Depression amongst caregivers of children and adolescents with perinatally-acquired HIV in Cape Town, South Africa

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Depression amongst caregivers of children and adolescents with perinatally-acquired HIV in Cape Town, South Africa

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Abstract

Background

Depression remains the most commonly diagnosed mental health disorder. It adds significantly to the global burden of disease and is responsible for the most years of life lost to disability in both men and women (Rehm & Shield, 2019). The successful roll-out of antiretroviral therapy (ART) to those living with HIV has resulted in the emergence of an increasing population of children and adolescents with perinatally acquired-HIV (PHIV) requiring care. Caregivers of PHIV are at increased risk for the development of depression due to parental, child and socio-economic factors. Few studies have focused on the specific factors associated with caregiver depression in the context of caring for ART-treated and untreated PHIV.

Aims and Objectives

The aims of this cross-sectional study are to assess the prevalence of depression in caregivers of PHIV compared with caregivers of a HIV-seronegative matched control group (HC). In the HIV-impacted families, a comparison will be drawn between the prevalence of depression in biological and non-biological caregivers. Factors associated with depression in this vulnerable group will be assessed using various caregiver, child and socio-economic measures.

Methods

Caregivers of 75 PHIV and 30 HC were selected from a community healthcare setting in Cape Town.

Results

There was no difference found between levels of depression in PHIV caregivers (biological or non-biological) and caregivers of HC. Internalising and externalising child behaviours, poor family resources (including basic needs, money, time for self and time for family) and limited social support were associated with depression in both caregiver groups. In caregivers of HC, parental stress was associated with higher levels of depression.

Conclusion

Factors independent of HIV status of children may be driving depression in caregivers of children and adolescents in Cape Town, South Africa where HIV is endemic. Thus, this study could facilitate a better understanding of depression in the context of caring for PHIV and better inform interventions in these vulnerable family systems.

Keywords**:** caregiver, depression, HIV, biological/non-biological, mental health

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Abbreviations and Glossary of terms

Adolescent: a person 10 – 19 years of age

ART: Antiretroviral therapy

Biological caregiver: caregiver who is the child's biological parent

CBCL: Child Behaviour Check List

CBCL: Child Behaviour Check List

CES-D: Centre for Epidemiologic Studies – Depression Scale

Child: a person 19 years of age or younger

Depression: defined by DSM 5 (Diagnostic and statistical Manual) as manifesting five (or more) of the following symptoms, which have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure – (1) depressed mood, (2) markedly reduced interest or pleasure, weight changes, (3) sleep disturbance, (4) psychomotor agitation or retardation, (5) fatigue, (6) feelings of worthlessness or guilt, (7) difficulty with thinking and concentration and (8) repeated thoughts of death

Eastern Cape: Province of Eastern Cape, South Africa

FRS: Family Resources Scale

FSS: Family Support Scale

HC: matched HIV-seronegative children and adolescent control group

HIVE: HIV-associated encephalopathy

HIV-impacted: individual with HIV-negative status but exposed to the effects of HIV while living in a household with others living with HIV and AIDS

HIV-seronegative: individual with an HIV-negative result

HIV-seropositive: individual living with HIV

KZN: Province of Kwazulu-Natal, South Africa

LMIC: low-to-middle income-country

Non-biological caregiver: caregiver who is not the child's biological parent

PHIV: children and adolescents with perinatally-acquired HIV

PLWHA: people living with HIV and AIDS

PSI: Parenting Stress Index

SA: South Africa

Western Cape: Province of Western Cape, South Africa

INTRODUCTION AND LITERATURE REVIEW

Title: Depression amongst caregivers of children and adolescents with perinatally-acquired HIV in Cape Town, South Africa

Background and Significance

Depression remains one of the most commonly diagnosed mental health disorders. Depressive disorders often have a protracted course and therefore add significantly to the global burden of disease. According to World Health Organisation's Global Health Estimates from 2017, there were more than 300 million people suffering from depression worldwide, 4.4% of the world's population (WHO, 2017). Depression is responsible for the most years of life lost to disability of all mental disorders in both men and women worldwide (Rehm & Shield, 2019). The South African Stress and Health (SASH) study found a 9.8% lifetime prevalence of a Major Depressive Disorder in South Africa (SA) with the highest lifetime prevalence for all mental disorders, including mood disorders, noted in the Western Cape, where the current study is planned (Herman et al., 2009; WHO, 2017). Maternal depression and depression in the context of caregiving, has been linked to various adverse outcomes in children and families (Turner & Honikman, 2016). HIV is endemic in SA with a prevalence of 13% (Maluleke, 2018) and people living with HIV and AIDS (PLWHA) have an increased risk for the development of depression with gender, employment status, parenting children and the stage of the disease noted as factors associated with increased risk for mental illness in this group. 11.1% of PLWHA in SA were found to fulfil criteria for a major depressive episode (Freeman et al., 2008). This would indicate that depression, in the context of maternal and caregiver mental health, especially in those with co-morbid HIV-infection, could present unique challenges in the South African context.

The widespread roll-out of HIV testing and treatment programmes in Sub-Saharan Africa has resulted in in a 49% reduction in AIDS-related deaths worldwide since 2010 (UNAIDS, 2020) . The sub-Saharan region has had the sharpest decline in AIDS-related deaths of all world regions. With the introduction of effective measures to reduce vertical transmission of HIV from mothers to infants, only 9% of new HIV infections worldwide are in children 0-14 years. However, of the new infections in children, 84% of were reported in sub-Saharan Africa (UNAIDS, 2020).

Consequently, children and adolescents with perinatally-acquired HIV (PHIV) are an emerging population with unique needs and challenges (Mellins & Malee, 2013). Antiretroviral therapy (ART) for the treatment of children was initiated in Africa in 2004 and this has seen the number of infants and children with HIV surviving to adolescence and adulthood. Access to ART for all, regardless of illness status or CD4 count, was only formulated into national guidelines from 2012 following the release of the CHER trial (Violari et al., 2008). Many PHIV born prior to 2012 would therefore not have been initiated on ART until later in the course of their illness.

PHIV live in environments with multiple stressors related to their own HIV-illness, the effects of HIV-illness on their parents and, in SA in particular, an HIV-endemic environment with high levels of poverty and violence. Perinatal HIV-infection can result in impairment in neurodevelopmental function (Hoare, 2015). Caring for PHIV can translate into caring for sick or disabled children (Kuo & Operario, 2009) and contribute to an increased risk of household poverty (Katana et al., 2020). These factors can create an environment for emotional and behavioural difficulties in PHIV. Caregivers of PHIV therefore, may have unique difficulties compared with caregivers of children in HIV-unimpacted households.

Carers of PHIV face individual and household struggles as they navigate HIV in their family units. Many are living with the effects of their own HIV-illness and the responsibility of managing a child or children also living with HIV. Caregivers may not be the biological parent of the child and have taken the responsibility of caregiving due to parental loss. This introduces a new family structure for the carer and child with the added difficulties of grief and loss. Grandparents and elderly family or community members are frequently called on to care for orphaned children. The caregiver may now be required to take responsibility for managing a child with an unfamiliar, chronic illness (Kalomo et al., 2017). Parental loss and orphanhood places financial strain on already limited family resources, especially in the context of the endemic poverty (Kagotho & Ssewamala, 2012). PHIV struggling with grief and loss along with their own illness can manifest emotional and behavioural problems adding to carer burden (Kefale et al., 2019). Usual family and community support may become more difficult to access under the weight of these burdens (Casale & Wild, 2013). These factors may contribute to an increased risk for depression in the carers of PHIV, especially in the sub-Saharan context.

In caregivers, the quality of parenting is significantly impacted by caregiver depression (Lachman et al., 2014). Considering an increasing PHIV population, the quality of care available to these youth is inextricably linked to the mental health of their caregivers. The literature suggests that caregivers of PHIV are at increased risk for depression (Casale et al., 2015; Katana et al., 2020; Kikuchi et al., 2017; Lachman et al., 2014; Ofori-Atta et al., 2019; Ogbonna et al., 2019). There appear to be multiple caregiver, child and socioeconomic factors which increase the risk for depression in carers. A review, published in 2013, found a link between social support and caregiver health in the context of HIV-illness in the carer. The review concluded that more research was needed on the subject, especially in a LMIC setting (Casale & Wild, 2013).

There is clearly a call for more research on PHIV and youth living with HIV along with those responsible for their care. It is necessary to clarify the many factors associated with depression in caregivers of PHIV, especially in sub-Saharan Africa, where the HIV burden is one of the highest worldwide. This will better inform outcomes for households impacted by HIV.

