Prevalence of Disability in a Cohort of HIV-Infected Children Attending an Urban Paediatric HIV Clinic in Johannesburg, South Africa

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ABSTRACT

Background:

With the success of evolving antiretroviral therapy (ART), human immunodeficiency virus (HIV) has become a chronic condition, however, children infected with HIV have been shown to have developmental difficulties and disabilities. This study aimed to investigate the extent of disability among a cohort of HIV infected children in South Africa and whether they are being referred and accessing rehabilitative services.

Methods:

A cross-sectional study was conducted at an HIV clinic in Johannesburg. Caregivers/parents were interviewed about their child, using the Ten Question Screen for Disability Questionnaire (TQSD) along with a general additional questionnaire devised by the researchers on medical history, services referred to and accessed and socioeconomic status (SES). Clinical data, from the child's clinic file were recorded.

Results

Of the 200 children whose caregivers/parents were interviewed, 50.5% experienced disabilities were 58.4% of those had more than one co-existing disability. Of the children who reported disability only 46% had been referred to one or more of the following support services; audiologist, physiotherapist (PT), psychologist, occupational therapist (OT) and/or speech and language therapist (SLT). Previous diagnosis of tuberculosis (TB), lower respiratory tract infections (LRTI) and low pre-combination ART (cART) CD4% were found to be associated factors in the presence of developmental disability and/or delay.

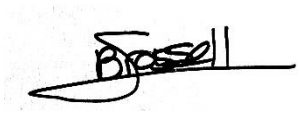
Conclusion

The prevalence of children with HIV and disability is high and these children are not being referred to and/or accessing the appropriate support services. Government policy and clinic practice need to shift their focus of management of children living with HIV, in order to integrate services that can assist children reach their developmental potential and improve their quality-of-life.

DECLARATION

I, Shane Elizabeth Brassell (Nee Hodges), declare that this research report is my own unaided work except for the help given by the persons listed under the acknowledgements. It is being submitted in partial fulfilment of the requirements of the degree of Master of Medicine (Child Health) at the University of the Witwatersrand. It has not been submitted before for any other degree or examination in any other university.

Signed this day in Cape Town



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Signature

07 /05 / 2018

Date

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LIST OF ABBREVIATIONS

Abbreviations below are used in text and/or in tables/figures presented in future chapters.

ADHD	Attention-Deficit Hyperactivity Disorder
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
ARV	Antiretroviral
Ax	Assessment
BAZ	BMI for AGE
BMI	Body Mass Index
BSID	Bayley Scales of Infant Development
BSITD	Bayley Scales of Infant and Toddler Development
cART	Combination Antiretroviral Treatment
CD4	Cluster of Differentiation 4
CMV	Cytomegalovirus
CNS	Central Nervous System
C-Section	Caesarean Section
DOBE	Department of Basic Education
DOH	Department of Health
DRC	Democratic Republic of Congo
DRM	Drug Resistance-associated Mutation
ELBW	Extremely Low Birth Weight
ENT	Ear, Nose and Throat Doctor (Otorhinolaryngologist)
ESRU	Empilweni Services and Research Unit
FPL	Food Poverty Line
GMDS	Griffiths Mental Development Scales
HAZ	Height for age
HIV	Human Immunodeficiency Virus
HIVE	HIV Encephalopathy
HPCSA	Health Professions Council of South Africa
IQR	Interquartile Range
IRIS	Immune Reconstitution Inflammatory Syndrome
K-ABC	Kaufman Assessment Battery for Children
LAMI	Low and Middle Income
LBPL	Lower Bound Poverty Line
LBW	Low Birth Weight
LRTI	Lower Respiratory Tract Infection
Optom	Optometrist
OT	Occupational Therapist
PCR	Polymerase Chain Reaction
PHC	Primary Health Care
PMTCT	Prevention of Mother-to-Child Transmission of HIV
PN	Peripheral Neuropathy
Psych	Psychologist

PT	Physiotherapist
Ref	Referral
RMMCH	Rahima Moosa Mother and Child Hospital
Rx	Treatment
SASLHA	South African Speech-Language-Hearing Association
SE	Standard Error Mean
SD	Standard Deviation
SES	Socioeconomic Status
SLT	Speech and Language Therapist
Std. Err. Mean	Standard Error Mean
UBPL	Upper Bound Poverty Line
TB	Tuberculosis
TBM	Tuberculosis Meningitis
TQSD	Ten Question Screen for Disability
UNAIDS	Joint United Nations Programme on HIV/AIDS
USA	United States of America
VLBW	Very Low Birth Weight
WAZ	Weight for Age
WHO	World Health Organisation

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CHAPTER 1

1. INTRODUCTION

"The children who many thought would never survive continue to be pioneers in the first-ever journey of perinatal HIV infection into adulthood" (Siberry et al., 2008 p.457)

Until recently the focus of paediatric human immunodeficiency virus (HIV) treatment has been on preventing mortality. With the introduction of combination antiretroviral therapy (cART), HIV is becoming a chronic condition in both adults and children, with many children infected with HIV, successfully transferring into adult services. Unfortunately the repercussions of a lower mortality and the shift towards chronic disease is higher morbidity rates. It has become generally accepted that increased survival of a chronic disease is associated with developmental changes and learning difficulties in children (Armstrong, 2006; Banks et al., 2015; Koekkoek et al., 2008). In addition literature has come to recognise the link between HIV and developmental disability (Abubakar et al., 2008; Baillieu and Potterton, 2008; Banks et al., 2015; Hanass-Hancock and Nixon, 2009) as well as the relationship between disability and lower socioeconomic groups (Ataguba et al., 2011; Simkiss et al., 2011) and poverty and HIV (Pons-Duran et al., 2016; Tladi, 2006; Wabiri and Taffa, 2013). Therefore, children with HIV who come from low socioeconomic environments are an exceptionally vulnerable group for developmental delay and disability. Additionally, people living with HIV are suffering a deterioration in their ability to participate in life (Banks et al., 2015; Nixon et al., 2011) and recent research has strongly recommended, the need for comprehensive neurological and functional assessments and management. (Banks et al., 2015; Devendra et al., 2013; R.Govender et al., 2011; Hilburn, Potterton & Stewart 2010). Access and referral to appropriate and supportive services should reflect the need of this group of children and swing towards chronic care, improving quality of life and supportive management (Bamford and Lyall, 2015).

"Neuro-disability" related to HIV occurs in 6-97% of infected children (Abubakar et al., 2008; Bagenda et al., 2006; Baillieu and Potterton, 2008; Banks et al., 2015; Benki-Nugent et al., 2015; Devendra et al., 2013; Donald et al., 2014; R. Govender et al., 2011; Kandawasvika et al., 2011; Lowick et al., 2012; Potterton et al., 2009; Rutar et al., 2015; Samia et al., 2013; Smith et al., 2008; Van Rie et al., 2007; Whitehead et al., 2014). This large range of percentage can be attributed to whether or not "neuro-disability" is identified as one specific disability such as hearing impairment or if the study groups a variety of neurodevelopmental difficulties, delays and disabilities together. This "neuro-disability" can

be as a direct result of the neurotrophic characteristics of HIV or indirectly via side effects of antiretroviral therapy (ART), opportunistic infections, side effects of treatment for the opportunistic infections (Hilburn, Potterton and Stewart 2010; Willen, 2006; Van Rie et al., 2007) or psychological effects of the consequences of parent illness and the stigma around HIV (Grover et al., 2007).

In addition to the direct effects of HIV, Donald et al. (2014) describe the "layering effect" of multiple compounding indirect factors affecting development in an HIV-positive paediatric population. These include clinical and socioeconomic factors such as timing of infection, prematurity, prolonged hospital stay, effects of exposure to ART on the developing brain in utero, immunological factors, prenatal drug exposure, effects of poor maternal health and resulting lack of opportunity for stimulation, malnutrition, family stress associated with illness and/or death of primary caregiver and orphan status (Donald et al., 2014; R. Govender et al., 2011; Hilburn et al., 2010; Willen, 2006). In addition, HIV-related opportunistic infections such as tuberculosis, meningitis, toxoplasmosis, cytomegalovirus (CMV), conjunctivitis primary central nervous system (CNS) lymphoma and otitis media can cause neurological damage affecting function (Buriti et al., 2013; Donald et al., 2014; Moschos et al., 2007).

There is abundant research on the positive and negative effects of ART. Early initiation has been shown to be effective at minimising the progression of HIV encephalopathy and resultant disability (Bagenda, 2006; Innes et al., 2014; Hilburn, Potterton and Stewart 2010; Kitahata et al., 2009; Laughton et al., 2013; Lindsey et al., 2007; Ruel et al., 2012; Violari et al., 2008). However, the side effects of ART in children can be disabling. Reported common side effects include; ototoxicity (Buriti et al., 2013), peripheral neuropathy, mitochondrial toxicity, immune reconstitution inflammatory syndrome (Donald et al., 2014) and cardiovascular complications (Siberry and Tindyebwa, 2014) which will all affect motor control or sensory function and therefore, the acquisition of new skills in developing children.

With these multitudes of factors affecting development it is clear that a child infected with HIV is at risk for developing one or more disabilities. The prevalence of developmental delay in infants and children infected with HIV is well documented. Many studies have researched the development of HIV infected infants in sub-Saharan Africa (Baillieu and Potterton, 2008; Hilburn, Potterton and Stewart 2010; Kandawasvika et al., 2011; McDonald et al., 2013; Potterton et al., 2009; Shead et al., 2010; Smith et al., 2012; Whitehead et al., 2014), but only a few have investigated developmental delays, difficulties and disability in children older than two years. Some studies have explored a single disability related to HIV in children, including epilepsy (Samia et al., 2013), hearing impairment (Christopher et al., 2013; Hrapcak et al., 2016; Torre et al., 2015), communication difficulties (Hattam et al., 2014), visual difficulties (Padhani et al., 2000; Rutar et al., 2015), behaviour disorders (R.

Govender et al., 2011; Grover et al., 2007; Koenig et al., 2011) and neurocognitive impairment (Kandawasvika et al., 2015; Sherr et al., 2017; Walker et al., 2013) while other studies have looked at developmental delay as a whole (Lowick et al., 2012; Ruel et al., 2012; Van Rie et al., 2007). Only two studies were identified that explored a range of disability in an older cohort of children infected with HIV. R.Govender et al. (2011) found abnormal neurology in 59% of a group of 78 children in Cape Town. However, this study focused solely on impairment and did not explore areas of activity or participation limitation and did not indicate how many of the children had single or co-existing disabilities. Devendra et al. (2013) took a larger cohort of children (n=296) in a case-controlled study in Malawi and investigated the prevalence of disability as well as identifying the requirements, opportunities and barriers for rehabilitation. Of their group of children, 33% of HIV-infected cases screened positive for disability, of which 49% had a single disability, 29% had two co-existing types of disability and 22% had more than three different coexisting types of disability.

Unfortunately many of the studies reviewed have very small study samples (n <300) when compared with a population of more than three million HIV-infected children living in sub- Saharan Africa (Donald et al., 2015). This large discrepancy makes it difficult to draw conclusions of association and impact in terms of the whole paediatric HIV infected population. The reason provided for small study samples were, loss to follow-up and time consuming measurement tools. All of the studies, be it on single or multiple aspects of development identified the "layering effect" as a possible confounding factor for concluding an association between HIV and developmental delay and/or disability.

1.1 Problem statement

In 2016 UNAIDS estimated that there are 320 000 children in South Africa living with HIV and the new infection rate among children is 12 000 a year (UNAIDS, 2017). With the advances in ARVs all these children will most likely grow up and will be required to be functioning and contributing members of society. However, these children are at risk for developmental delay and disability which could cause an increasing burden to health care and the social and economic development of South Africa. If these difficulties and disabilities are prevented and/or treated timeously with the correct processes of identification and intervention, the burden to health care and society in general may be minimised. Currently there are no studies on the prevalence of child disability related to HIV in children older than two years in the Gauteng region of South Africa or the referral and use of services available to this population. If the magnitude of this problem is identified, finances and structures can be allocated and put in place to prevent, assist and manage these potential disabilities.

1.2 Aim

The aim was to examine the prevalence of disability in a cohort of HIV-infected children at Empilweni Services and Research Unit (ESRU) at Rahima Moosa Mother and Child Hospital (RMMCH), determine factors associated with HIV related disability and whether this population are being referred and/or accessing the rehabilitative services available to them.

1.3 Study Objectives

1. Estimate the prevalence of disability in a cohort of HIV-infected children between the ages of 2-9 years of age at RMMCH in Johannesburg, South Africa.
2. Provide insight into the rehabilitative services that are being accessed by this population.
    - What rehabilitative services are available to this population?
    - Is this population being referred to these services?
    - Are these services being utilised by this population?
    - What are the facilitators and barriers to accessing rehabilitative services?
3. Examine factors associated with HIV related disability;
    - Individual Factors
        - Age
        - Sex
    - Anthropometric factors
    - Birth Factors
        - Mode of Delivery
        - Gestational age
        - Birth Weight
    - Clinical Factors
        - Pre-ART
            - CD4 cell count
            - CD4%
            - Viral Load
        - Childhood and opportunistic infections/diseases
        - Number of hospitalisations
    - Treatment Factors
        - Age at the start of cART
        - Duration on cART
        - Treatment adherence
        - Maternal ART

- Socioeconomic Status
  - Monthly household income
  - Orphan Status
  - Main caregiver education

1.4 Significance of the study

The outcomes of this study will provide clinicians and policy makers with much needed information on the prevalence of disability in this population. In conjunction with other similar studies from ESRU (Potterton et al., 2016; Whitehead et al., 2014), the outcomes of this study will assist in the planning and provision of and referral to appropriate supportive and habilitation services for children infected with HIV at ESRU and potentially other facilities. In addition, this study, in conjunction with others (Chetty and Hanass-Hancock, 2016, 2015; Cobbing et al., 2017, 2014, 2013; Devendra et al., 2013; Egeraat et al., 2015; Maddocks et al., 2018; Potterton et al., 2016) can be used to reinforce the importance of rehabilitative services in the chronic management of children and adults with HIV and the outcomes can be used to motivate for the active integration of rehabilitative services into HIV care facilities.

1.5 Conclusion

HIV has become a chronic condition which affects a child's susceptibility to developmental delays and disabilities. The services supporting these children need to make a shift in focus from survival to chronic, supportive and quality-of-life management.

CHAPTER 2

2. LITERATURE REVIEW

"This shift toward chronicity has significant implications for health and health care, and requires a parallel shift in thinking" (Nixon et al., 2011, p. 3).

This chapter reports on developmental delay and childhood disability in paediatric HIV. It will define disability and developmental delay and review the epidemiology of paediatric HIV and childhood disability. It will then go on to discuss possible aetiologies of disability in children, associated with HIV infection, taking a closer look at the pathogenesis of HIV and the developing CNS, opportunistic infections, ART and the "layering effect." Literature from previous studies looking at the prevalence of delayed development, specific impairment of children living with HIV and measurement tools will be discussed. To conclude this section, a review of the literature on services available and recommendations for appropriate services will be presented.

Literature was sourced through comprehensive searches on the following databases: Cochrane Collaboration, EBSCO Host, Google Scholar, Medline, Pubmed, and ScienceDirect. The following are the key words that were used in searches: ART, ARV, children, cognition, communication, CNS, developmental delay, disability, encephalopathy, epilepsy, hearing, HIV, paediatric, seizures and vision.

2.1 Definitions of Development, Disability & Habilitation

"Neurodevelopment" and "child development" are often used interchangeably however, there is a difference. "Child development" is what can be observed, while "neurodevelopment" are the processes that are behind what is observed (Maes, 2016). Child development is the simultaneous development of motor (gross and fine), sensory, speech, language, emotional, behaviour and cognitive processes (Boivin et al., 2015; Couper, 2016), while neurodevelopment is the development of the neuronal networks and pathways, the wiring and firing that enable child development to occur (Boivin et al., 2015; Maes, 2016; Merrian-Webster, 2017). However, neurodevelopment and child development do not occur in a vacuum and there is an intricate inter-relationship between neurodevelopment, genetics and environment that play a complex role in child development (Boivin et al., 2015; Couper, 2016; Maes, 2016).

There is limited neutral language when it comes to describing and defining disability (Simkiss et al., 2011). Over the years, disability has been defined in many ways, using a number of models including biomedical, philanthropic, sociological or socio-political definitions. Function and consequently disability is a complex, multifactorial and often subjective concept (Altman et al., 2001). The most commonly used definition is from the World Health Organisation (WHO) which defines disability as "an umbrella term, covering impairments, activity limitations, and participation restrictions. An impairment is a problem in body function or structure; an activity limitation is a difficulty encountered by an individual in executing a task or action; while a participation restriction is a problem experienced by an individual in involvement in life situations." (WHO, 2011). There is however, often disagreement when "disability" needs to be classified into domains and severity (Altman et al., 2001). How can one compare the ability to participate in a sports match to the ability to participate and achieve in a classroom situation? Or compare visual impairment with hearing loss? In children, the definition of disability becomes even more complex, as many practitioners would rather give a label of "developmental delay" as opposed to "disability." It is universally accepted that children who show delay in attaining developmental milestones are at risk for developing functional and participatory difficulties and/or disabilities. At what point in a child's life does the line of "developmental delay" end and "disability" begin? This question is beyond the scope of this report, however, it is something to keep in mind. For the purpose of this report the term "developmental delay" will relate to below norm scores for developmental measurement tools and perceptions of the caregiver/parent that their child is not achieving milestones within universal and family norms. "Disability" is defined under the WHO definition of impairments, activity limitations, and participation restrictions on a spectrum of mild to severe.

"Rehabilitation" implies the re-acquiring of skills that existed but are now lost. A child with developmental delay or developmental difficulty has never developed those skills in the first place (O'Toole, 2003). Therefore, "habilitation" is used to describe assisting a child with developmental delay or developmental difficulties to acquire functional and participatory skills. A summary of these definitions can be found in Table 8.1 (Appendix 1).

2.2 Epidemiology

HIV infection rates are finally beginning to decrease in sub-Saharan Africa, but the sheer numbers of people infected are still a major cause for concern. In 2015 the Joint United Nations Programme on HIV/AIDS (UNAIDS, 2017) estimated that there were seven million people in South Africa living with HIV of which, 240 000 were children between the ages of 0-14 years. The mid-year population estimates of South Africa for 2017 estimated that 7.06 million South Africans were living with HIV which is approximately 12.5% of the total South African population (Stats SA, 2017a).

There is a lack of recent studies of the prevalence of disability in general paediatric populations. The 2001 South African Census on the prevalence of disability reported that 2% of children under 10 years were disabled (Stats SA and Lehohla, 2005), while other studies have estimated the prevalence between 5.2% and 6.4% (Christianson et al., 2002; Couper, 2002; Gladstone, 2010; G. Saloojee et al., 2007). The Census 2011: Profile of Persons with Disability in South Africa, reported that 10.8% of children between 5-9 years old had disabilities (Stats SA and Lehohla, 2011). This is much higher than other studies. However, it was noted that this may be due to parents misreporting on their children by classifying them as unable to perform or have difficulty performing functions when in actual fact the child was not old enough to be expected to perform those functions (Stats SA and Lehohla, 2011).

Prevalence of disability appears to be much higher in the HIV-infected population. Abnormal neurological signs, impairment and developmental delay have been reported in 9.4-90% of children with HIV (Banks et al., 2015; Kandawasvika et al., 2011; Lowick et al., 2012; Samia et al., 2013; Smith et al., 2008, 2012; Walker et al., 2013). It is reported that 23-70% of children with HIV experience physical disabilities (Baillieu and Potterton, 2008; Banks et al., 2015; Devendra et al., 2013; Foster et al., 2006; Myezwa et al., 2009; Potterton et al., 2009; Van Rie et al., 2007; Whitehead et al., 2014), while 6.4-36% have hearing difficulty (Banks et al., 2015; Devendra et al., 2013; R. Govender et al., 2011; Hrapcak et al., 2016; Makar et al., 2012; Palacios et al., 2008; Torre et al., 2012, 2015), 6-67% have problems with vision (Devendra et al., 2013; R. Govender et al., 2011; Ikoona et al., 2003; Kestelyn et al., 2000; M'bongo Zindamoyen et al., 2013; Padhani et al., 2000; Rutar et al., 2015), 8.9-97% have neurocognitive and behaviour difficulties (Devendra et al., 2013; Donald et al., 2014; R. Govender et al., 2011; Grover et al., 2007; Kandawasvika et al., 2015; Lowick et al., 2012; Martin et al., 2006; Myezwa et al., 2009; Nozyce et al., 2006; Potterton et al., 2009, 2016; Smith et al., 2012; Van Rie et al., 2007; Whitehead et al., 2014) and those with communication difficulties amount to 7.5-82% of children with HIV (Baillieu and Potterton, 2008; Devendra et al., 2013; Makar et al., 2012; Rice et al., 2013; Van Rie et al., 2008; Whitehead et al., 2014). These large percentage ranges are most likely due to differences in sample size, age range of children assessed, assessment method, location of study (i.e. developed vs. developing country), ART-initiated or ART-naive and type of participant (e.g. in-patient vs. outpatient) and will be discussed in depth under the heading "Developmental Delay and Disability."

2.3 Pathogenesis

These disabilities in children with HIV are often termed "neuro-disabilities" as they can be the direct consequence of the neurotrophic traits of HIV. In addition, these impairments can be caused secondarily by opportunistic infections, the side effects of ARTs, other treatments for opportunistic

infections (Hilburn, Potterton and Stewart 2010; Willen, 2006; Van Rie et al., 2007) and/or psycho-social factors (Grover et al., 2007; Lowenthal et al., 2014).

The types of disability and comorbidities in adults differ to those of children and are well documented (Banks et al., 2015; Myezwa et al., 2009, 2011). In adults, HIV attacks a mature CNS, while in children; HIV invades a developing foetal and infant CNS. Studies have shown that HIV may be expressed differently depending on the timing of contagion during gestation, the viral load and perhaps the genetic background of the foetus (Boivin et al., 2015; Lyman et al., 1990; Yan, 2015). In a number of studies looking at aborted foetuses and in vitro studies, HIV in CNS tissue as well as observed changes in cells and the developing structure of the CNS was detected (Lyman et al., 1988, 1990; Schwartz et al., 2007; Seth and Major, 2005; Vazeux et al., 1992; Wigdahl et al., 1987) which indicates a possible causal relationship between HIV and atypical neurological function in children exposed to HIV in utero (Angelini et al., 2000; Benki-Nugent et al., 2015; Crowell et al., 2015; Lyman et al., 1990; Seth and Major, 2005; Van Rie et al., 2007). Once HIV has infiltrated the CNS it has an assortment of mechanisms through which it triggers atypical neuronal function. These mechanisms include the inflammatory state of the brain as well as direct infection of certain brain cells. HIV-infected brain microglial cells and macrophages invade the CNS causing an inflammatory response (release of viral proteins, pro-inflammatory cytokines and nitric oxide) which results in a cascade of neurotoxic events causing neuronal injury (Benki-Nugent et al., 2015; Crowell et al., 2015; Everall et al., 2005; Van Rie et al., 2007). In addition, it is thought that neuronal loss and demyelination during early brain development is due to the direct infection of the neuroblasts, astrocytes and oligodendrocyte progenitor cells with HIV (Angelini et al., 2000; Everall et al., 2005; Gorry et al., 2003; Seth and Major, 2005; Van Rie et al., 2007). Van Rie et al. (2007) remarked that foetal astrocytes may be more vulnerable to HIV infection, because the developing CNS may be more susceptible to alterations in astrocyte function which could result in infected astrocytes playing a fundamental role in paediatric HIV encephalopathy.

Antiretroviral (ARV) drugs infiltrate the CNS to differing extents. Consequently local viral replication in the CNS can occur in individuals who have lower levels of ARV drugs crossing the blood-brain barrier, creating a reservoir of HIV infection in the CNS (Crowell et al., 2015; Fois and Brew, 2015; Gavin and Yogev, 1999; Gray et al., 2014, 2016; Hellmuth et al., 2015; Martínez-Bonet et al., 2015). This HIV reservoir theory, along with persistent intrusion of HIV into the CNS has been thought to contribute to the poor neurodevelopment of children with HIV (Crowell et al., 2015).

HIVE can result in a cascade of events causing developmental delays and impairment (Donald et al., 2014; Hilburn, Potterton and Stewart 2010; Willen, 2006; Walker et al., 2013). HIVE has a variety of clinical manifestations that have been classified into three subtypes; Sub-acute, Plateau and Static.

