cognition	0.18	.67	.06	.07
Total Competence				
Group	< .001	.97		
Global cognition	< .001	.98		
Group x Global cognition	0.23	.64	.04	.08
PSI				
Parent domain				
Group	0.18	.68		
Global cognition	< .001	.99		
Group x Global cognition	0.05	.83	.01	.06
Child domain				
Group	0.19	.66		
Global cognition	0.33	.57		
Group x Global cognition	1.23	.28	.09	.19
Total Stress				
Group	0.01	.92		
Global cognition	0.08	.78		
Group x Global cognition	0.48	.49	.04	.10
Life Stress				
Group	1.37	.25		
Global cognition	0.09	.77		
Group x Global cognition	1.48	.24	.32	.22

Outcome variable	*F*	*p*	R^2	Observed power
FRS				
Group	0.34	.56		
Global cognition	0.06	.82		
Group x Global cognition	0.31	.58	.11	.08
FSS				
Group	0.01	.92		
Global cognition	0.15	.70		
Group x Global cognition	0.06	.81	.01	.06
CES-D				
Group	0.01	.94		
Global cognition	2.22	.15		
Group x Global cognition	0.15	.71	.40	.07
WHO QoL				
Group	3.66	.07		
Global cognition	1.81	.19		
Group x Global cognition	0.34	.57	.23	.09

Note. R^2 here indicates the amount of variance in the outcome variable accounted for by entire model (i.e., the two main effects and the interaction term taken together). CIS = Columbia Impairment Scale; CMS = Children's Motivation Scale; CBCL = Child Behaviour Checklist; PSI = Parental Stress Index; FRS = Family Resources Scale; FSS = Family Support Scale; CES-D = Center for Epidemiological Studies - Depression scale; WHO QoL = World Health Organization Quality of Life scale.

Case Studies

To try and demonstrate that, although subtle, there are between-group differences that might be interesting at the clinical level, I will now review three case studies. One case was selected from each of the three groups. The case studies take an in-depth look at the lowest- and highest-functioning children in the HAART-naïve and HAART-treated groups, respectively, and the highest functioning child in the control group. These three participants were selected by examining the global cognitive *z*-scores. A *z*-score of 0 indicates that a child performed at exactly the average relative to participant's in this study's HIV-negative control group. Any *z*-score above 0 indicates a child functioning above that average, whereas any score below 0 indicates a child functioning below that average. By looking at one participant at each end of the spectrum, I aimed to demonstrate that there are functional (albeit subtle) differences between children in the HAART-naïve group. Because the HAART-naïve participants constituted the main group of interest for this study, I chose the worst performer of the HAART naïve-group and compared it to the two best performers for both the HAART-treated and Control groups. In so doing, I hoped to emphasize any subtle differences between these children. For each case, I examined each child's functional, emotional, and behavioural

functioning (as reported by his/her mother), as well as his/her mother's subjective quality of life and well-being.

Case 1: XF – Lowest-functioning HAART-naïve participant. This Black African Xhosa-speaking female participant was aged 11 years and 6 months at the time of testing (DOB: 28/12/1998), and was repeating Grade 4. Her global cognitive *z*-score was -0.23. The measures were completed by her biological mother, who was a single parent aged 47 years. The mother, who had completed 12 years of formal education, was unemployed at the time of testing.

XF's mother reported that they lived in a township area in a shack/sink structure with four rooms. The house was occupied by five people: XF, her mother, two siblings, and XF's grandmother. The annual household income was in the ZAR0 - ZAR35 000 range, placing them in the lowest income bracket reportable for the study within which this one was nested. XF's mother reported that they did not have any of the following amenities in their home: running tap, electricity, flush toilet, television, adequate clothing, or a study area for XF.

XF's mother's CIS ratings placed her in the normal range of functioning with regard to social interactions, parental relationships, and everyday activities. This report was consistent with that on the CMS, which indicated that she had normal levels of motivation for her age and that she did display any apathetic tendencies.

Regarding CBCL ratings, XF's mother reported that she showed clinical levels of internalizing, but not externalizing, problems (i.e., she was more likely to cry when faced with challenges than to respond with anger), and that her overall competence at dealing with challenges in her environment was poor. Her mother also reported that the total number of problems XF was facing was in the "borderline" range (i.e., close approaching the clinical range). On the items within the Competence scale, XF's mother reported that she scored within the normal ranges for daily and social activities, but that she was in the clinical range for school functioning. This reported low functioning on the school-related items is reinforced by the fact that XF was repeating grade 4. On the items related to psychological syndromes, XF's mother reported that she scored within the normal range for anxious/depressive, withdrawn/depressive, social problems, attention problems, rule-breaking, and conduct problems. The mother's report indicated, however, that XF scored within the clinical range for somatic complaints (for example, she stated that XF often complained of constipation and dizzy spells) and in the borderline range for thought problems (for example, she stated that XF was often distractible) on the internalizing and externalizing problems subscale. On the DSM-related items, XF's mother reported that she was functioning

at a normal level in terms of anxiety problems, attention deficit/hyperactivity problems, and oppositional-defiant problems. The mother reported that XF scored within the borderline clinical range for conduct problems, however, and in the clinical range for affective and somatic problems (i.e., she showed a slight tendency toward depressive symptoms and reported quite an extensive range of somatic problems, including dizzy spells, headaches, general body aches and pains, and nausea). The latter might not be surprising considering XF's HIV-positive status. XF's reported internalizing problems are consistent with her mother's reports on items related to thought and affective problems: Her mother reported that XF often feels sad, lonely, guilty, and lacks energy and cries a lot.

Regarding total parental stress, as measured by the PSI, XF's mother scored within the highly stressed range. She scored in that range on both the Parent and Child subdomains of the PSI, meaning that she is distressed by her own personal characteristics in her role as a parent, and is also distressed by the characteristics of her child which might not meet her expectations). XF's mother reported a non-significant number of general life stressors, however.

Regarding family resources (as measured by the FRS) and support (as measured by the FSS), XF's mother reported not unsatisfactory levels on both. For example, she reported not having adequate medical care for her family and not having any support at all from relatives. Furthermore, this mother was clinically depressed, according to the score derived from her CES-D self-report, even though she reported, via the WHO QoL, being satisfied with her overall quality of life and feeling that her life was meaningful.

Case 2: VB – Highest-functioning HAART-treated participant. This Black African Xhosa-speaking male participant was aged 11 years and 2 months at the time of testing (DOB: 13/10/2000), and was in Grade 5. He had repeated Grade 1 and Grade 2. His global cognitive *z*-score was +1.02. The measures were completed by his biological mother, who was a single parent aged 46 years. The mother, who had completed 12 years of formal education, was employed on a part-time basis as a domestic cleaner.

VB's mother reported that they lived in a township area in a brick-built structure with four rooms. The house was occupied by seven people: VB, his mother, four siblings, and VB's nephew. The annual household income was in the ZAR0 - ZAR35 000 range, placing them in the lowest income bracket reportable for the study within which this one was nested. His mother reported that they did not have any of the following amenities or resources in their home: enough food to eat, adequate clothing, or a study area for VB.

VB's mother's CIS ratings placed him in the functionally impaired range with regard to social interactions, parental relationships, and everyday activities. This report was consistent with that on the CMS, which indicated that he had slightly lower levels of motivation for his age and that he displayed slight apathetic tendencies.

Regarding CBCL ratings, VB's mother reported that he showed clinical levels of internalizing, and borderline clinical levels of externalizing, problems (i.e., he was very likely to have feelings of worthlessness and engage in fights), and that his overall competence at dealing with challenges in his environment was poor. His mother also reported that the total number of problems VB was facing was in the normal range. On the Competence scale items, VB's mother reported that he scored within the normal range for social activities, but that he was in the borderline clinical range for school functioning and daily activities. Low functioning on the school and daily living subtest is reinforced by the fact that he had previously repeated grades and that, according to the CIS, his overall functioning was impaired. On the items related to psychological syndromes, VB's mother reported that he scored within the normal range for anxious/depressive, withdrawn/depressive, social problems, somatic complaints, thought problems, attention problems, rule-breaking, and aggressive behaviours. On the DSM-related items, VB's mother reported that he was functioning at a normal level in terms of anxiety problems, attention deficit/hyperactivity problems, oppositional-defiant problems, and conduct problems. She reported that he scored within the borderline clinical range for affective and somatic problems (i.e., she indicated that he was likely to experience a general lack of interest and headaches). Overall, with regard to his behaviour VB's mother noted that he was clearly experiencing some somatic problems; these might have been related to his HIV-positive status and the fact that he was on HAART treatment, which could have side effects. The reports of internalizing problems are consistent with reported functioning within the borderline clinical range for affective problems. Finally in terms of the CBCL, VB's mother reported that he sometimes expressed suicidal thoughts and feelings of worthlessness.

Regarding total parental stress, as measured by the PSI, VB's mother scored within the highly stressed range. She reported high levels of stress on the Child, but not the Parent, domain of the PSI. This pattern of data suggests that she felt confident in her ability as a parent, but was struggling to cope with the characteristics of her child that did not meet her expectations or that she found challenging. She also reported a significant number of life stressors (for example, the recent death of an immediate family member).