Literature Review

The literature search aimed to identify articles published between 2004 and October 2020. A systematic search was conducted, using the following search terms: ‘caregiver’, ‘HIV’, ‘adolescent’, ‘depression’, ‘mental health’, ‘Africa’, ‘South Africa’. The data bases searched were PubMed and PsycInfo and the references of the selected articles from the databases were searched for further relevant studies.

Twenty-two studies were identified, relevant to the search terms. Despite the literature search covering 2004 - 2020, no relevant articles were identified prior to 2012, 17 articles were published between 2012 and 2018 and 6 articles between 2018 and 2020 indicating few recent studies on this highly relevant topic.

Location

Search terms for this study stipulated studies originating in Africa. A review article analysed worldwide studies including Africa (Casale & Wild, 2013). All other articles were based in sub-Saharan Africa. HIV is endemic in this region and it would stand to reason that much of the available research would originate from this area. Four studies compared data from more than 1 sub-Saharan region: 3 studies based in SA and Malawi and 1 study reflecting combined data from SA, Zimbabwe, Uganda and Malawi. Seventeen studies were based in a single sub-Saharan country.

Eleven studies were based in SA – five from Kwazulu Natal (KZN), 1 from the Eastern Cape, 2 from the Western Cape and in 3 studies where the region within SA was not specified. There were 4 studies based in Malawi and Uganda, 2 studies from Rwanda and single studies from Namibia, Kenya, Ethiopia, Ghana and Nigeria.

Time Period

Despite searching the literature from 2004, the time period over which studies were conducted was from 2008 – 2018. Eight studies did not specify the time period over which the study was conducted. A single longitudinal study ran from 2011 – 2014 and a second cross-sectional study utilised data from a larger longitudinal study which had run from 2008 – 2012.

Participants and group description

Twenty-two studies were selected – this number included a single review article. There was a total of 13 355 study participants (where child-caregiver dyads were classified as a single study participant). The study with the least number of participants was 29 and the highest was 2477. The mean number of study participants per study was 635,95.

In the studies selected, the participants in 15 studies were child-caregiver dyads. 6 articles focused mainly on child-outcomes, 8 on caregiver-outcomes and 7 focused on both child and carer outcomes. A single review article compared various studies of HIV-impacted caregivers and children.

Caregiver characteristics

Primary caregiver was defined in different ways but the consensus in articles was that a primary caregiver should be responsible for the care needs of the child and that the child should spend most of the week living in the caregiver's home. A caregiver could be a

biological (parent) or non-biological carer and did not need to be a family member unless specified in inclusion criteria.

Gender: Familiar et al (2016) studied only female HIV-seropositive caregivers of children aged 2-5 years. Casale (2015) also focused on women in the care-giving role (Casale et al., 2015). No further studies focused specifically on gender although articles did comment on the preponderance of female caregivers with little mention of male caregivers.

Age: All studies included caregivers over the age of 18 years and there were no studies which included children under the age of 18 years caring for younger siblings or family members. Elderly caregivers over the age of 60 years were focused on in a single article only (Kalomo et al., 2017).

HIV status: Familiar (2016) studied HIV-seropositive carers only (Familiar et al., 2016). Casale (2015) compared the effects of living with HIV and other illnesses while caring for children (Casale et al., 2015). In papers where the focus was orphaned children, the knowledge of the HIV status of the carer was not required for inclusion into the study (Kuo et al., 2012). In the remaining studies, the HIV status of caregivers was commented on but not required for inclusion into studies.

Biological vs non-biological carers: no study focused specifically on biological and non-biological carers in inclusion criteria.

Caregivers of orphans: three studies described carers of AIDS-orphaned children – Kagoto (2012) broadly included caregivers of AIDS-orphans while Kalomo (2017) specified carers over the age of 60 years who were not biological parents of the AIDS-orphaned child and noted that the HIV status of the child was established as part of inclusion criteria (Kagotho & Ssewamala, 2012; Kalomo et al., 2017). A study in KZN, SA compared the effects on mood

due to caring for children orphaned by AIDS, orphaned for other reasons compared with non-orphaned children – this was in the context of an HIV endemic area (Kuo et al., 2012).

Characteristics of children

Age: The World Health Organisation classifies children as 19 years and younger and adolescents as 10 – 19 years of age (WHO, 2013). The age range of the children studied varied considerably with the youngest children described being 2 years old and no studies describing adolescents older than 18 years. The age range in 12 studies straddled childhood and adolescence while 2 studies described children aged between 2-7.5 years. Only 4 studies could be strictly classified as studies of adolescent subjects.

HIV status: most studies included caregiver-child dyads. In the studies reviewed, 14 cohorts were caregivers of PHIV. Four of these studies included HIV-seronegative child control groups. Three studies focused on caregiver HIV status and the HIV status of the children in the dyad was not specified. A single study included 3 arms, namely HIV-exposed and infected children, HIV-exposed but negative children and HIV unexposed and negative children. A single orphan study, based in an HIV-endemic area, included children whose HIV status was unknown. A second orphan study included arms for AIDS-orphans, those orphaned due to other causes and non-orphaned children where the HIV status of the children was not included.

Orphaned children: two articles studied depressive symptoms in carers of AIDS orphaned children in high HIV prevalence areas in Southern Africa (Kagotho & Ssewamala, 2012; Kalomo et al., 2017). In a South African study, an arm for children orphaned by causes other than AIDS was also added (Kuo et al., 2012) The HIV status of the children was not required for inclusion into these studies.

ART status of children: ten studies included PHIV on ART while 7 studies included PHIV children not on ART or where current treatment with ART was not specified. Katana (2020) focused specifically on the economic and mental health burden of biological and non-biological caregivers of PHIV adolescents aged 12-17 years who were on ART (Katana et al., 2020).

Cognitive screening of children: Sherr (2016) included neurocognitive screening of PHIV subjects but treatment with ART was not commented on (Sherr et al., 2016). Familiar (2020) screened PHIV participants on ART for neurocognitive impairment. (Familiar et al., 2020). Louw (2016) compared mood disturbance in caregivers of PHIV children aged 6-16 years on ART, with and without HIV encephalopathy (HIVE) to an HIV-seronegative control group (Louw et al., 2016)

Study designs

Most studies were cross-sectional in nature with 16 studies based on this design. Louw (2016) described a cross-sectional descriptive analytic design while Ogbonna (2019) noted a cross-sectional and comparative design. Phillips (2013) utilised a quasi-experimental design (Phillips, 2013), Webster (2019) a community-based longitudinal study (Webster et al., 2019) and Ng (2015) a case control design (Ng et al., 2015). There was a single systematic review included (Casale & Wild, 2013).

Control groups

Twenty-two studies were included in the literature review. There was a single review article and in the remaining 21 studies, 11 studies included a control group while 10 studies had no control group.

Measures

Various measurement tools were used to evaluate depressive symptoms in caregivers. The most frequently used validated measures to assess depression was the Centres for Epidemiological Studies Depression Scale (CES-D). Four studies utilised the Hopkins Symptom Check List (HSCL). Two studies made use of the Patient Health Questionnaire (PHQ), a study validated in 2 Kenyan studies and used in a study in Nigeria and a number of South African studies while Kefale (2019) obtained data on depressive symptoms using the WHO Self-reporting Questionnaire (Kefale et al., 2019). Skeen and Sherr (2016) used the Shona Symptom Questionnaire which is a measure designed for use in Zimbabwe (Sherr et al., 2016; Skeen et al., 2014). Studies using non-validated measures utilised a 90-minute survey combining measures adapted from 3 previous studies used in Africa (Kagotho & Ssewamala, 2012) and a 2019 study where responses to 15 questions on depression and anxiety were used to draw conclusions (Webster et al., 2019).

Findings

The burden of caring for PHIV has impacted many households worldwide and carers of these children are hypothesised to be more at risk for depressive illness. Sub-Saharan Africa carries a significant proportion of PHIV (UNAIDS, 2020) and various studies in the region confirm risk for depressive illness in this group of caregivers.

A Nigerian study in 2019 reported severe depression in 48.3% of caregivers of PHIV on ART (Ogbonna et al., 2019). A study in Kenya of adolescents with PHIV found 10.7% of their primary carers screened above the cut-off for depressive symptoms (Katana et al., 2020). In Namibia, Kalomo (2017) found that 83% of caregivers of PHIV older than 60 years scored in the depressive range (Kalomo et al., 2017), while a study of a cohort of Malawian and South African carers of PHIV found psychological morbidity in 28% and suicidal ideation in 12.2% of these caregivers (Skeen et al., 2014). A review of the literature revealed

distinct caregiver characteristics, characteristics in the children and socio-economic factors which contribute to the burden of depression in this group of carers.