Sub-acute encephalopathy is severe and involves cognitive deterioration, seizures and loss of milestones resulting in dysfunction. Plateau encephalopathy involves subtle declines in areas of motor and cognitive ability; Static encephalopathy manifests as non-progressive neurological deficits and a slow rate of skills acquisition (Hilburn, Potterton and Stewart 2010; Mitchell, 2006; Willen, 2006). The WHO has set out diagnostic criteria for HIVE. A clinical diagnosis is defined as "at least one of the following, progressing over at least two months in the absence of other illness; a) Failure to attain or loss of developmental milestones or loss of intellectual ability; b) progressive impaired brain growth demonstrated by stagnation of head circumference; c) acquired symmetrical motor deficit accompanied by two or more, of the following: paresis, pathological reflexes, ataxia and gait disturbances." A definitive diagnosis is defined as "Neuroimaging demonstrating atrophy and basal ganglia calcification and excluding other causes" (WHO, 2007, p. 37). As a clinical diagnosis is subjective and neuroimaging is expensive and therefore, not routinely used, clinicians run the risk or falsely diagnosing or under-diagnosing HIVE. Donald et al. (2015) found that HIVE was frequently missed in children with severe or milder forms. The study proposed busy clinics and a lack of further examinations and specialized services as the reason for under-diagnosis (Donald et al., 2015). The presence of HIV encephalopathy (HIVE) is a good predictor of disability (Everall et al., 2005; Mitchell, 2006; Shanbhag et al., 2005; Smith et al., 2008, 2012). Consequently, by missing a diagnosis of HIVE, the opportunity of early identification and treatment delays can be lost.

Some studies have shown that pre-treatment virological status can be used to predict neurodevelopmental fallout. Shanbhag et al. (2005) found an association between pre-treatment CD4% ($p < 0.001$) and viral load ($P = 0.06$) and neurocognitive functioning. However, other studies have found no such association (Devendra et al., 2013). These two studies, were published eight years apart and where one was researched in New York (Shanbhag et al., 2005), the other took place in a less developed country, Malawi (Devendra et al., 2013).

2.4 Layering Effect

Armstrong (2006) pointed out that if a child has a chronic illness, this does not safeguard against other risk factors for neurodevelopmental disability. As HIV has become a chronic disease, this sentiment applies for HIV too. Over and above the focused effects of HIV there are multiple compounding factors affecting development which include clinical and socioeconomic factors such as timing of infection, prematurity, prolonged hospital stay, effects of exposure to ART on the developing brain in utero, immunological factors, prenatal drug exposure, effects of poor maternal health and resulting lack of opportunity for stimulation, malnutrition, family stress associated with illness and/or death of the primary caregiver and orphan status (Donald et al., 2014; R. Govender et al., 2011; Hilburn et al., 2015; Sherr et al., 2014b, 2017; Willen, 2006). Donald et al. (2014) termed these factors the "layering effect"

and many studies have concluded that this “layering effect” may be a confounding factor in their results. Some aspects of this “layering effect” are discussed here and others will be discussed under future headings.

2.4.1 Prematurity

Preterm birth is classified into mild preterm (32-36 weeks), very preterm (28-31 weeks) and extremely preterm (<28 weeks). However, gestational age is not always accurate therefore, professionals prefer to classify prematurity by birth weight, where extreme low birth weight (ELBW) is less than 1000g, very low birth weight (VLBW) is 1000-1500g and low birth weight (LBW) is between 1500 and 2500g.

Maternal HIV has been associated with increased risk of preterm birth (Arab et al., 2017; Uthman et al., 2017; Xiao et al., 2015; Zack et al., 2014). In addition a systematic review showed that initiating ART pre-conception, increases the likelihood of preterm delivery (Uthman et al., 2017) but other studies disagree. Chagomerana et al. (2017) looked retrospectively at 3074 women in Malawi who gave birth between April 2012 and November 2015. These women had started ART before 27 weeks gestation and the study found no significant association between ART and preterm birth, with preconception ART particularly protective of premature and low weight births. These findings are in contrast to the review by Uthman et al. (2017) who reviewed 11 studies with 19189 mother/infant pairs, which were collectively conducted between 1986 and 2011. The review concluded that women who started ART before conception were at significantly increased risk for preterm birth. However, the review did conclude that as ART has been shown to reduce HIV transmission from mother to child and concluded that the benefits far outweigh the risks (Mofenson, 2016; Uthman et al., 2017). The Malawian study (Chagomerana et al., 2017) was conducted later than most of the other studies in Uthman et al.’s (2017) review, therefore, changes in ART regimes may explain the difference in outcome between the two studies. In addition, the review had five studies (of 11) from low resourced countries while the rest were from developed countries and none of the studies reviewed were in Malawi. However, a review does have greater validity than a retrospective cross sectional study.

It is commonly accepted that prematurity is linked with mortality as well as short and long term neurodevelopmental difficulties and disability in the survivors (Acharya et al., 2016; Rogers and Hintz, 2016; Spittle and Treyvaud, 2016; Taylor and Clark, 2016) with the incidence of neonatal mortality and morbidity increasing with decreasing gestation/birth weight (Ballot et al., 2012; Couper, 2016; Moutquin, 2003). Jarjour (2015) showed that extremely preterm children have a low probability of developing typically while very and mild preterm infants have milder impairments relating to domains such as executive function (Taylor and Clark, 2016) and sensory modulation difficulties (Bröring et al., 2017). There is some documentation that a low birth weight (<2500grams) is a risk factor for

difficulties with developmental motor skills, cognition and behaviour (Hutchings and Potterton, 2014; Walker et al., 2007). As a result, it has been recommended that mothers infected with HIV need particular prenatal care to minimise other risk factors of premature birth and possible resulting morbidity (Arab et al., 2017).

2.4.2 Socioeconomic Status

Socioeconomic status (SES) is a multidimensional concept. It is a measure of total economic and sociological factors that affect the status of an individual or a group (e.g. neighbourhood) in society (Hackman and Farah, 2009; Howe et al., 2012). Household income, education, occupation (employment status) and industry are elements often used to establish and analyse SES. Children are not able to establish their own SES and therefore, their SES is inherited from their parents or caregivers until they are able to establish themselves independently of their carers (Hackman and Farah, 2009). Elements of SES in sub-Saharan Africa that relate to health and developmental concerns in children include maternal education, birth spacing, food security, household income, living environment (house hold size, house structure), access to health care and geographical location (Boyede et al., 2013; Gilbert and Walker, 2002; Heaton et al., 2016; Kandawasvika et al., 2015; McDonald et al., 2013; Nkonki et al., 2011; Wamani et al., 2004).

In South Africa, a common indication of measuring SES is; Rands, per person, per month. This is categorised into thresholds of Food Poverty Line (FPL), Lower Bound Poverty Line (LBPL) and Upper Bound Poverty Line (UBPL). The 2017 thresholds for FPL, LBPL and UBPL were R531pp/month, R758pp/month and R1138pp/month respectively (Stats SA, 2017b). In 2015, 55.5% of South Africans were living below the UBPL and 33.3% of people residing in Gauteng were living below the UBPL (Stats SA, 2017b).

Poor SES has been associated with disability and developmental delay as well as HIV infection (Banks et al., 2017; Boivin et al., 2015; Hackman and Farah, 2009; Heaton et al., 2016; Johnson and Budlender, 2002; Manomano and Selebogo, 2017; Sibanda and Doctor, 2013; Wabiri and Taffa, 2013; Wamani et al., 2004). However, Simkiss et al. (2011) reviewed 24 primary studies and 13 reviews on the "relationship of childhood disability with family and household social circumstances in low and middle income (LAMI) countries"(Simkiss et al., 2011, p. 3) and concluded that empirical evidence on the association between childhood disability and low household SES in LAMI countries is inconsistent and contradictory. This is interesting as the general assumption due to social and biological observations is that there would be an association. There may be a number of reasons for this conclusion; Simkiss et al. (2011) did note that there is not necessarily a lack of research supporting the association between SES and childhood disability but more a paucity of robust evidence on this topic. Limitations

were found in the lack of standardised definition of disability and dissimilarity of measures of household SES. Other reviews have indicated that limitations in studies may arise due to different perceptions of SES in different cultures and countries and because it is difficult to unscramble the independent effects of SES from the genetic or biological differences on health disparities and brain development (Boivin et al., 2015; Sibanda and Doctor, 2013). However, a more recent systematic review, which included 150 studies, indicated a substantial link between low SES and disability. This review found that 81% of the studies appraised found significant association between low SES and increased rate of disability (Banks et al., 2017).

Women of low SES and therefore, their offspring, are particularly vulnerable of contracting HIV. A cross sectional study in a large sample of adults (n=14384) in South Africa found a high prevalence of HIV among low socioeconomic groups in general but women were particularly vulnerable (Wabiri and Taffa, 2013). Not only does coming from an environment of low SES put one at risk for contracting HIV, but HIV and acquired immune deficiency syndrome (AIDS) affect the wealth of a household, intensifying pre-existing deprivation thereby, creating a cycle of HIV and poverty (Bachmann and Booysen, 2003; Manomano and Selebogo, 2017; Omotoso and Koch, 2017).

Boivin et al. (2015) describes a complex mutual interaction between environment (SES), genetics and brain health and development (Figure 2.1). As described, HIV infects and affects the brain, especially the developing brain and in South Africa low SES and HIV have been complexly entangled together with a clear association between HIV infection and low SES (Gilbert and Walker, 2002; Johnson and Budlender, 2002; Tladi, 2006; Wabiri and Taffa, 2013). Individual genetics can influence HIV-expression (Lyman et al., 1990) and epigenetic changes have been associated with HIV (Yan, 2015). Therefore, Boivin et al.'s (2015) model can be adapted to incorporate HIV to illustrate the complex interactions of these factors in South Africa (Figure 2.2).

Consequently, despite some study limitations, it is apparent that low SES is a common factor in both disability/developmental delay and HIV. Therefore, in a group with similar SES, one could attempt comparing HIV and disability/developmental delay to each other.

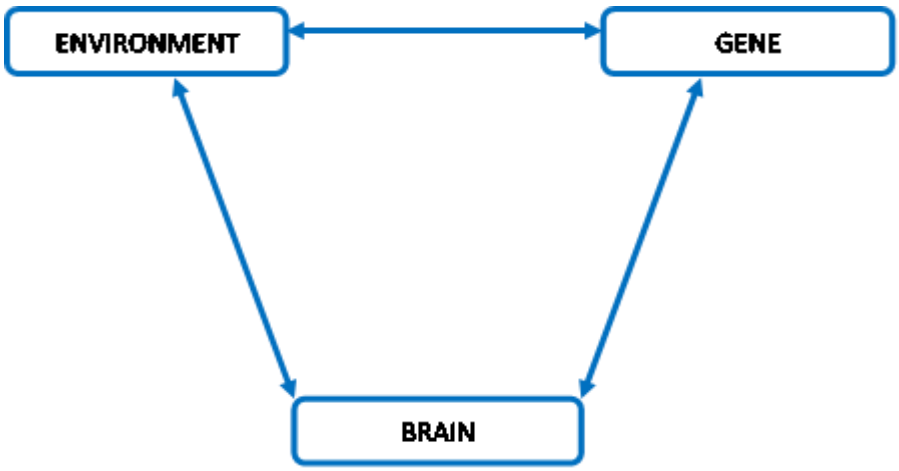

Figure 2.1: Boivin et al. (2015), p.159: Interaction between environment (SES), genetics and brain development/health

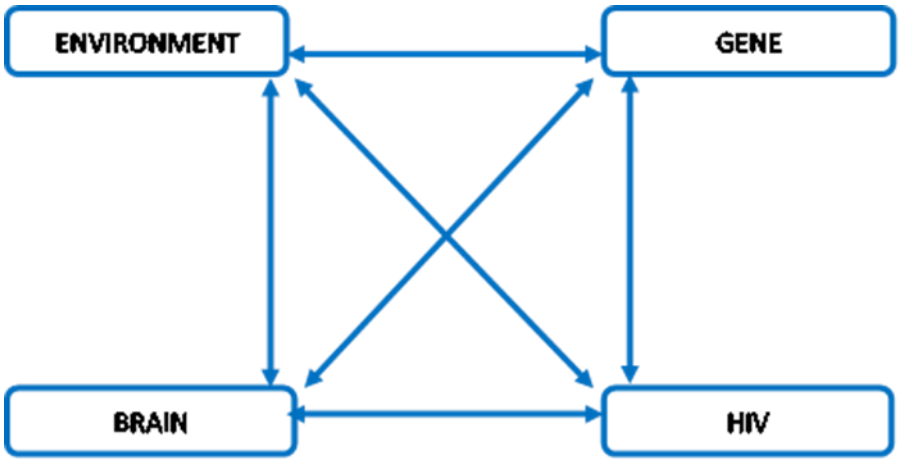

Figure 2.2: Mutual interaction between environment (SES), genetics, HIV and brain development/health.

2.4.3 Nutrition

Not only is malnutrition, stunting and wasting contributed to by socioeconomic and environmental factors (Brink et al., 2014; Keino et al., 2014; Said-Mohamed et al., 2015), there is a plethora of literature that have studied the links of nutrition, stunting and wasting with HIV and child development (Abubakar et al., 2009; Brink et al., 2014; Danaei et al., 2016; Eley and Nuttall, 2007; Jesson et al., 2015; McDonald et al., 2013; McGrath et al., 2012; Omoni et al., 2017; Said-Mohamed et al., 2015; Shead et al., 2010; Sherr et al., 2017). Studies have shown that underweight, undernourished, wasting or stunting can indicate current and/or future problems in motor and cognitive development (Abubakar et al., 2009; McDonald et al., 2013; Pollack et al., 1996). Underweight children are usually

identified using weight-for-age (WAZ) calculations, while stunting is defined by height-for-age (HAZ) and wasting is defined as BMI-for-age (BAZ). Any Z-score below -2 is considered stunted (HAZ), underweight (WAZ) or wasted (BAZ). The prevalence of malnutrition, stunting and wasting in children in South Africa is high (Brink et al., 2014; Said-Mohamed et al., 2015) but especially in those children infected with HIV (Bobat et al., 2001; H. Saloojee et al., 2007). Low WAZ has been found to have a prevalence of 10 – 57% in children with HIV (Jesson et al., 2015; Potterton et al., 2016; Seth et al., 2017; Sherr et al., 2017; Van Rie et al., 2008), while stunting has been identified in 18 – 59% of these children (Cames et al., 2017; McDonald et al., 2013; Seth et al., 2017; Sherr et al., 2017; Van Rie et al., 2008). Wasting has been noted in 6-47% of HIV-positive children (Cames et al., 2017; McDonald et al., 2013; Potterton et al., 2016). Additionally, the magnitude of this problem is reflected in the mean Z-scores for WAZ, HAZ & BAZ found in samples of children living with HIV. Mean WAZ Z-scores in these children have been found between -2.12 and -3.36 (Abubakar et al., 2009; H. Saloojee et al., 2007; Shead et al., 2010; Whitehead et al., 2014). H. Saloojee et al. (2007) found HAZ Z-score of -3.71 and ten years later Omoni et al. (2017) found a mean HAZ Z-scores of -2.38 in children living with HIV. The differences in the extent of wasting and stunting depend on rural versus urban locations (Bobat et al., 2001; Said-Mohamed et al., 2015; H. Saloojee et al., 2007) and earlier studies have a much more prevalent incidence of underweight, stunting and wasting (Shead et al., 2010; Van Rie et al., 2008), compared to later studies (Potterton et al., 2016). However, babies and younger children have much lower mean Z-scores than older children (Abubakar et al., 2009; Omoni et al., 2017; Shead et al., 2010; Whitehead et al., 2014). Unfortunately, recent research has found that ARV therapy make little difference in the prevalence of stunting, malnutrition and wasting (Jesson et al., 2015; Omoni et al., 2017; Seth et al., 2017; Sherr et al., 2017). Nutritional education of caregivers and health care workers as well as nutritional supplementation has been shown to affect growth in children living with HIV (Kelly and Coutts, 2000; Sunguya et al., 2013b, 2013a, 2014, 2017). As a result, the role of a dietician is vital in the team that manages a child with HIV (Abubakar et al., 2009; McDonald et al., 2013).

2.4.4 Orphanhood

Orphanhood has been associated with poor developmental outcomes but particularly in the arenas of mental and cognitive development and health. Early studies showed an association between poorer educational outcomes and orphanhood (Ardington and Leibbrandt, 2010; Beegle et al., 2006). In addition, although maternal death has a stronger negative effect on schooling outcomes, paternal death is associated with poorer socioeconomic status (Ardington and Leibbrandt, 2010; Beegle et al., 2006). In Southern Africa, many orphans are fostered by extended family rather than institutionalised (Ardington and Leibbrandt, 2010; Monasch and Boerma, 2004). This puts strain on the foster home's capital expenses (Deininger et al., 2003; Monasch and Boerma, 2004), affecting their SES. More

recently Sharp et al. (2015) reviewed 87 articles published later than 2005 on the mental health effects of AIDS orphanhood on HIV-negative children. A number of impairments were identified among the children including internalizing problems (anxiety, depression and post-traumatic stress), social functioning difficulties, school functioning problems and externalising problems such as; Attention Deficit Hyperactivity Disorder (ADHD), acting out, aggression, delinquency and risky sexual behaviours. In addition, this study agreed with Lowenthal et al. (2014) that orphan status is associated with high levels of stress. In an effort to control confounding factors the study excluded research on HIV-positive orphans, however, studies comparing cognitive scores of HIV-infected children and HIV-exposed but uninfected children found little difference between these the groups and hypothesized that this is due to the in utero exposure to HIV (Bagenda et al., 2006; Gay et al., 1995; Lazarus et al., 2015; Smith et al., 2012). The other studies, referenced above, found their study sample in a population where HIV was highly prevalent but did not control for orphanhood as a result of HIV or consider if the orphan was HIV-positive or negative. Therefore, an orphan who is HIV-exposed but uninfected may have cognitive and schooling difficulties due to in-utero exposure or orphan status or both. This makes attributing a child's mental and cognitive developmental health to orphan or HIV status difficult. Regardless of the source of a child's difficulty, an orphan with HIV is at a high risk of developing mental, cognitive and scholastic difficulties.

2.4.5 Opportunistic infections

Neurological damage with resultant developmental delay or functional impairments can be caused by HIV-related opportunistic infections such as TB, meningitis, CMV, toxoplasmosis, conjunctivitis and otitis media (Buriti et al., 2013; Donald et al., 2014; Ikoona et al., 2003; M'bongo Zindamoyen et al., 2013; Moschos et al., 2007). Thankfully, many of the opportunistic infections and other common childhood disorders are not as common as they were before the introduction of ARV therapy. But children who are HIV-infected are still at a higher risk of contracting these infections and the resultant sequelae (McAuley, 2014; Slyker, 2016). R. Govender et al. (2011) found that 15% of their cohort had prior CNS opportunistic infections. TB is particularly prevalent in children with HIV and is one of the most common causes of meningitis in children (Wolzak et al., 2012). Depending on the study setting, 5.8- 56% of children with TB are co-infected with HIV (Rabie et al., 2015). Moreover, latent HIV in monocytes can be reactivated by *mycobacterium tuberculosis* and managing co-infection can pose difficulties due to drug interactions (R. Govender et al., 2011). Tuberculosis meningitis (TBM) in particular has many complications that can result in mortality and disability including hydrocephalus, cerebrovascular disease and immune reconstitution inflammatory syndrome (IRIS) (van Toorn and Solomons, 2014). Tuberculomas of the CNS can also form resulting in death or disability (van Toorn and Solomons, 2014).

Despite CMV being less common due to the introduction of ART; children with delayed diagnosis and/or ARV treatment initiation are still at risk for contracting CMV. Adverse developmental outcomes associated with CMV include hearing loss, IRIS and poor neurocognitive development (Slyker, 2016). Congenital toxoplasmosis has a variety of manifestations, much of which is subclinical but it can cause life-long sequelae including chorioretinitis, strabismus, blindness, intracranial calcifications, hydrocephalus, microcephaly, jaundice, developmental delay, epilepsy and hearing impairment (McAuley, 2014).

Respiratory tract infections are common in children with HIV with lower respiratory tract infections (LRTI) and allergic rhinitis, the most prevalent (Donald et al., 2014; Graham, 2003; Linhar et al., 2014; Stokes and Tankersley, 2011; Zar, 2004). Both LRTI and allergic rhinitis easily become recurrent and chronic in children with HIV (Linhar et al., 2014; Stokes and Tankersley, 2011). These types of infections do not affect child development directly, however, they have secondary implications. An ill child is less likely to move and explore, they have a lower quality of life (Meltzer, 2001), decreased school attendance and secondary cognitive and behavioural fallout (Armstrong, 2006; Meltzer, 2001; Nixon et al., 2011). Conjunctivitis and otitis media can have a similar effect and are still incredibly common in children with HIV but will be discussed under “Vision” and “Hearing” respectively.

2.4.6 Antiretroviral Therapy

There is a plethora of research on the effects of ART, highlighting both positive and negative aspects. Early initiation in infants has been shown to improve virologic control, is more effective at limiting the size of the HIV reservoir in the CNS (Martínez-Bonet et al., 2015) and may curtail the advancement of HIVE along with ensuing disability and developmental delay (Bagenda et al., 2006; Benki-Nugent et al., 2015; Crowell et al., 2015; Innes et al., 2014; Kitahata et al., 2009; Laughton et al., 2013; Lilian et al., 2017; Lindsey et al., 2007; Penazzato et al., 2014; Ruel et al., 2012; Shiau et al., 2017; Violari et al., 2008). Consequently it is important to start ARV treatment at an early age to optimize developmental outcomes (Benki-Nugent et al., 2015). This was reflected in the National Consolidated Guidelines for the Prevention of Mother-to-Child Transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults 2015, which introduced “Immediate initiation of infant ART with first positive HIV PCR test, whilst waiting for confirmatory test results” and “provision of ART for all children under five years, regardless of their CD4 cell count or clinical staging” (South African National Department of Health, 2015, p. 15).

A study in Central Africa showed that although children under 24 months were enrolling at HIV clinics, only half of them were initiated on treatment (Adedimeji et al., 2017). If a child is not initiated on treatment he/she will not be able to reap the benefits of improved neurodevelopment. Benki-Nugent

et al. (2015) concluded that disease development, unsatisfactory response to ART and poor growth is associated with later milestone accomplishment in HIV-infected children. Furthermore, of neurodevelopment concern is a seemingly high virological failure rate in children (25.4%) when compared with adults (9.1%) who are on long term ART (Muri et al., 2017; Shiau et al., 2017) and the emergence of HIV drug resistance-associated mutation (HIV-DRM) in this population. Virological failure and the presence of HIV-DRM were found to be associated with younger age of cART initiation, treatment interruptions, female sex and non-nucleoside reverse transcriptase inhibitor regimes (Muri et al., 2017).

Other studies have shown, that while cART is effective at controlling immunological status, therefore, reducing opportunistic infections sequelae and improving survival it does not directly improve neurodevelopmental functioning (Crowell et al., 2015; Devendra et al., 2013; Lindsey et al., 2007; Sherr et al., 2017). This may be attributed to the CNS functioning as a reservoir for the HI-Virus and drugs not adequately penetrating the blood-brain-barrier (Crowell et al., 2015; Van den Hof et al., 2017). Antiretroviral therapy can cause its own functional impairments. Frequent adverse effects include; ototoxicity (Buriti et al., 2013; Thein et al., 2014), peripheral neuropathy (Peters et al., 2014), mitochondrial toxicity and IRIS (Donald et al., 2014). These disorders can influence motor control and/or sensory function which in turn will affect neurodevelopment and child development and consequently the development of new skills.

There is an abundance of research on peripheral neuropathy (PN) in adults with HIV. The prevalence of which is thought to be about 31% (Benevides et al., 2017). However, not much research has been done on PN in children. Studies have shown that distal sensory polyneuropathy in children is a potential side effect of stavudine based cART (Cherry et al., 2009; Peters et al., 2014; Sankhyan et al., 2015). A Peruvian study found a prevalence of 13% of PN in HIV-infected children (Esteban et al., 2008). In contrast, Peters et al. (2014) found that 28% of their cohort of 185 rural South African HIV-infected children had PN and a year later Benjamin et al. (2015) found a 36% prevalence in a cohort of urban South African children. In the Peruvian study the children were aged 18 months to 18 years, which is a large range and children often only start to present with PN at an older age because the risk is higher at this time (Cherry et al., 2009). The South African studies had age ranges of 5-14 years (Peters et al., 2014) and 4-10 years (Benjamin et al., 2015). Peters et al. (2014) and Benjamin et al. (2015) found that PN was underdiagnosed in their cohorts and recommended regular neurological and gross motor screening and assessments for this population. Physiotherapy has been shown to be beneficial in improving symptoms of PN (Tumusiime et al., 2015) and should be incorporated as early as possible into intervention strategies (Benjamin et al., 2015; Tumusiime et al., 2015).