Regarding family resources (as measured by the FRS) and support (as measured by the FSS), VB's mother reported not unsatisfactory levels of both. For example, she reported not having adequate indoor plumbing and having very little support from her friends. This mother was clinically depressed, according to a score derived from her CES-D self-report (for example, she stated that she lacked energy and felt that everything was an effort for her). She did, however, reported on the WHO QoL that she was satisfied with her overall quality of life and that she felt satisfied with herself as a person.

Case 3: SM – Highest-functioning control participant. This Black African Xhosa-speaking male was aged 10 years and 3 months at the time of testing (DOB: 20/06/2000), and was in Grade 5. He had never repeated a grade. His global cognitive *z*-score was +0.79. The measures were completed by his biological mother, who was married and aged 38 years. The mother, who had completed 12 years of formal education, was unemployed at the time of testing.

SM's mother reported that they lived in a township area in a shack/sink structure with four rooms. The house was occupied by five people: SM, his parents, and two siblings. The annual household income was in the ZAR0 - ZAR35 000 range, placing them in the lowest income bracket reportable for the study within which this one was nested. His mother reported that they did not have any of the following amenities or resources in their home: enough food to eat, adequate clothing, or a study area for SM.

SM's mother's CIS ratings placed him in the functionally impaired range with regard to social interactions, parental relationships, and everyday activities. However, his mother reported via the CMS that he had normal levels of motivation for his age and that he not did display any apathetic tendencies.

Regarding CBCL ratings, SM's mother reported that he showed clinical levels of internalizing and externalizing problems (i.e., he was likely to experience feelings of being unloved and to often lie and cheat), and that he showed normal levels of overall competence at dealing with challenges in his environment. His mother also reported that the total number of problems SM was facing was in the clinical range (i.e., that he encountered significantly more than the average number of problems faced by a child of his age). On items within the Competence scale, SM's mother reported that he scored within the normal ranges for daily living, social activities, and school functioning. This report of normal functioning is consistent with the fact that he was performing well at school and had not repeated any grades. On items related to psychological syndromes, SM's mother reported that he scored within the normal range for withdrawn/depressive, somatic problems, and social problems.

She also reported, however, that he scored within the borderline clinical range for anxious/depressive problems (for example, his mother reported him as being self-conscious) and in the clinical range for thought problems (i.e., she stated that he sometimes showed tendencies toward distractibility), attention problems (i.e., she stated that he failed to finish tasks sometimes), rule-breaking behaviour (i.e., she stated that he used foul language sometimes), and aggressive behaviour (i.e., she reported incidents of vandalism) on the internalizing and externalizing problems subscale. On the DSM-related items, SM's mother stated that he was functioning at a normal level in terms of anxiety problems and somatic problems, but that he scored within the borderline clinical range for attention deficit/hyperactivity problems, and in the clinical range for affective, oppositional defiant, and conduct problems. His mother reported that SM was not experiencing somatic problems, which is to be expected considering his HIV-negative status. According to his mother's report, SM exhibited both internalizing and externalizing problems, reinforced by scores within the clinical ranges for affective problems and conduct problems. SM's mother also reported that he showed having problems with attention.

Regarding total parental stress, as measured by the PSI, SM's mother scored within the highly stressed range. She reported high stressed levels on the Child domain, but not the Parent, domain of the PSI (i.e., she reported feeling comfortable in her ability as a parent, but found that her child was difficult to understand). She also and reported a significant number of life stressors (for example, she stated that recently there had been substantial decrease in household income).

Regarding family resources (as measured by the FRS), SM's mother reported unsatisfactory levels (for example, not having enough food for at least 2 meals a day). Regarding family and social support (as measured by the FSS), she reported satisfactory levels. This mother was also clinically depressed, according to a score derived from her self-report on the CES-D (e.g., she reported having crying spells a lot of the time). She reported on the WHO QoL, however, that she was satisfied with her overall quality of life.

Table 8
Case studies: comparison of raw scores and diagnostic ranges.

	Case 1: XF - Lowest functioning HAART-naive		Case 2: VB - Highest functioning HAART-treated		Case 3: SM - Highest functioning control	
Outcome Variable	Raw score	Diagnostic Range	Raw score	Diagnostic range	Raw score	Diagnostic range
CIS	3	Normal	31	Impaired	24	Impaired
CMS	36	Normal	24	Apathetic	38	Normal
CBCL						
Internalizing	71	Clinical	65	Clinical	65	Clinical
Externalizing	57	Normal	61	Borderline	77	Clinical
Total Problems	63	Borderline	60	Normal	74	Clinical
Total Competence	34	Clinical	32	Clinical	46	Normal
PSI						
Parent domain	154	Stressed	127	Normal	116	Normal
Child domain	122	Stressed	119	Stressed	154	Stressed
Total stress	276	Stressed	246	Stressed	350	Stressed
Life stress	4	Non-significant	25	Significant	18	Significant
FRS	53	Unsatisfied	67	Unsatisfied	47	Unsatisfied
FSS	24	Unsatisfied	23	Unsatisfied	16	Unsatisfied
CES-D	16	Depressed	21	Depressed	47	Depressed
WHO QoL	85	Satisfied	70	Satisfied	64	Satisfied

Notes: [a]Diagnostic range: a term used to indicate the level of functioning based on the cut-off scores for each scale. CIS = Columbia Impairment Scale, CMS = Children's Motivation Scale, CBCL = Child Behaviour Checklist, PSI = Parental Stress Index, FRS = Family Resources Scale, FSS = Family Support Scale, CES-D = Center for Epidemiological Studies – Depression scale, WHO QoL = World Health Organization Quality of Life scale

Comparison of the three cases. When comparing these three cases at an in-depth clinical level we can see that there are indeed differences between them. The lowest functioning HAART-naïve child (XF) performed poor on only three out of the six outcome variable related to child functional and emotional impairment. The highest functioning HAART-treated child (VB) performed poorly on five out of the six outcome variables, and the control child (SM) performed poorly on four out of the six outcome variable. It would seem that the HAART-treated and control cases were overall more functionally impaired than the HAART-naïve case.

Both XF and VB's (i.e., both were HIV-positive participants) mothers reported that their children experienced internalizing problems. Their mother's also reported that their children often complained of somatic problems. XF and VB had previously failed grades at school, but overall they seemed to be able to function in social situations and deal with everyday problems. SM's (i.e., the control participant) mother also reported that her child had internalizing problems, but did have somatic complaints. SM had not previously repeated any grades at school.

VB's mother reported that he displayed borderline levels of externalizing problems, while SM's mothers reported that her child displayed clinical levels of externalizing behavioural problems.

Regarding parental functioning the mothers all expressed feelings of being stressed and depressed, but stated that, overall, they were happy with their quality of life. All three mothers reported a lack of support from extended family and friends. The mothers also reported a general lack of resources (e.g.: enough money to pay bills, enough food for two meals a day, etc.).

When comparing cases at a qualitative level, the differences observed are only miniscule. These three children (and their parents) appeared to not differ that much from each other. Hence, the review of these three cases confirms, from a qualitative and clinical perspective, what the inferential statistics suggested.

DISCUSSION

The objectives of this study are summarized by these two questions:

1. Relative to HIV-negative controls, are HAART-naïve children truly asymptomatic, and is there a difference, in terms of functional, behavioural, and emotional impairment, between being HAART naïve and HAART treated?

2. Does caring for a HIV-infected child significantly affect the parental experience in terms of stress, depression, and subjective quality of life?

Child Functional Impairment

Regarding the first question, statistical analyses revealed no significant between-group differences in terms of parent-reported functional, emotional, and behavioural status, or in terms of objectively-measured neuropsychological status. In fact, the data (mean scores on the scales pertaining to child functional impairment) suggested that participants in all groups were functioning normally. Hence, Hypothesis 1, which stated that HIV-positive children will demonstrate more behavioural and emotional difficulties, and more functional impairment, than HIV-negative controls, was disconfirmed by initial between-group statistical analyses.

This finding stands in contrast to that reported by Nozyce et al. (2006), who found that clinically stable HIV-infected HAART-treated children (N = 298) manifested significant behavioural difficulties compared to their uninfected counterparts. Mellins et al. (2003) also found high rates of emotional and behavioural problems in HIV-infected HAART-treated children (N = 96). However, in contrast to Nozyce et al. (2006) and consistent with this study, Mellins et al. (2003) also found that, when compared to HIV-exposed negative controls (N = 211), there was no significant association between the observed psychological problems and disease presence in the patient group. Furthermore, Mellins and colleagues' data suggested that demographic characteristics (e.g., gender of the child, ethnicity, and maternal education) were the strongest correlates of impaired behavioural and emotional functioning.

Inspection of individual data collected for this study suggested that, within each of the three groups, there were children who might be characterized as functionally impaired and those who might be characterized as functioning normally. Hence, I conducted a set of secondary statistical analyses to determine if there was a significant difference in the distribution of functionally impaired children to normally functioning children across the three groups (i.e., to examine whether a child scored within the normal or clinical range on various scales was contingent upon group status). Normal cases were defined here as children who scored below the cut-off score on a particular diagnostic test. For example, if a child scored below 16 on the CIS, she would be considered to be functioning normally in the domains assessed by that test. Clinical cases were defined here as children who scored above the cut-off on a diagnostic test. For example, if a child scored above 16 on the CIS, she would be considered functionally impaired in the domains assessed by that test.