Caregiver characteristics

Gender: Women are disproportionally affected by HIV in SA. Of the 7 500 000 adults living with HIV in SA, 4 700 000 (62.67%) are women (UNAIDS, 2018).Care needs for children traditionally fall to women and there were no studies that focused on male caregivers of PHIV. A single study by Kuo in 2012 found that female gender was associated with an almost two-fold increase in depression in orphan caregivers in a rural cohort in KZN, SA (Kuo et al., 2012).

HIV-status: Being HIV-seropositive imparts an increased risk for the development of psychological distress and depression in carers of PHIV. In a Ghanaian study of 446 child-carer dyads caring for PHIV on ART, HIV-seropositive status in the caregiver was significantly associated with caregiver depression. HIV-seropositive carers were also found to have lower HIV knowledge, worse HIV illness perceptions and greater perceived HIV stigma (Ofori-Atta et al., 2019). Skeen (2014) studied a combined South African and Malawian cohort of 979 child-carer dyads and found that 28% of the cohort reported psychological morbidity above the clinical cut-off while 12.2% expressed suicidal ideation. Of interest is that South African subjects reported more psychological distress than Malawian subjects (Skeen et al., 2014). In a further South African cohort, Kuo (2012) noted a significant association between being an AIDS-ill caregiver of AIDS orphans and experiencing more poverty, more depression and less positive parenting experiences than those caregivers who were healthy or experienced other non-HIV related illness (Kuo et al., 2012). A larger study also conducted in KZN, SA of 2199 AIDS-ill caregivers-AIDS-orphan

dyads revealed increased risk of clinical depression in AIDS-ill caregivers and chronically ill caregivers compared with healthy controls (Casale et al., 2015).

Medical co-morbidities other than HIV: In 2015, a South African cohort of caregivers of youth in an HIV-endemic area, found that those at higher risk for depression were carers living with HIV and carers who were chronically ill with other illnesses (Casale et al., 2015). Kalomo (2017) studied elderly carers of PHIV and found that in carers over the age of 60 years, high levels of depression were significantly associated with underlying co-morbid illness in the caregiver (Kalomo et al., 2017).

Relationship to child (biological vs non-biological caregivers): Sherr (2017) contrasted parent and child outcomes in a group of PHIV and found that biological parents were better parents. Better parenting was associated with less problematic behaviour and better self-esteem in children which in turn impacted positively on caregiver mental health (Sherr et al., 2017). A study on the emotional and behavioural problems in PHIV on ART in Ethiopia found higher odds of behavioural and emotional difficulties in PHIV with non-biological caregivers. Those PHIV who had lost both parents fared worse from a behavioural and emotional perspective than those whose parents were still living (Kefale et al., 2019).

Child Characteristics

HIV status of child: A longitudinal study conducted in South Africa and Malawi in HIV-impacted households, found an increased risk of caregiver depression if the caregiver or child in their care was HIV-seropositive (Sherr et al., 2016). Studies based in other sub-Saharan nations, namely Kenya and Nigeria found carers of PHIV reported increased depression in caregivers of PHIV. The Kenyan study found 10.7% of participants were depressed (Katana et al., 2020), while caregivers of HIV-seropositive children in the

Nigerian study were 24 times more likely to report psychosocial disorders than the caregivers of HIV-seronegative children (Ogbonna et al., 2019).

Louw studied a South African cohort of 108 caregivers of PHIV on ART with and without cognitive impairment. Caregiver depression was higher in both groups of children compared with lifetime prevalence rates noted in the general South African population. (Louw et al., 2016).

Interestingly, in a small cohort of carers of AIDS-orphaned children over 60 years, caring for an HIV-seropositive child was not associated with increased depressive symptoms while financial difficulties and co-morbid chronic illness impacted depressive symptomatology significantly (Kalomo et al., 2017).

Treatment status of the child: In the studies reviewed, the treatment status of PHIV did not appear to affect caregiver depression. Phillips studied a small cohort of PHIV children and found that raising an HIV-seropositive child, regardless of whether that child was ART-naïve or ART-treated, had no significant effect on the parental experience and overall parental well-being compared to raising an HIV-seronegative child (Phillips, 2013).

Neurocognitive status of the child: A recent study conducted in various regions in Sub-Saharan Africa (SA, Uganda, Zimbabwe and Malawi) concluded that increased caregiver depression is not associated with cognitive impairment in PHIV but those carers who were depressed reported more executive dysfunction in their children. This would raise concern for the impact of carer depression on behavioural outcomes in this vulnerable group of children (Familiar et al., 2020). Louw (2016) studied emotional and behavioural problems in PHIV on ART and reported higher rates of caregiver depression in those caring for children with and without HIV-associated encephalopathy (HIVE) compared with a control group of caregivers

of HC. More adverse emotional and behavioural outcomes in children appear to be associated with HIV-seropositivity in the child and depression in the caregiver (Louw et al., 2016).

Behavioural and emotional difficulties: Numerous studies have noted the association between depressed caregivers and behavioural difficulties in PHIV. Kikuchi (2017) sought to examine the interconnectedness of the mental health of caregivers and those they care for. This was done in the context of PHIV on ART and it was found that caregiver depressive symptoms were positively associated with depressive symptoms in the children. The study concluded that caring for the mental health of caregivers would ultimately impact positively on the child and disrupt a negative feedback cycle of mutual depression (Kikuchi et al., 2017).

In the Eastern Cape region of South Africa, Lentoor (2016) studied the psychological function of caregivers who cared for PHIV and found a significant association between caregiver depression and child emotional difficulties (Lentoor et al., 2016).

In KZN region of South Africa, Bhana (2016) noted lower total child difficulties scores with lower caregiver depression. (Bhana et al., 2016). Lachman (2014) studied a different KZN cohort and found that having an AIDS-ill caregiver or AIDS-orphaned children in the home impacted positive parenting practices and was significantly associated with higher levels of carer depression, poverty and child behaviour issues than HIV-unimpacted homes (Lachman et al., 2014).

In Ethiopia, Kefale (2019) found a significant association between PHIV caregiver's mental distress and externalising behaviour in the youth in their care. This was amplified if the caregiver was not a biological parent of the PHIV and if both the parents of the child were deceased (Kefale et al., 2019).

In a study with Malawian and South African participants, HIV burden in the household influenced child problem behaviour due to a positive association with caregiver depression. It was observed that depressed parents may have used harsher physical punishments with children in their care in the context of their own mental illness and disease challenges along with other stressors related to HIV in the home (Sherr et al., 2016). A Rwandan study of protective factors for suicidal ideation and behaviour in PHIV and HIV-impacted children, found an increase in suicidal ideation in PHIV whose caregivers reported mental health issues (Ng et al., 2015).

In an Eastern Cape cohort of caregivers of PHIV on ART, caregiver depression was found to be a stronger predictor of emotional and behavioural problems than HIV-seropositivity in the children while there was a significant association between caregiver depression and child emotional difficulties (Lentoor et al., 2016). Louw (2016) studied a Cape Town cohort of PHIV on ART and their carers and found that the risk for suicidal ideation and behaviour in children was higher with certain parenting factors, depression in the child and depression in the caregiver (Louw et al., 2016). Webster (2020) studied dyads of PHIV school-going children and their carers by using an informal measure to assess symptoms of depression and anxiety in the carers. Findings noted reduced child well-being associated with caregiver depression and anxiety in the context of low social support (Webster et al., 2019).

Orphan hood: HIV/AIDS has created the devastating phenomenon of orphanhood which has impacted individual carers and children as well nuclear and extended families as relatives are called on to bear the responsibility of caring for orphaned children. A study conducted in Ethiopia on 423 carer-PHIV dyads found that HIV-impacted youth who have lost both parents have increased odds of behavioural and emotional problems compared with those who still have living parents. (Kefale et al., 2019).

In a high HIV-endemic area in KZN, SA, 30.3% of carers of orphans met criteria for depression with a higher prevalence of depression in those caring for orphans than non-orphans. There was no difference in the prevalence of depression in those caring for children orphaned by HIV and those orphaned in other circumstances (Kuo et al., 2012)

Socio-economic factors

Lack of social and economic support is a significant driver of depression in PHIV caregivers. The combined burden of HIV illness in the household and poverty appear to contribute to increased levels of depression in those caring for PHIV.