In 2013, a review concluded that the data on the safety of ARV-therapy, in particular protease inhibitors, in HIV-infected pregnant woman are generally inconclusive and that the value of antiretroviral treatment substantially eclipses the side effects (Azria et al., 2013). However, more recently a study in Botswana showed that exposure to in-utero/maternal ART may have negative consequences on infant growth and development (Powis et al., 2016). There are insufficient studies focussing on the effect of ART exposure on long term health outcomes and growth in people with HIV (Locks et al., 2017). All of these findings need to be taken into account when providing supportive services.

2.5 Developmental Delay and Disability

With these multitudes of factors affecting development it is clear that a child infected with HIV is at risk for developing one or more disability. Nixon et al. (2011) anticipated that at a population level, in adults, disability will develop into an ordinary part of living with HIV. ARV treatment extends the lifetime of people living with HIV but they will experience oscillations of poor health, wellness and disability (Nixon et al., 2011). These sentiments are no less applicable to children. The nature of disability in children growing up with ART treated HIV tends to be subtle but the effect is still significant in a child's life (Potterton et al., 2016; Sherr et al., 2017) with many children experiencing a substantial loss of quality of life (Devendra et al., 2013; Sherr et al., 2017). However, many of the minor disabilities are overlooked by outpatient and inpatient settings as urgent medical concerns are often more of an immediate priority (Lowenthal et al., 2014).

The prevalence of developmental delay in infants and children with HIV is well documented. Outcomes of studies from developed countries do not necessarily apply to the developing-country context as it is a poorly-resourced environment with a high prevalence of poverty, opportunistic infections, malnutrition and culturally different child-rearing environments (Hilburn, Potterton and Stewart 2010). Developmental delay and early identification of HIV in infants in sub-Saharan Africa have been the topic of many papers. Some studies have explored a single disability related to HIV in children, including epilepsy, hearing impairment, language impairment, visual difficulties, behaviour and psychiatric disorders and neurocognitive impairment.

2.5.1 Epilepsy

Two studies on HIV and epilepsy took place in Cape Town. One study estimated that 11.5% of the children who were infected with HIV had an additional diagnosis of epilepsy (R. Govender et al., 2011) while two years later a more in-depth study estimated the occurrence of epilepsy in a hospital-based cohort to be 7.6% (Samia et al., 2013). The difference in prevalence may be due to the difference in sample sizes; 78 in R.Govender et al.'s (2011) study versus 354 in Samia and colleagues' 2013 study,

and the differences in definition of epilepsy (i.e. incidence of a seizure compared with a clinical diagnosis of epilepsy) and the fact that R.Govender et al. (2011) looked at outpatients while the other study examined inpatients. The studies were done at the same hospital only two years apart. Despite the differences, this is considerably higher than the prevalence of epilepsy among the general population of African children. A Tanzanian study estimated a 0.29% prevalence (Burton et al., 2012), while in Ghana the prevalence of epilepsy among the paediatric population is estimated to be 1% (Ae-Ngibise et al., 2015). A South African study on adults and children also fell into this bracket with a 0.7% prevalence (Wagner et al., 2014). Additionally, Samia et al. (2013) noted that children with disability and/or developmental delay were more common among children with both HIV and epilepsy, rather than HIV-infected children without epilepsy indicating that co-existing disabilities appear to be more common among HIV-positive children.

2.5.2 Hearing

Almost all of the studies focusing on the association between hearing impairment and HIV have found a high prevalence of hearing loss among children infected with HIV (Buriti et al., 2013; Christopher et al., 2013; Hrapcak et al., 2016; Khoza-Shangase and Turnbull, 2009; Makar et al., 2012; Palacios et al., 2008; Torre et al., 2012, 2015). Torre et al. (2012) found in their study in United States of America (USA), that 20% of HIV-positive children had hearing loss. In India they found that 32% of their sample had difficulty hearing (Makar et al., 2012). A study in Uganda identified hearing loss in 33% of their sample (Christopher et al., 2013) but in a more recent study in Malawi the prevalence of overall hearing loss in children with HIV was 24% (Hrapcak et al., 2016). The Indian study had a small sample group (n=67) which may account for the higher prevalence in comparison to the American (n=231) and Malawian (n=380) studies, but the Ugandan study had a large sample (n=370) too. These differences may be explained by differences in available ARV regimes as the Malawian study was conducted 3-4 years after the Indian and Ugandan study.

Conductive hearing loss in children with HIV has been attributed to both acute and chronic otitis media (opportunistic infection) (Hallbauer et al., 2014; Palacios et al., 2008; Tiedt et al., 2013; Torre et al., 2016) while sensorineural hearing loss is credited to HIV infection, opportunistic CNS infections (e.g. toxoplasmosis, CMV, TB and cryptococcosis) and ototoxic drugs (ART and TB antibiotics) (Harris et al., 2012; Khoza-Shangase, 2011; Khoza-Shangase and Turnbull, 2009; Thein et al., 2014). Aminoglycosides used in TB treatment are infamous for being ototoxic (Harris et al., 2012, 2012, Khoza-Shangase, 2011, 2013). Many children with HIV become infected with and are therefore, treated for TB. Similarly certain ART drugs and drug regimens are considered ototoxic (Harris et al., 2012; Khoza-Shangase, 2011; Thein et al., 2014). Buriti et al. (2013) found a significant association between hearing loss and ART use as well as hearing loss and otitis media. In the USA study most

hearing loss was of sensorineural origin (Torre et al., 2012), while the Malawian study found that most of the hearing loss was due to conductive shortcomings and it was hypothesised that this was due to frequent ear infections (Hrapcak et al., 2016). As the sample size was similar, this difference could be attributed to differences in ARV regimes or access to health care; there may have been a lack of identification and treatment of otitis media in Malawi.

It is clear that this population of children is at high risk for developing hearing difficulties with consequent speech and learning problems (Makar et al., 2012). Hrapcak et al. (2016) echoed Hallbauer et al. (2014) and Tiedt and colleagues' (2013) sentiments by noting that children with HIV and hearing loss were less likely to attend school, had less developed emotional and cognitive functioning and tended to exhibit other disabilities too.

Hence, many studies have recommended that audiologists and otolaryngologists need to be involved in the assessment and management of these children and that routine ototoxicity screening is an important part of that management (Christopher et al., 2013; Govender et al., 2015; Harris et al., 2012; Hrapcak et al., 2016; Khoza-Shangase and Turnbull, 2009). The Health Professions Council of South Africa (HPCSA) Early Hearing Detection and Intervention Programmes in South Africa Position Statement 2007 has recommended universal new-born screening in hospitals ("screening programmes should screen 95% of infants before discharge or before 1 month of age") and at Primary Health Care (PHC) Clinics ("Screening programmes should screen 95% of infants attending their 6-week immunisation visit") (HPCSA, 2007, p. 12). In addition, this document recommends a risk-based surveillance strategy to recognise acquired, late-onset, and progressive hearing loss as soon as possible. The HPCSA Position has published risk indicators which in addition to others include; HIV infection, parental or caregiver concern regarding hearing, speech, language, and/or developmental delay, postnatal infections associated with sensorineural hearing loss and recurrent or persistent otitis media. Yet, studies in South Africa have shown that although paediatric physicians are aware of the role of audiologists, there is a lack of awareness of all these risk factors set out by the HPCSA Position Statement 2007, including HIV and associated ototoxic drugs. Hence appropriate referrals are not materialising (Kanji and Kara, 2013; Khoza-Shangase et al., 2010; Khoza-Shangase and Jina, 2013). What is even more concerning is that a recent study in two provinces in South Africa identified that no PHC clinics were conducting formal hearing screening due to financial and personnel restraints (Petrocchi-Bartal and Khoza-Shangase, 2016).

2.5.3 Speech & Language

A study in Kenya looked at language development in very young children (8-15 months) and found significantly poorer language scores within the HIV-positive children (Alcock et al., 2016) which was in

keeping with findings of a South African study which found 45% of their cohort of under 12 month old children presented with a language delay (Whitehead et al., 2014). Baillieu and Potterton (2008) in a slightly older sample of HIV-infected children (18-30 months) found that 82.5% of their sample had global language delay which is reflected in Van Rie et al.'s (2008) result (85% of their sample had delayed language expression and 77% had delayed language comprehension). However, this study was looking at the neurodevelopment of HIV-positive preschool-aged children in the Democratic Republic of Congo (DRC). Another study of much older children 9-16 years concluded that HIV-positive children had poor language ability (Brackis-Cott et al., 2009). It seems prudent to conclude that children living with HIV have a higher risk of having poor or delayed language development that begins in early development and carries through into high school and possibly even adulthood. Optimistically, Whitehead et al. (2014) implied that the number of HIV-positive children presenting with a language delay at less than 12 months decreased at a follow-up six months later. These outcomes were attributed to the increased access infants now have to ARV-therapy. However, this study had only 27 participants, while the other studies had between 206 and 262 participants (Alcock et al., 2016; Brackis-Cott et al., 2009) with the exception of Baillieu and Potterton (2008) who had a sample of 40 children.

The South African Speech-Language-Hearing Association (SASLHA) has published guidelines regarding optimal early communication intervention. The SASLHA has identified neonatal care units, postnatal wards, PHC clinics and facilities, nursery schools, day care facilities and pre-schools at optimal assessment and intervention locations (Bardien et al., 2011). Hattam et al. (2014) identified 203 candidates for early communication intervention at a Gauteng HIV outreach clinic, however, only 1 child (0.5%) had been referred to a speech and language therapist (SLT). This low referral rate was attributed to a lack of knowledge of the clinic doctors regarding current literature about communication disability risk factors and the importance of an SLTs role in treating children infected with HIV.

2.5.4 Vision

There are many ocular manifestations of HIV which can involve all parts of the eye and ocular adnexae and are mainly attributed to opportunistic infections (P. Govender et al., 2011, p. 2; R. Govender et al., 2011; Rutar et al., 2015). The prevalence of ocular manifestations is reported in 50 to 100% of adults infected with HIV (Govender et al., 2010; Ikoona et al., 2003). In children, however, this prevalence is much lower, sitting at 23%-67% (R. Govender et al., 2011; Ikoona et al., 2003; Kestelyn et al., 2000; M'bongo Zindamoyen et al., 2013; Padhani et al., 2000; Rutar et al., 2015). Padhani et al. (2000) found that children who were HIV-positive have a 10% prevalence of atypical visual acuity when matched with HIV exposed but uninfected children and Rutar et al. (2015) found a high prevalence

(18%) of strabismus in a cohort of 22 HIV-infected children on cART, while there was no significant difference in prevalence of other "vision-threatening" diseases (Rutar et al., 2015). This is interesting as other studies stated the following as the most common paediatric ocular manifestations; conjunctivitis (12-13%) (Ikoona et al., 2003; M'bongo Zindamoyen et al., 2013), perivasculitis (3-38%) (Ikoona et al., 2003; Kestelyn et al., 2000; M'bongo Zindamoyen et al., 2013), keratoconjuctivitis sicca (dry eye syndrome) (3- 9%) (M'bongo Zindamoyen et al., 2013; Rutar et al., 2015) and molluscum contagiosum (6 – 12%) (Ikoona et al., 2003; M'bongo Zindamoyen et al., 2013) all of which can affect vision. Rutar et al. (2015) conducted their study in the USA while the other studies were conducted in developing countries in Africa. Additionally, these findings may be attributed to the fact that Rutar et al. (2015) had a cohort of twenty-two while the other studies ranged from 109 – 208 participants and may be more statistically significant. However, many of the Africa-based studies noted that vitamin A deficiency in their study communities may be contributing to their higher prevalence of affected vision (Ikoona et al., 2003; Kestelyn et al., 2000; Padhani et al., 2000).

Padhani et al. (2000) reflected that the lower prevalence of ocular manifestation in children compared with adults may be as a result of difficulties of diagnosis in small children while Kestelyn et al. (2000) considered it a result of survival bias.

For many years visual difficulties have been associated with learning problems (Kurtz, 2006; Paranjpe et al., 2016) and preschool visual screening has long been recommended (Newman et al., 1996). This is reflected in HPCSA's Minimum Standards for Child Health Care and the South African Integrated School Health Policy which requires vision screening for all ages, but particularly pre-school children (DOH and DOBE, 2013; HPCSA, 2017). HIV-related opportunistic infections, such as conjunctivitis can have an impact on a child's school performance. A recent Indian study found a high prevalence of conjunctivitis in a group of children with low school grades (Paranjpe et al., 2016) and identified that these children had concentration problems. Another study found a significant association between conjunctivitis and migraines in children (Wang et al., 2016), which could affect learning. Not only can conjunctivitis cause temporary and/or permanent damage causing visual impairment, but prolonged and/or repetitive use of corticosteroid treatment of chronic conjunctivitis can cause cataracts and glaucoma (Sheppard et al., 2016). Therefore, children infected with HIV are at a much higher risk of temporary and/or permanent vision impairing conditions that will affect their academic learning potential and participation in daily life.

2.5.5 Behaviour & Mental Health

Detection of behaviour and psychiatric problems at a very young age is difficult (Donald et al., 2014; Mwaba et al., 2015). Behaviour challenges and cognitive fallout are often only detected at school age

and by then opportunities for early intervention are missed (Mwaba et al., 2015). It is thought that neurobehavioural problems occur in 61-81% of children with HIV (R. Govender et al., 2011; Grover et al., 2007) while these problems manifest in only 18% of the children in a control group (Grover et al., 2007). ADHD is a reported common behavioural problem, with 14-20% of infected children reaching cut-off scores for ADHD (Donald et al., 2014; R. Govender et al., 2011; Nozyce et al., 2006) while 30% had mild to moderate hyperactivity. When compared with the general population, in which ADHD is prevalent in 8.6% of the children (R. Govender et al., 2011) it can be deduced that HIV-positive children have an increased susceptibility for developing ADHD.

In addition many children fall into the mild-moderate range for neurobehavioural and psychiatric problems, with parents reporting socio-emotional problems, depression, sub-scale lethargy and social withdrawal in their children (Donald et al., 2014; R. Govender et al., 2011; Grover et al., 2007). Proposed aetiologies for these problems include direct infection and the effect of HIV on the frontal cortices and basal ganglia (R. Govender et al., 2011). However, Grover et al. (2007) proposed that the causes are of a multifactorial nature which are secondary to HIV and attributed to external factors including multiple medical and psychological stresses due to chronic illness, prenatal drug exposure, family environment, age of parents, level of parent education, parental absence, changes in caregivers, nutrition and poverty. This is in line with the psychological stressors that adolescents with HIV experience described in Lowenthal et al.'s (2014) review and Sherr et al.'s (2014) study. Lowenthal et al. (2014) described how children and adolescents with vertically contracted HIV experience cumulative and recurrent stressors such as family (parent & sibling) deaths, financial and care responsibility for younger siblings and/or ill family members, discrimination, stigma, fear of being "abnormal," fear of illness and morbidity, dealing with morality and an uncertain future. Additionally, Sherr et al. (2014) found negative effects of parent and/or adult HIV on children. Furthermore, orphan status has been shown to have its own risk factors for developmental health issues including psychological distress, loss of educational opportunities and impoverishment (Lowenthal et al., 2014; Sharp et al., 2015; Sherr et al., 2014). As a result of these multitude of risk factors for behaviour and mental health impairment, preventative and supportive psychological intervention for children with HIV is vital (Grover et al., 2007; Lowenthal et al., 2014; Sherr et al., 2014a, 2017).

2.5.6 Neurocognition

Many studies have shown that children infected with HIV are vulnerable to neurocognitive delay and fallout from an early age (Amzel et al., 2013; Hoare et al., 2016; Phillips et al., 2016; Sherr et al., 2009, 2014b, 2017). Early studies showed that infected infants (3-24 months) attained low Mental Scores on the Bayley Scales of Infant Development (BSID) when compared to their exposed but uninfected peers. However, both groups became progressively delayed over time (Gay et al., 1995). A Cape Town pilot

study researched neurocognitive function in children 0-13 years using a variety of measurement tools. They observed significant neurocognitive deficits in children with HIV which remained static despite the initiation of cART (Smith et al., 2008). A more recent study found neurocognitive disorders in 46% of their HIV cohort (Phillips et al., 2016) while another study found HIV-positive children between the ages of 4-13 years to have considerable neurocognitive delay (Sherr et al., 2017). Other studies describe more subtle and specific impairments that involved processing speed, simultaneous and sequential processing, planning, perceptual reasoning, visual reaction times, visio-spatial and motor integration, memory insufficiency and adaptive domains in older children infected with HIV (Bamford and Lyall, 2015; Donald et al., 2014; Hoare et al., 2016; Koekkoek et al., 2008; Phillips et al., 2016; Potterton et al., 2016; Ruel et al., 2012; Smith et al., 2012).

While literature agrees on the presence of neurocognitive delay and disability in children with HIV when compared to their uninfected peers (Sherr et al., 2014b, 2017), there are differing opinions as to the relationship between the HI-virus, neurocognition, and the effect, if any, that cART has on the development of neurocognition. Studies show that early cART initiation and subsequent virologic suppression is associated with improved neurocognitive outcomes later on in childhood (Crowell et al., 2015). This could indicate an association between HIV infection with subsequent encephalopathy of the CNS and neurocognitive function. However, one study did not find any difference in IQ scores in HIV-positive children when compared to their uninfected peers (Lazarus et al., 2015) and other studies compared pre-cART and post-cART neurocognitive scores and found no significant improvement (Sherr et al., 2017; Smith et al., 2012). A further study found no significant difference in neurocognitive scores between children infected with HIV, children exposed but uninfected and HIV naïve children (Bagenda et al., 2006). This could indicate that symptoms are due to in utero changes in the brain's anatomy and function as a result of being exposed (Jankiewicz et al., 2017). Smith et al. (2008) and Bagenda et al. (2006) executed their research in South Africa and Uganda respectively, while the other studies were based in the USA (Crowell et al., 2015; Lazarus et al., 2015; Smith et al., 2012). The studies which found no significant association between ART and improved neurocognition supported other literature showing links between poor cognitive development and poor nutrition, changes in home and family structure due to HIV related disease among caregivers, poor socioeconomic status and low level of maternal education (Bagenda et al., 2006; Boyede et al., 2013; Mwaba et al., 2015; Potterton et al., 2016; Ruel et al., 2012; Smith et al., 2008).

The fact that the CNS acts as a reservoir for HIV and there are limitations of ARV-therapy crossing the blood-brain barrier are two factors that could contribute to the lack of changes in cognitive development despite ARV treatment (Crowell et al., 2015; Fois and Brew, 2015; Van den Hof et al., 2017). Other proposed reasons for the differences in outcome of the studies may be cross sectional

design with limited longitudinal follow-up and lack of control groups (Crowell et al., 2015; Lazarus et al., 2015; Smith et al., 2008) or differences in outcome measures. The USA studies used the Wechsler Intelligence Scale for Children (WISC) (Crowell et al., 2015; Lazarus et al., 2015; Smith et al., 2012), while one of the African studies used the Kaufman Assessment Battery for Children (K-ABC) (Bagenda et al., 2006) and the other used a variety of measures including the Griffiths Scales of Mental Development (GSMD) (Smith et al., 2008). Regardless of etiology, children infected with HIV are vulnerable to neurocognitive problems, especially those that come from depressed socioeconomic backgrounds and early preventative therapy could be vital in minimising the risk of later neurocognitive complications (Sherr et al., 2017; Smith et al., 2012).

2.5.7 Neurodevelopment & Child Development

It is convenient for researchers, specialists and practitioners to look at child development in different categories such as cognition, motor development, speech development, behaviour etc. But a child does not develop in different boxes, each area develops simultaneously. All neurological systems are connected with the brain as the coordinator (Thelen, 1995). Therefore, ideally, one needs to look at development as a whole, rather than in separate fragments (Couper, 2016; Thelen, 1995). In addition, milestones and "stages of development" are based on "normal development" of children with an unharmed brain. A child perinatally exposed and infected with HIV does not have an intact, "normal" brain due to the contamination of the brain tissue with HIV (Jankiewicz et al., 2017; Schwartz et al., 2007; Seth and Major, 2005). Therefore, their development will not be that of a child with an intact CNS (Armstrong, 2006; Jankiewicz et al., 2017; Maes, 2016; Sherr et al., 2017). This concept is reflected in the plethora of studies that have researched development as a whole in children infected with HIV (Abubakar et al., 2008; Baillieu and Potterton, 2008; Jelsma et al., 2011; Kandawasvika et al., 2011; Laughton et al., 2013; Lowick et al., 2012; Mwaba et al., 2015; Potterton et al., 2009, 2016; Ruel et al., 2012; Shead et al., 2010; Van Rie et al., 2007, 2008; Whitehead et al., 2014). Many of these studies have been done on very young children and as HIV has become a chronic disease it is important to look at how older children are developing and what kind of quality of life they experience.

Only a few studies were identified that explored a range of developmental domains in an older cohort of children infected with HIV. Van Rie et al. (2008) looked at the neurodevelopment of HIV-positive children aged 1.5 -6 years in the DRC and found 29% of the cohort had gross motor delays, 60% had severe cognitive function delay, 85% had delayed language expression and 77% had delayed language comprehension. Although their control group was made up of five girls and five boys for every six month age category (n=90) their case cohort was still small (n=35), which did not allow for logistic regression analysis. Lowick et al. (2012) assessed development in a small (n=30) cohort of HIV-positive children of five and six years of age from Soweto, South Africa and found a 83.4% prevalence of severe

delay in the HIV-infected children, compared with the children in the control group which had a prevalence of developmental delay of 53.3%. Ruel et al. (2012) had a larger sample (cohort: n=93; control: n=106) from Uganda, and agreed with the findings of other studies that HIV-infected children had substantial motor and cognitive insufficiencies. More recently, Potterton et al. (2016) looked at a cohort (n=68) of children 3-5 years old at an urban research facility in Johannesburg. They found overall developmental delay in 55.8% of their cohort. Both Potterton et al. (2016) and Lowick et al. (2012) had very similar cohorts. Both studies used the same measurement tool and found a similar distribution of delay where hearing and speech domains were most affected and personal-social domains were the least involved (Potterton et al., 2016). Interestingly, Van Rie et al. (2008) and Ruel et al.'s (2012) studies used ART-naive HIV-infected children while Lowick et al. (Lowick et al., 2012) and Potterton et al. (2016) used children already initiated on ART. All four studies found significant developmental delay in children infected with HIV. However, Potterton at al.'s (2016) results, although still significantly high, were much lower than the prevalence in Lowick and colleague's (2012) study. This was attributed to better access and earlier ART initiation in the later study (Potterton et al., 2016). Lowick et al. (2012) and Potterton et al. (2016) both used the GSMD while Ruel et al. (2012) used K-ABC and Bruininks-Oseretsky Test for Motor Proficiency and Van Rie et al. (2008) used a variety of other assessment tools. It is therefore, more straightforward to compare Potterton et al. (2016) and Lowick et al. (2012) studies to each other than to the other studies.

Only two studies were identified that explored a range of disability in an older urban cohort of children infected with HIV. R.Govender et al. (2011) found abnormal neurology in 59% of a group of 78 children in Cape Town (23% had visual impairments, 6.4% had hearing impairments, 11.5% had epilepsy, 5% had peripheral neuropathy and 61% were found to have neurobehavioural problems). While Devendra et al. (2013) took a more statistically significant cohort of children (n=296) for a case controlled study in Malawi and found 33% of their cases screened positive for disability (6% reported visual impairments, 36% had hearing impairments, 6% experienced seizures, 33% had physical disability, 53% had cognition impairment and 46% reported communication difficulties). The difference in prevalence of disability between these two cohorts may be due to sample size, differences in measurement tools and that Devendra et al. (2013) used a control group whereas R.Govender et al. (2011) did not. The Cape Town study had a larger percentage of ART-naïve participants (14%) compared to the Malawian study (7%) which may account for why the prevalence was higher in R.Govender et al.'s (2011) study.

Interestingly in the Cape Town study only 6.4% had hearing impairments and 23% had visual impairments but in the Malawian study only 6% had visual impairments but 36% had hearing loss. This may be due to more participants being on ART in the Devendra et al. (2013) study and therefore,

increased likelihood of ototoxicity. It may be due to the different locations of the studies, where different environments may have different risk factors for hearing and visual problems or different settings have different resources and education focused on hearing and visual impairments. In addition, there were differences in measurement tools or definitions/categorization of hearing and visual impairment may have differed between studies.