Statistical analyses revealed that the distribution of clinical versus normal cases within each group was not significantly different. One might infer, then, that group status did

not predict whether a participant was functionally impaired or not. Otherwise stated, being HIV-positive and on HAART, for example, did not mean certain (or even probable) functional impairment relative to being HIV-negative.

Another group of secondary statistical analyses arose from the thought that there might be interaction effects, not initially hypothesized, between some of the measured variables. Hence, I decided to investigate the possibility of an interacting variable. Poor neuropsychological functioning has been linked to high viral loads (Jeremy et al., 2005), and for this reason I decided to investigate cognitive performance as a potential interacting variable in a series of univariate ANOVAs. The results of these analyses revealed no significant interaction effects between two predictors (group status and global cognition) on any of the child functional impairment and parental well-being outcome variables. The fact that this interaction was not statistically significant suggests that childrens' behavioural and emotional functioning, and parents' stress, depression, and quality of life, are not differentially influenced by neurocognitive functioning, regardless of whether the child is HIV-negative or HIV-positive.

To follow up and add to the statistical analyses described above, I reviewed three individual cases. My thoughts here were that if I could make an in-depth clinical examination of a subset of the children, aspects of functioning not clearly defined by the statistical analyses might become apparent. Further, taking a closer, qualitative look at cases might also reveal social issues not measured by the questionnaires and scales.

Hence, I selected three children: the lowest-functioning (by global cognitive status) HAART-naïve child, the highest-functioning HAART-treated child, and the highest-functioning Control child. I chose participants with these ranks because comparing them would optimize the chances of finding the kinds of significant group-based differences upon which the study's major questions attempted to focus.

Comparisons of the three children's scores on the outcome scales completed by their mothers suggested there were not many differences in their functional, emotional, and behavioural status. For instance, each mother reported functional impairment on at least half of the outcome measures, and each reported that her child was in the 'clinically impaired' range on the CBCL Internalizing subscale (i.e., that the child displayed low self-confidence, and traits such as shyness and nervousness). This observation of similar functional, emotional, and behavioural profiles, regardless of group and despite variation in global cognitive status, supported the conclusions drawn from the statistical analyses.

Regarding intellectual functioning, developmental psychologists agree that, generally, cognition proceeds through three simple phases: maturation, stabilising, and age-related decline (Bates et al., 1999). All participants in this study were in the maturation phase (i.e., they were of an age where they were acquiring and learning new cognitive skills). Aside from cognitive development, the maturational phase is also a stage of important social, behavioural, and emotional development. Unfortunately, this developmental trajectory can be derailed by numerous factors, making the maturational phase a particularly sensitive period in the individual's development (Bornstein, 1989). These risk factors may include unstable or multiple caregivers, caregiver alcohol and/or drug use, poverty, and low maternal education (Smith et al., 2006). Brooks-Gunn and Duncan (1997) examined the effects of poverty on child developmental impairment. They found that children growing up below the poverty line experienced higher incidences of negative outcomes in physical health, cognitive ability, and school achievement, and in overall behavioural and emotional functioning.

The sociodemographic statistics and case studies described above make it clear that the participants in this study emerged from low-SES backgrounds and lived in particularly poverty-stricken surroundings. It stands to reason, therefore, that all of them (even the children in the Control group) would be experiencing some form of developmental impairment.

Furthermore, impairment in any one area of development is often associated with impairment in another. For instance, Cook et al. (1994) found a negative association between the presence of child behavioural problems and general intellectual functioning. Similarly, Hinshaw (1992) reported an association between externalizing behaviours and cognitive deficits in early development.

Clearly, then, interpretation of the parents' responses to the questionnaires, and the childrens' neuropsychological test performance, must be made with consideration of the family's social and economic circumstances. At the time of testing, two of the three case-study parents were unemployed, and all reported that they lacked certain basic amenities (e.g., running tap water, a flush toilet, and electricity) and that they were generally struggling under the burden of inadequate resources. It could be possible that because these children are so severely disadvantaged in terms of their social and economic circumstances that we are unable to find significant differences elsewhere with regards to their everyday functioning. It could also be possible that because of the circumstances in which they grew up, they are all functioning at similar (low) levels, regardless of their HIV status. Hence, between-group differences, if they do exist, are lost in statistical methodology.

Ishida et al. (2012) state that the association between HIV serostatus and SES is inconsistent in developing countries; the direction of association is unclear, and there are certainly no established causal links (Hargreaves et al., 2008; Parkhurst, 2010). Other studies have, however, found significant associations between HIV serostatus and educational achievement, but not between HIV serostatus and household wealth (Barnighausen et al., 2007). Still other studies report no association between HIV prevalence and SES (Gillespie et al., 2007; Wojciki, 2005).

What these mixed reports suggest is that, if there is a link between HIV and SES, it is a complex one that is not easily explained by single-mode methods. The above review highlights the importance of knowledge distribution or education at a community level. This means that if you are well informed, regardless of your household wealth, you are either more or less likely to be affected by the HIV virus.

Perhaps an alternative way of explaining the lack of significant between-group differences is to examine the possibility of the presence of protective factors, as suggested by Cluver and Gardner (2007). Those authors conducted a qualitative study of 60 HIV-positive South African children, interviewing both the children and their caregivers. They found that the psychological well-being of those children was influenced by a number of perceived risk factors (e.g., parental bereavement, lack of caregiver presence and poverty) and perceived protective factors (e.g., access to medical care, safe play areas, and support from friends and extended family).

The presence of protective factors might help buffer the psychological effects of being HIV-positive, but at the same time these protective factors may also boost psychological well-being in HIV-negative children. All of the children who participated in this study came from severely disadvantaged circumstances. Although their home circumstances were not at all ideal, all children who participated appeared to have loving and actively present caregivers, as evidenced by the following: All HIV-positive children (HAART-naïve and HAART-treated) were receiving medical care at their respective community clinics, and all the children were attending school. Although some were obtaining poor grades, just being part of the mainstream school system may have helped boost their overall morale.

Although there were no between-group differences with regard to child functional, emotional, or behavioural impairment, it remains possible that the HIV-positive, HAART-naïve children will grow into the kinds of deficits that I hypothesized they would be experiencing (i.e., that these deficits would only become apparent near the end of adolescence and at the start of early adulthood). An adolescent twin study looking at the trajectory effect

of age and gender on comorbidity of disorders found that overall diagnosis of disorders increased with age (Simonoff et al., 1997). However, these trajectories are not simple linear psychological developmental paths, but are complex, with various environmental factors also being influential. Feng, Shaw, and Silk (2008) studied the developmental trajectories of boys aged 2-10 years and found that if parents reported anxiety during early childhood, the children were more likely to be diagnosed with anxiety and depressive disorders in later childhood and adolescence. The same authors also found that maternal mental health attributes (specifically, maternal depression) differentially affected developmental trajectories over time, increasing symptoms of anxiety. Feng and colleagues' findings were supported by a similar study looking at the association between maternal anxiety and depression and aggravation of child/adolescent mental health problems (Fatori, Bordin, Curto, & Paula, 2013). This latter study found that child/adolescent mental health problems increased as maternal anxiety and depression increased.

The abovementioned studies on child developmental and psychological trajectories focus mainly on child internalizing behaviours. Reef, Diamantopoulou, van Meurs, Verhulst, and van der Ende (2009) studied the developmental trajectories of child externalizing behaviours and their association with adult mental disorders. They found that aggression, opposition, property violation, and status violations during childhood were strongly associated with an increase in disruptive behaviour during adulthood. They also found that children on a high-level externalizing trajectory were more likely to experience both internalizing and externalizing disorders in adulthood.

Hence, child developmental trajectories are influenced by numerous internal and external factors and play an important role in the diagnoses of both adolescent and adulthood disorders. Each child who participated in this study was on his/her own developmental path, a path that will determine mental health at a later life stage.

Parental Well-being

The study's second main question was whether there were significant between-group differences in terms of the parental experiences of the adults raising these children. Again, this question was answered in the negative: There were no such differences. Parents of HIV-positive children, regardless of whether those children were HAART naïve or HAART treated, were not more stressed, were not more depressed, and were not less satisfied with their quality of life than parents of HIV-negative controls. In fact, the data suggest that, on average, the parents in all three groups were clinically stressed and depressed, but were satisfied with their quality of life. Hence, Hypothesis 2, which stated that parents/caregivers

of HIV-positive children will report experiencing more stress and depression, and poorer subjective quality of life, than will parents/caregivers of HIV-negative children, was also disconfirmed by the initial between-group statistical analyses.

In a recent South African study, Potterton, Stewart, and Cooper (2007) studied parental stress associated with caring for HIV-infected infants (N = 122, mean age of infants = 18.50 months, SD = 8.10). Their findings revealed that, at baseline, parents reported high levels of stress, similar to those reported in this study. The authors of that study recognised that, although caring for a HIV-infected child is stressful, HIV is not the only factor contributing to the overall level of parental stress. Parenting in itself is stressful, even if your child is not chronically ill. Other factors which may also contribute to parental stress are financial constraints, lack of employment, lack of adequate medical care, lack of educational opportunities, and the parent's own physical and mental health.

In the current study, the statistical analyses suggested that parents of HIV-negative children were as stressed as parents of HIV-positive children. This observation, then, implies that child HIV-status alone does not determine the level of parental stress, supporting the argument made by Potterton et al. (2007).