In a study conducted in rural Uganda, the authors found that in the face of HIV-seropositivity, reduced economic and social support factors predicted mental health difficulties in carers (Familiar et al., 2016). A second Ugandan study of caregivers of AIDS-orphans, found that better cash savings and better support systems correlated with lower depression scores in carers. (Kagotho & Ssewamala, 2012).

A study based in an HIV endemic area of SA also noted associations between increased caregiver depression and low income, lack of access to running water and hunger in households caring for AIDS-orphans (Kuo et al., 2012). Lentoor (2016) studied a cohort of carers of PHIV on ART in the Eastern Cape, SA and concluded that there was significant association between greater depression and lower perceived resources (Lentoor et al., 2016). In KZN, Lachman found positive parenting in carers of both PHIV and AIDS-orphans was reduced in the face of higher poverty, higher depression and less social support. (Lachman et al., 2014).

Skeen compared a South African and Malawian cohort of PHIV carers and concluded that perceived lack of support from the community, living with a sick family member and household unemployment all contributed to psychological morbidity and suicidal ideation in

the carers. Of interest is that those in the South African cohort experienced more psychological morbidity and suicidal ideation than individuals in the Malawian cohort (Skeen et al., 2014).

Kalomo's study (2017) of elderly Namibian carers of PHIV found a significant association between depressive illness and financial strain. Those carers who had knowledge of government assistance grants reported less depression (Kalomo et al., 2017). Kuo (2012) also commented on an association between the presence of childhood and household support grants and less depression in caregivers of AIDS-orphans (Kuo et al., 2012).

In a study of South African female carers of PHIV in 2013, it was concluded that protective resources, such as social support, may be insufficient to protect women against the effects of HIV when living in adverse social circumstances. The authors felt that the impact of HIV-related stressors on mental health may be too large to absorb the impact of these stressors (Casale & Wild, 2013).

A review article by the same author published in 2012 confirmed the importance of social support in the context of caring for PHIV and the lack of empirical research in LMIC at that time. It was observed that direct, indirect and total costs of caregiving for PHIV were higher among caregivers with a positive screen for depressive symptoms compared to those without depressive symptoms (Casale & Wild, 2012).

Aims

Specific Aim 1

To assess the prevalence of depressive symptoms in caregivers of children and adolescents with perinatally-acquired HIV (PHIV) and compare this to the prevalence of depression in a group of caregivers caring for a matched HIV-seronegative control group of children and adolescents (HC) in a Cape Town cohort.

Specific Aim 2

In primary caregivers of PHIV, we will compare the prevalence of depressive symptoms in biological parents of PHIV versus non-biological caregivers of PHIV.

Specific Aim 3

To explore the caregiver, child, and socio-demographic factors associated with depression in individuals caring for PHIV and HC.

Objectives

1: To establish the prevalence of depression in caregivers of PHIV compared with caregivers of HC.

(a) A cohort of primary caregivers-PHIV dyads will be selected from Infectious Disease Services at Community Health Centres in the Cape Town area.
(b) A control cohort of primary caregivers and HC youth dyads will be selected from the community surrounding the specified Community Health Centres.
(c) The Centres for Epidemiological Studies Depression Scale (CES-D Scale) will be administered to both groups.

2: To ascertain whether the prevalence of depression is different between biological carers of PHIV children compared with those who are non-biological carers of PHIV.

(a) The caregiver-PHIV dyad group will be divided into biological and non-biological carers and the CES-D scores of parents (presumed HIV-infected) will be compared with the scores of other non-biological carers.

3: To identify specific lifestyle factors that are more affected in the households of PHIV dyads compared with caregivers of HC dyads. Caregivers in the cohort will complete measures to assess lifestyle factors and quality of life – a Sociodemographic Questionnaire, Parenting Stress Index, Family Resources Scale, Family Support Scale, WHO Quality of Life Scale, Asset Index, Child Neuropsychological Battery and Child Behaviour Check List.

Overall description of Project and Methodology

Study Design

This study is cross-sectional study. The current study will be housed within a larger research study conducted at Groote Schuur Hospital from 2010-2014 under the University of Cape Town (UCT) The larger study is focused on the neuropsychiatric, neuroimaging and neuropsychological characteristics of PHIV and the Principal Investigator is Prof J. Hoare. 'White matter micro-structural changes in ART-naive and ART-treated children and adolescents infected with HIV in South Africa' (A. J. Hoare et al., 2015)

A number of papers have been published based on the parent study (Jacqueline Hoare, 2015; J. Hoare, J. P. Fouche, N. Phillips, J. A. Joska, K. A. Donald, et al., 2015; J. Hoare, J. P. Fouche, N. Phillips, J. A. Joska, R. Paul, et al., 2015; J. Hoare et al., 2016; Louw et al., 2016; N. J. Phillips, 2013) However an investigation of caregiver depression and associated factors has not yet been done.

Study Setting

Once candidates had been recruited form community clinics associated with University of Cape Town, assessments were planned for the Psychiatry outpatient Department (J2) at Groote Schuur Hospital, Cape Town, South Africa

Study Participants and Sampling

Caregiver-adolescent dyads were recruited from Infectious Diseases Community Health Centres at Khayelitsha Site C (Nolungile) and Kuyasa Clinics, Woodstock Community Health Centre and Mitchells Plain Community Health Centre along with a cohort from the Paediatric Neurology service at the Red Cross Children's Hospital in Cape Town, Western Cape.

The study coordinator selected 2-3 eligible subjects from each of these sites per day. The selected adolescent/children and their parent/caregiver were then invited to participate in the study. When a subject declined, the next subject on the list was invited. The folders of subjects who fulfilled criteria were then reviewed and a screening interview was done.

Controls

30 control dyads were selected from schools and community health centres in the areas surrounding the community health centres where the HIV-affected cohort were drawn. This was to allow for the matching of gender, race, sex and ancestry of caregivers and children in the HIV-unaffected cohort. This group was drawn from schools and community health centres in the same areas to control for education quality and socio-economic status.

Inclusion Criteria

a. Carer-child dyads: Primary caregivers with a child between the ages of 6 and 16 years were included

b. Caregivers of children who have a positive HIV diagnosis established with initial and confirmatory tests.

c. Both caregivers of children who have not previously used anti-retroviral medications (ART naive) AND those who are currently taking anti-retroviral treatment (ART)

d. Caregivers of children who attend an out-patient clinic.

Exclusion Criteria

a: Caregivers who refused to sign informed consent for themselves or their child

b: Caregivers of children with the following medical conditions:

Uncontrolled medical condition - such as poorly controlled diabetes mellitus, epilepsy, active tuberculosis requiring admission in the child.

Identified central nervous system neurological condition (other than HIV) - such as CNS infections e.g. TB Meningitis, Cryptococcal Meningitis, documented cerebrovascular accident and lymphoma in the child

c: Caregivers of children in whom there is a strong positive history of drug or alcohol exposure in pregnancy

d: Caregivers of children where there is a history in the child of a head injury with a duration of loss of consciousness of >30 minutes, AND/OR requiring overnight admission to hospital

e: Caregivers of children with a history of perinatal complications such as prematurity, hypoxic ischemic encephalopathy or neonatal jaundice requiring exchange transfusion.

f: Caregivers of children where there is a contra-indication to MRI scanning - such as metal or claustrophobia.

Instruments and Measures

Various instruments and measures will be utilised during the study. Specific measures are required to assess the caregiver, the child and the socioeconomic circumstances of the caregiver-child dyad. All scales are translated into Xhosa - the translation process included forward and back-translation (authentication) where the translated test instructions were translated into English again. This was to ensure that there were no discrepancies between the original and translated instructions and that the instructions remain culturally suitable in the Xhosa translation. The scales are administered in the home language of the subject or the language of their choice. The participating caregivers will be assisted by trained research assistants fluent in Xhosa and English.

Centre for Epidemiologic Studies – Depression Scale (CES-D)

The CES-D is a 20-item scale devised for use within community populations (Knight, Williams, McGee, & Olaman, 1997) and will be used to measure depressive symptoms in caregivers in the 2 weeks preceeding the interview. It is a combination of the Beck Depression Inventor*y* (Beck, 1996*)*, the Zung Self-Rating Depression Scale (Zung, 1965), the Raskin Scale (Gardener, 1968) and the Minnesota Multiphasic Personality Inventory Depression Scale (Hathaway, 1942). 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. That study reported a sensitivity of 91% using a cut-off score of 16. This measure has been used in the past in HIV-affected populations in South Africa (Bryant et al., 2015; Joska et al., 2010; Nöthling, Martin, Laughton, Cotton, & Seedat, 2013) and has been validated in English, Afrikaans and Xhosa in the region. (Baron, Davies, & Lund, 2017). See Appendix A.