Govender et al. (2011) focused solely on impairment but did not indicate how many of the children had single or co-existing disabilities. Of the 33% that screened positive for disability in Malawi, 49% had a single disability, 29% had two co-existing types of disability and 22% had three or more different coexisting types of disability. This reaffirms findings of other authors researching a specific impairment who found that multiple or co-existing disability and developmental delay was more common in children with HIV. Disability was more common in children with HIV and epilepsy (rather than epilepsy without HIV) (Samia et al., 2013), Smith et al. (2008) concluded that receptive and expressive language delay in HIV-infected children is a good predictor of academic failure and consequently hearing impairment was associated with language and cognitive fallout (Hallbauer et al., 2014; Hrapcak et al., 2016; Tiedt et al., 2013).

A systematic review can give a comprehensive overview of the association between a variety of disabilities and HIV, yet, only three systematic reviews on paediatric disability were identified which included studies from sub-Saharan Africa. One study concluded that motor development and sensorimotor skills were most affected but there were contradicting data regarding intellectual ability (Abubakar et al., 2008). Unfortunately, this review only included six articles and therefore, a definitive conclusion cannot be drawn. Another study reviewed 21 articles of which seven (33%) had been conducted in Sub-Saharan Africa and concluded that children infected with HIV are at a high risk for impairment, particularly cognitive difficulties and that this population needs to be monitored carefully and specific education and intervention strategies need to be put in place (Sherr et al., 2014a). Banks et al. (2015) appraised 61 published articles between 1995 and 2013, of which 16 studies were on infants and children, to determine the relationship between HIV and the prevalence of disability in sub-Saharan Africa. Four of the sixteen articles reviewed had also been systematically reviewed in Sherr et al. (2014) and three different articles had been evaluated in Abubakar et al. (2008). The study concluded that disability is strongly associated with HIV infection and is common in sub-Saharan Africa. Regrettably many of the studies appraised in Abubakar et al. (2008), Sherr et al. (2014) and Banks et al. (2015) have very small study samples (n <300), when compared with the population (more than three million HIV-infected children living in sub-Saharan Africa (Donald et al., 2015)), which makes it difficult to draw conclusions of association and impact as results were not always statistically significant. The reasons provided in the reviews for small study samples were, loss to follow-up and

time consuming measurement tools. It is clear that there is a significant lack of studies, as many of the reviews had overlapping literature and a lack of longitudinal follow-up studies. Much of the literature found, consisted of cross sectional studies and occasional case controlled studies but of a cross sectional nature.

2.6 Measurement Tools

There is a surprising lack of congruency among the studies regarding the choice of outcome measurement tools for development and disability in children with HIV. This may be accredited to the fact that measurement tools are generally designed for specific age bands. There is not one tool that can be used from birth to adolescence and so studies identify tools that will be most applicable to the age band they are studying. Table 8.2 (Appendix 2) is a list of developmental, cognitive, behavioural and communication outcome measurement tools among the studies reviewed. Some studies choose to use screening tools while others use full assessment outcome measures.

2.6.1 Assessment Tools

The BSID I, II and III appear to be the most commonly used in South African studies on HIV-positive children followed by the Griffiths Scales of Mental Development. The Wechsler Intelligence Scale for Children (WISC) III and IV edition have been commonly used in research but typically in resource-rich countries.

The BSID is a norm referenced, descriptive test and was originally published in 1969 (Connolly et al., 2013; Lennon et al., 2008), reviewed in 1993 (BSID-II) and again in 2006 (Bayley Scales of Infant and Toddler Development BSITD-III) (Lennon et al., 2008). Its aim is to measure developmental functioning under the domains of cognition, language, social-emotional, motor behaviour and adaptive behaviour (Lennon et al., 2008) and is for ages 1-42 months. It has been standardised in South Africa although black African infants tend to perform better on the Bayley-III than its norms which were developed in the USA (Rademeyer and Jacklin, 2013). There has been international criticism as there appears to be a lack of consistency between the BSID-II and the BSITD-III (Acton et al., 2011; Ballot et al., 2012; Campbell et al., 2013; Connolly et al., 2013; Reuner et al., 2013). Campbell and colleagues (2013) advised that children scoring less than average on the BSITD-III at an early age should be monitored carefully and followed up if need be. All editions of the BSID are standardised for children up to 42 months. It is therefore, not suitable for evaluation of children older than three and a half years old.

The GSMD have a slightly larger age range from one month to five years and 11 months, however, norms were developed on British children and norms for South African children have still not been developed (Amod et al., 2007; Jacobs, 2016; Laughton et al., 2010). Yet, the GSMD has been used and

researched in South Africa (Amod et al., 2007; Jacobs, 2016; Laughton et al., 2010, 2013; Lowick et al., 2012; Luiz et al., 2001; Potterton et al., 2016; Smith et al., 2008).

The BSITD-III included children with mental, physical, or behavioural difficulties as 10% of their standardization sample (Albers and Grieve, 2007). Conversely, the BSID-II and the GSMD are based on norms of a healthy population of children (Cromwell et al., 2014). As described above, due to the neurotrophic nature of HIV and considering it is infecting a developing brain, these children will never develop according to "the norm" (Armstrong, 2006; Maes, 2016). Therefore, this needs to be taken into account when assessing HIV-infected children with healthy norm referenced outcome measurement tools.

The BSID and GSMD along with many of the other tools are time consuming (Spittle et al., 2008). They are used both as a research tool and as clinical assessment tools, but as the assessment takes between 45minutes and an hour. This makes it difficult to use routinely in clinical practice, especially with limited staff resources, undertrained employees and busy clinics. Many of the other tools described in Table 2.3 have not been validated for South Africa and lack concurrent validity with each other (Spittle et al., 2008; Tieman et al., 2005). As a result there is a lack of consistency between studies which means it is difficult to explicitly compare studies.

2.6.2 Screening Tools

Screening tools are more efficient and affordable for clinical use in busy and overburdened facilities. In 2010 the new South African "Road to Health Booklet" was introduced and contains the only nationally implemented developmental screening tool in South Africa. The booklet contains a checklist focusing on development of children from 14 weeks to 18 months with a few questions for children three years and 5-6 years old. However, this booklet has been found to be ineffective at identifying children at risk for developmental delay and disability and gives limited indication for referral if problems are identified (Jonker and Stellenberg, 2014; van der Linde et al., 2015). In addition studies have found that the booklet is underused and clinic staff do not possess the knowledge in which to utilise or interpret the booklet correctly (Cloete et al., 2013; Jonker and Stellenberg, 2014; Tarwa and De Villiers, 2007).

Two screening tools have been developed in South Africa focusing on the developmental health of children with HIV. The Infant Gross Motor Screening Test (IGMST) was developed in Gauteng to evaluate gross motor function in HIV-infected infants from six to 18 months old and published in 2010 (Hilburn et al., 2011). Preliminary testing suggested excellent psychometric properties (Hilburn et al., 2011). The other screening tool was developed and validated in the Western Cape. It is the Red Cross War Memorial Children's Hospital (RCWMCH) Developmental Screening tool and is an excellent

adjunct to the IGMST as it is designed to screen children between the ages of nine to 36 months for moderate to severe developmental delay (Boyede et al., 2016, 2015). This tool has acceptable psychometric properties, as it has a high sensitivity but low specificity (Boyede et al., 2015). Currently there are no HIV-specific screening tools that have been developed for children with HIV who are older than three years.

Many studies recommended the WHO Ten Question Screen for Disability (WHO TQSD) as a much less time-consuming tool to screen for any developmental delays and/or disabilities in a child, older than two years, may be experiencing (Belmont, 1984; Christianson et al., 2002; Couper, 2002; Devendra et al., 2013; Durkin et al., 1994, 1995; Gottlieb et al., 2009; Ibrahim and Bhutta, 2013; Muga, 2003; Mung'ala-Odera et al., 2006; Singhi et al., 2007; Stein et al., 1986; Thorburn et al., 1992; Zaman et al., 1990). The WHO TQSD is an internationally validated screening tool for resource-poor settings used to identify disability in a child, 2-9 years old. This is completed by asking the caregiver to compare their child's functional ability to his or her peers in a number of domains, including developmental milestones, speech, hearing, vision, seizures, learning and comprehension (Devendra et al., 2013; Gottlieb et al., 2009). The TQSD is freely available and a quickly administered tool for disability screening and has been used in developing countries around the world (Christianson et al., 2002; Couper, 2002; Devendra et al., 2013; Durkin et al., 1994; Gottlieb et al., 2009; Ibrahim and Bhutta, 2013; Muga, 2003; Mung'ala-Odera et al., 2006; Singhi et al., 2007; Thorburn et al., 1992; Zaman et al., 1990). It is strictly a screening tool and not a diagnostic tool (Durkin et al., 1994; Gottlieb et al., 2009) and has successfully been used to screen populations of HIV-infected children (Devendra et al., 2013). It has a high sensitivity (80-100%) for profound developmental disabilities (Durkin et al., 1994; Singhi et al., 2007), however, it has demonstrated a high false positive for cognitive impairments (Thorburn et al., 1992) and visual and hearing impairments (Durkin et al., 1995; Singhi et al., 2007), especially those on the milder spectrum, resulting in over-referral. Nevertheless studies have shown that the children with false positives had milder problems, such as ear infections and benefited from the referral and subsequent treatment (Singhi et al., 2007; Zaman et al., 1990).

2.7 Services

As discussed, the majority of children infected with HIV have a different developmental trajectory from a typical child and as a result are vulnerable to a variety of disabilities. The presentation of HIV in a developing child evolves and can often be unpredictable and multi-systems based (Banks et al., 2015). In addition, in the South African context, most of these children hail from resource-poor settings and therefore, the "layering-effect" plays a role in their development too. In 2011, Nixon and colleagues predicted that in Sub-Saharan Africa HIV-related disabilities in low socioeconomic

backgrounds will be more “acutely disabling” due to limited access to rehabilitation and chronic health care services.

The Children’s Act 38 of 2005 stipulates provision of necessary support services for children with difficulties or chronic illness. Evidently there is a need for evolving, appropriate and accessible preventative and supportive services as well as appropriate and efficient referral protocols for children infected with HIV. Many studies have echoed these sentiments in recommending comprehensive neurological and neurocognitive assessments (Banks et al., 2015; Devendra et al., 2013; Govender et al., 2011; Hilburn, Potterton & Stewart 2010), improved screening and early identification tools (Hilburn et al., 2011; Hrapcak et al., 2016; Kandawasvika et al., 2011), growth monitoring (Isanaka et al., 2009), nutritional assessment and management (Abubakar et al., 2009; Eley and Nuttall, 2007), education support (Kathard et al., 2011; Sherr et al., 2014b; Wium and Louw, 2013) and psychological support and interventions (Grover et al., 2007; Lowenthal et al., 2014; Sherr et al., 2014b). Physiotherapy, occupational therapy and speech and language therapy have been shown to be important in supporting child development as well as in the management of HIV (Chetty and Hanass-Hancock, 2016; Cobbing et al., 2013; Hattam et al., 2014; Joubert, 2010; Lecuona et al., 2016; Maddocks et al., 2018; Potterton et al., 2016; van Jaarsveld, 2014).

More than 20 years ago a model was developed by Armstrong and Horn (1996) which has implications for the management of children with chronic illness (Armstrong, 2006). This model is especially applicable to children growing up with HIV, because a child’s neurodevelopment and consequently child development can be compromised by HIV infection. Armstrong and Horn (1996) recommended that the assessment of neurocognitive function must be repeated over time as new domains of specific difficulty or impairment will be found at several points in time across a child’s life (Armstrong, 2006). This concept does not only need to be applied to cognitive function but all neurological development, activity and participation function including gross and fine motor, speech, hearing, vision etc. These reoccurring impairments are not necessarily part of a process of new injury but rather a failure of the brain to develop in order to support specific functional abilities at the anticipated time. This neurodevelopmental model recommends that the ideal opportunity for developmental habilitation and mediation is not when deficits are detected but in expectancy of their occurring (Armstrong, 2006; Boivin et al., 2015).

However, despite multitudes of recommendations and appropriate referral, these services seem not to be widely available to this population of children and adolescents. Many other studies have lamented the lack of available services in sub-Saharan Africa (Banks et al., 2015; Chetty and Hanass-Hancock, 2015; Cobbing et al., 2014; Donald et al., 2014; R. Govender et al., 2011; Govender et al.,

2015; Grover et al., 2007; Hilburn et al., 2010, 2011, 2015; Hrapcak et al., 2016; Kandawasvika et al., 2011; Lowenthal et al., 2014; Nixon et al., 2011). Other studies have highlighted the failings of South African Health Services to provide adequate early detection, surveillance and developmental screening (Chetty and Hanass-Hancock, 2015; Department of Social Development et al., 2012; Fick, 2017; Jonker and Stellenberg, 2014; Saloojee and Bamford, 2006) and further studies have identified a lack of referral to these services (Devendra et al., 2013; Hattam et al., 2014; Maddocks et al., 2018). Devendra et al. (2013) sought to identify the requirements, opportunities and barriers for rehabilitation in children with HIV in Malawi. The study found that 67% of the cases identified with a disability had never attended any rehabilitative service, many of these cases had never been referred and those that had been referred reported distance and transport costs as a barrier to accessing services.

In addition, Chetty and Hanass-Hancock (2016) have recognised the need for South African rehabilitation services to evolve in response to the "era of HIV as a chronic disease" (Chetty and Hanass-Hancock, 2016, p. 132). In an effort to overcome environmental constraints, fiscal challenges, and institutional limitations, they propose the Chetty Model

Concomitant political, social and financial commitment is needed across many sectors to enable HIV services to respond to the evolving all-encompassing needs of a developing HIV-infected child and to be able to provide these holistic services at a community, clinical and policy level. (Banks et al., 2015; Boivin et al., 2015; Donald et al., 2014, 2015; Nixon et al., 2011).

2.8 Conclusion

HIV has become a chronic condition. Children living in South Africa, who are infected with HIV have a higher risk of developing mild to severe impairments in all spheres of development. Whether these impairments are due to the primary neurotrophic characteristics of HIV or secondary due to opportunistic infections, treatment side effects, socioeconomic status or other social or clinical factors, these children are vulnerable to developing not one but many different impairments that can affect function, participation and achievement throughout their life. Despite a multitude of recommendations regarding early and continual identification of developmental delay, varied neurodevelopmental trajectories and disability, appropriate referral and support services are often not available to this population. In addition, there are no HIV-specific screening tools to help identify developmental problems in children infected with HIV who are older than three years old. Furthermore, there is a need for more robust, longitudinal studies on children who are HIV-positive to support protocols and policy makers to assist with improving identification of disability, referral processes and access to services.

CHAPTER 3

3. METHODS

This chapter will discuss the locations of the study, ethical considerations, study design, subjects, materials and measurements, the procedures used to collect data, and data analysis.

3.1 Location

Rahima Moosa Mother and Child Hospital (RMMCH) is a government (Gauteng Provincial Government, 2017a) and academic hospital (University of the Witwatersrand, 2017) located in Coronationville in Johannesburg. It has a large, Gauteng, catchment area comprising of City of Johannesburg Metropolitan Municipality and parts of the West Rand and Sedibeng District Municipalities. RMMCH provides a range of services and care. Over and above emergency services and inpatient care, outpatient services include child psychiatry/psychology, dental, dietetics, ENT/respiratory clinic, neurodevelopmental clinics, obstetrics and gynaecology, occupational therapy, orthopaedics, pharmacy, physiotherapy, podiatry, radiology/radiography, social work and speech and language therapy (Boraine, 2017; Gauteng Provincial Government, 2017a; Rose, 2017; Wikipedia and Conlinp, 2018). In addition RMMCH hosts Empilweni Services and Research Unit (ESRU)(ESRU, 2018a), which provides outpatient care and treatment to children living with HIV. ESRU was the location for this study.

ESRU is one of the largest paediatric HIV treatment clinics in the Gauteng province and in South Africa with over 1600 children in active follow-up. The service division of ESRU offers outpatient care to children ranging from infants to adolescents who are HIV exposed (infected and uninfected). The clinic is open four days a week where children receive regular care services including medical management (nurses and doctors) and adherence counselling. A dietician and social worker are available at the clinic for referrals and children can be referred to the RMMCH inpatient or outpatient services or external services, such as primary health care facilities, other tertiary facilities (e.g. Helen Joseph Hospital) (Gauteng Provincial Government, 2017b) or specialist services such as victim support units (The Teddy Bear Clinic, 2018). The research division of ESRU provides a platform for researches to conduct studies at ESRU and have access to their data bases and patients. As a result, much valuable research has been produced at this clinic (Abrams et al., 2016; ESRU, 2018b; Fortuin-de Smidt et al., 2017; Kuhn et al., 2014; Potterton et al., 2016; Sherman et al., 1999; Shiau et al., 2017; Technau et al., 2017a, 2017b, 2017c; Whitehead et al., 2014)

3.2 Ethical Considerations

Ethical guidelines as defined by the HPCSA were adhered to (HPCSA, 2008). The study protocol was approved by the University of Witwatersrand Human Research Ethics Committee (Medical) (HREC) (Clearance number M160450; Appendix 3). Based on confirmation of ethical clearance, permission was obtained from RMMCH and ESRU to conduct the study (Appendix 4). Informed consent was requested from the main caregiver. Prior to consent, an information sheet containing the purpose, aims and objectives of the study was given to the caregivers and explained to them in detail (Appendix 5). Participation was voluntary and caregivers/parents were free to withdraw at any time, with no implication to their clinical care. Assent was not required as it is only the parent/caregiver that is being interviewed (HREC, 2016). Any material or information obtained during the study was considered strictly confidential. The use of file numbers and allocated study numbers as identifiers assisted with keeping children anonymous. All identifying material (e.g. name, photographic material, ID documents) were excluded.

3.3 Study Design

This was a cross-sectional study of children infected with HIV, from two to nine years old. A cross-sectional design was chosen as it best suited the resources available to the researchers (Portney and Watkins, 2009). The main caregivers of children who met the inclusion criteria were invited to participate in the study interview. Data were collected between July 2016 and March 2017.

3.4 Subjects

Consecutive sampling was utilized. Children were screened and then recruited from the waiting rooms at ESRU. The caregivers of consecutive children who met the inclusion criteria were invited to participate by providing the information sheet (Appendix 5) and consent form (Appendix 6). Using Raosoft software, an optimal sample size was calculated at 254, based on an expected prevalence of 33% (Devendra et al., 2013) and the clinic population size of children 2-9 years (n=1000). Recruitment continued until a sample size as close to optimal as possible, was obtained within the time frame restrictions.

- Inclusion criteria
    - Known HIV-positive status
    - Between the ages of 2-9 years (to allow the use of the WHO TQSD).
    - Accompanied by a caregiver eligible to give consent on behalf of the child.

- Exclusion Criteria
    - Caregivers not willing to sign consent or participate in the study.
    - Caregivers with limited information/knowledge about the child.
    - Children who had a disability due to a known cause (e.g. asphyxia, cancer, foetal alcohol syndrome, genetic conditions, poliomyelitis, prematurity, (brain) malformation, rickets and trauma).

3.5 Data Collection and Tools

Once consent was obtained the caregiver was taken through the questionnaire by the researcher and a translator, who translated the questions into the language of the caregiver's choosing. Categorical data were collected via the administration of the WHO TQSD (Appendix 7) coupled with a General Additional Questionnaire comprising of the referral, available and access to services data (Appendix 8) and sociodemographic information (e.g. education, medical history, household size, location, income, asset ownership etc.) (Appendix 9). The TQSD was used to achieve the first study objective (estimate prevalence of disability), while the General Additional Questionnaire and clinical file information was used to achieve Objective Two and Three (provide insight into the rehabilitative services that are being accessed and examine factors associated with HIV related disability.)

Once interviews were completed, the researcher systematically examined ESRU clinical records of those children whose parents/caregivers had given consent. The clinical records were used to complete the general additional questionnaire (Appendix 8, Heading 4, Clinical Factors) (e.g. age of diagnosis with HIV and the start of cART treatment, failed/poor adherence to treatment, number of hospitalisations, growth parameters before treatment started and opportunistic infections/diseases), obtain blood count data and referral notes to available services. Email communication with ESRU assistant manager (Rose, 2017), informal communication with clinic staff (nurses and doctors) and online presence (ESRU, 2018a; Gauteng Provincial Government, 2017a) were methods used to further ascertain available services to this population.

The WHO TQSD is a parent or caregiver proxy disability screening tool. It is time-efficient (10-15minutes) and freely available and has been widely used and recommended, particularly for developing countries (Christianson et al., 2002; Couper, 2002; Devendra et al., 2013; Durkin et al., 1995, 1994; Gottlieb et al., 2009; Ibrahim and Bhutta, 2013; Muga, 2003; Mung'ala-Odera et al., 2006; Singhi et al., 2007; Thorburn et al., 1992; Zaman et al., 1990). In addition, studies have used it successfully with populations of HIV-infected children (Devendra et al., 2013). It has a high sensitivity (80-100%) for severe developmental disabilities (Durkin et al., 1994; Singhi et al., 2007). For these reasons a pilot study was not deemed necessary. However, literature criticizes it for displaying high

false positive results for cognitive impairments (Thorburn et al., 1992) and visual and hearing impairments (Durkin et al., 1995; Singhi et al., 2007), particularly those with milder impairment, resulting in a possible over-referral. Still, research has demonstrated that children whose caregivers indicated a false positive on the TQSD had minor problems, such as otitis media and benefited from assessment and consequent treatment (Singhi et al., 2007; Zaman et al., 1990).

The questionnaire developed to establish socioeconomic position used in this study, has been based primarily on Barbarin and Khomo's (1997) Household Economic and Social Status Index and UNICEF's Demographic and Heath Surveys – Household Characteristics (The DHS Programme, 2015). Both of which are accepted measures of socio-economic position. Common measures of socio-economic position identified through literature include asset-based measures, consumption expenditure, education, income, occupation, participatory wealth ranking and subjective measures (Howe et al., 2011, 2012). The questionnaire included many of the above measures except participatory wealth ranking as it is not feasible due to the type of study proposed.

3.6 Procedure

All caregivers agreeing to participate in the questionnaires were individually taken to a private room, where information about the study was given to them in English and read and/or translated to them in a language of their choice. If they were willing they were taken through the consent procedure and the interview began. Caregivers/parents were free to ask questions in order to clarify interview questions. Each child/caregiver pair enrolled in this study was assigned a study number prior to the interview. Data obtained from the caregiver were collected on site. If the caregivers raised any concerns regarding their child, a referral letter addressed to the clinic doctors was given to them in order for the clinic staff to assess the parent's concern further. Data from the file were collected on a different day from the interviews, and children were identified by collating the study code with the clinic file number and clinic research number. Time frames are presented in Table 3.1.

Table 3.1 Research Report Time Frames

Activity	Time Frame
Proposal	April 2016
Ethical clearance & approvals	May 2016
Data Collection	July 2016 – February 2017
Analysis	April 2017 – August 2017
Write up	August 2017 – January 2018
Publication	Pending: June 2018

3.7 Data Analysis

Data were evaluated for omitted values and outliers. Counts were used to establish the prevalence of disability among the cohort of HIV-positive children. WHO Anthro (version 3.3.2) was used to calculate anthropometric Z-scores.

Data were analysed using STATA 14 (DataCorp) USA and Microsoft Excel 2013. Levene's test was used to assess quality of variances. The Chi-square test, Fisher's Exact test, t-Test and Mann–Whitney U test were used to calculate the significance of association (p-value) between disability and clinical and socioeconomic factors. A logistic regression was used to analyse any factors significantly associated with the presence of disability.

- Individual Factors
    - Age
    - Sex
- Anthropometric factors
- Birth Factors
    - Mode of Delivery
    - Gestational age
    - Birth Weight
- Clinical Factors
    - Pre-ART Blood Counts
        - CD4 cell count
        - CD4%
        - Viral Load
    - Childhood and opportunistic infections/diseases
    - Number of hospitalisations
- Treatment Factors
    - Age at the start of cART
    - Duration on cART
    - Treatment adherence
    - Maternal ART
- Socioeconomic Status
    - Monthly household income (Rands, per person, per month)
    - Orphan Status
    - Main caregiver education

Frequencies and proportions were used to describe what rehabilitative services are available to this population and which of these services are being utilised by this population. These descriptive statistics were used to indicate what the facilitators and barriers are to accessing rehabilitative services. Specific tests for each objective are presented in Chapter 4: Results.

3.8 Conclusion

This chapter has discussed the locations of the study, ethical considerations, study design, subjects, measurement tools, the procedures used to collect data, and statistical methods employed to analyse the data. The results of this study will be presented in Chapter Four.

CHAPTER 4

4. RESULTS

A total of 208 caregivers were interviewed during the study. From these interviews information was collected on 214 children. Brief descriptive group demographics will be presented on caregivers and children including age and sex. This will be followed by the results of the TQSD. Data on services received will then be described, followed by exploring possible confounding and/or associated factors.