Regarding parental stress, Silver, Westbrook, and Stein (1998) investigated the levels of distress in parents who had children with chronic health conditions (which included, but were not limited to, asthma, diabetes, epilepsy, kidney disease, cerebral palsy, hearing loss, and Down syndrome). They found that the parents of children who had chronic conditions with functional limitations (eg., epilepsy, cerebral palsy, etc) were more stressed than parents of children who did not have the accompanying functional limitations. Although the levels of parental stress in the Silver et.al. study were high, they were not as, for instance, those of parents who care for HIV-infected children (Potterton et.al., 2007).

Because the levels of parental stress across the three groups in the current study were so high, one must assume that factors besides the child's HIV status also add to these levels. All HIV-positive children enrolled for this study had acquired the virus via vertical transmission, which means that at least one of the parents was also HIV-positive, adding to parental stress levels. Poverty and poor social circumstances all add to the parental stress. For instance, Emerson (2004) stated that poverty has a pervasive impact on the mental health of parents and their children. He suggested that poverty is associated with poor parental well-being and, consequently, poor parenting practices.

Taking a more general look at sub-Saharan Africa, Gentilini and Chieze (1990) state that the AIDS pandemic has huge economic implications for a country as whole, in the sense

that AIDS leads to high mortality rates, which in turn leads to loss of productivity. This chain of events is evident in South Africa, where unemployment rates are high. In a more recent study, Bor et al. (2012) found that early initiation of ARV treatment prevented loss of employment due to HIV. The same authors also reported that re-employed rates were quite high after about 4 years after starting ARV treatment. The results of this study are supported by an earlier study in which they predict that sub-Saharan African countries most affected by the pandemic will be, on average, 30% poorer than countries not affected by HIV and AIDS (Ferreria, Pessôa, & Santos, 2011). Ferreria et al. also predict that schooling will decrease by as much as 40% due to the effects of HIV and AIDS, but also note that these figures are drastically reduced by the introduction of appropriate medical treatment.

The findings from these two studies indicate that ARV treatment does not only have medical benefits for HIV infected individuals, but economic benefits for countries as well. It is important to take into consideration the economic climate in which people find themselves when making inferences about how they might be affected. In this particular study all the participants came from low income brackets, which should be considered together with the fact that in South Africa as a whole unemployment rates are high. Prevention of loss of employment is also important. Having access to ARV treatment and proper schooling are important factors to take into account when looking at SES.

The above review highlights the importance of SES factors associated to HIV-infection. Reviews are mixed, and the exact casual links between various factors (i.e.: such as loss of productivity, unemployment, low income, tec.) are not clearly defined. What is evident though is that the physical effects of the HIV disease will result in loss of productivity, and ultimately, unemployment. This then in turn leads to loss of income and families living in poverty.

Earlier mentioned studies have demonstrated the association between poverty and child functional impairment and development. Poverty also affects the parental experience and consequently parental practices.

Limitations and Recommendations for Future Research

The first major limitation of the current study is its relatively small sample size. The sample of 29 participants was not adequate to achieve optimal statistical power to detect between-group differences on the instruments administered. Obviously, then, a larger sample size would have served my purposes better.

Several difficulties during both recruitment and actual study administration made achieving a larger sample challenging, however. One of these difficulties emerged from the

fact that the current healthcare policy in South Africa is to start all children, regardless of CD4 count, on ARV treatment. Hence, the research team struggled to recruit HAART-naïve children. For this particular study, I was only able to recruit 9 HAART-naïve participants. Another difficulty with regards to recruitment was that the larger study had, at the time, ethical approval to recruit from only one community clinic. The rate of recruitment was dependent on the referral rate of patients to the study by the clinic staff.

For all statistical analyses, I was unable to achieve the optimum power of .80. In fact, the average power achieved across all outcome variables was very low (.13). This low power means that my sample size was too small to detect any significant differences between the groups. An a priori power calculation revealed that, at the current effect size estimates, I would have required an *N* of 339 participants across the three groups to achieve statistical significance. What this calculation suggests, then, is that in real-world terms the effect HIV status has on child functional impairment and parental stress is very small. Hence, one might argue that the relationship investigated here does not have clinical significance[4]. The current data set needs to be examined in a different way.

Although my primary recommendation would be to recruit larger numbers of participants, another option might be to re-define what makes someone HAART naïve. As was the case in the larger study within which this one was nested, participants who were on HAART treatment for a period of less than 6 weeks could be considered HAART naïve. This re-definition could help increase the numbers of HAART-naïve group participants. However, in light of the new healthcare policy surrounding HIV, one might have to consider grouping together the HAART naïve and HAART treated groups to create an overall HIV-positive group in order to achieve greater numbers.

A second limitation of this study, also methodological, was the absence of a control group who were HIV-negative but experiencing a chronic medical illness without any obvious cognitive effects. Including such a control group would have allowed direct inferences about, for instance, the specific effects of raising an HIV-positive child on the parental experience. In the initial stages of the research, the team attempted to recruit a group of epileptic children to fulfil this control purpose. Unfortunately, these attempts were unsuccessful.

Having a medical control group, for example a group of parents of epileptic children, would help to strengthen the argument that HIV as a chronic (and sometimes fatal) illness

[4] Clinical significance is define here as the change between "the range of the dysfunctional population or within the range of the functional population" (Jacobson & Truax, 1991).

significantly affects parental well-being. The hypothesis here could possibly be that parents of HIV-infected children are more stressed than parents of children with other chronic medical illnesses and more stressed than controls.

A third limitation of this study is that the children themselves were not interviewed, and did not fill out questionnaires, regarding their functional capabilities, behaviour, and emotions, and that the research team did not make direct observations of their behavioural, emotional, and functional status. The reason for having parents complete measures about their child (and not having the child themselves complete these type of measures) was to decrease the load of testing placed on the children themselves. The researchers of the larger study felt that the neuropsychological test battery the children were required to complete was demanding enough and that more burden should not be placed on them, given their young age.

Given feasibility, a clinical interview with each of the children could be valuable for gaining information regarding the child's own insight into his/her level of functioning. The child self-report version of the CBCL has previously been used successfully in research with South African children (Cluver, Gardner, & Operario, 2006).

Another very important limitation of the study was that there was no quantifiable measure of SES. Participants completed a sociodemographic questionnaire that only required them to give general information regarding their social and economic circumstances. Neither this study, nor the larger one within it was nested, used a formal index or scale to give a quantifiable measure of SES. Hence, I could not use SES as a predictor variable in my statistical analyses.

More thorough data collection focusing specifically on SES would be beneficial. For example, using a scale like the ASSET Index (Myer, 2008) will help classify these individuals into different groups stratified by SES. In-depth research into how SES can affect the functional, emotional, behavioural, and neurocognitive functioning of children is needed. Research into how SES affects the parental experience in terms of parental stress, depression and subjective quality of life, could also be of great value in the current South African setting. One might also possibly study SES as an interacting factor on child functional impairment and parental well-being. A multi-level study is required, which investigates various sources of influence on child functional impairment and parental well-being. Fang et al. (2008) suggests that social and cultural aspects should be considered, because SES alone is not enough to explain the observations (i.e. serostatus and prevalence).

CONCLUSION

The study described here focused on investigating differences in functional impairment of HIV-positive HAART-naïve children compared to their HIV-positive HAART-treated and HIV-negative counterparts. I examined various aspects of functioning (e.g., motivation, internalizing and externalizing problems, competencies, etc.). In comparing HIV-positive and HIV-negative children, I also sought to determine if there are differences within the HIV-positive group (i.e., between HAART-naïve and HAART-treated subgroups). In so doing, I attempted to answer the question of whether the HAART-naïve participants could truly be viewed as asymptomatic.

The second major aim of this study was to investigate the parental experience, and overall parental well-being, in parents of HIV-positive children (both HAART-naïve and HAART-treated) and parents of HIV-negative children. More specifically, I addressed the question of whether levels of child functional impairment and behavioural/emotional difficulties were associated with levels of parental stress and parents' subjective quality of life.

Statistical analyses indicated no detectable between-group differences with regard to child functional, behavioural, and emotional impairment, and with regard to parental stress, depression, and subjective quality of life. Child global cognitive ability was not a statistically significant predictor of those outcomes, either independently or in interaction with group status. In-depth qualititative review of three individual cases supported these quantitative data.

The absence of detectable between-group differences might be explained in three ways: (1) the participants' social and economic circumstances are so harsh that these effects far overshadow the relatively subtle effects that HIV infection might have on the child and the family; (2) the presence of factors such as loving and present caregivers, adequate medical care, and being part of a schooling system protects HIV-positive children against functional, behavioural, and emotional impairment, and shields their parents from experiencing poor quality of life; or (3) these children are still growing into their developmental deficits.

To build onto the findings of this study, future research should focus on investigating the following: gathering detailed and quantifiable measures of SES, and then examine its far-reaching effects on the well-being of HIV-infected children and their parents/caregivers; identifying and finding ways to increase the availability of protective factors for buffering the psychological effects of being HIV-positive; and conducting longitudinal investigations into

the developmental and psychological trajectories of child and adolescent mental health. More thorough investigation into the possible child developmental deficits in HIV-positive HAART-naïve children is needed; such investigation should include detailed measures of family SES so as to tease out the effects of that factor from the effects of the illness itself.