Parenting Stress Index (PSI)

The PSI is a 120-item scale which assesses parental stress as it pertains to prominent functional characteristics and/or difficulties in the child. 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 scale incorporates Child and Parent domains with specific subscales in each domain. A score is then calculated for each domain and combined to give the Overall Total Stress Score. An additional Life Stress Score measures the caregivers perceived stress outside of the parent-child relationship.

WHO Quality of Life Scale (WHO QoL 100)

The WHO QoL 100 assessment scale is a measure of life satisfaction of adults/parents. It is a 26-item instrument and was devised through the collaboration of contributors from 15 varied cultural backgrounds and provides an assessment of subjectively experienced quality of life rather than assessment of objective items. The brief version to be utilised in this study has psychometric properties comparable to the full version and is considered a sound, cross-culturally reliable and valid instrument for the measurement of quality of life (Gururaj, 2008)

Child Behaviour Checklist (CBCL)

The CBCL is a measure or a child's competencies and problem behaviours. It is administered to children 6-18 years and requires a parent to rate their child's competence in domains of firstly, general functioning and secondly, emotional and behavioural problems. Administration of the measure provides a Total Competence score and a Total Problem score which is then further classified into an (1) Internalising Scale (depression/withdrawal. Anxiety and somatic behaviours, an (2) Externalising Scale (cruel, aggressive and delinquent

behaviours) and a (3) Total Problems Scale (other problem behaviours such a immaturity or hyperactivity). (Achenbach, 2001)

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 and the measure has been translated into more than 70 languages, and is used globally (Albores-Gallo, 2007). This measure has been used in an HIV and South African context in past studies (A. J. Hoare et al., 2015; Louw et al., 2016)

Neuropsychological Battery

A standard battery of neuropsychiatric tests was administered to each participant. The battery aims to evaluate the general intellectual functioning of the child as well as assess specific cognitive domains. These are standardised tests, commonly used in research and clinical setting to assess neuropsychological parameters within paediatric populations in South Africa. The distribution of each of these tests is strictly controlled by various psychometric service providers which ensures reliability and validity (Jacqueline Hoare et al., 2012; J. N. Phillips et al., 2019).

The list of tests included is

- Lang Hand questionnaire
- CAT-Rapid
- TEA-Ch (version B)
- Digit Span
- Colour Trails
- BNT Coding
- RCF
- RCF – 3 minute recall

- Nepsy Inhibition – Shapes: naming, inhibition, switching
- Nepsy Inhibition – Arrows: naming, inhibition, switching
- WISC Symbol Search
- HVLT – 1, 2, 3
- RCF – 30 min delayed
- HVLT – 5 minute delayed, recognition
- WASI
- VFLU – phonemic, category
- IHDS
- Finger tapping test – dominant, non-dominant

  Grooved Pegboard – dominant, non-dominant

Socio-demographic Questionnaire

The socio-demographic questionnaire assesses general demographic questions related to caregiver, child and socioeconomic indices within the household. It was devised for the greater study. See Appendix B.

Family Resources Scale (FRS)

The FRS is a 30-item scale (Dunst, 1986) used to measure the adequacy of tangible resources in a home with young children. The scale reviews specific resources required by a household to meet the needs of the family as a whole. This measure will be used to assess the family's access to particular resources eg. healthcare for the family, money to pay monthly bills. The instrument shows good internal consistency (Cronbach's $\alpha = 0.92$) and test-retest

reliability (r = 0.52) (Spratt, Saylor, & Macias, 2007). This has been used in the South African setting in the Western Cape in past studies. (N. J. Phillips, 2013) See Appendix C.

Family Support Scale (FSS)

The FSS (Dunst, 1986) measures the perceived level of social and family support to which caregivers have access. Participants report the amount of support from various sources to which they have access. This study utilises information generated on available social support. The scale developers report that the instrument shows good internal consistency (Cronbach's α = 0.77). Test-retest reliability ranges from .35-.76 for the various subscales, and is .80 for the total score (Hanley, Tassé, Aman, & Pace, 1998) The FSS has been used in South African settings in the past studies (N. J. Phillips, 2013) See Appendix D.

Asset Index

The Asset Index is a questionnaire used to measure socio-economic status. A score is calculated which can then be used as a measure for poverty. The current study will use the Asset Index devised by Myer et al (J. N. Phillips et al., 2019)

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Depression amongst caregivers of children and adolescents with perinatally-acquired HIV in Cape Town, South Africa

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The authors declare that they have no conflict of interest

Data Availability Statement

Data sharing and availability is not applicable to this article as no new data were created or analysed in this study.

Geolocation Information

This project was conducted in Cape Town, South Africa. All participants who participated in the study are South African citizens.

Depression amongst caregivers of children and adolescents with perinatally-acquired HIV in Cape Town, South Africa

Abstract

Depression is a common mental health disorder, adding significantly to the global disease burden. Studies have shown that caregivers of children and adolescents with perinatally acquired HIV (PHIV) are at increased risk for developing depression. Few studies have differentiated between depression in biological versus caregivers of non-biological PHIV. This cross-sectional study aimed to assess the prevalence of depression in caregivers of PHIV compared with matched caregivers of HIV-seronegative controls (HC) as depression prevalence in biological and non-biological caregivers of PHIV. The dyads were drawn from an urban community population in Cape Town. Factors associated with depression were assessed using various caregiver, child and socio-economic measures. Independent t-test sampling was run on PHIV and HC dyads with identical sampling performed on the biological and non-biological PHIV dyads. Bivariate correlations were conducted to identify factors associated with caregiver depression and quality of life. There was no significant difference between depression in PHIV caregivers (biological or non-biological) and HC caregivers. Internalising and externalising child behaviours, poor resources and limited social support were strongly associated with depression in both caregiver groups while parental stress in HC caregivers was associated with depression. Factors other than the child HIV status are driving depression in caregivers.

Keywords: caregiver, depression, HIV, biological/non-biological, mental health

Introduction

Depression adds significantly to the global burden of disease and is ranked as the single largest contributor to global disability (WHO, 2017). HIV-seropositive individuals are at higher risk for the development of depression with 11.1% of people living with HIV in South Africa (SA) fulfilling criteria for a major depressive episode (Freeman, Nkomo, Kafaar, & Kelly, 2008). Maternal depression in the context of caregiving has also been linked to adverse outcomes in children (Turner & Honikman, 2016).

In addition to neurodevelopmental and cognitive impairment (Hoare et al., 2015), caring for PHIV can translate into caring for sick or disabled children who may have lost one or both parents to HIV (Kuo & Operario, 2009) with exacerbation of poverty in HIV-impacted households, especially in low-to-middle income countries (LMIC) (Katana et al., 2020).

PHIV caregivers navigate their own HIV-illness compounded by medical co-morbidities other than HIV (Kalomo, Lee, & Besthorn, 2017). The elderly take on the care of orphaned children placing strain on already limited family resources, especially in the context of the current endemic poverty in SA (Kagotho & Ssewamala, 2012). These factors can increase the risk for depression in the PHIV caregivers, especially in the sub-Saharan context. Caregiver depression has been shown to significantly impact the quality of parenting, reinforcing a damaging cycle (Lachman, Cluver, Boyes, Kuo, & Casale, 2014).

Few studies have investigated depression in non-biological carers (non-parent) compared with biological (parent) carers and the impact of PHIV emotional and behavioural problems and neurocognitive impairment on caregiver depression. There is a need for more research on PHIV and their caregivers. Clarity around the many factors associated with

depression in caregivers of PHIV, will better inform interventions to improve outcomes for families affected by HIV.

Methods

Study setting and design

This cross-sectional study is nested within a larger study investigating the neuropsychiatric, neuroimaging and neuropsychological complications of PHIV (Hoare et al., 2015). The current study focuses on the mental health of caregivers of PHIV compared with caregivers of HC.

This study was conducted at the Department of Psychiatry and Mental Health at the University of Cape Town at Groote Schuur Hospital, Cape Town, South Africa.

Study Participants

Caregiver-adolescent dyads were recruited from four Infectious Diseases Community Health Centres in Cape Town and the Paediatric HIV services at the Red Cross Children's Hospital in Cape Town, Western Cape. All caregivers who were not biological parents of the PHIV were denoted as non-biological (even if biologically related in other ways e.g., biological grandmother).