Seven subjects were excluded because they did not fall into the age bracket of 2-9 years. Three were excluded because of insufficient data and two were excluded due to the caregiver not being a direct relative of the child. One child had cerebral palsy due to birth asphyxia and one child had foetal alcohol syndrome. Both were excluded. The data regarding 200 children were analysed.

4.1 Descriptive Group Statistics

Of the 200 children, just over half (50.5%) of the sample were male (n=101). The range of ages was two years to eight years and 11 months. The mean age of the sample was six years and five months (76.8 months) with a standard deviation (SD) of two years (24.5 months). A summary of group statistic are presented in Table 8.3 (Appendix 10) and are presented later in this chapter in Table 4.4. The distribution of ages is presented in Figure 4.1.

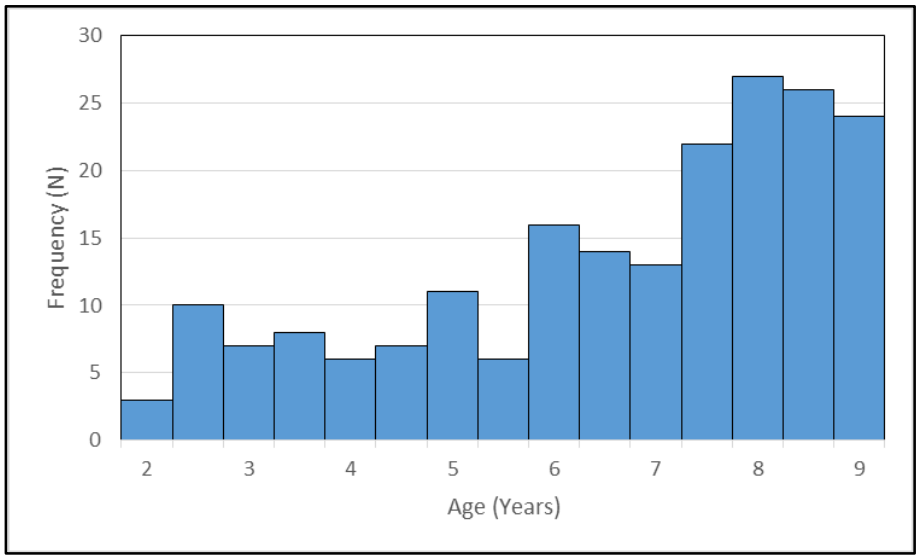

Figure 4.1: Distribution of age

The majority (64%) of the caregivers interviewed were the children's mothers, 12% were their grandmothers, 9% were fathers and 3% were aunts. Five percent did not indicate their relationship to the child. The remaining 7% was made up of grandfathers, great aunts, sisters, a foster mother and an adopted father.

Carers were asked the reasons for the child being cared for by a family member other than the child's mother or father (biological, adopted or foster) (n=37). Eleven (6%) did not answer the question. Reasons given included; mother, both parents and grandmother have passed away (62%), mother and/or father was at work (19%), parents are not the main caregiver/abandoned child (14%) and mother is very ill (5%). Distributions are shown in Figure 4.2.

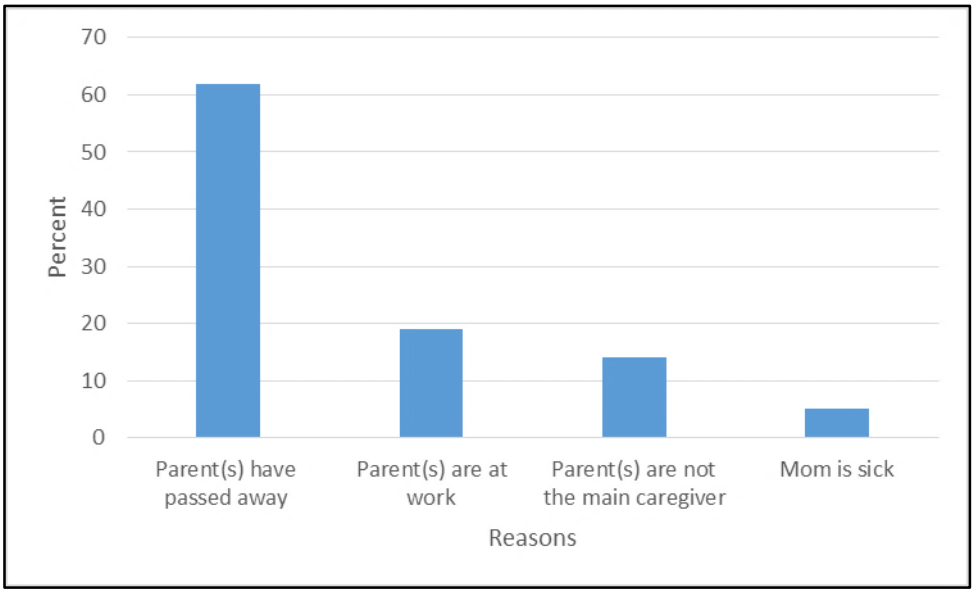

Figure 4.2: Reasons for parents not bringing their children to the clinic

4.2 Developmental Delay & Disability

A child could score positive on the TQSD for severe disabilities as well as for mild or subtle disabilities. The TQSD classifies the disabilities into developmental delay, seizures, physical, visual, hearing, speech and language and cognitive and behavioural impairments. Clinical notes on any official diagnoses that could influence neurodevelopment and/or child development, such as CMV, epilepsy, HIVE, meningitis, childhood and/or opportunistic infections, otitis media and PN were noted.

4.2.1 Prevalence of Disability by Ten Question Screen for Disability.

Of the sample, 50.5% (n=101) screened positive for disability on the TQSD.

On further analysis, of those with positive TQSD outcomes, 42 (41.6%) reported a single difficulty, 32 (31.7%) reported two coexisting disabilities, 20 (19.8%) reported three coexisting disabilities and nine (6.9%) reported four or more coexisting disabilities. Figure 4.3 presents these percentages.

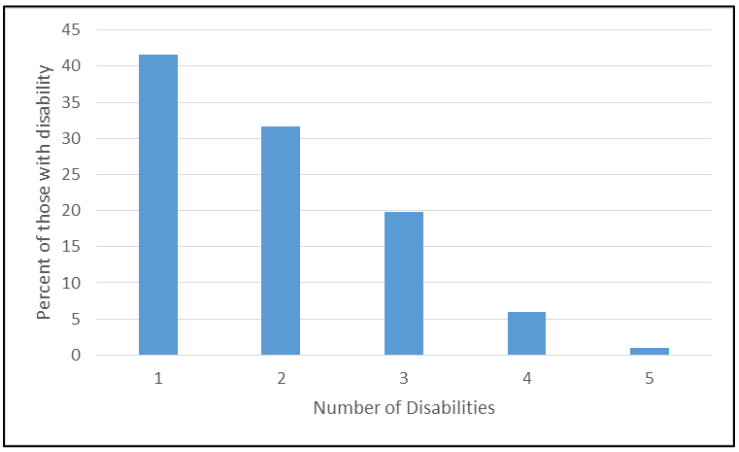

Figure 4.3: Percentage of those with one or coexisting disabilities

4.2.2 Distribution of Disabilities

When analysing the distribution of different types of disability; developmental delay was the most common reported difficulty (27%). The next most common was cognitive and behavioural difficulties (20.5%) followed by communication difficulties (16.5%). Distributions of disabilities are presented in Table 4.1 and Figure 4.4.

Table 4.1: Distribution of disabilities

Disability/Delay	**Caregiver-Reported: n (% of sample) n=200**
Developmental Delay	54 (27)
Physical	25 (12.5)
Vision	17 (8.5)
Hearing	18 (9)
Communication	34 (16.5)
Cognitive/Behavioural	41 (20.5)
Seizures	5 (2.5)
Total Disabilities Recorded	192*

**58.4% of those with disabilities had >1 disability, therefore, total no. of disabilities, will not match the total no. of children with caregiver-reported disability.*

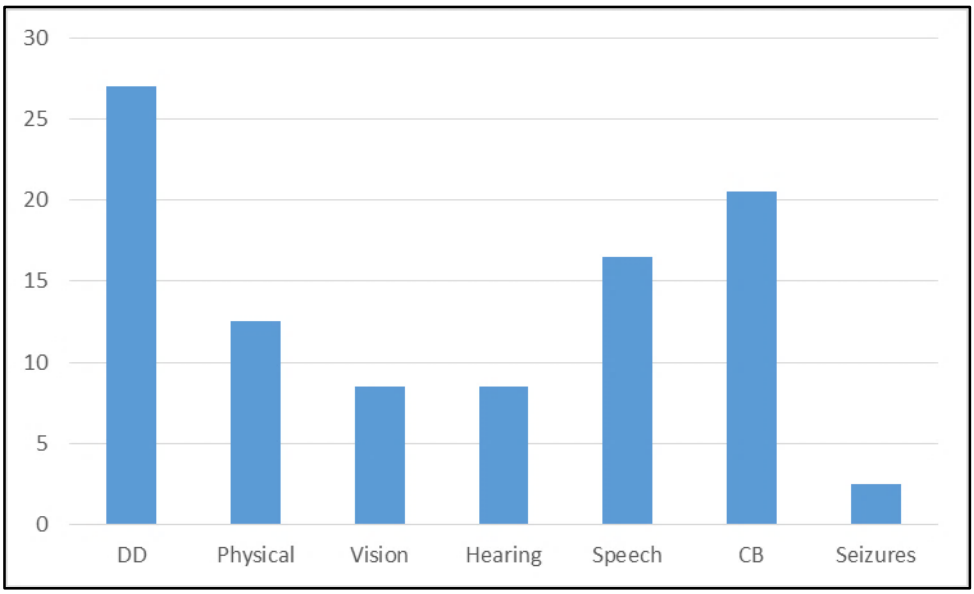

Figure 4.4: Distribution of difficulties in children with HIV

Abbreviations: DD: Developmental Delay, CB: Cognitive and Behavioural Difficulties

4.2.3 Developmental Delay

Of the entire sample, 54 (27%) reported developmental delay of which, 24 (44.4%) reported developmental delay only with no further difficulties. The remaining 30 (55.6%) reported further disabilities including physical, hearing, visual, cognitive and behavioural difficulties as well as seizures and pain

The majority of those with developmental delay were born full term (83.3%). No significant association was found between gestational age and caregiver-reported developmental delay (Chi Square p = 0.207). However, results need to be interpreted cautiously due to the low number of premature births in the sample (Table 4.6).

Only 18 of the 54 (33.3%) with developmental delay were referred and assessed by a physiotherapist (PT) (n=15) and/or occupational therapist (OT) (n=7).

Table 4.2 and Table 4.3 presents a more comprehensive breakdown of services.

4.2.4 Physical Disability

Twenty five (12.5%) caregivers/parents reported physical disability in their children of which, eight (32%) were for a physical disability only (which included pain). Nine of the 25 (36%) had reported previous developmental delay. Therefore, 70 (35%) children reported developmental delay (n=54) and/or physical disability (n=25).

Three of the 25 children (12%) with physical impairments were born before 34 weeks gestation. Two children (8%) were previously diagnosed with HIVE (neither of whom were born premature). None of the children were diagnosed with cerebral palsy.

Only 12 (42.9%) of children with caregiver-reported physical disability were referred to a PT and/or an OT. All 12 had been referred to physiotherapy and four of those children had also been referred to occupational therapy. Only 11 children had actually been assessed by a PT and all four had been assessed by an OT. A more comprehensive breakdown of services is presented in

Table 4.2 and Table 4.3.

4.2.5 Vision

Seventeen (8.5%) caregivers reported visual difficulties in their children.

Conjunctivitis was diagnosed in 34 children (17% of the entire sample group); half of which (n=17) were positive for disability on the TQSD. However, there was no significant association between caregiver-reported visual difficulties and clinically diagnosed conjunctivitis (Chi square p = 0.471).

Pterygium was recorded as present in two children (1%) and strabismus was recorded in the file of four (2%) children. No caregiver reported and no notes on congenital toxoplasmosis were found in the clinic files.

Table 4.3 shows supportive services accessed by those with visual difficulties. Of the 17 children whose carers reported visual difficulties, three (17.6%) were referred and assessed by an optometrist and two (11.8%) were seen by an OT.

4.2.6 Hearing

Of those children who's caregivers reported hearing difficulty (n=18), two (11.1%) had an official diagnosis of hearing loss/deafness. Of the 18, four (24%) reported difficulty with hearing only, while the remaining 14 (76%) children had other disabilities.

Otitis media was documented in 38 (19% of the total sample) of the clinic files assessed. Of the 18 children with hearing difficulty, five (27.8%) reported otitis media. There was no significant association between the incidence of otitis media and caregiver-reported hearing problems (chi-square p = 0.228) (Table 4.13).

Nine of the 18 children (53%) with reported hearing problems; described an additional speech and/or language difficulty. Furthermore, six of the 18 (33.3%) children with hearing difficulty had had previous developmental delay. None of the children with hearing difficulty had previous CMV.

Five (27.7%) of the children reporting hearing difficulties had been referred to an audiologist and/or SLT. Only four (22.2%) were assessed by an audiologist and three (16.7%) were assessed by an SLT. These results are presented in Table 4.3.

4.2.7 Speech & Language

Of the carers interviewed, 34 (17% of entire sample) reported a speech and/or language impairment in their children. Of those reporting these difficulties, ten (29.4%) reported additional hearing problems (24 (70.6%) reported no hearing difficulty). Caregiver-reported hearing difficulty and speech difficulty were found to be significantly associated (chi-square p <0.001).

Of those with speech difficulties (n=34), six (17.6%) had a previous diagnosis of otitis media, however, no significant association was found (Chi square p = 0.698) between the incidence of otitis media and caregiver-reported speech difficulty.

Table 4.2 and Table 4.3 presents the breakdown of services received by the children with caregivers who reported speech and/or language delay/disability. Only 10 (29.4%) of those experiencing speech and/or language difficulties (n=34) were referred to speech and language service by ESRU and seven children (20.6%) were assessed. Six (17.6%) children with speech and/or language difficulties were referred and assessed by an audiologist.

4.2.8 Cognitive & Behavioural

Forty-one (21%) of caregivers/parents reported cognitive and behavioural difficulties among their children. One caregiver reported a diagnosis of ADHD and two other children were on Ritalin. One child attended a special school and another child was not attending school at all despite being the appropriate age for school.

Only three (7.3%) of the 41 children reportedly experiencing cognitive and behavioural difficulties were referred to a psychologist and four children (9.8%) were assessed by a psychologist. Table 4.2 and Table 4.3 present a more comprehensive breakdown of these services.

4.2.9 Seizures

Seizures were caregiver-reported in five children (2.5%) while epilepsy was diagnosed and noted in the files of three children (1.5%). Only one child with caregiver-reported seizures was diagnosed with epilepsy and two children diagnosed with epilepsy had not been reported by their caregivers. None of the caregivers reported seizures only in their children. All of them had other delays and disabilities including cognitive, behavioural, emotional, physical and hearing difficulties.

4.2.10 Peripheral Neuropathy

Two children (1%) had an official diagnosis of PN while in another child's file, it was noted that the child complained of sore feet and hands but had no diagnosis of PN.

4.3 HIV Encephalopathy

In the file notes of eight children (4%) it was noted that they had previously been diagnosed with HIVE and a diagnosis was being queried for one child but was not confirmed either way. This sample was too small to perform any measure-of-association tests. Seven of the nine (eight diagnosed with HIVE and one possible diagnosis) reported disability, three had a single difficulty while four had two co-existing disabilities. Four reported developmental delay, three reported speech difficulties, two had physical difficulties and two had visual problems.

4.4 Available, referred and accessed services

4.4.1 Available

The clinic provides waiting room information sessions and talks. The RMMCH dietician gives talks on nutrition while the nurses, councillors and social workers cover the "*Flipster Support Club Tool*" Programme (Right to Care and Mwanandimai, 2015) which discusses adherence, disclosure, lifestyle and diet. For adolescents it includes teenage pregnancy, drug and alcohol abuse.

Supportive service providers accessed by the sample included; audiologist, dentist, dietician, HIV counsellor, OT, optometrist, PT, psychologist, special schools, social worker and SLT. These, including frequencies and percentages, are presented in Table 4.2.

The sample, as a whole had been seen by a number of medical practitioners which included cardiologists, dermatologists, endocrinologists, ENT/Respiratory clinic, general practitioners, gynaecologists, ophthalmologists (eye clinic), orthodontists, orthopaedic surgeons, paediatricians (developmental clinic), rheumatologists, plastic surgeons, radiologists and urologists. Some children had also seen traditional healers. Other support networks include the *Psychosocial Helpline* which can provide social worker and counsellor advice during office hours and the *B-wise* Mobi-site (Department of Health, 2015) is aimed at young South Africans seeking medical advice.

Table 4.2: Support services: referred and accessed

Service Provider	Clinic Referrals from File	Patient Reported Referral from any practitioner	Patient Reported seeing provider	Patient would like referral to provider
Audiologist	6 (3)	19 (9.5)	29 (14.5)	28 (14)
Dentist	23 (11.5)	.	59 (29.5)	48 (24)
Dietician	65 (32.5)	.	8 (4)	9 (4.5)
HIV Counsellor	200 (100)	.	16 (8)	16 (8)
Learning support	0 (0)	.	0	4 (2)
Optometrist/eye clinic	9 (4.5)	28 (14)	41 (20.5)	21 (10.5)
Occupational therapist	10 (5)	11 (5.5)	13 (6.5)	2 (1)
Play Therapist	0	.	0	12 (6)
Psychologist/School Assessment	8 (4)	7 (3.5)	4 (2)	24 (12)
Physiotherapist	9 (4.5)	41 (20.5)	40 (20)	5 (2.5)
Speech and Language Therapist	11 (5.5)	18 (9)	13 (6.5)	12 (6)
Social Worker	48 (24)	.	2 (1)	2 (1)

Of those interviewed, 62 (31%) were happy with their current services and did not need to see other service providers, two were uncertain and the remainder, 136 (68%), wanted to be referred or re-referred to one or more additional service providers. Dentists, audiologists, psychologists and optometrists were the most commonly requested service.

4.4.2 Referral and Assessment

Both frequency of referral and frequency of assessment were obtained through the General Additional Questionnaire. However, “Clinic referral” referred to a question asking, if the staff at ESRU had ever referred the child/caregiver pair to a support service, and “assessment” was if they had ever been to see a service provider, whether they had been referred by ESRU or another source.

A total of 74 (37%) children in the whole sample had been referred to one or more support service. Forty six of the 74 (62.1%) had scored positive of the TQSD and the remaining 28 (37.9%) reported no disability.

Of the entire sample of caregivers, 81 (40.5%) reported their child had been assessed by one more service provider(s). Forty-eight (59.3%) of which had caregiver-reported disability and 33 (40.7%) did not. Figure 4.5 represents the distribution of the referral and assessment of these services. In addition, the study site is a research unit, hence, 18 (22.2%) of the children that had a developmental assessment, were for research purposes only, where a child was part of a cohort. Therefore, not all assessments were as a result of a referral due to neurodevelopmental concern.

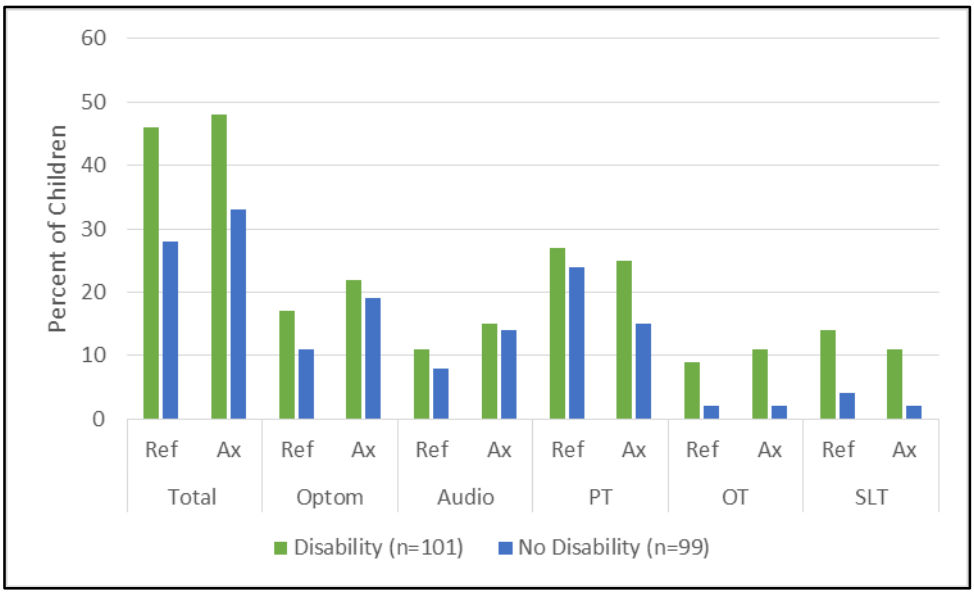

Figure 4.5: Distribution of referral and assessment of support services

Abbreviations: Audio: Audiologist; Ax: Assessment; Optom: Optometrist; OT: Occupational therapist; Psych: Psychologist; PT: Physiotherapist; Ref: Referral; SLT: Speech and language therapist.

4.4.2.1 Referral of those with disabilities

Of those carers who reported a difficulty in their child (n=101), 46 (45.5%) had been referred to one or more of the following support services; audiologist, OT, optometrist, PT, psychologist and/or SLT. Ten (21.7%) of the caregivers with children who had been referred for services admitted to never attending the assessment appointment. Reasons for this included no time to take the child to be assessed, no money for transport or for service, the child or parent/caregiver was sick on the appointment day, the service provider cancelled, an appointment or referral letter was never given to the patient and 20% did not know why they never followed up on the appointment. Distribution is shown in Figure 4.6.

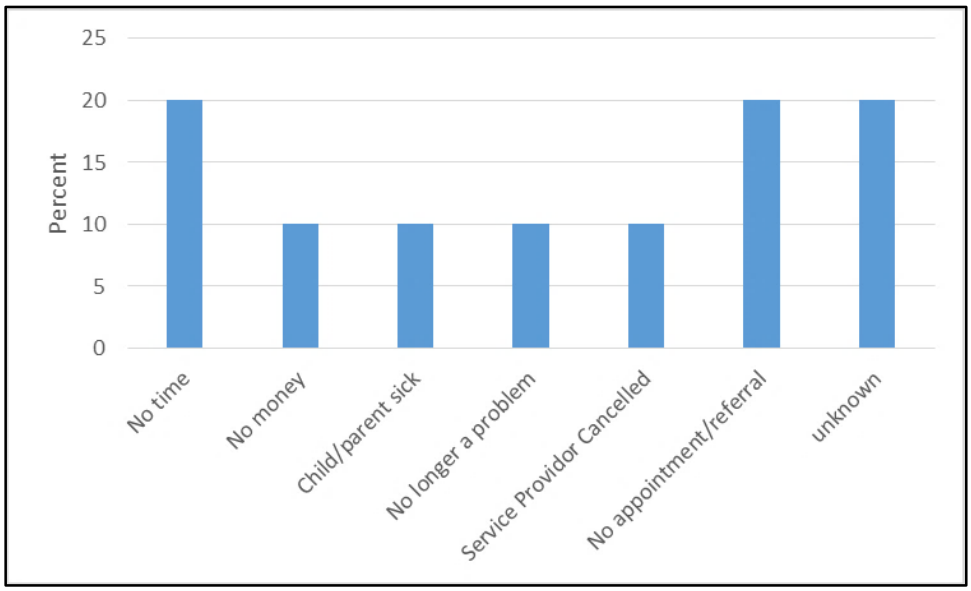

Figure 4.6: Reasons for not going to assessment

4.4.2.2 Distribution of Services to those with disabilities

Many of the children with disabilities reported low frequencies of referral to (45.5%) and assessment (47.5%) by supportive services. These are detailed in Table 4.3. Many children had co-existing disabilities, therefore the total number of referrals and/or assessments (Table 4.3) is not the sum of referrals and/or assessments within each disability category.