This is one of the first studies conducted in South Africa focusing specifically on child functional impairment in HIV, and on the well-being of parents of HIV-infected children. In 2010, about 390 000 of new infections globally were among children (UNAIDS, 2011). These infections are due to MTC transmission, meaning in 2010 there were 390 000 new HIV-infected parent-child dyads worldwide. Research regarding the well-being of this group of people (both parents and children) is thus very important.

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APPENDIX A

DEMOGRAPHICS QUESTIONNAIRE

A. PARENT / CAREGIVER DEMOGRAPHICS

Sex: MALE FEMALE
Age: _____
DOB: _____
Marital status: MARRIED SINGLE DIVORCED
WIDOWED
Race: WHITE COLOURED BLACK AFRICAN
OTHER
Religion: _____
Home Language / Mother Tongue: ENGLISH AFRIKAANS isiXHOSA
OTHER
Other languages in which you are fluent: _____
Employed: YES NO
If YES, please describe what type of work you do:
_____
Are you dependent on a disability grant? YES NO

B. OBSTETRICS HISTORY

Any birth complications: YES NO
If yes, please specify:
_____
Emergency C-section: YES NO
If yes, please explain:
_____
Routine checkups followed: YES NO
If no, why not:
_____
Alcohol use during pregnancy: YES NO
If yes, please explain (frequency and quantity):
_____
Drug use during pregnancy: YES NO
If yes, please explain (quantity, frequency and type):
_____

C. CHILD / PATIENT DEMOGRAPHICS

Sex: MALE FEMALE
Age: _____
DOB: _____
Race: WHITE COLOURED BLACK AFRICAN OTHER
Religion: _____
Home Language / Mother Tongue: ENGLISH AFRIKAANS isiXhosa OTHER
Other languages in which your child is fluent: _____

D. CHILD / PATIENT MEDICAL HISTORY

Most recent CD4 count: _____ Date taken: _____
Most recent viral load: _____ Date taken: _____

Significant / traumatic head injuries: YES NO
If yes, please specify the following:
When/how long ago:
_____
Was child unconscious (could not wake child up):
_____
Was child hospitalised and for how long:
_____
Did the child require stitches:
_____
Brain scans done and when:
_____

Alcohol use: Previous YES NO
Alcohol use: Current YES NO
If yes, please specify quantity and frequency:
_____

Drug use: Previous YES NO
Drug use: Current YES NO
If yes, please specify quantity, frequency and type:
_____

Has your child ever been diagnosed with any psychiatric illness: eg: depression, psychosis, anxiety, etc: YES NO
If yes, please specify:
_____
Is your child currently receiving treatment for a psychiatric illness: YES NO

If yes, please explain:

_____

Please explain your child's current HAART treatment regime:

_____

_____

Has your child had any HIV related illnesses: YES NO

If yes, please specify: eg: TB, pneumonia, meningitis, etc.

_____

Is your child currently receiving treatment for an HIV related illness: YES NO

If yes, please explain:

_____

Has your child had any surgical procedures done? Please explain:

_____

_____

Does your child have any other medical conditions: YES NO

If yes, please specify: eg: diabetes, asthma, epilepsy, etc:

_____

E. EDUCATION LEVEL OF CHILD

Highest grade completed at school:

_____

Current grade:

_____

If child is not presently attending school, please specify their daily activities. Are they at home? At a care facility?

_____

Has he/she repeated any grades at school? YES NO

School setting: RURAL URBAN

F. GENERAL INFORMATION

Which best describes the area you live in?

SURBURBAN URBAN RURAL

TOWNSHIP

What is the name of the area you live in?

_____

Size of the house (number of rooms in the house):

_____

Number of people who live in the house:

_____

Who lives in your house (e.g., father, mother, grandmother, etc):

Annual Household Income:

i.	0 – 35 000	☐
ii.	36 000 – 50 000	☐
iii.	51 000 – 80 000	☐
iv.	81 000 – 100 000	☐
v.	101 000 – 120 000	☐
vi.	121 000 – 150 000	☐
vii.	151 000 and more	☐

Do you have the following amenities at home:

i.	Tap with running water		YES		NO
ii.	Electricity / Gas		YES		NO
iii.	Flush toilet in house	YES		NO	
iv.	TV	YES		NO	
v.	Adequate clothing for child	YES		NO	
vi.	Enough food to eat for at least 2meals per day		YES		NO
vii.	Child's own study/homework area or space	YES		NO	

APPENDIX B

COLUMBIA IMPAIRMENT SCALE (CIS) PARENT VERSION

Question		Parent Response						
In general, how much of a problem do you think he/she has with:		No problem	Very small problem	Some problem	Moderate problem	Very bad problem	N/A	Don't know
1	Getting into trouble?	0	1	2	3	4		9
2	Getting along with you? (or his/her mother or female caregiver)	0	1	2	3	4	8	9
3	Getting along with you? (or his/her father or male caregiver)	0	1	2	3	4	8	9
4	Feeling unhappy or sad?	0	1	2	3	4		9
How much of a problem would you say he/she has:								
5	With his/her behaviour at school?	0	1	2	3	4		9
6	With having fun?	0	1	2	3	4		9
7	Getting along with adults other than you?	0	1	2	3	4		9
How much of a problem does he/she have:								
8	With feeling nervous or afraid?	0	1	2	3	4		9
9	Getting along with his/her brother and/or sister?	0	1	2	3	4	8	9
10	Getting along with other kids his/her age?	0	1	2	3	4		9
How much of a problem would you say he/she has:								

11	Getting involved with activities like sport or hobbies?	0	1	2	3	4		9
12	With his/her school work?	0	1	2	3	4		9
13	With his/her behaviour at home?	0	1	2	3	4		9

APPENDIX C

MOTIVATION SCALE

Directions: Please circle the number on the scale below each question which best describes your child's motivation.

1. Starts playing (games, activities) on his/her own.
   For example, gathering materials for a game, cooking.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

2. Seems to put little effort into anything.
   For example, choosing clothing, getting ready for school, cleaning up.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

3. Does things on his/her own.
   For example, household chores, homework, getting ready for a trip.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

4. Finishes projects he/she starts.
   For example, colouring a picture, earning a scout badge, or pursuing a hobby.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

5. Approached activities with intensity, energy, or enthusiasm.
   For example, wants to be best at a sport, excited about visiting a new place.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

6. Is interested in things.
   For example, new TV shows, new clothes, new toys, new books.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

7. Makes plans, asks to do things in future.
   For example, taking a trip, having a party, getting a new toy.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

8. Is curious. For example, wants to understand things, know about different people, places, activities, or how things work.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

9. Is interested in learning new things.
   For example, learning the alphabet, learning a new sport, taking driver's education.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

10. Shows expected emotional responses.
    For example, happy when rewarded or surprised, sad when hurt, angry when insulted.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

11. Has to be told what to do in his/her free time.
    For example, playing with a toy or game, or making a phone call to a friend.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

12. Wants to be with friends.
    For example, invites friends to play, calls on the phone, or arranges social events.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

13. Talks freely, sharing his/her ideas with those present.
    For example, likes to talk on the phone, talks a lot with family and friends, likes to express his/her ideas on a topic.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

14. Does not appear interested or concerned about his/her own problems.

For example, being silly at school, not doing homework, lying.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

15. Lacks energy and often appears fatigued.
    For example, when important activities occur, when requests are made.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

16. Does not appear interested or concerned about his/her family or friends.
    For example, illness of a family member, being rejected or ignored by a close friend, being included in social events.

0	1	2	3	4
Never or rarely Occurs	1-3 times during a month	1-3 times per week	4-6 times per week	1 or more times a day

APPENDIX D

FAMILY RESOURCE SCALE

For each response write the number response that best describes how well the needs are met on a consistent basis in your family (that is, month-in and month-out). Eg: 1. Food for 2 meals a day: 3

NA= Does not apply

1= Not at all adequate

2= Seldom adequate

3= Sometimes adequate

4= Usually adequate

5= Almost always adequate

1. Food for 2 meals a day : _____
2. House or apartment: _____
3. Money to buy necessities: _____
4. Enough clothes for your family: _____
5. Heat for your house or apartment: _____
6. Indoor plumbing/water: _____
7. Money to pay monthly bills: _____
8. Good job for yourself or spouse: _____
9. Medical care for your family: _____
10. Public assistance(SSI, AFDC, Medicaid. Etc: _____
11. Dependable transportation (own transport or provided by others): _____
12. Time to get enough sleep/rest: _____
13. Furniture for your home or apartment: _____
14. Time to be by yourself: _____
15. Time for family to be together: _____

16. Time to be with children: _____
17. Time to be with spouse or close friend: _____
18. Telephone or access to phone: _____
19. Babysitting for your child(ren): _____
20. Child care/day care for your child(ren): _____
21. Money to buy special equipment/supplies for child(ren): _____
22. Dental care for your family: _____
23. Someone to talk to: _____
24. Time to socialize: _____
25. Time to keep in shape and looking nice: _____
26. Toys for your child(ren): _____
27. Money to buy things for self: _____
28. Money for family entertainment: _____
29. Money to save: _____
30. Travel/vacation: _____

THANK YOU

APPENDIX E

FAMILY SUPPORT SCALE

Name: _____

Date of assessment: _____

Instructions: We are going to present you with a list of people and groups that often are helpful to members of a family raising a child. Please choose one of the numbers on the card to describe how helpful sources have been to your family during the past 3 – 6 months. If a source of help has not been available to your family during this period, check the not available response.