Convenience and snowball sampling methods were used to recruit 86 caregiver-PHIV dyads and 30 caregiver-HC dyads who were selected from schools and community health centres in the areas surrounding the community health centres where the PHIV cohort was drawn. The cohorts were matched for race, sex, ethnicity, and socio-economic status.

Inclusion Criteria

Eligible caregivers were primary caregivers of PHIV between the ages of 6 and 16 years, attending an infectious diseases clinic. PHIV in the dyad were included irrespective of their

use or non-use of ART. PHIV status was confirmed via hospital records or confirmatory HIV testing. Children with uncontrolled medical conditions, previous head injuries, known significant perinatal complications and identified central nervous system neurological conditions other than HIV, such as CNS infection, cerebrovascular accident and CNS malignancy were excluded from the study along with caregivers of children in whom there was a strong positive history of substance use during pregnancy. There were no specific exclusion criteria applied to the caregivers of the children, except that they were required to be the primary caregiver of the child enrolled into the study.

Procedures

Informed consent for participation was obtained from the caregiver and assent from the child. Consent forms were given in English and isiXhosa and consent was obtained by trained research assistants fluent in both English and isiXhosa. The study was conducted at a separate site from the site of routine care to ensure confidentiality. Data was collected and stored using participant codes and saved on a password protected database with strict confidentiality protection.

Measures

Centres for Epidemiological Studies - Depression scale (CES-D) is a 20-item scale devised for use within community populations (Knight, Williams, McGee, & Olaman, 1997; Radloff, 2000) The WHO Quality of Life Scale (WHO QoL) is a measure of life satisfaction utilising subjectively experienced items as reported by the adult caregiver in the dyad.

The Parenting Stress Index (PSI) is a self-reported scale with domains assessing parental distress, parent-child dysfunctional interaction and behaviours of the child impacting parenting behaviours and child outcomes. The sub-scales are combined to report a total parental stress score (Abidin, 1995; Potterton, Stewart, & Cooper, 2007). The FRS is a 30-item

scale used to measure the adequacy of tangible resources in a home with young children (Dunst, 1986; Spratt, Saylor, & Macias, 2007) while the FSS measures the perceived level of social and family support to which caregivers have access (Hanley, Tassé, Aman, & Pace, 1998)

The Child Behaviour Checklist (CBCL) measured child competencies and problem behaviours – scores are calculated for internalising child behaviour problems, externalising child behaviour problems and total child behaviour problems (Achenbach, 2001; Albores-Gallo, 2007; Rescorla, 2005)

Data Analysis

Data was directly collected into a study generated Case Report Form which included forms to capture demographic, clinical and serological data, as well as data from instruments administered. Data was analysed using the SPSS 26 statistical software package. Descriptive statistics were conducted to describe both the sample and the data (means, standard deviation, normality and other categorical classifications) with regards to caregiver depression and child behavioural and cognitive impairment.

An independent samples t-test was performed to compare the prevalence of depression in caregivers of PHIV and caregivers of HC. This analysis was then repeated comparing depressive symptoms in biological PHIV caregivers and non-biological PHIV caregivers.

Bivariate correlations were conducted to identify factors associated with caregiver depression and quality of life. The data was normally distributed, and a parametric correlation was performed with the Pearson co-efficient reported for all groups, namely, biological caregivers of PHIV, non-biological caregivers of PHIV and caregivers of HC.

Results

The final study sample included 86 caregivers of PHIV and 34 caregivers of HC. The groups were well matched for age, sex, race and socioeconomic status of the children. PHIV caregivers were receiving significantly more support in the form of disability grants than caregivers of HC *(p = 0.027)*.

HIV disease variables in the PHIV group were obtained in line with their routine care. The range of CD4 cell counts in PHIV was 0 – 1938 *(M = 853.36; SD: 437.41)* – ART-naïve subjects were included in the study and a single subject recorded a CD4 count of 0 and mean viral load = 22284.49 (see visual representation). Twenty-three children were ART-naïve; 33 children were on first line ART treatment ZDV, 3TC and NVP, 9 children were on second line treatment ZDV, 3TC, NVP and ABAC while 1 child was on the third line regimen D4T, 3TC, NVP and NLF.[1]

There was no significant difference between quality of life, parental stress and child behaviour outcomes measured in either PHIV (biological and non-biological) or HC caregivers.

The mean score for depression according to the CESD scale in the PHIV caregivers *(M = 13.3)* and caregivers of HC *(M = 13.65)* fell below the threshold of 16, which is indicative of high risk for clinical depression (Table 2). Table 3 compares depression between biological and non-biological PHIV caregivers. A mean score of 16.07 *(SD = 12.27)* was reported for biological PHIV caregivers placing them in the depressed range while non-biological PHIV caregivers remained below the cut-off for depression with a mean score of 13.35 *(SD = 10.61)*. This, however, did not approach significance in any of the groups.

[1]Zidovudine (ZDV); Lamivudine (3TC); Nevirapine (NVP); Abacavir (ABAC); Stavudine (D4T); Nelfinavir (NLF)

There are no statistically significant differences between the groups on QoL total scores - biological caregivers of PHIV had a mean score of *63.49,* while non-biological PHIV caregivers had a mean score of *56.88* and caregivers of HC *54.68* on WHO QoL.

Both parental groups, whether biological or non-biological, reported high stress levels in both the parent and total life stress domains on the PSI. Caregivers of HC scored slightly higher than caregivers of PHIV in all PSI domains, not reaching statistical significance *(p = .257).*

No correlations were found between caregiver variables (age, marital status, ethnicity and parental stress) and depression in PHIV caregivers. The age of biological caregivers of HC was inversely correlated with quality of life *(R = 0,09; p = 0.034)*, indicating that, in the general population, being older was associated with a lower quality of life. In caregivers of HC, correlations between depression and parental stress in the child domain *(R = 0.44; p = 0.010)*, parent domain *(R = 0.48; p = 0.004)* and total stress domain *(R = 0.52; p =0.002*) on the PSI, reached statistical significance.

The CBCL was used to assess child competency and problem behaviours. Mean scores for competency behaviours in PHIV was *M = 36.56* and in HC was *M = 40.48* while problem behaviours reflected *M = 57.52* in PHIV and *M = 56.92* in HC. In both caregivers of PHIV and caregivers of HC, there was a significant positive association between depression in carers and internalising child behaviour problems *(PHIV: R = 0.35; p = 0.001; HC: R = 0.57; p = 0.000)*, externalising child behaviour problems *(PHIV: R = 0.35; p = 0.001; HC: R = 0.44; p = 0.009)* and total child behaviour problems *(PHIV: R = 0.39; p = 0.000 ; HC: R = 0.54; p = 0.001)* as measured by the CBCL.

Caregiver depression was associated with fewer family resources *(PHIV: R = 0.23; p = 0.029; HC:R = 0.65; p = 0.006)* and less perceived family support *(PHIV:R = 0.27; p =*

0.011; HC: R = 0.43; p = 0.010) in both PHIV caregivers and caregivers of HC. Of interest was a significant positive correlation between depression and quality of life in both groups *(PHIV: R = 0.21; p = 0.047; HC:R = 0.42; p = 0.013*).

Discussion

The study anticipated that PHIV caregivers would experience more depression than those caring for HIV-seronegative children and that biological caregivers would be more depressed that non-biological caregivers. Although the mean scores for depression were slightly higher in PHIV caregivers than HC caregivers, this didn't reach statistical significance. Parental stress levels were high in both groups, suggesting that factors other than the child HIV status contribute to stress in all caregivers of children included in this study. Child behavioural problems , namely internalising and externalising behaviours, were associated with increased depressive symptomatology in all caregivers, irrespective of child HIV status. In both PHIV and HC caregivers, fewer family resources and less perceived social support appeared to be an important aspect in caregiver depression. HC caregivers also found the stress of parenting in their environment an additional factor associated with higher levels of depression. An unanticipated positive correlation was found between caregiver depression and higher quality of life in both PHIV and HC carers - it is unclear what is driving this outcome. These findings suggest that raising a child in an urban, low socioeconomic environment with fewer resources and reduced social support may be associated with caregiver stress and depression (Jörns-Presentati et al., 2021).

The current study included participants from low socioeconomic environments in Cape Town. Despite the high prevalence of HIV within this community, PHIV caregivers in this study were not more likely to become depressed than their HC caregivers. A Namibian supports this finding; however, caregivers were over 60 years old where additional factors

such as poverty and caregiver co-morbid chronic illness appeared to contribute to higher levels of depression in addition to HIV burden in the home (Kalomo et al., 2017). Our study confirms the findings of Louw's study (2016) where no significant difference in depression between PHIV caregivers and carers of HC caregivers was found(Louw, Ipser, Phillips, & Hoare, 2016).