Table 4.3: Distribution of services to those reporting disability

Disability/delay (total n reported)	**Supportive services, n** (% of those with disability)											
	Audiologist		**PT**		**Psychologist**		**Optometrist**		**OT**		**SLT**	
	Clinic Ref	**Ax**	**Clinic Ref**	**Ax**	**Clinic Ref**	**Ax**	**Clinic Ref**	**Ax**	**Clinic Ref**	**Ax**	**Clinic Ref**	**Ax**
Developmental Delay (54)	8 (14.8)	10 (18.5)	15 (27.7)	15 (27.7)	2 (3.7)	2 (3.7)	5 (9.3)	10 (18.5)	5 (9.3)	7 (13)	8 (14.8)	5 (9.3)
Physical (25)	4 (16)	5 (20)	12 (48)	11 (44)	2 (8)	2 (8)	4 (16)	6 (24)	4 (16)	4 (16)	4 (16)	4 (16)
Vision (17)	3 (17.6)	2 (11.8)	4 (23.5)	4 (23.5)	1 (5.9)	1 (5.9)	3 (17.6)	3 (17.6)	1 (5.9)	2 (11.8)	1 (5.9)	1 (5.9)
Hearing (17)	5 (29.4)	4 (23.5)	4 (23.5)	3 (17.6)	0 (0)	1 (5.9)	1 (5.9)	0 (0)	3 (17.6)	3 (17.6)	5 (29.4)	3 (17.6)
Speech (33)	6 (18.2)	6 (18.2)	12 (36.4)	11 (33.3)	0 (0)	0 (0)	5 (15.2)	5 (15.2)	4 (12.1)	4 (12.1)	10 (30.3)	7 (21.2)
Cognitive/Behavioural (41)	5 (12.2)	4 (9.8)	11 (26)	9 (22)	3 (7.3)	4 (9.8)	7 (17.1)	8 (19.5)	2 (4.9)	2 (4.9)	5 (12.2)	3 (7.3)
Seizures (5)	1 (20)	1 (20)	1 (20)	1 (20)	0 (0)	0 (0)	1 (20)	1 (20)	1 (20)	1 (20)	0 (0)	0 (0)
Total no. of Ref or Ax	19	26	41	40	7	4	28	41	11	13	18	13

Abbreviation: Ax: Assessment; OT: Occupational therapist; PT: Physiotherapist; Ref: Referral; SLT: Speech and language therapist

4.4.2.2.1 Audiologist

Twenty nine caregivers (14.5% of entire sample) reported that their children had seen an audiologist. Two had speech and hearing difficulties, two reported hearing difficulties only and four had speech difficulties only.

Of the 17 children with caregivers that reported hearing difficulties, five (29.4%) were referred to an audiologist (four were assessed) and only six (18.2%) children with a reported speech difficulty had seen an audiologist. Of the entire sample, 38 (14%) caregivers wanted their child to be referred to an audiologist (Table 4.3).

4.4.2.2.2 Optometrist

Of the 200 children interviewed, 41 (20.5%) caregivers reported that their child had been assessed by an optometrist or at the eye clinic. Therefore, conversely, 79.5% of these children had never had their vision assessed by an optometrist. Of those 41, 22 (53.7%) had reported no difficulty and three (7.3%) had reported visual difficulties. These three made up 17.6% of all those who reported visual difficulties (n=17). The remainder of the 41 (n=16) had other problems not categorised under vision. Ten of the 34 children who had previous conjunctivitis (29%) had seen an optometrist.

4.4.2.2.3 Physiotherapist

Forty children (20% of entire sample) reported being assessed by a PT. Of those assessed by a PT, 13 (32.5%) were assessed only. Of those 13, seven (53.8%) were assessed for research purposes and not due to developmental concern. Eight (20%) children had previously received inpatient physiotherapy only and 19 (47.5%) continued to receive outpatient therapy. At the time of the interviews, five children were receiving physiotherapy.

Six children (15%) who had been assessed by a PT (n=40) had caregiver-reported developmental delay and physical impairment and nine of the 40 (22.5%) reported developmental delay only. Therefore, of those with developmental delay (n=54), 15 (27.8%) had seen a PT. Of those reporting physical disability (n=25), only 11 (44%) had been assessed by a PT.

4.4.2.2.4 Occupational Therapist

Of the 54 children with developmental delay, six (11.1%) had been assessed by an OT. Cognitive and behavioural difficulties were found in 41 children and two (4.9%) of them had been assessed by an OT. Of the 13 children who had seen an OT, nine (46.2%) had received outpatient treatment, five (38.5%) were assessed only and two (15.4%) were seen as an inpatient only. Therefore, only eight (4%) children received occupational therapy on an outpatient and/or inpatient basis. At the time of the interview, one child was still receiving OT.

4.4.2.2.5 Speech and Language Therapist

Thirteen caregivers had reported that their child had been assessed by an SLT. Three of which had reported hearing difficulties (23.1%) and seven reported speech difficulties (53.8%).

Of those who were assessed by a SLT (n=13), five (38.5%) children were assessed only and eight (61.5%) children continued to receive treatment. At the time of the interview four (30.8%) children were receiving SLT.

4.4.2.2.6 Psychologist

Forty one carers (20.5% of entire sample) reported cognitive and behavioural difficulties in their children. Four of which (9.8%) had been assessed by a psychologist. Three of these children had been referred by the clinic, the fourth was referred from another source.

4.4.3 Assessment locations

Distribution of assessment locations is shown in Figure 4.7. Vision and hearing tests were most commonly done at an unknown facility, which is likely to be another tertiary referral hospital in the area. School testing was the second most common location followed by hospital assessments. No vision and/or hearing tests were done at PHC clinics.

Physiotherapy, occupational therapy, speech and language assessments were more commonly done in hospital and at a research facility.

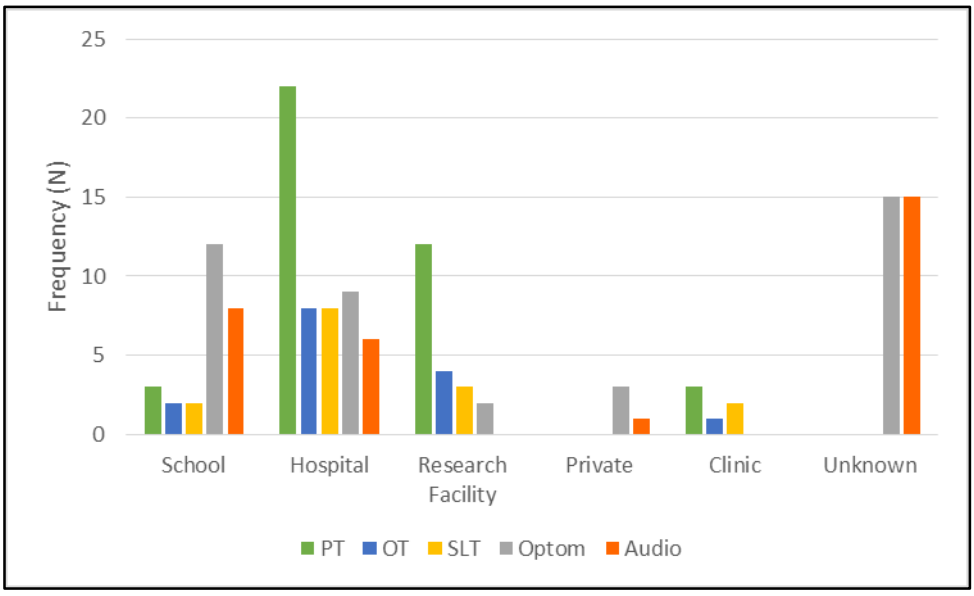

Figure 4.7: Location of assessments

Abbreviations: Audio: Audiologist; Optom: Optometrist; OT: Occupational therapist; PT: Physiotherapist; SLT: Speech and language therapist.

4.4.4 Frequency of Treatment

Of the 81 children that had ever been assessed by a support service provider; 43 (53.1%) attended therapy services for more than an assessment. Of these children (n=43), 19 (44.2%) children attended once a month. A third (30%) of all physiotherapy treatments took place on a daily inpatient basis and another third (30%) were seen as an outpatient with once a month appointment dates. Speech and language therapy appointments occurred on an outpatient once a month basis, 88% of the time and one child was seen by a SLT 2-3 times a week. Half (50%) of the OT sessions, took place once a month and a quarter (25%) were seen on an inpatient basis. These distributions are shown in Figure 4.8.

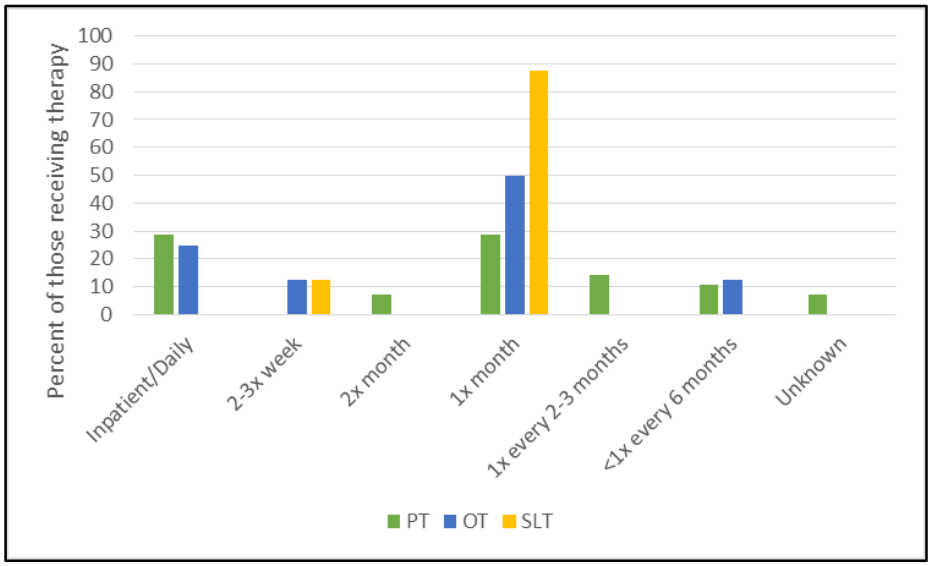

Figure 4.8: Frequency of therapy appointments

Abbreviations: OT: Occupational therapist; PT: Physiotherapist; SLT: Speech and language therapist.

4.4.5 Barriers to receiving therapy

The majority of children receiving physiotherapy, occupational therapy or speech and language therapy stopped attending therapy because they were discharged either from the inpatient facility or from outpatient services. Very few carers admitted that the reason for stopping services was due to transport difficulties or that the therapy was not helping. These results are detailed in Figure 4.9. One carer reported that she did not know why she stopped taking her child to occupational therapy and another carer reported that she was not re-referred to speech therapy services when she relocated cities.

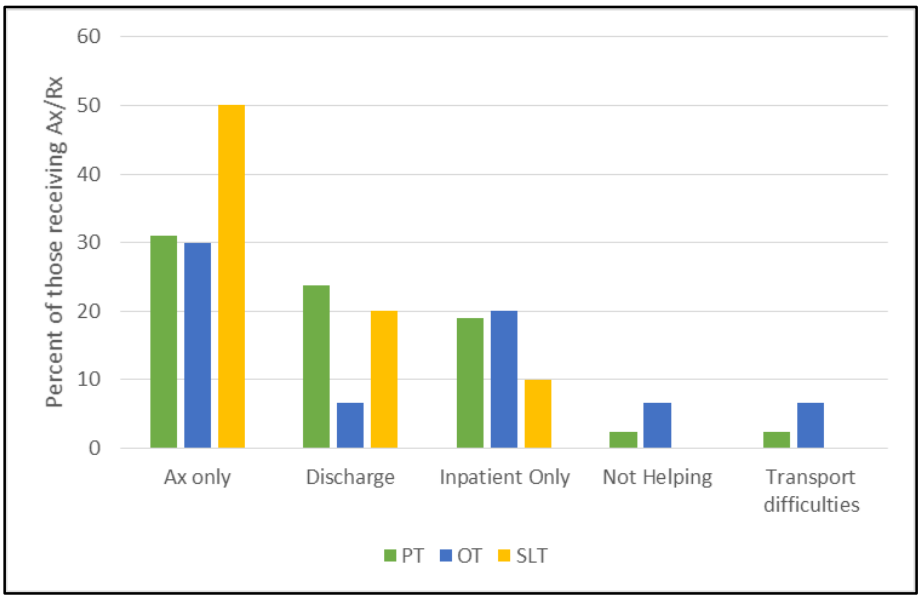

Figure 4.9: Reasons for no longer attending therapy

Abbreviations: Ax: Assessment; OT: Occupational therapist; PT: Physiotherapist; SLT: Speech and language therapist.

Ten children were receiving outpatient physiotherapy (n=5), occupational therapy (n=1) and/or speech and language therapy (n=4) at the time of the interview. When asked if there was anything that made attending therapy difficult; four caregivers/parents reported that they had no problems and six reported problems accessing these services. Three reported that transport was difficult and therapy services were too far from the home. Two indicated that there was no money for transport and one mother said she found it difficult to take time off work.

4.5 Possible Confounding or Contributing Factors

Possible factors associated with childhood disability are presented below. In addition, a compilation of these factors are presented in Table 8.3 (Appendix 10).

4.5.1 AGE & SEX

Those with disabilities tended to be older than those without disability. The mean age of those with disabilities was six years and seven months (SD: +-24 months) while the mean age for those without disabilities was six years and two months (SD: +-25 months). However, an independent samples t-test showed no significance in age between the two groups (p = 0.071). Data for age is presented in Table 4.4.

Slightly more males reported disability (50.5%). However, no significant association was found (p = 0.480) when a chi-square test was performed to investigate the possibility of an association between sex and disability. Frequencies are presented in Table 4.4.

Table 4.4: Group statistics of age and sex in relation to disability

Variable	Total	With Disability	Without Disability	P-Value
Total N	**200**	**101**	**99**	
AGE (Months)	Range: 24-107			
Mean	76.78	79.87	73.63	0.071
SD	24.46	23.89	24.76	
Std. Err. Mean		2.38	2.48	
Median	84	86	78	
IQR	59-96	66-99	56-95	
Sex (male), n (%)	101 (50.5)	54 (53.5)	47 (46.5)	0.480

Abbreviation: N: number; IQR: Interquartile Range; SD: Standard Deviation; Std. Err. Mean: Standard Error Mean

4.5.2 Anthropometric Data

Anthropometric data (height and weight) were recorded for each child on the date of the parent/caregiver interview. Weight-for-age (WAZ), height-for-age (WAZ) and Body Mass Index (BMI)-for-age (BAZ) and their corresponding Z-scores were calculated using WHO Anthro (Version 3.3.2). The results are shown in Table 4.5 and distributions are shown in Figure 4.10. A Z-score of <-2.00 indicates that an individual may be underweight (WAZ), stunted (HAZ) or wasted (BAZ). Of the entire sample, 20 (10.2%) children were underweight, 24 (12.2%) children were stunted and nine (4.6%) were wasted.

The interquartile ranges for all Z-scores were all within the norm values for height, weight and BMI according the WHO Growth Chart guidelines. Yet, all median and mean values were below the 50th percentile.

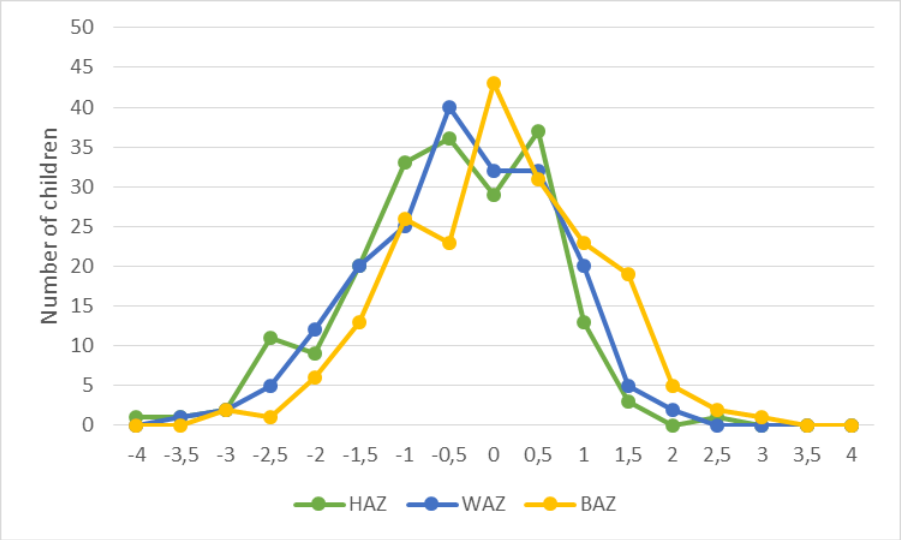

Figure 4.10: HAZ, WAZ and BAZ Z-score distribution

Levene's test scores were not significant for WAZ, HAZ and BAZ, thus independent samples t-tests were performed. No significant association was found when examining disability and HAZ or disability and BAZ but a statistically significant association was found when investigating WAZ and disabilities (p = 0.014). Those with disabilities were more likely to have a lower WAZ score and are therefore, more likely to be underweight. Group statistics are presented in Table 8.3 (Appendix 10) and Table 4.5.

Table 4.5: Group statistics for WAZ, HAZ & BAZ

Variable	Total	With Disability	Without Disability	P-Value
WAZ Z-score				
Total N	**194**	**100**	**94**	
Mean	-1.16	-0.78	-0.42	0.014
SD	1.62	1.01	1.01	
Std. Err. Mean		0.10	0.10	
Median	-0.56	-0.69	- 0.41	
IQR	-1.31 to 0.15	-1.54 to 0.04	- 0.97 to 0.29	
WAZ Z-score <-2	20 (10.3)	12 (12)	8 (8.5)	
HAZ Z-score				
Total N	**196**	**100**	**96**	
Mean	-1.66	-0.88	-0.60	0.064
SD	1.76	1.14	0.97	
Std. Err. Mean		0.11	0.10	
Median	-0.63	-0.88	-0.57	
IQR	-1.38 to 0.08	-1.46 to 0.08	-1.28 to 0.11	
HAZ Z-score <-2	24 (13.8)	17 (17)	7 (7.3)	
BAZ Z-score				
Total N	**193**	**100**	**93**	
Mean	-0.05	-0.37	-0.08	0.058
SD	0.56	1.06	1.03	
Std. err. Mean		0.11	0.11	
Median	-0.21	-0.4	-0,02	
IQR	-0.94 to 0.52	-1.08 to 0.29	-0.73 to 0.64	
BAZ Z-Score <-2, n (%)	9 (4.7)	5 (5)	4 (4.3)	

Abbreviation: N: number; IQR: Interquartile Range; SD: Standard Deviation, Std. err. Mean: Standard Error Mean

4.5.3 Birth Factors

Birth factors of gestational age, mode of delivery and birth weight were investigated for any association with disability. These results are presented in Table 4.6.

4.5.3.1 Mode of Delivery

Of the caregivers interviewed, three were uncertain as to the mode of delivery of the child. Normal delivery was reported in 77.2% of the sample and caesarean sections (C-Sections) occurred 22.8% of the sample. A Chi square test showed no significant association in the presence of disability between different modes of delivery ($p = 0.292$). This result should be interpreted with caution due to the high prevalence of natural births.

4.5.3.2 Prematurity

When analysing gestation, prematurity was initially divided into three groups, >37weeks, 34-36 weeks and <34weeks. However, the frequency of births before 36 weeks was too small for statistical testing. Hence, the groups were adjusted to premature (<37 weeks) and term (>37weeks). No significant association was found between gestational age and mode of delivery (Chi-square test $p = 0.274$).

A chi-square test was performed to determine an association between developmental difficulty and gestational age but no significant association was found ($p = 0.075$). Frequencies are shown in Table 4.6.

4.5.3.3 Birth Weight

Sixty four children (32%) had no recorded data on birth weight. Data on 136 children were analysed.

As expected, birth weight was significantly lower in the group born preterm ($P < 0.001$). In addition, birth weight was significantly associated to WAZ Z-score ($p = 0.0001$).

When investigating birth weight and caregiver-reported childhood disability, the mean birth weight for those with a difficulty was 2.92kg (SD: 0.67kg) and those without was 3.12kg (SD: 0.63kg) Distributions are presented in Table 8.3 (Appendix 10) and Table 4.6. There is a trend of significant association between birth weight and caregiver-reported disability ($p = 0.051$). However, results need to be interpreted with care due to the low number of ELBW and VLBW children.

Prenatal ART was not associated with a lower birth weight.

Table 4.6: Birth factors possibly associated with disability

Variable		Total	With Disability	Without Disability	P-Value
Mode of Delivery, n (%)					
Total N		**197**	**99**	**98**	
Normal		152 (77.2)	70 (70.7)	82 (83.7)	0.292
C-Section		45 (22.8)	29 (29.3)	16 (16.3)	
Prematurity, n (%)					
Total N		**195**	**99**	**96**	
>37 weeks		172 (88.2)	83 (83.8)	89 (92.7)	0.075
<37 weeks		23 (11.9)	16 (16.2)	7 (7.3)	
	34-36 weeks	12	9 (9.1)	3 (3.1)	
	<34 weeks	11	7 (7.1)	4 (4.2)	
Birth Weight					
Total N		**136**	**64**	**72**	
Mean (kg)		3,03	2.92	3.12	0.051
SD (kg)		0.66	0.67	0.63	
Median (kg)		2.97	2.9	3.04	
IQR (kg)		2.64 – 3.49	2.53 – 3.4	2.8 – 3.52	
Distribution of Birth weight, n (%)					
	ELBW	1 (0.7)	1 (1.6)	0 (0)	
	VLBW	2 (1.4)	0 (0)	2 (2.8)	
	LBW	18 (13.2)	13 (20.3)	5 (6.9)	
	Typical BW	115 (84.6)	50 (78.1)	65 (90.3)	

Abbreviation: BW: Birth Weight; C-Section: Caesarean Section; ELBW: Extremely Low Birth Weight, LBW: Low Birth Weight; N: number; IQR: Interquartile Range; SD: Standard Deviation, VLBW: Very Low Birth Weight.

4.5.4 Number of Admissions

Distribution of the number of hospitalisations is given in Table 4.7. Forty six caregivers (23 with children with disabilities and 23 without) did not answer the question. Children who had never been admitted to hospital came to a total of 44 (28.6%). A total of 110 (71.4%) children had known admissions to hospital. Of those who had been admitted, 61 (55.5%) had caregiver-reported difficulties and 49 (44.5%) had reported no problems.

Of the children with known admissions history and reporting a disability (n=78), 61 (78.2%) had at least one admission into hospital. Fewer children reporting disability had never been admitted. Yet, this association was not statistically significant (p = 0.368 using a chi-square test).

Table 4.7: Distribution of number of admissions

Variable	Total	With Disability	Without Disability	P-Value
Total N	**154**	**78**	**76**	
Never	44 (28.6)	17 (21.8)	27(35.5)	0.368
Once	75 (48.7)	40 (51.3)	35 (46.1)	
> Once	35 (17.5)	21 (26.9)	14 (18.4)	

4.5.5 Clinical Factors and Antiretroviral Therapy (ART)

There were no ART data for nine children, however, the remaining 191 (95.5%) children in the sample were already initiated on ARV therapy.

4.5.5.1 Blood Count Data

Pre-treatment and the most recent blood count data were recorded and group statistics are presented in Tables 4.8, 4.9, 4.10 and 4.11. CD4 cell counts, CD4 percentages and viral load data were not available for all children and these numbers are included in these tables.

*Table 4.8: CD4 cell count (10*6/1cells/mm3)*

		Pre-treatment	Latest
N	**Valid**	156	177
	Missing	44	23
Mean		1064.83	1252,29
Std. Dev.		814.44	595.31
Median		803	1088.5
IQR		487.75 - 1524.75	1192 - 1488
Minimum		4	46
Maximum		5039	4087

Table 4.9: CD4 %

		Pre-treatment	Latest
N	**Valid**	150	164
	Missing	50	36
Mean		21.44	34.65
Std. Dev.		11.25	9.58
Median		19.08	39
IQR		13.75 - 28	35.23 – 40.46
Minimum		1	3.6
Maximum		72.4	76

Table 4.10: Viral load cells/mL

		Pre-treatment	Latest
N	**Valid**	144	144
	Missing	56	6
	TLTD	0	50
Mean		10187879.28	55209.37
Std. Dev.		70489049.16	590530
Median		160045	878
IQR		521904.5 - 2050000	433 - 1745
Minimum		52	21
Maximum		710000000	7080000

Pre-ART blood count data indicate that 45 children (30.2%) had severe immunosuppression (CD4% <15%) and 56 children (37.6%) had moderate immunosuppression (CD4% 15%-25%). More than 84% of those with documented pre-treatment viral load data (n=144) had viral loads more than 50 000cells/mL.

The most recent blood count results for CD4% (n=164), show that five children (3%) indicated severe immunosuppression, 19 (11.6%) children showed moderate immunosuppression and the remainder (n=140) had no immunosuppression. Of those children with up-to-date viral load data (n=194), 50 (25.8%) had viral loads too small to detect or less than 20cells/mL.

4.5.5.1.1 Pre-treatment Blood Counts

4.5.5.1.1.1 Pre-treatment CD4 Count

The overall mean CD4 count was 1064.83 x 10*6/1 cells/mm3. Those reporting a disability had a lower mean CD4 count than the mean of and those without disability. However, there was no significant association in the pre-treatment CD4 counts between those with a difficulty and those without (p = 0.183), statistics are presented in Table 4.11.