For example, if your parents were not helpful to your family during the past 3 – 6 months, choose (1) - "Not at all helpful". If they were sometimes helpful, choose (2) – "Sometimes helpful". Choose (3) if they were generally helpful, (4) if very helpful, (5) if extremely helpful. If your parents are no longer living, choose (0) which tells me they were not available during this time period.

		0 Not available	1 Not at all helpful	2 Sometimes helpful	3 Generally helpful	4 Very helpful	5 Extremely helpful
1	Your parents						
2	Your spouse or partner's parents						
3	Your relatives/kin (other you're your parents)						
4	Your spouse or partner's relatives/kin						
5	Spouse or partner						
6	Your friends						
7	Your spouse or partner's friends						
8	Your own children						
9	Other parents						
10	Co-workers						
11	Parent groups						
12	Social groups/clubs						
13	Church members/minister						
14	Your family or child's physician						
15	Early childhood intervention programs						
16	School/day care centre						
17	Professional helpers(social, worker,therapist,teacher, etc)						
18	Professional agencies(public health, social services,mental health, etc)						

APPENDIX F

CENTER FOR EPIDEMIOLOGIC STUDIES DEPRESSION SCALE (CES-D), NIMH

Below is a list of the ways you may have felt or behaved. Please indicate how often you have felt this way during the past week.

		During the Past Week			
		Rarely or none of the time(less than 1 day)	Some or little of the time(1-2 days)	Occasionally or a moderate amount of the time(3-4 days)	Most or all of the time(5-7 days)
1	I was bothered by things that usually don't bother me.				
2	I did not feel like eating, my appetite was poor.				
3	I felt that I could not shake off the blues even with help from family and friends				
4	I felt I was just as good as other people				
5	I had trouble keeping my mind on what I was doing.				
6	I felt depressed.				
7	I felt that everything I did was an effort.				
8	I felt hopeful about the future.				
9	I thought my life had been a failure.				
10	I felt fearful.				
11	My sleep was restless.				
12	I was happy.				
13	I talked less than usual.				
14	I felt lonely.				
15	People were unfriendly.				
16	I enjoyed life.				
17	I had crying spells.				
18	I felt sad.				
19	I felt that people disliked me.				
20	I could not get going.				

APPENDIX G

PATIENT INFORMATION AND CONSENT FORM
FOR THE STUDY: Diffusion Tensor Imaging of HIV-positive Children and Their Psychocognitive and Behavioural Profiles.

HIV Positive patients

Principal Investigator: Dr J Hoare

Dear Participant

You and your child are requested to participate in a medical research study that is being done at Red Cross Children's Hospital in the School of Child and Adolescent Health, University of Cape Town. The following describes the study and you and your child's role. Please take some time to read the information presented here carefully, and feel free to ask any questions.

Background
We are doing a study on how HIV affects children's learning, development and behaviour. We want to compare tests of development (learning, memory, language and attention), psychosocial scales (trauma, life events, depression, anxiety and adaptability) and brain scans from children with HIV to children who do not have HIV.

If you are willing to allow your child to participate in this study, your child must be *HIV positive and currently not physically ill.*

HIV infection may cause slow development in a child. This can be either because of the virus itself or infections that the child may get. Even if a child seems well and is going to school, the HIV infection may affect some functions - like interfering with learning, with good memory, with doing mathematics, and with attention and behaviour.

We also want to learn about how caring for a child affects you as a parent. Parents, who have to care of a HIV-positive child, may experience more stress and difficulties than parents whose children do not have HIV. We want to compare test of parental stress of parents of children who are HIV-positive, to parents of children who are HIV-negative.

Children are often exposed to different kinds of trauma under various circumstances. We would like to find out more about the kinds of trauma certain children may experience.

Purpose of the Study
The aim of this study is to measure tests of development (learning, memory, language, attention) and tests of behaviour and brain scans in healthy HIV-positive children and in healthy HIV negative children. The HIV-positive children's performance will be compared to the performance of healthy HIV-negative children. This will improve our understanding and management of children with HIV.

Procedures in the Study
Your involvement in the study will require you to visit the study doctor/team on three occasions. Two of the sessions will take place at Red Cross Children's Hospital (RXH), and

during these sessions neuropsychological, developmental and behavioural tasks will be completed by your child. This includes the brain scan, but this will be done at Tygerberg Hospital.

Confirmation of HIV diagnosis
If you are invited to participate in this study, it means that your child has *already been diagnoses as being HIV positive,* and has been referred to this study. Your child is unique in that he/she will have acquired the infection via mother to child transmission, and not via a blood transfusion or unhygienic needles.

Your child is currently attending a clinic for regular checkups. With your permission, we will contact the clinic which you and your child are attending to gain access to information in your clinic folders. During the course of your participation you will be asked certain medical questions regarding your child most recent CD4 count, viral load, and current treatment regime.

Neuropsychological and psychological testing
The study research assistant will ask your child to complete a number of pencil and paper tests which involve some writing and drawing as we tests their memory, concentration and planning abilities. Many of these are like a normal IQ test that your child may have completed at school. All of these tests are important and will help us to determine if HIV has any effects on these aspects for your child's brain. This session will take approximately 2½ - 3 hours long. At another session you child will be asked questions about what kinds of things they have experienced in their everyday lives, as well as questions about their emotional state.

While your child completes these tasks, we will ask you as the parent / guardian to complete psychological measures pertaining to your child's overall development, as well as your experiences as a parent. These tests are important and will help us to determine the amount of stress and anxiety you may experience as a parent, and how this relates to your child's development.

Brain scanning procedure
All brain scans will be done at a specialized facility at Tygerberg Hospital. A special brain scan (an MRI scan) will be done on your child – this examination is not harmful and it is not painful. Your child will be asked to lie still on a special bed while the scanner takes the pictures of your child's head - this will be for a maximum of 30 minutes. Some children may find the machine a bit scary. If your child is very anxious or scared or unable to lie still for that long, we will not continue with the examination.

Neurological examination
You child will be required to undergo a neurological examination which will be performed by a study doctor. The purpose of this examination is to check that your child's sensory and motor responses, and also their reflexes, are functioning properly and that there is no damage to their nervous system. To test this, the doctor will ask your child to do a series of playful activities, for example touching their nose or their ankles. These tasks are not harmful to your child. If your child is anxious, you may accompany him/her in the examination room.

Procedure for drawing of bloods

This part of the study involves the long-term storage of DNA (genetic) taken from a sample of your child's blood for future analysis. Genetic material, also called DNA, can be obtained from small samples of blood. Previous studies have shown that HIV infection can have damaging effects on the brain. We are however unsure as to how serious these effects may be in young children. In this part of the study, we hope one day to be able to use genetic material, such as we will be collecting, to assist us in identifying genes that will tell is what people may be particularly vulnerable to experience harmful effects, and what genetic patterns are likely to make people more susceptible to becoming infected with the HIV virus. Before the brain scan is done, a registered nurse will draw a small amount of blood from your child. This procedure will not be harmful to your child. Your child may feel a light prick when the needle is inserted into his/her arm, but will not experience any pain. The needle is connected to a thin plastic pipe and the blood then flows into a small blood sample tube. The test will require about 1 teaspoon of blood, and is performed only once.

Your blood will only be used for genetic research that is directly related to this study looking and diffusion tensor in HIV-infected children. Also if the researchers wish to use your stored blood for *additional research in this field* they will be required to apply for permission to do so from the Human Research Ethics Committee at UCT. If you do not wish your blood specimen to be stored after this research study is completed you will have an opportunity to request that it be discarded when you sign this consent form.

Follow ups
You and your child may be asked to attend a follow up session. If you are asked to come for a follow up, it will be one year from the date of your first enrollment to this study. The study procedures for the follow up, will be the same as for this time.

Your Part in the Study
While your child is being tested by members of the study team, you will also be asked to completed questions by another member of the study. You will complete a general demographics form, and other psychological tests pertaining to your child's mental health and yours. These tests are not harmful, but may ask some sensitive questions about your life. Our researchers will do all they can to emotionally support you while you complete these forms. It is important for us that you answer these questions truthfully, so that we can better understand you as a parent, and your needs.

For the first session, a trained research assistant will interview your child at RXH. During this session your child will complete the neuropsychological tasks previously described. During the second session, a registered social worker will interview your child about their behavioural and emotional well-being. Your child will then be given another appointment to go Tygerberg hospital, on a day that is convenient for you, where the brain scan will be done. We will try to arrange these sessions so as to not interfere with your child's normal school routine. These sessions may be booked after school hours where possible. Transport money and food vouchers will be provided for you and your child for each these visits.

Risks to You and Your Child
There are only low or minimal risks associated with your participation in this study. If you feel tired at any point during any of the visits, you should please ask your study

doctor/psychologist for a rest. If for some reason you are unable to complete a visit on a particular day we may reschedule to complete the assessments at another time.

There are no direct risks in having blood taken for genetic testing.

Furthermore, there are no known risks for your child for either the psychological tests or the brain scan. The brain scan does not involve any radiation.

Benefits to You and Your Child
Although there is no direct benefit for you or your child, the results of this research may help to inform us to what the common school and behaviour problems are that healthy HIV-positive children can have. This will help us to decide if we need to consider extra treatments and/or interventions for these children.