Other studies have highlighted high levels of depression in PHIV caregivers in various sub-Saharan cohorts in Nigeria (Ogbonna, Emodi, Ikefuna, & Ojinnaka, 2019), Kenya (Katana et al., 2020), Namibia (Kalomo et al., 2017) Malawi and SA (Skeen, Tomlinson, Macedo, Croome, & Sherr, 2014). Studies from Kenya and Namibia didn't include a control arm. The Nigerian study found higher levels of psychosocial disorders in those caring for PHIV compared with caregivers of HC but used a different measure to assess depression than the CES-D (Ogbonna et al., 2019).

Our study draw attention to high stress levels present in both PHIV and HC caregivers in this South African cohort. Skeen (2014) confirmed that parenting PHIV in SA is more distressing than parenting PHIV in Malawi despite HIV prevalence in both (Skeen et al., 2014). Phillips (2013) also reported that caring for PHIV children, whether on ART or ART-naïve did not significantly impact parental well-being compared with HC caregivers (Phillips, 2013). SA appears to have factors inherent in its societal make-up that make it a more stressful place to parent compared with other sub-Saharan countries, despite similar HIV prevalence.

A finding from our study, strongly supported by the literature, is the link between symptoms of depression in all caregivers and the behavioural expressions of the children in their care, irrespective of child HIV status. We hypothesised a perpetuating cycle between caregiver stress, exacerbation of caregiver depression and adverse child behaviours. Louw

(2016) came to similar conclusions in SA (Louw et al., 2016) while studies from Rwanda (Kikuchi et al., 2017) (Ng, Kanyanganzi, Munyanah, Mushashi, & Betancourt, 2014), Ethiopia (Kefale, Boka, Mengstu, Belayneh, & Zeleke, 2019), Uganda (Webster et al., 2019) and Malawi (Sherr, Skeen, Hensels, Tomlinson, & Macedo, 2016) reported similar findings. Aside from Louw's (2016) study, the aforementioned studies lacked control groups and the findings pertained to PHIV caregivers-child dyads only. Kefale's study (2019) found fewer emotional and behavioural problems in children of biological caregivers whereas our study found equal association between biological and non-biological PHIV carers and adverse child behaviour (Kefale et al., 2019). Studies on cohorts in SA, Zimbabwe, Uganda and Malawi confirmed the potential impact of PHIV caregiver and HC caregiver depression on child behavioural outcomes (Familiar et al., 2020). This link has been noted in a national (Sherr et al., 2016) and regional context in the Western Cape (Louw et al., 2016), KZN (Bhana et al., 2016) and Eastern Cape (Lentoor, Asante, Govender, & Petersen, 2016) in SA. Depressed parents and distressed children reinforce one another's behaviour and there is a call to actively address parental depression to alleviate child emotional difficulties and optimise family functioning.

A concern raised in the literature is more depression reported in PHIV caregivers living with HIV themselves (Ofori-Atta et al., 2019). Our study was unable to comment on this as the larger study focused on child outcomes and caregiver HIV status wasn't an inclusion criterion. Our analysis, also consistently supported by South African and Sub-Saharan literature, is increased depression in PHIV caregivers with limited family resources and social support. Ugandan (Familiar et al., 2016); (Kagotho & Ssewamala, 2012), Namibian (Kalomo et al., 2017) and Malawian cohorts confirm these findings as do regional studies in SA namely the Eastern Cape (Lentoor et al., 2016), KZN (Lachman, Cluver, Boyes, Kuo, & Casale, 2014) and Western Cape (Louw et al., 2016). The combined study in

Malawi and SA contrasting the 2 cohorts, confirmed this finding and noted more significant depressive symptomatology in participants from SA. Our study concluded that this is also relevant to HC caregivers reflects the experience of all caregivers in our cohort. Parenting children in a low socio-economic environment in SA puts parents at risk for depression.

The positive association between depression and quality of life in both PHIV and HC caregivers allows pause for thought. Measures such as the WHO QoL are heavily reliant on the subjective experience, possibly influenced by cultural and regional perspectives of the concept of quality of life. Chronic poverty may allow for a normalisation of quality of life below what is considered internationally acceptable.

Our study found that PHIV caregivers received significantly more financial assistance such as social grants. Further associations confirmed lower social support linked to increased depression. Access to, and the understanding of pathways of government assistance has been shown to reduce depression in elderly PHIV caregivers (Kalomo et al., 2017). Our analysis also found poorer quality of life in elderly HC caregivers, which is concerning.

Limitations and Opportunities for further study

The larger study within which this study was nested focused on child characteristics and outcomes and important data such as the HIV status of the caregivers was not collected. Although it can be implied that biological parents of PHIV would be HIV-seropositive, there is the possibility that a portion of caregivers of HC may also have been HIV-seropositive but avoided vertical transmission to their children. The interplay between resources, support, quality of life and depression appear to be unclear and are beyond the scope of this study. Future studies utilising data appropriate for multivariate and regression analysis of these variables would be useful to clarify what appears to be a more complex relationship than initially anticipated between the aforementioned variables in the South African context.

Qualitative research in SA examining the cultural experience, perception and perspective of constructs reflected in the WHO QoL and international measures such as the Global Multidimensional Poverty Index and their relationship to depression could shed light on depression in all tiers of South African society.

Sample limitations included a small sample size and results based on secondary data analysis collected for a larger study where recruitment matched child and not caregiver/family criteria.

Literature on the limitations of self-report measures is extensive and could inform the methods of data collection in future studies (Kimberlin & Winterstein, 2008).

Recommendations

The effect of HIV illness on levels of depression in PHIV caregivers and HC caregivers could be explored as an additional caregiver factor influencing depression in both cohorts. Co-morbid illness other than HIV in caregivers wasn't recorded and may affect associations with depression, as suggested in the literature. This would have been valuable to comment on in elderly caregivers as elderly caregiving of children in South Africa is common (Ntuli & Madiba, 2021). Further research comparing factors driving depression in older and younger PHIV caregivers is needed. There would be value in exploring the impact of social grants on mental health outcomes in PHIV and HC carers as PHIV could have access to more formal financial and social assistance in a SA, putting HC caregivers at risk for adverse mental health

outcomes.

The literature on caregiver depression in this unique cohort highlights differences based on countries and exploring the origins of these differences could be the focus of further study.

Research into programmes to provide combined screening for childhood distress and caregiver mental health difficulties would add value to both groups by improving the function of families and the greater community.

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Conflict of Interest

The authors deny any conflict of interest

Tables

Table 1

Sample Characteristics

Variables	Group		
	Caregivers of PHIV (N = 86)	Caregivers of Healthy Controls (N = 34)	p
Caregiver Variables			
Caregiver Age			
Mean (SD)	42.34(10.153)	41.24(8.367)	0,580
Range	22-65	24 - 62	
Caregiver gender (Male/Female)	4/82	0/34	0,204
Caregiver Race (Black African/Coloured/White)	70/8/1	30/4	0,903
Relationship to child (Biological/ Non-biological)	29/27	16/7	0,786
Employment status (Unemployed/ Employed)	50/28	23/11	0,720
On Disability Grant (Yes/No)	57/18	31/2	0,027
Size of house[a]			
Mean (SD)	2.96 (1.81)	3 (1.95)	0,919
Range	1-12	1-12	
Number of occupants			
Mean (SD)	6.08 (3.86)	6.74 (4.43)	0,432
Range	2-25	4-25	
Variable for overcrowding[b]			
Mean (SD)	2.54 (1.62)	2.619 (1.49)	0,810
Range	0.6-8	1-8	
Child Variables of the Caregiver			
Child age			
Mean (SD)	10.12 (2.43)	10.08 (2.17)	0,928
Range	6-16.6	6.1 – 17.2	
Child Gender (Male/Female)	47/39	18/16	0,867
Child Race (Black African/Coloured)	79/5	32/2	0,988
Highest Grade passed			
Mean (SD)	2.92 (1.88)	2.97 (1.85)	0,886
Range	0-9	0 - 8	
CD4 count		-	

Mean	853.36	-
(SD)	(437.41)	
Range	0 - 1938	-
Viral Load		-
Mean	22284.49	-
(SD)	(124551.56)	
Range	0-904105	-
ARV regimen		
Naïve / First / Second / Third[c]	23 / 33 / 9 / 1	-

NOTES: a: number of rooms in the house. b: Number of occupants per room in the house. c: ARV naïve / First line ARV / Second line ARV / Third line ARV.