4.5.5.1.1.2 Pre-treatment CD4%

The sample (n=150) had a mean CD4% of 21.44% (+-SD 11.25%). Those reporting a difficulty had a mean of 19.15% (+-SD 10.96%) and those without a disability had a mean of 23.43% (+-SD 11.47%). As shown in Table 4.11, a significant p-value of 0.021 was identified when analysing CD4% and occurrence of disability. Children with a lower pre-treatment CD4% are more likely to have one or more disabilities reported by their caregivers. Additionally, low CD4% was found to be significantly associated with the occurrence of TB (p = 0.0067) but none of the other recorded childhood and/or opportunistic infections.

4.5.5.1.1.3 Pre-Treatment Viral Load

Viral load group statistics are presented in Table 4.11. More children with positive TQSD outcomes had higher pre-treatment viral loads than those with negative TQSD outcomes. No homogeneity was met with a Levene's test and so a Mann-Whitney U test was performed on pre-treatment data and TSQD results. No significant association was found between those with a higher pre-treatment viral load and those with caregiver-reported disability (P=0.689).

Table 4.11: Group statistics of pre-ART blood count data

Variable	Total	With Disability	Without Disability	P-Value
Pre-Treatment Blood Count Data				
CD4 Count				
Total N	**156**	**76**	**80**	
Mean CD4 Count 10*6/1 cells/mm3	1064.83 (SD: 814.44)	975.66 (SD: 840.02) (Std. Err. Mean: 96.36)	1149.54 (SD: 785.24) (Std. Err. Mean: 87.79)	0.183
CD4 %				
Total N	**150**	**76**	**74**	
Mean CD4%	21.44 (SD: 11.25)	19.15 SD: 10.96) (Std. Err. Mean: 1.27)	23.43 (SD: 11.47) (Std. err. Mean: 1.33)	0.021
CD4% Thresholds, n (%)				
<15%	48 (32.2%)	31 (40.8)	17 (23)	
15-25%	66 (44.3)	33 (43.4)	33 (44.6)	
>25%	36 (24.2)	12 (15.8)	24 (32.4)	
Viral Load, cells/mL				
Total N	**144**	**68**	**76**	
Mean Viral Load, cells/mL	10187879 (SD: 70489049)	19130134 (SD:100669931)	1961005 (SD: 2955962)	0.689
Viral Load Thresholds, n (%)				
<50	0	0	0	
50 - 1000	3 (2.1)	1 (1.5)	2 (2.6)	
1000 - 10 000	8 (5.6)	1 (1.5)	7 (9.2)	
10 000 - 50 000	11 (7.6)	3 (4.4)	8 (10.5)	
>50 000	122 (84.7)	63 (92.6)	59 (77.6)	

4.5.5.2 HIV Treatment Factors

Treatment factors are presented in Table 4.12 and are summarised in Table 8.3 (Appendix 10).

4.5.5.2.1 Age of starting ART

Information regarding age of starting ART was available for 189 children. There were big differences between the mean and median scores of age of starting ART. The mean age for starting ART was 20.27 months (SD: 3.89). However, the median age for starting ART was 10.5 months with an interquartile rage of 4-27 months. This difference is due to 16 (9.9%) children being initiated on ART between the ages of 5 – 9 years. This affected the mean score. Distributions are presented in Table 4.12.

The children with caregiver-reported disability, on average started ART later in life than those that did not. Those reporting a difficulty started at a median age of one year (mean 20.5 months), while those without a difficulty reported started ART at a median age of nine months (mean 18.47 months). However, despite this difference, there was no significant association between the age of starting ART and occurrence of disability (independent samples t-test p = 0.578). Descriptive statistics and associations are shown in Table 4.12.

4.5.5.2.2 Duration of ART

The sample of children were on cART for a mean of four years nine months (57.2 months) (SD: 28.3 months). Those reporting disability had been on cART for a mean of four years 10 months (58.4 months) (SD: 29 months). Those without disability had been on cART for a mean of four years and eight months (56 months) (SD: 27.6 months). The mean sample age was over six years while age of cART initiation was less than two years. Therefore, more children had been on cART for longer, due to average older age of the sample.

No significant association was found between the presence of disability and the amount of time a child was on cART (p = 0.556). Group statistics are shown in Table 4.12.

4.5.5.2.3 Defaulting treatment

Frequencies and percentages are presented in Table 4.12. Information regarding defaulting treatment was only found in 139 (69.5%) of the whole sample. More than a third (n=51, 36.7%) of those had previously defaulted on treatment.

More of those with disability defaulted treatment (n=28, 38.4%) but there was no significant association (Chi-square test p = 0.726) between defaulting treatment and the existence of difficulties in a child. But with 30% of the sample missing this data, this could influence the results.

4.5.5.2.4 Maternal ART

No significant association between maternal ART during gestation and caregiver-reported difficulty was found (Chi square p = 0.193). No significant association was found between maternal ARV treatment and prematurity (Chi-square p = 0.606) or birth weight (p = 0.441). Nonetheless, this must be interpreted with caution due to the small number of preterm births in the sample (Table 4.6).

Table 4.12: Group statistics of HIV treatment factors

Variable	Total	With Disability	Without Disability	P-Value
Age of starting cART (Months)				
Total N	**189**	**93**	**96**	
Mean	20.27	20.53	18.47	0.578
SD	3.89	24	22.79	
Std. err. Mean		2.68	2.53	
Median	10.5	12	9	
IQR	4-27	5 – 29.75	3.88 – 25.5	
Age bands of starting ART, n (%)				
<6 months	71 (37.6)	30 (32.3)	41 (42.7)	
6 - 12 months	32 (16.9)	19 (20.4)	13 (13.5)	
12 - 24 months	32 (16.9)	16 (17.2)	16 (16.7)	
24- 36 months	23 (12.2)	11 (11.8)	12 (12.5)	
36 - 48 months	7 (3.7)	3 (3.2)	4 (4.2)	
48 - 60 months	8 (4.2)	6 (6.5)	2 (2.1)	
60 - 107 months	16 (8.5)	8 (8.6)	8 (8.3)	
Duration on cART (Months)				
Total N	**183**	**94**	**89**	
Mean	57.2	58.4	56	0.556
SD	28.3	29	27.6	
Std. err. Mean		2.53	2.31	
Median	62	64	60	
IQR	31 - 81	30.25 - 83	34.63 - 79	
Duration bands, child was on ART, n (%)				
<12 months	13 (7.1)	7 (7.4)	6 (10.1)	
12 - 24 months	20 (10.9)	8 (8.5)	12 (13.5)	
24 - 48 months	38 (20.8)	18 (19.1)	20 (22.5)	
48 - 72 months	49 (26.8)	23 (24.5)	26 (29.2)	
72 - 107 months	63 (34.4)	38 (40.4)	25 (28.1)	
Treatment Defaulting, n (%)				
Total N	**139**	**73**	**66**	
Ever defaulted treatment	51 (36.7)	28 (38.4)	23 (34.8)	0.726
Maternal ART, n (%)				
Total N	**188**	**95**	**93**	
Maternal ART	52 (27.7)	22 (23.2)	30 (32.3)	0.193

4.5.6 Childhood and/or Opportunistic Infections

A variety of common childhood and/or opportunistic infections were experienced by 149 children (74.5%). Of those children, 44 (29.5%) had one recorded disorder/infection, and the remaining 105 (70.5%) had more than one.

Chi Square tests were used to find the p-value for each childhood and/or opportunistic infection presented in Table 4.13.

"Skin disorders" includes, eczema, herpes simplex, herpes zoster, molluscum contagiosum, *tinea capitus*, *sarcoptes scabiei* and undiagnosed rash. Skin disorders were the most common infection/disorder (53.5%).

TB was the second most common opportunistic infection (37%) followed by LRTI (24.5%) and upper respiratory tract infections (URTI) (24%). Congenital toxoplasmosis was not found to be recorded in clinical files. Seven children had a file-recorded diagnosis of CMV and another seven had a file-recorded diagnosis of meningitis. These were too few to calculate an association between CMV or meningitis and disability.

Conjunctivitis, otitis media, oral thrush, skin disorders and URTI had no significant association to caregiver-reported disability.

Of the entire sample, 74 (37%) had a previous official diagnoses of TB. Using the Chi-square test, a significant association between TB and the presence of a difficulty was found (p = 0.003). TB was also found to be significantly associated with pre-treatment CD4% (p = 0.007).

A significant association was found (p = 0.049) between LRTI and caregiver-reported disability. No relationship was found between LRTI and TB (p = 0.397).

Table 4.13: Distribution of common childhood and/or opportunistic infections

Variable	Total	With Disability	Without Disability	P-Value
Opportunistic Infections, n (%)				
Total N	**200**	**101**	**99**	
Cytomegalovirus	7 (3.5)	3 (3)	4 (4)	Too small
Conjunctivitis	34 (17)	17 (16.8)	17 (17.2)	0.949
Lower Respiratory Tract Infect.	49 (24.5)	31 (30.7)	18 (18.2)	0.049
Meningitis	7 (3.5)	5 (5)	2 (2)	Too small
Otitis Media	38 (19)	20 (19.8)	18 (18.2)	0.858
Oral Thrush	29 (14.5)	18 (17.8)	11 (11.1)	0.229
Skin disorders	107 (53.5)	60 (59.4)	57 (57.6)	0.886
Tuberculosis	74 (37)	49 (48.5)	25 (25.3)	0.003
Upper Respiratory Tract Infect.	48 (24)	25 (24.8)	23 (23.2)	0.063

4.5.7 Socioeconomic Factors

4.5.7.1 Household Location & Income

Children lived a mean of 26km from the study site clinic. Four child/caregiver pairs (2%) lived in hostels or houses shared with non-relatives, nine (8.5%) lived in flats, 42 (21%) lived in single rooms, 54 (27%) lived in shacks and 83 (41.5%) lived in houses.

Figure 4.11 shows the distribution of household monthly income. The entire sample earned a mean R5235p/m (Median: R3300/pm). Three quarters of the sample earned less than R6350 a month. Children with difficulty came from homes with lower mean household monthly income than children with no disability. However, no statistically significant association between monthly household income and disability in children with HIV (p = 0.127) was found. These results should be interpreted cautiously as there was not an even income distribution with only 25% earning more than R6350.

A mean size of a household was 4.5 people (median: 4). The sample had a mean Rands, per person, per month (Rands/person/month) of R1342.17 (SD: R1513.02). The UBPL for 2017 is R1138/person/month. Of the sample that provided income information (n=196), 118 (60.2%) lived below the UBPL. Of these, 60 (30.6%) lived below the FPL (<R531/person/month) and 32 (16.3%) lived below the LBPL. No association was found between disability and Rands/person/month. Distributions are presented in Figure 4.12 and Table 4.14.

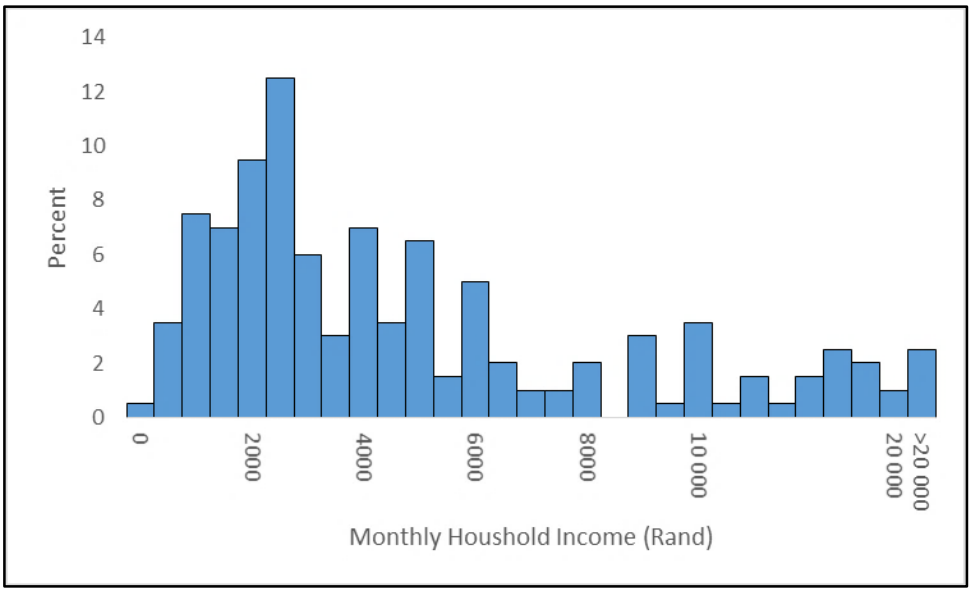

Figure 4.11: Household monthly income distribution

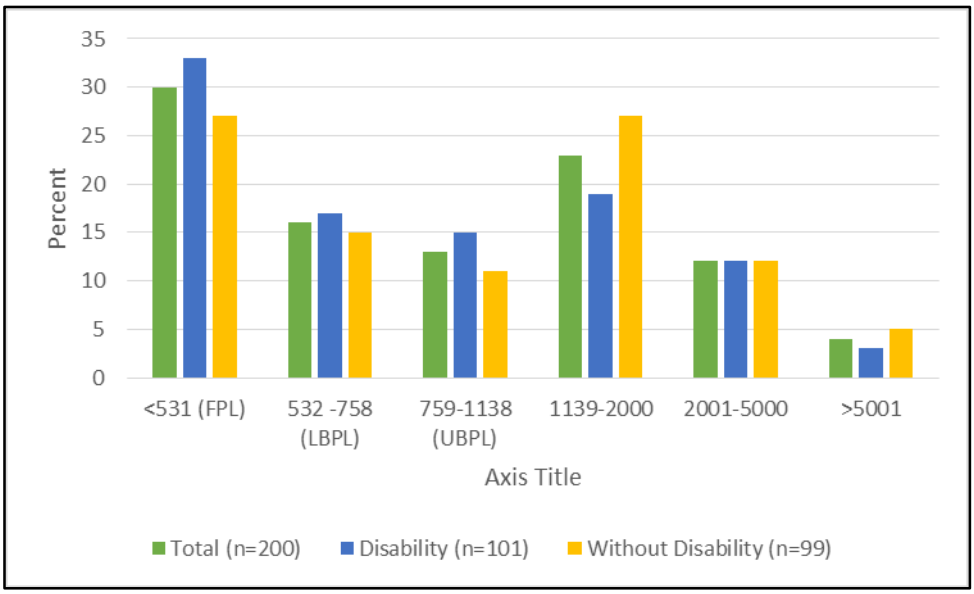

Figure 4.12: Distribution of income (Rands) per person per month.

Abbreviation: FLP: Food Poverty Line; LBPL: Lower Bound Poverty Line; UBPL: Upper Bound Poverty Line

4.5.7.1 Orphan Status

Orphan status was unknown for nine children. Thirty-three (17.28%) children were orphans and 18 (54.5%) orphans had caregiver-reported disability. There was no significant association between orphan status and the presence of disability (Chi- Square p = 0.568). No significant association was found between orphan status and cognitive and behavioural difficulties.

4.5.7.2 Caregiver's education

Five caregivers (2.5%) did not answer the question regarding the main caregivers' education. The majority, 57 of 195 caregivers (29.2%) had a Grade 10-11 education, followed by a matric or vocational training (n=45, 24.1%) and Grade 7-9 education (n=42, 21.5%). A chi-square test showed no significant association (p = 0.226) between the main carers education and the existence of a difficulty in a child. These statistics are presented in Figure 4.13 and Table 4.14.

Table 4.14: Socioeconomic factors

Variable	Total	With Disability	Without Disability	P-Value
Household Income				
Total N	**196**	**99**	**97**	
Mean Monthly Household Income (Rands)	5235 (SD: 5813) (SE: 436)	4653 (SD: 4829) (SE: 725)	6337 (SD: 7110) (SE: 485)	0.127
Mean Rands/person/month	1342.17 (SD: 1513.02)	1205.31 (SD: 1402.15)	1486.34 (SD: 1613.29)	
Rand/person/month thresholds, n (%)				
< R531 (FPL)	60 (30.6)	33 (33.3)	27 (27.8)	
R532- R758 (LBPL)	32 (16.3)	17 (17.2)	15 (15.5)	
R759 - R1138 (UBPL)	26 (13.3)	15 (15.2)	11 (11.3)	
R1139 – R2000	46 (23.5)	19 (19.2)	27 (27.9)	
R2001 – R5000	24 (12.2)	12 (12.1)	12 (12.4)	
>R5001	8 (4.1)	3 (3)	5 (5.2)	
> R5000	8 (4.1)	3 (3)	5 (5.2)	
Orphan Status				
Total N	**191**	**94**	**97**	
No. of orphans	33 (17.3)	18 (19.1)	15 (15.5)	0.568
Main Caregiver Education				
Total N	**195**	**100**	**95**	
No School	6 (3.1)	3 (3)	3 (3.2)	0.226
< Grade 7	10 (5.1)	6 (6)	4 (4.2)	
Grade 7-9	42 (21.5)	27 (27)	15 (15.8)	
Grade 10-11	57 (29.2)	28 (28)	29 (30.5)	
Matric/Vocational training	47 (24.1)	22 (22)	25 (26.3)	
1-2y college/technikon	29 (14.9)	13 (13)	16 (16.8)	
>3y University	4 (2.1)	1 (1)	3 (3.2)	

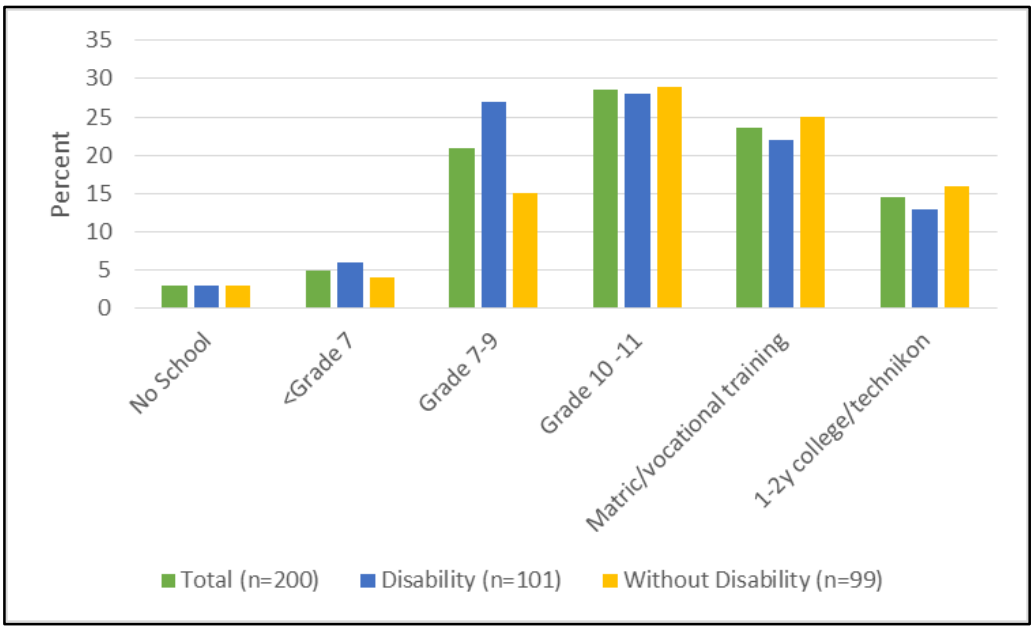

Figure 4.13: Main caregivers' education level

4.5.8 Logistic Regression Model

WAZ Z-score, pre-treatment CD4%, a medical history of TB and/or LRTI were found to be significantly associated with disability. Additionally, a trend of significance was found between birth weight and the presence of disability in children infected with HIV. TB and pre-treatment CD4% were significantly associated (p = 0.0067) therefore both of these factors could not be used in logistic regression analysis. WAZ Z-score and birth weight were significantly associated (p = 0.0001) and therefore both factors could not be used in a logistic regression. Birth weight, CD4% and LRTI were used in a logistic regression model. With 109 observations and a p-value for the model of 0.0003, pre-treatment CD4% and LRTI remained significantly associated to the occurrence of disability but birth weight did not. Values are presented in Table 4.15.

Table 4.15: Logistic regression results between occurrence of disability and birth weight, CD4% and LRTI

	Coefficient	**Std. Err**	**P- value**
Birth Weight	-0.33	0.32	0.3000
CD4 %	-0.49	0.02	0.0240
LRTI	1.75	0.56	0.0020

4.6 Conclusion

More than half of the sample scored positively on the TQSD for disabilities many of whom have two or more coexisting disabilities. A summary of possible confounding or associated factors are shown in Table 8.3 (Appendix 10). Possible factors that were associated with increased likelihood of disabilities in children with HIV in this study were a medical history of TB and/or LRTI and/or a low pre-ART CD4%. No clinical or socioeconomic confounding factors were identified. There are many different medical and supportive services available to the children at the study site. In spite of this very few children were referred to supportive services considering the high prevalence of disability.

CHAPTER 5

5. DISCUSSION

"As children infected with HIV live longer, relatively healthier lives, the impact of even subtle impairments becomes more significant" (Potterton et al., 2016; p.3).

This chapter will explain the study design, discuss the results and relate the findings to previous studies. It will discuss the limitations, implications and recommendations for services and the development of future studies.

This study found that 50.5% of a cohort of children infected with HIV had developmental and functional disabilities. These findings are consistent with other studies from Southern Africa (Devendra et al., 2013; Lowick et al., 2012; Potterton et al., 2016; Van Rie et al., 2008) and have a large impact considering the absolute numbers of children infected with HIV in sub-Saharan Africa.

5.1 Study Design

This study interviewed a group of caregivers whose children were between the ages of two and nine years. These children attended an urban HIV clinic in Johannesburg. The study site clinic is a well-established urban service and research unit and is an exclusively paediatric HIV clinic. PHC clinics and peri-urban and rural clinics do not have the same specialization and resources that the study site has. This needs to be taken into account when interpreting the results. These results cannot be generalised to the population of South African HIV-infected children.

5.2 Disabilities Experienced by Children

5.2.1 Results of Ten Question Screen for Disability

Just more than half (50.5%) of the sample screened positive on the TQSD for one or more disabilities. This prevalence is much higher than the 2-6% prevalence found in disability studies on the general South African paediatric population (Christianson et al., 2002; Couper, 2002; Gladstone, 2010; G. Saloojee et al., 2007; Stats SA and Lehohla, 2005) or even the reportedly inflated 10% prevalence conveyed in the Census 2011: Profile of Persons with Disability in South Africa. All studies referenced above, used screening tools to identify disability and they all used similar study designs to the current study. Christianson et al. (2002) and Couper (2002) used the TQSD in rural South African populations while Stats SA and Lehohla (2005) and Census 2011 used census survey questions in rural and urban populations. Therefore, this large difference in prevalence between the current study and that of the

general population, is unlikely to be due to differences in data collection tools or difference in the classification of a “disability”.

This study’s findings are similar to those of R.Govender et al. (2011) who found neurological impairment in 59% of their sample of HIV-positive children between the ages of three months and 12 years old using the Denver II Developmental Screening tool, a neurological exam and the Aberrant Behaviour Checklist. Devendra et al. (2013) used the same measurement tool as the current study (TQSD) in their study in Malawi and therefore, had the same age range yet, found the prevalence of disability to be less, at 33%. However, Devendra et al. (2013) did postulate that there may have been a lack of understanding of what could qualify as a disability and that there was a low level of awareness amongst their sample. This study’s sample had slightly different SES characteristics to the Devendra et al. (2013) study which may contribute to the current sample having a better awareness of the difficulties their child may experience, therefore, resulting in a higher prevalence. These SES differences will be discussed later in this chapter.

Of the 101 children who reported disabilities in the current study, 42% had a single difficulty and 58% reported more than one difficulty (31% had two co-existing impairments, 27% had more than three co-existing disabilities). Devendra et al. (2013) found a similar distribution (49% had a single disability, 29% had two co-existing types of disability and 22% had three or more). It is evident that children born with HIV experience a broad spectrum of disabilities with a high risk of multiple impairments. These two studies emphasise the need for a holistic and multidisciplinary approach to the management of these children.