Confidentiality
You and your child's test results will be kept confidential (private) and will only be used by the members of this study for the purpose of research. If any information from this study gets published, we will make sure that your personal details will remain confidential at all times.

This study has been approved by the Committee for Human Research of the University of Cape Town (UCT). It will be conducted according to Medical Research Council guidelines on good clinical practice (2003) as well as the Declaration of Helsinki Guidelines (Edinburgh, 2000), which provide detailed guidelines that relate to the ethical conduct of studies involving human subjects.

Voluntary Participation
You and your child's participation are entirely voluntary. You or your child is not under any obligation to participate. If you choose not to allow your child to participate, it will not affect you or your child negatively or prevent your right to future health care services. You have the right to withdraw your child from the study at any time.

You have the right to ask questions at any time about any aspect of the study. If you have any queries, you can contact Jackie Hoare on 021 404 2134/2164

You are entitled to a signed copy of this document.

If you agree to take part, please complete the following section:

ASSENT OF MINOR

I (*Name of Child/Minor*) _____ have been invited to take part in the above research project entitled**: Diffusion Tensor Imaging of HIV-positive Children and Their Psychocognitive and Behavioural Profiles.**

The study doctor/nurse and my parents have explained the details of the study to me and I understand what they have said to me.

- They have also explained that this study will involve 3 assessments which include interviews, filling questionnaires, a physical examination, blood sampling, and a brain scan.
- I also know that I am free to withdraw from the study at any time if I am unhappy.
- By writing my name below, I voluntarily agree to take part in this research project. I confirm that I have not been forced either by my parents or doctor to take part.

_____

Name of child **(To be written by the child if possible)**

DECLARATION BY PARENT/LEGAL GUARDIAN

By signing below, I *(name of parent/legal guardian)* _____ agree to allow my child (*name of child*) _____ who is ___ years old, to take part in a research study entitled: **Diffusion Tensor Imaging of HIV-positive Children and Their Psychocognitive and Behavioural Profiles.**

I declare that:

- I have read or had read to me this information and consent form and that it is written in a language with which I am fluent and comfortable.
- If my child is older then 7 years, he/she must agree to take part in the study and his/her ASSENT must be recorded on this form.
- 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 let my child take part.
- I may choose to withdraw my child from the study at any time and my child will not be penalised or prejudiced in any way.
- My child may be asked to leave the study before it has finished if the study doctor or researcher feels it is in my child's best interests, or if my child does not follow the study plan as agreed to.
- I understand that genetic material will be collected from blood samples

☐ I agree that my child's blood sample can be stored for research purposes, subject to the approval of the Human Research Ethics Committee (HREC) of UCT, provided that all information is kept confidential. I can choose to request at any time that my stored sample be destroyed. I have the right to receive confirmation that my request has been carried out.

OR

☐ Please destroy my blood sample as soon as the current research project has been completed. **(Tick the option you choose**)

Signed at (*place*) _____ on (*date*) _____20____

_____

Signature of parent/legal guardian

DECLARATION BY INVESTIGATOR

I *(name)* _____ declare that:

- I explained the information in this document to (*name of child and parent)*_____
  I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understand 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

DECLARATION BY INTERPRETER

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

- I assisted the investigator (*name*) _____
  to explain the information in this document to
  (*name of parent/legal guardian*) _____
  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 parent/legal guardian fully understands the content of this informed consent document and has had all his/her questions satisfactorily answered.

Signed at (*place*) _____on (*date*) _____20_____

_____
Signature of interpreter

PARTICIPANT INFORMATION LEAFLET

We are doing a study on children's learning, development and behaviour.
We also want to learn about how caring for a child affects you as a parent.

Procedures in the Study
Your involvement in the study will require you to visit the study doctor/team on three separate occasions. Two sessions at RXH and another session at TBH.

Neuropsychological and psychological testing
The study research assistant will ask your child to complete a number of pencil and paper tests which involve some writing and drawing as we tests their memory, concentration and planning abilities. This session will take approximately 2½ - 3 hours long. While your child completes these tasks, we will ask you as the parent / guardian to complete psychological measures pertaining to your child's overall development, as well as your experiences as a parent.

Brain scanning procedure
All brain scans will be done at a specialized facility at TBH. A special brain scan (an MRI scan) will be done on your child – this examination is not harmful and it is not painful. The scan will take about 30 minutes.

Neurological examination
You child will be required to undergo a neurological examination which will be performed by a study doctor. The purpose of this examination is to check that your child's sensory and motor responses, and also their reflexes, are functioning properly and that there is no damage to their nervous system.

Risk and Benefits
There are no major risks involved in participating in this study. You and your child will be making a valuable contribution to the field of medical and psychological knowledge. Transport money and food vouchers will be provided for each of your visits. All your personal information and test results will be kept strictly confidential

Questions and queries:
Bulelwa Mtukushe
(t) 021 404 7625 / 021 404 7626

APPENDIX H

PATIENT INFORMATION AND CONSENT FORM
FOR THE STUDY: Diffusion Tensor Imaging of HIV Affected Children and Their Psychocognitive and Behavioural Profiles.

HIV Negative controls

Principle Investigator: Dr J Hoare

Dear Participant

You and your child are requested to participate in a medical research study that is being done at Red Cross Children's Hospital in the School of Child and Adolescent Health, University of Cape Town. The following describes the study and you and your child's role. Please take some time to read the information presented here carefully, and feel free to ask any questions.

Background
We are doing a study on how HIV affects children's learning, development and behaviour. We want to compare tests of development (learning, memory, language and attention), psychosocial scales (trauma, life events, depression, anxiety and adaptability) and brain scans from children with HIV to children who do not have HIV.

You may participate in this study if your child is ***healthy and not HIV positive.***

Infection may cause slow development in a child. This can be either because of the virus itself or infections that the child may get. Even if a child seems well and is going to school, the infection may affect some functions - like interfering with learning, with good memory, and with attention and behaviour.

We also want to learn about how caring for a child affects you as a parent. Parents, who have to care of a positive child, may experience more stress and difficulties than parents who have children who are negative. We want to compare test of parental stress of parents of children who are negative, to parents of children who are positive.

Children are often exposed to different kinds of trauma under various circumstances. We would like to find out more about the kinds of trauma certain children may experience.

Purpose of the Study
The aim of this study is to measure tests of development (learning, memory, language, attention) and tests of behaviour and brain scans in healthy positive children and in healthy negative children. The positive children's performance will be compared to the performance of healthy negative children. This will improve our understanding and management of children with HIV.

Procedures in the Study
Your involvement in the study will require you to visit the study doctor/team on three occasions. Two of the sessions will take place at Red Cross Children's Hospital (RXH), and during these sessions neuropsychological, developmental and behavioural tasks will be

completed by your child. The brain scan will be done at the third session, and this will take place at Tygerberg Hospital's (TBH) Cape Universities Brain Imaging Center (CUBIC).

HIV testing procedure
Since your child is a ***healthy HIV negative participant*** in this study, with your permission we are going to do a very simple screening procedure to test for HIV infection. It is important that we are able to exclude HIV as a confounding factor when looking at the development of normal healthy children. This test will be done at your first study visit, prior to doing any of the neuropsychological tasks.

If your child is negative, he/she will be enrolled into this study with your permission as parent/guardian. If your child tests positive, he/she will still be able to participate in this study, but only after his/her immediate medical needs have been taken care of. Having an HIV test done can cause feelings of anxiety and worry. These kinds for feelings are normal. We will take every step possible to ensure that you are comfortable with having your child take the HIV test. We will perform an HIV rapid test, which will require your child to have a finger prick for a drop of blood. The test results are immediately available. As part of this procedure, you and your child will be counseled both prior to taking the test and afterwards, regardless of the test outcome.

<u>What are your rights?</u>

- To make your own decision about whether to be tested for HIV or not;
- To be provided with all the information necessary regarding harm and risks of taking or not taking an HIV test
- To be given an opportunity and time to ask any questions related to the infection and have them answered to your satisfaction; this includes any questions that your child might have
- To have a session of counselling for you and your child before and after the result of the test is known
- To have your child's test results treated in confidence
- To ask ANY questions about any part of this study

If as a result of your participation in this research study your child is initially diagnosed as positive, the results will be revealed to you. This can either be done privately or together with your child. You will then be referred by the study doctor to the Infectious Disease Family Clinic at Groote Schuur Hospital or to your local clinic for immediate counseling and medical treatment.

If your child has already had a recent HIV test, he/she will not need to redo the test to participate in this study, but with your permission, we will have to gain access to the information from the clinic at which he/she was tested.

Neuropsychological and psychological testing
The study research assistant will ask your child to complete a number of pencil and paper tests which involve some writing and drawing as we tests their memory, concentration and planning abilities. Many of these are like a normal IQ test that your child may have completed at school. All of these tests are important and will help us to determine if HIV has any effects on these aspects for your child's brain. This session will take approximately 2½ - 3 hours long. At another session you child will be asked questions about what kinds of things

they have experienced in their everyday lives, as well as questions about their emotional state.

While your child completes these tasks, we will ask you as the parent / guardian to complete psychological measures pertaining to your child's overall development, as well as your experiences as a parent. These tests are important and will help us to determine the amount of stress and anxiety you may experience as a parent, and how this relates to your child's development.