Table 2

Comparison of depression and quality of life in PHIV caregivers and caregivers of healthy controls

	Group						
Outcome variable	Caregivers PHIV (N = 86)	Caregivers HC (N = 34)	df	F	p	95% CI	t
WHOQoL[a]							
Mean (SD)	59.53 (32.96)	54.68 (32.73)	117	0.06	0.469	(-18.07 – 8.36)	-0.72
Range	0 – 360	202 – 362					
CESD[b] Total score							
M (SD)	13.30 (11.69)	13.65 (11.85)	118	0.01	0.885	(-4.36 – 5.05)	0.14
Range	0 - 50	0 - 47					
PSI[c] Child Domain							
M (SD)	113.79 (30.98)	119.48 (20.84)	108	0.36	0.337	(-6.00 - 17.38)	0.96
Range	0 - 160	77 - 174					
PSI[c] Parent Domain							
M (SD)	138.31 (39.10)	147.42 (24.98)	108	0.51	0.220	(-5.533 - 23.758)	1.23
Range	0 - 213	109 - 212					
PSI[c] Total stress							
M (SD)	252.10 (67.23)	266.91 (41.04)	108	0.32	0.257	(-10.21 - 39.82)	1.17
Range	202 - 362	0 - 360					
FSS[d]							
M (SD)	27.06 (18.33)	25.29 (21.44)	117	1.36	0.652	(-9.50 - 5.97)	-0.45
Range	0 – 86	0 - 90					
FRS[e]							
M (SD)	60.14 (35.23)	52 (35.39)	118	0.21	0.257	(-22.29 - 6.01)	-1.13
Range	0 – 134	0 - 117					

NOTES: a: World Health Organisation Quality of Life Scale. b: Centers for Epidemiological Studies Depression scale. c: Parental Stress Index. d: Family Support Scale. e: Family Resources Scale

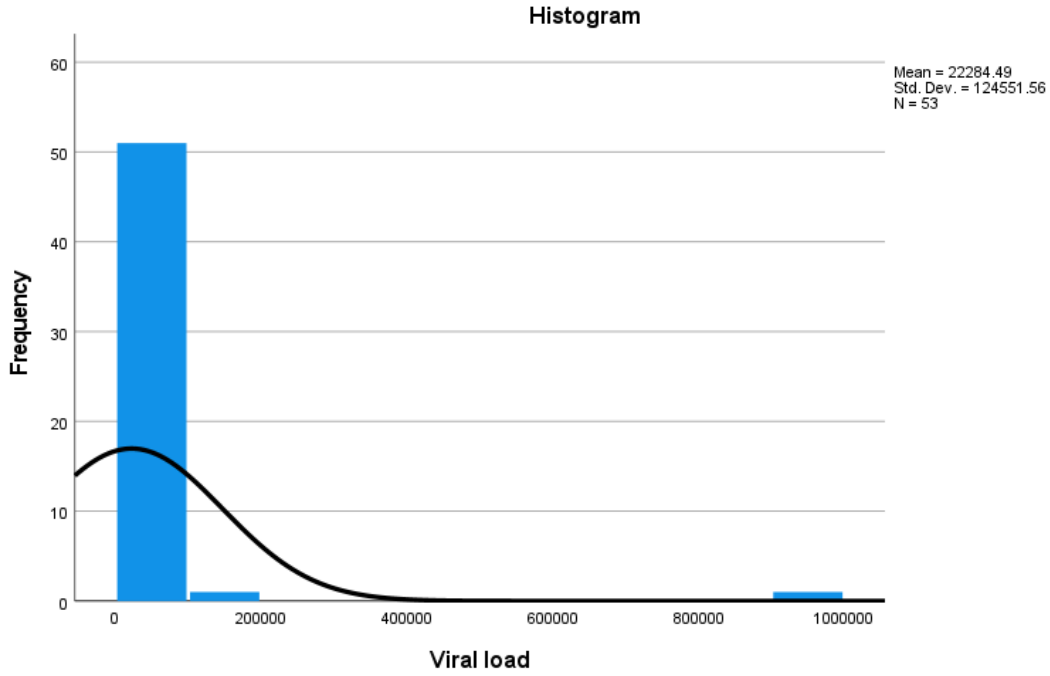
Table 3

Comparison of depression and quality of life in PHIV Biological Caregivers and PHIV Non-Biological Caregivers

Outcome variable	Group		df	F	p	95% CI	t
	PHIV Biological Caregivers (N = 45)	PHIV non-biological Caregivers Control (N = 34)					
WHOQoL[a]							
Mean (SD)	63.49 (29.28)	56.88 (34.77)	76	2.51	0.366	-7.86 – 21.08	0.91
Range							
CESD[b]							
Mean (SD)	16.07 (12.37)	13.35 (10.61)	77	0.62	0.309	-2.56 – 7.98	1.02
Range							
PSI[c] Child Domain							
Mean (SD)	119.07 (24.46)	119.74 (8.95)	74	0.00	0.898	-11.09 – 9.74	-0.12
Range							
PSI[c] Parent Domain							
Mean (SD)	147.69 (32.62)	142.87 (24.67)	74	0.10	0.489	-8.97 – 18.61	0.69
Range							
PSI[c] Total stress							
Mean(SD)	266.76 (53.65)	262.61 (38.86)	74	0.18	0.714	-18.27 – 26.56	0.36
Range							
FSS[d]							
Mean (SD)	30.00 (17.47)	25.94 (20.81)	76	0.43	0.352	-4.58 – 12.70	0.93
Range							
FRS[e]							
Mean (SD)	61.04 (31.974)	58.65 (38.447)	77	1.90	0.763	-2.56 – 18.18	0.30
Range							

[a] World Health Organisation's Qualify of Life scale. [b] Centers for Epidemiological Studies Depression scale. [c] Parental Stress Index. [d] Family Support Scale. [e] Family Resources Scale

Visual Representation



Visual representation of HIV viral load mean in PHIV

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APPENDIX A

Center for Epidemiologic Studies Depression Scale (CES-D), NIMH

Below is a list of the ways you might have felt or behaved. Please tell me 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 a little of the time (1-2 days)	Occasionally or a moderate amount of 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 my family or 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 dislike me.	☐	☐	☐	☐
20. I could not get "going."	☐	☐	☐	☐

APPENDIX B

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 check-ups 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: e.g.: 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: e.g.: 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: e.g.: 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): 74

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 C

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). E.g.: 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. Childcare/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 D

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 membership/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 E

PARENT QUESTIONNAIRE AND ASSET INDEX

GENERAL INFORMATION

Full name (Parent):	
Telephone:	Work: ( ) Home: ( ) Cell:
How would you describe your ethnicity / race?	1. Black 2. Coloured 3. White 4. Asian 5. Other(specify):
Home Language:	
Full name (Child):	
Gender:	M F
Date of Birth:	
Grade:	

HOUSEHOLD INCOME: (Please circle appropriate number)

Household income per year:	1. R0 2. R1 – R5 000 3. R5001 – R25 000 4. R25 000 – R100 000 5. R100 001+

PARENTAL EDUCATION: (Please circle appropriate number)

	Biological mother	Biological father	Guardian
Highest level of education reached? Mark one response for each person as follows: 1. 0 years (No Grades / Standards) = No formal education (never went to school)	1. 2. 3.	1. 2. 3.	1. 2. 3.

2. 1-6 years (Grades 1-6 / Sub A-Std 4) = Less than primary education (didn't complete primary school) 3. 7 years (Grade 7 / Std 5) = Primary education (completed primary school) 4. 8-11 years (Grades 8-11 / Stds 6-9) = Some secondary education (didn't complete high school) 5. 12 years (Grade 12 / Std 10) = Secondary education (completed senior school) 6. 13+ years = Tertiary education (completed university / technikon / college) 7. Don't know	4. 5. 6. 7.	4. 5. 6. 7.	4. 5. 6. 7.

APPENDIX F

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 check-ups. 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 test 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 enrolment 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 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.
 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 test 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 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 92

APPENDIX G
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 counselled both prior to taking the test and afterwards, regardless of the test outcome.

What are your rights?

 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 counselling 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 test their memory, concentration and planning abilities. Many of these are like a normal IQ test that your child may have completed at school. All 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 pacemakers, 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 centre 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 enrolment 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 test 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 101

APPENDIX G

INSTRUCTIONS TO AUTHORS

Submitting a Journal article to AIDS Care

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