Brain scanning procedure
All brain scans will be done at a specialized facility at Tygerberg Hospital. A special brain scan (an MRI scan) will be done on your child – this examination is not harmful and it is not painful. Your child will be asked to lie still on a special bed while the scanner takes the pictures of your child's head - this will be for a maximum of 45 minutes. During that time your child may rest and close his/her eyes. Having an MRI scan done is a safe procedure if you and your child have been screened correctly for the presence of any magnetic material on or inside you such as pace-makers, surgical clips and metal objects. A formal screen for this will be done by one of the study research assistants prior to the scanning session. When the magnet inside the machine is switched on, it will make some loud banging noises. At this time you will feel nothing and the noise is not harmful to you or your child in any way. Your child will be given soft ear plugs to wear during the procedure to minimize possible discomfort associated with this experience.

Some children may find the machine a bit frightening. If your child is very anxious or scared, you will be allowed to accompany your child inside the scanning room. We will make sure that it is safe for both you and your child to go inside the MRI scanning room and to undergo scanning. Your child may feel slightly dizzy immediately after the scan. This is completely normal. The radiographers at the scanning center are qualified and trained to be alert to the effects of the scanning procedure on participants. Your child's need will be attended to immediately, should the need arise. We will make every effort to ensure that your child is comfortable doing the scan. Materials will be provided to prepare your child before the scan, for example a flow diagram for the scanning procedure, as well as a video. If your child is still afraid or unable to lie still for that long, we will not continue with the examination.

Follow ups
You and your child may be asked to attend a follow up session. If you are asked to come for a follow up, it will be one year from the date of your first enrollment to this study. The study procedures for the follow up, will be the same as for this time.

Your Part in the Study
While your child is being tested by members of the study team, you will also be asked to completed questions by another member of the study. You will complete a general demographics form, and other psychological tests pertaining to your child's mental health and yours. These tests are not harmful, but may ask some sensitive questions about your life. Our researchers will do all they can to emotionally support you while you complete these forms. It is important for us that you answer these questions truthfully, so that we can better understand you as a parent, and the difficulties you experience while caring for your child.

For the first session, a trained research assistant will interview your child at RXH. During this session your child will complete the neuropsychological tasks previously described. During

the second session, a registered social worker will interview your child about their behavioural and emotional well-being. Your child will then be given another appointment to go Tygerberg hospital, on a day that is convenient for you, where the brain scan will be done. We will try to arrange these sessions so as to not interfere with your child's normal school routine. These sessions may be booked after school hours where possible. Transport money and food vouchers will be provided for you and your child for each these visits.

Risks to You and Your Child
There are no risks involved in doing an HIV test. However, waiting for and receiving the test result may be a difficult time because of the complex emotions involved in a time such as this. If you are in need of support, please telephone the study contact (investigator) who gave you this information before you had the test done.

If you or your child feels tired at any point during any of the visits, you should ask your study doctor/psychologist for a rest. If for some reason you are unable to complete a visit on a particular day we may reschedule to complete the assessment at another time.

Furthermore, there are no known risks for your child for either the psychological tests or the brain scan. The brain scan does not involve any radiation.

Benefits to You and Your Child
Although there is no direct benefit for you or your child, the results of this research may help to inform us to what the common school and behaviour problems are that healthy HIV-positive children can have. This will help us to decide if we need to consider extra treatments and/or interventions for these children.

We acknowledge that we cannot provide intervention or treatment, as part of this study. If it is detected that your child has developmental delay, we will provide you will a detailed report, and with your permission we will forward it to the relevant educational department to be dealt with accordingly. A detailed report will be important in determining what type of intervention your child may need. Further treatment for your child will be at your own expense.

Confidentiality
You and your child's test results will be kept confidential (private) and will only be used by the members of this study for the purpose of research. If any information from this study gets published, we will make sure that your personal details will remain confidential at all times.

This study has been approved by the Human Research Ethics Committee (021 406 6492) of the University of Cape Town (UCT). It will be conducted according to Medical Research Council guidelines on good clinical practice (2003) as well as the Declaration of Helsinki Guidelines (Edinburgh, 2008), which provide detailed guidelines that relate to the ethical conduct of studies involving human subjects.

Voluntary Participation
You and your child's participation are entirely voluntary. You or your child is not under any obligation to participate. If you choose not to allow your child to participate, it will not affect you or your child negatively or prevent your right to future health care services. If you do not want your child to be tested for HIV, this means that you and your child will not be able to participate in this study. The reason for this is that it is important that we are able to exclude

HIV disease as a factor in our findings and your child's performance. You have the right to withdraw your child from the study at any time.

You have the right to ask questions at any time about any aspect of the study. If you have any queries, you can contact Jackie Hoare on 021 404 2134/2164.

You are entitled to a signed copy of this document.

If you agree to take part, please complete the following section:

ASSENT OF MINOR

I (*Name of Child/Minor*) _____ have been invited to take part in the above research project entitled**: Diffusion Tensor Imaging of HIV-positive Children and Their Psychocognitive and Behavioural Profiles.**

The study doctor/nurse and my parents have explained the details of the study to me and I understand what they have said to me.

- They have also explained that this study will involve 3 assessments which include interviews, filling questionnaires, a physical examination including a blood test, and a brain scan.
- I also know that I am free to withdraw from the study at any time if I am unhappy.
- By writing my name below, I voluntarily agree to take part in this research project. I confirm that I have not been forced either by my parents or doctor to take part.

_____

Name of child **(To be written by the child if possible)**

DECLARATION BY PARENT/LEGAL GUARDIAN

By signing below, I *(name of parent/legal guardian)* _____ agree to allow my child (*name of child*) _____ who is ___ years old, to take part in a research study entitled: **Diffusion Tensor Imaging of HIV-positive Children and Their Psychocognitive and Behavioural Profiles.**

I declare that:

- I have read or had read to me this information and consent form and that it is written in a language with which I am fluent and comfortable.
- If my child is older than 7 years, he/she must agree to take part in the study and his/her ASSENT must be recorded on this form.
- 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 let my child take part.
- I may choose to withdraw my child from the study at any time and my child will not be penalised or prejudiced in any way.
- My child may be asked to leave the study before it has finished if the study doctor or researcher feels it is in my child's best interests, or if my child does not follow the study plan as agreed to.

Signed at (*place*) _____ on (*date*) _____20____

_____
Signature of parent/legal guardian

DECLARATION BY INVESTIGATOR

I *(name)* _____ declare that:

- I explained the information in this document to (*name of child and parent)*_____
  I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understand 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

DECLARATION BY INTERPRETER

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

- I assisted the investigator (*name*) _____
  to explain the information in this document to
  (*name of parent/legal guardian*) _____
  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 parent/legal guardian fully understands the content of this informed consent document and has had all his/her questions satisfactorily answered.

Signed at (*place*) _____on (*date*) _____20_____

_____
Signature of interpreter

PARTICIPANT INFORMATION LEAFLET

We are doing a study on children's learning, development and behaviour.
We also want to learn about how caring for a child affects you as a parent.

Procedures in the Study
Your involvement in the study will require you to visit the study doctor/team on three separate occasions. Two sessions at RXH and another session at TBH.

Neuropsychological and psychological testing
The study research assistant will ask your child to complete a number of pencil and paper tests which involve some writing and drawing as we tests their memory, concentration and planning abilities. This session will take approximately 2½ - 3 hours long. While your child completes these tasks, we will ask you as the parent / guardian to complete psychological measures pertaining to your child's overall development, as well as your experiences as a parent.

Brain scanning procedure
All brain scans will be done at a specialized facility at TBH. A special brain scan (an MRI scan) will be done on your child – this examination is not harmful and it is not painful. The scan will take about 30 minutes.

Neurological examination
You child will be required to undergo a neurological examination which will be performed by a study doctor. The purpose of this examination is to check that your child's sensory and motor responses, and also their reflexes, are functioning properly and that there is no damage to their nervous system.

Risk and Benefits
There are no major risks involved in participating in this study. You and your child will be making a valuable contribution to the field of medical and psychological knowledge. Transport money and food vouchers will be provided for each of your visits. All your personal information and test results will be kept strictly confidential

Questions and queries:
Bulelwa Mtukushe
(t) 021 404 7625 / 021 404 7626

APPENDIX I

WELL DONE!

YOU COMPLETED A WHOLE RANGE OF NEUROPSYCHOLOGICAL TESTS AS PART OF RESEARCH

Awarded to: _____

Date: _____ Signed: _____

APPENDIX J

NEUROPSYCHOLOGICAL TEST BATTERY

LangHand questionnaire
CAT-Rapid
TEA-Ch (versionB) – sky, score, creature counting, sky DT, opposite world
Digit Span – forward, backward
Colour Trails – 1, 2
BNT
Coding – A or B (depending on age)
RCF – copy
RCF – 3 minute recall
Nepsy Inhibition – Shapes: naming, inhibition, switching
Nepsy Inhibition – Arrows: naming, inhibition, switching
WISC Symbol Search - A or B (depending on age)
HVLT – 1, 2, 3
RCF – 30 min delayed
HVLT – 5 minute delayed, recognition
WASI – vocab, block, similarities, matrix
VFLU – phonemic, category
IHDS
Finger tapping test – dominant, non-dominant
Grooved Pegboard – dominant, non-dominant