5.2.2 Neurodevelopment

It is well understood that HIV infects and affects the CNS and can be particularly detrimental to the developing foetal and infant brain (Angelini et al., 2000; Benki-Nugent et al., 2015; Crowell et al., 2015; Everall et al., 2005; Gorry et al., 2003; Gray et al., 2014, 2016; Schwartz et al., 2007; Van Rie et al., 2007). As a result of an affected neurological system, the developmental trajectory of a child with HIV is not expected to be that of a typical child (Armstrong, 2006; Maes, 2016; Sherr et al., 2014a). Therefore, it is not surprising that developmental delay was the most common reported difficulty in this study (27%). These results echo a 2015 review which found that developmental delay was highly prevalent in most of the studies reviewed and concluded that developmental delay is significantly linked with HIV (Banks et al., 2015). Early studies found a very high prevalence (63-90%) of developmental delay in children with HIV (Lowick et al., 2012; Potterton et al., 2009; Ruel et al., 2012; Van Rie et al., 2008). A more recent study reported a slightly lower occurrence of developmental delay in 3-5 year old children infected with HIV (55.8%) (Potterton et al., 2016). This is still much higher than

the 27% found in the current study. Both the Potterton et al. (2016) and the current study were conducted at the same study site. However, the current study relied on caregiver reported data while Potterton et al. (2016) used the GSMD. This study had a higher mean age (76.8 months) than the 2016 study (46.8 months). This may contribute to the caregivers/parents' perception of developmental delay, where mild delays may be seen as cognitive and behavioural fallout or speech difficulties rather than failure to achieve gross motor milestones (Glascoe, 1994).

This study found that 12.5% of carers reported physical problems (defined as function and participation limitations) in their children. This was much less than Devendra et al. (2013) reported (33%). However, this study differentiated between physical disabilities and developmental delay. The TQSD has one question pertaining to delayed milestones of a child and one question regarding physical limitations. The Malawian study combined these two into one category, while the current study defined a difference between developmental delay and physical disability. When this study combined the developmental delay and physical disability occurrences, the prevalence was 35% which is similar to the findings of Devendra et al. (2013) in Malawi.

PN was only diagnosed in two (1%) children's whose parents/caregivers participated in the study. Benjamin et al. (2015) found a 36% prevalence of PN in children from the same site. These findings reflect Peters et al. (2014) and Benjamin et al. (2015) conclusion that PN is severely underdiagnosed in this population. Both of these studies recommended regular neurological screening and assessments for children infected with HIV.

This study has shown a high prevalence of developmental delay and/or physical disabilities. In addition, research shows that most beneficial time to address neurodevelopmental difficulties in children with chronic disease is not when they present, but in anticipation and prevention of disability (Armstrong, 2006). Hence, this would indicate that early developmental intervention for children born with HIV should be a universal requirement.

5.2.3 Vision

Visual difficulties were reported in 8.5% of the cohort which is higher than Devendra et al.'s (2013) findings in Malawi (6%), but much lower than other studies which found a 16-67% prevalence (R. Govender et al., 2011; Ikoona et al., 2003; Kestelyn et al., 2000; M'bongo Zindamoyen et al., 2013). However, the Malawian study used caregiver/parent proxy reported data from the TQSD (same as the current study) and their result is closer to the current study's result. Other studies were less recent and data were collected by thorough ocular assessments. These results reflect Padhani et al. (2000) concerns that visual difficulties are more difficult to identify in children and therefore, are not necessarily recognised by caregivers. In addition conjunctivitis was present in 17% of the cohort of

which half reported visual difficulty. Caregivers may not be aware of the functional implications that conjunctivitis, especially recurrent conjunctivitis, could have on a child's vision and learning capacity (Kurtz, 2006; Paranjpe et al., 2016; Sheppard et al., 2016; Wang et al., 2016).

The prevalence of conjunctivitis in the current study (17%) was only slightly higher than the results found by Ikoona et al. (2003) (12%) and M'bongo Zindamoyen et al. (2013) (13%). This study found a low incidence of pterygium (1%) and strabismus (2%) compared with other studies (Ikoona et al., 2003; M'bongo Zindamoyen et al., 2013; Padhani et al., 2000; Rutar et al., 2015) which also found a high prevalence of perivasculitis, keratoconjunctivitis sicca, *ocular molluscum contagiosum*, conjunctiva xerosis and CMV retinitis among HIV-infected children (Ikoona et al., 2003; Kestelyn et al., 2000; M'bongo Zindamoyen et al., 2013; Padhani et al., 2000; Rutar et al., 2015). However, no data were collected, either caregiver-reported or file-reported on these conditions. This study's results were generated from HIV clinic notes and caregiver-reported data, whereas the other studies were based on comprehensive ophthalmic assessments, which may explain the lack of data on these ocular conditions in this study.

5.2.4 Hearing

Studies that incorporated comprehensive hearing assessments found the prevalence of hearing difficulties to be between 20-33% (Christopher et al., 2013; Hrapcak et al., 2016; Torre et al., 2012). However, parent/caregiver reported hearing difficulties in children have been recorded at around 12% (Devendra et al., 2013). In keeping with this trend, this study found a lower prevalence (9%) of hearing difficulties via caregiver proxy reporting. It is curious that studies using the TQSD, which purportedly renders high false positives for hearing impairment (Durkin et al., 1995), results in a lower prevalence of hearing impairment than studies which include an audiological assessment. This may be due to an actual lower prevalence of hearing difficulty in this study's population. However, Devendra et al. (2013) and Hrapcak et al. (2016) conducted their studies at the same clinic in Malawi. Devendra et al. (2013) used the TQSD and found half the prevalence of hearing difficulties (12%) as Hrapcak et al. (2016) found (24%), using an audiological examination. Hence, it may be more cautious to interpret that the lower prevalence found by this study may indicate that caregiver-reported hearing problems may not be a reliable indicator of hearing difficulty. There are many factors that could influence the hearing of a child infected with HIV over its lifetime, so, rather than relying on parental concern only, regular hearing screening and assessment by audiologists is important (Kanji and Kara, 2013; Khoza-Shangase et al., 2010; Khoza-Shangase and Turnbull, 2009).

5.2.5 Speech & Language

Studies conducted in Sub-Saharan Africa, which investigated speech delay and language insufficiencies in HIV-positive children, found the prevalence of communication delay to be between 45-85% (Alcock et al., 2016; Baillieu and Potterton, 2008; Potterton et al., 2016; Van Rie et al., 2008; Whitehead et al., 2014). This wide range has been attributed to changes in ARV treatment regimens protocols and access (Whitehead et al., 2014). This study found a lower prevalence of speech and language difficulties (17%). This may have been due to the other studies using comprehensive outcome measures such as the BSID or the GMDS to assess speech and language ability. However, Whitehead et al. (2014) did conclude that speech and language delay improved with time and as this study had, on average, an older cohort than previous studies (Alcock et al., 2016; Baillieu and Potterton, 2008; Potterton et al., 2016; Van Rie et al., 2008; Whitehead et al., 2014), caregivers/parents may not have reported any difficulty.

5.2.6 Cognitive and Behavioural

There is consistency among the literature that cognitive and behavioural difficulties are definitively linked with HIV (Sherr et al., 2014a). However, there are some discrepancies when it comes to prevalence of cognitive and behavioural impairment. Just over a fifth (21%) of the caregivers interviewed, reported cognitive, behavioural and emotional difficulties in their children. This prevalence is consistent with Potterton et al. (2009), but is generally lower than findings of other similar studies conducted in sub-Saharan Africa (45-97%) (Baillieu and Potterton, 2008; R. Govender et al., 2011; Hoare et al., 2016; Hutchings and Potterton, 2014; Lowick et al., 2012; Potterton et al., 2016; Van Rie et al., 2008; Whitehead et al., 2014). Only two papers reviewed in this study, found a lower prevalence (11-16%) of cognitive and behavioural problems than this current study (Devendra et al., 2013; Kandawasvika et al., 2015). All in all, the prevalence of cognitive and behavioural difficulties ranges from 11 – 97%. Sherr et al. (2014) hypothesized in their review that this wide range is due to the inconsistencies of outcome measures used and the resultant differences in age-bands of assessments. The average age of the samples in these studies, varied greatly, from five months to eight years. Comprehensive outcome measures that had been used were the BSID (Baillieu and Potterton, 2008; Hutchings and Potterton, 2014; Potterton et al., 2009, 2016), Denver-II (R. Govender et al., 2011), GSMD (Lowick et al., 2012), McCarthy Scales of Children's Abilities (Kandawasvika et al., 2015), PDMS (Van Rie et al., 2008) and the WISC-IV (Hoare et al., 2016). Devendra et al. (2013) and the current study were the only studies to use a caregiver-report screening tool, which resulted lower-than-average (according to the literature) prevalence of cognitive and behavioural impairments in both studies.

In this study, caregivers of 41 (21%) children expressed concerns regarding their child's learning, concentration, behaviour and emotional status but only three had ever been referred to a psychologist. This discrepancy may be due to a lack of the parent/caregiver reporting these disabilities to clinicians, or reflect the more subtle nature of the cognitive and behavioural disability these children are facing that are not being identified by either parent/caregiver or clinician (Bamford and Lyall, 2015; Donald et al., 2014; Phillips et al., 2016; Potterton et al., 2016; Ruel et al., 2012; Sherr et al., 2014a; Smith et al., 2012).

5.2.7 Seizures

Five carers reported seizures in their children but only one child overlapped with the three that have official epilepsy diagnoses. This discrepancy may be due to the fact that carers would have reported any seizure whether it was related to epilepsy or due to severe acute illness such as acute gastroenteritis, while only a diagnosis of epilepsy would be noted in the clinic file. Children diagnosed with epilepsy and on medication may not have been reported as their seizures are controlled and the interviewee may never have witnessed a seizure in the child.

Prevalence of seizures in the sample was 2.5% which is lower than the findings of Devendra et al. (2013) in Malawi (6%). This study found diagnosed epilepsy in 1.5% of the sample. This prevalence is consistent with studies of the general population of children living in sub-Saharan Africa (Ae-Ngibise et al., 2015; Burton et al., 2012; Wagner et al., 2014). This may be attributed to improved treatment regimens which increase the strength of the immune response, thereby lowering the incidence and/or severity of acute illness, which in-turn results in decreasing the risk of occurrence of febrile or acute symptomatic seizures. However, more research is needed in this area to explain these differences.

Two Cape Town studies on children with HIV found much higher prevalence of epilepsy (7.6-11.5%) (R. Govender et al., 2011; Samia et al., 2013). In addition, the difference between the current study and the Cape Town studies may be attributed to changes in ARV treatment regimes. R.Govender et al. (2011) used a small sample size (n=78) and 14% were ART-naive compared with the current study which had 95.5% of the sample on ART. Samia et al. (2013) had a larger sample of inpatients (n=354) while the current study used clinic outpatients.

5.3 Services

A wide range of medical and supportive services seem to be available to this population of children, however, limited information on child development is presented to caregivers/parents at the study site. Only information on nutrition, lifestyle and adherence were provided in waiting room information sessions. The *B-wise mobi-site is* more focused on personal (aimed at adolescents and young adults) health rather than child development (Department of Health, 2015) and is only accessible to carers

with a smart mobile phone. No research was found on the benefit and extent of the utilization of this mobile application in the South African population.

Physiotherapy, occupational therapy and speech and language therapy were commonly accessed at the hospital. Those receiving regular treatment, usually had appointments once a month. Audiologists and optometrists were more likely to be seen at an "unknown facility" (which is possibly another referral hospital for these services in the area) or at school, than at a clinic or RMMCH. The most common referrals made by the HIV clinic were to the HIV counsellor (100%), dietician (32.5%), social worker (24%) and dentist (11.5%). However, of those that reported disability, less than half (45.5%) were actually referred to any support services including audiologist, learning support, OT, optometrist, PT, psychologist or SLT. Of those that were referred, 21% admitted to never accessing these services due to financial (for transport or service) constraints, transport difficulties or cancellation of appointment either due to patient illness or service provider cancellation. These reasons are similar to the reasons Devendra et al. (2013) found in Malawi. Many studies have made proposals and recommendations about early initiated, comprehensive, universal, regular and continual neurodevelopmental assessment and treatment by allied health professionals (Abubakar et al., 2008, 2009; Banks et al., 2015; Devendra et al., 2013; Eley and Nuttall, 2007; Grover et al., 2007; Hilburn et al., 2010, 2011, 2015; Hrapcak et al., 2016; Isanaka et al., 2009; Kandawasvika et al., 2011; Lowenthal et al., 2014). Proposals and recommendations which have been brought to the attention of South African health care professionals, policy makers and government. However, the results of this present study indicate, that overall, very few children are referred and/or are accessing these services. Further study needs to be conducted into the lack of referrals to determine if it is a lack of;

1) Straightforward referral and awareness that HIV management needs to shift from life-saving focus to a holistic focus (Lowenthal et al., 2014).

2) Available and accessible resources and service provision in South Africa (Department of Social Development et al., 2012; Donald et al., 2014; R. Govender et al., 2011; Hutchings and Potterton, 2014; Jonker and Stellenberg, 2014; Lowick et al., 2012; Saloojee and Bamford, 2006; Smith et al., 2008).

3) Or, a combination of the two.

5.3.1 Audiology Referrals and Assessment

The HPCSA Early Hearing Detection and Intervention Programmes in South Africa Position Statement 2007 recommends universal new-born screening in hospitals and PHC facilities as well as many other studies have expressed the need for ongoing surveillance for individuals who have a high risk of hearing loss, such as children infected with HIV (Christopher et al., 2013; Govender et al., 2015; Harris

et al., 2012; HPCSA, 2007; Hrapcak et al., 2016; Khoza-Shangase and Turnbull, 2009). Considering this, the percentage of the current sample who reported visiting an audiologist was incredibly low (14.5%). In addition none of the children who had audiological screening/assessments had had these screening/assessments at a PHC clinic. This reflects Petrocchi-Bartal and Khoza-Shangase's (2016) findings, that formal hearing screenings were not being conducted at any PHC clinics in Gauteng and one other province in South Africa, despite HPCSA guidelines and recommendations (HPCSA, 2007).

Of those whose caregivers/parents reported concern regarding hearing, only five (29.4%) children were referred to an audiologist and six (18.2%) children with a reported speech difficulty were referred for a hearing assessment. This is higher than the Ear Clinic referral rate Devendra et al. (2013) found in their study. This low referral and assessment of children for a service that is intended to be universal may be attributed to poor awareness of risk factors for hearing loss among paediatric physicians (Kanji and Kara, 2013; Khoza-Shangase et al., 2010; Khoza-Shangase and Jina, 2013) or a possible lack of hearing screening services at a primary health care level (Petrocchi-Bartal and Khoza-Shangase, 2016). This lack of service is apparent as carers of 28 children (14% of entire sample) reported that they would like to be referred to have their child's hearing tested.

5.3.2 Optometry/Eye Clinic Referrals and Assessment

Literature has found that ocular manifestations of HIV occur in 23-67% of children (P. Govender et al., 2011; Ikoona et al., 2003; Kestelyn et al., 2000; M'bongo Zindamoyen et al., 2013; Padhani et al., 2000; Rutar et al., 2015), some of which are asymptomatic (P. Govender et al., 2011). Some of these manifestations and have known long term implications as well as treatment side effects (Kurtz, 2006; Paranjpe et al., 2016; Sheppard et al., 2016). As a result, studies have recommended mandatory, regular, comprehensive ophthalmic examination for all children but most especially those who are HIV-positive (P. Govender et al., 2011; Padhani et al., 2000). Considering this, it is surprising that 79.5% of children in this study had never been assessed by an optometrist or an eye clinic. This percentage is worrying considering the National Integrated School Health Policy states that all children will have regular vision screening throughout their school years (DOH and DOBE, 2013). In addition, only 12 children (29%) who were assessed were assessed at school. Even more concerning is the small amount of referral to ocular health services from health care service providers (14%) and of those with caregiver-reported visual difficulties (n=17) only three children (17.6%) had been referred to an optometrist and/or Eye Clinic. This is considerably lower than what was found in Malawi, where 57% of those with reported visual difficulties had visited the Eye Clinic (Devendra et al., 2013). This difference could relate to different protocols in place at the different study site locations, different approaches to ocular health awareness among health care professionals and/or caregivers/parents, or differences in vision screening services. Due to the high risk of visual difficulties in children living

with HIV, visual screening should be an integral part of HIV treatment clinics and paediatric management.

5.3.3 Physiotherapy and Occupational Therapy Referrals and Assessment

The role of physiotherapy and occupational therapy in assessing and managing children with HIV and the subsequent neurodevelopmental fallout has been highlighted and in many studies it is coupled with recommendations on regular developmental screening and follow-up services. (Baillieu and Potterton, 2008; Banks et al., 2015; Hilburn et al., 2010, 2011, 2015, Potterton et al., 2009, 2016; Tumusiime et al., 2015). However, it appears that these services are under-referred to and underutilised (Devendra et al., 2013). Very few children reporting developmental delay and/or physical difficulty were referred to physiotherapy and or occupational therapy services. These results are similar to the referral rate children with physical disability experienced in Malawi (Devendra et al., 2013). Of the children that had physiotherapy assessments with no follow up treatment (n=13), 53.8% of these assessments were for research purposes only rather than referral due to developmental concern. This lack of referral for children with HIV may be due to a lack of insight of the requirements for early intervention and PT and OT referral by study site clinicians or that the focus of treatment is still predominantly on survival and those children with more chronic and quality-of-life difficulties are overlooked (Lowenthal et al., 2014). As PTs were seen more frequently during inpatient stays but less frequently (once a month) for out-patients the limited referral and treatment may be due to a lack of physiotherapy resources (personnel and financial) which limits a clinicians ability to refer.

OTs have a wide spectrum of expertise which aim to improve physical, sensory, functional, participatory, cognitive and psychological well-being in children and adults (Joubert et al., 2008; Lecuona et al., 2016; van Jaarsveld, 2014) and they have an important role in the management of HIV (Joubert et al., 2008). Yet, only eight children (4% of sample) had ever been treated on an outpatient and/or inpatient basis. More investigation is needed as to the lack of utilisation of these services.

PTs and OTs need to play an active part servicing paediatric HIV treatment clinics. Health care professionals and caregivers should receive more information and training regarding neurodevelopment and child development as well as potential red and yellow flags regarding developmental problems. Regular developmental screening services for children living with HIV can assist with earlier and better identification of developmental difficulties in order for early intervention to take place and be beneficial.

5.3.4 Speech and Language Referral and Assessment

Due to the multilingual nature of children in schools in South Africa, recommendations have been made for SLTs to be an integral part of schooling for all children attending public schools in South

Africa (Kathard et al., 2011; Wium and Louw, 2013). The SASLHA has also indicated the need for SLTs in neonatal care units, postnatal wards, PHC clinics and facilities, nursery schools, day care facilities and pre-schools (Bardien et al., 2011). In addition, research has reported global language delay in the majority (45-85%) of HIV-infected children between the ages of eight months and 16 years (Alcock et al., 2016; Baillieu and Potterton, 2008; Brackis-Cott et al., 2009; Hattam et al., 2014; Van Rie et al., 2008; Whitehead et al., 2014). Therefore, screenings for speech and language difficulties, should be a regular feature of the management of children infected with HIV (Hattam et al., 2014). Considering these recommendations and guidelines, it is concerning that only 6.5% of the sample had been assessed by a SLT. Of those with a speech difficulty (n=33), only 30.3% were referred to an SLT and of those with a hearing difficulty (n=17), only five (29.4 %) were referred to an SLT. Hattam et al. (2014) found similar low referral rates in their Gauteng study and speculated that many South African medical health practitioners are unaware of the implications of not referring children to speech and language service and "are not cognisant of the important role that the speech-language therapist and audiologist have in the assessment and treatment of the HIV infected child, as well as their role within the interdisciplinary team" (Hattam et al., 2014, p. 375).

5.3.5 Psychologist and Learning Support Referral and Assessment

Primary cognitive and psychiatric problems such as neurocognitive delay, ADHD and depression (Donald et al., 2014; R. Govender et al., 2011; Grover et al., 2007; Nozyce et al., 2006) as well a secondary neurocognitive fallout, psychological and psychosocial complications (Amzel et al., 2013; Bamford and Lyall, 2015; Gay et al., 1995; Grover et al., 2007; Lowenthal et al., 2014; Potterton et al., 2016; T. D. Ruel et al., 2012; Sharp et al., 2015; Smith et al., 2008, 2012) are common in children infected with HIV from an early age. Many studies have expressed how vital monitoring and ongoing psychological care are in the management of children with HIV (Abubakar et al., 2008; Amzel et al., 2013; Donald et al., 2014; R. Govender et al., 2011; Grover et al., 2007; Lowenthal et al., 2014; Lowick et al., 2012; Smith et al., 2012). It is therefore disturbing, that only three children (1.5% of the entire sample) in this study had been assessed by a psychologist or learning support services. Of the sample, 24 carers (12%) said they would like a referral for their child to a psychologist or learning support service.

The "Flipster Support Club Tool" (Right to Care and Mwanandimai, 2015) covers mental health issues such as stress, self-esteem and emotions, however, it is mainly aimed at adolescents. By the time a child has become a teenager, cognitive and behavioural issues are already present with consequent neurological changes and the opportunity for early prevention and interventions have been missed (Mwaba et al., 2015). There is a need for improved awareness regarding the subtle but significant cognitive difficulties a child living with HIV may be experiencing. Psychologists ought to be an integral

part in the multi-disciplinary team managing children with HIV. Regular monitoring of a child's mental health should to be a requirement for children infected with HIV (Grover et al., 2007; Lowenthal et al., 2014; Sherr et al., 2014b).

5.3.6 Barriers to referral, assessment and continued treatment

The researchers of this study found very similar barriers to therapy as Devendra et al. (2013) in Malawi and similar studies based on rehabilitation of adults with HIV (Chetty and Maharaj, 2013; Cobbing et al., 2014; Maddocks et al., 2018). According to the current study's results, a lack of referral appears to be the first barrier to receiving rehabilitative services. Maddocks et al. (2018) found this lack of referrals were due to a poor understanding of roles and hegemony which prevent effective and cohesive collaboration between professionals. In addition, Chetty and Maharaj (2013) identified organizational differences, role restrictions and environmental structure as barriers to collaboration between nurses and allied health professionals.

Barriers to attending assessment appointments and continuing with therapy include socioeconomic factors. Transport was a common barrier. Either, obtaining transport was difficult, or the carer had no money for transport or the service provider was too far which indicates expense in terms of time and money. Considering patients travelled a mean of 26km to be at the clinic, this indicates that support services are not easily accessible and available to this population. Furthermore, other caregivers indicated that due to the distance, they were unable to acquire time off work to take their child to support services. Allied health profession services need to be more widely available at PHC facilities in communities (Chetty and Hanass-Hancock, 2015, 2014; Cobbing et al., 2017, 2014) as well as taking an active role in multidisciplinary HIV clinic settings (Cobbing et al., 2013). The Chetty Model is currently being researched to assist with collaboration between government health care providers and the community to improve the model of care of people living with HIV (Chetty and Hanass-Hancock, 2016, 2015, 2014; Hanass-Hancock and Alli, 2015). Discussion of the Chetty Model and its benefits to managing children with HIV are beyond the scope of this paper, however it may prove to be a useful tool in providing access of rehabilitative services to this population.

Another barrier is a lack of follow-up if the appointment is missed. Missed appointments were due to a sickly carer or child or due to the provider cancelling. However, no follow-up date or referral are given post cancellation. Systems should be put in place in the health sector to ensure patients are re-issued with appointment dates and carers need education and awareness to take responsibility for ensuring and requesting another appointment date. Very few caregivers/parents stopped attending therapy because they felt it was not helping. However, caregivers/parents need to be educated and awareness created regarding purpose and expectations of therapy. Furthermore, if caregivers would

like to terminate therapy, they need to be aware to inform the therapist in order for follow-up to be put in place, especially with regards to school placement and support.

5.4 Possible Factors Associated with Disability

5.4.1 Sample Size

Much of the research on childhood disability in HIV-infected children have been done on smaller sample sizes. Data were collected and analysed on 200 children. Compared with other Southern African studies on HIV and disability, this is only one of six studies found that have sample sizes more than 100 participants (Range: n=122–380) (Devendra et al., 2013; Hrapcak et al., 2016; Potterton et al., 2009; Samia et al., 2013; Sherr et al., 2017). As a result this study has more power than some studies but less than others. Yet, the sample was taken from only one clinic which reduces generalizability.

5.4.2 Age & Sex

Of the entire sample, the mean age was six years five months (SD: 2 years) and 50.5% of the sample were male. The majority of studies conducted in sub-Saharan Africa have almost even ratios of male/female. Some, like this study have marginally more males (Alcock et al., 2016; R. Govender et al., 2011; Hoare et al., 2016; Jelsma et al., 2011; Potterton et al., 2016; Samia et al., 2013; Shead et al., 2010; Smith et al., 2008), while slightly more papers have a minor female dominance in their samples (Bagenda et al., 2006; Devendra et al., 2013; Hrapcak et al., 2016; Hutchings and Potterton, 2014; Kandawasvika et al., 2011, 2015; Khoza-Shangase and Turnbull, 2009; Lowick et al., 2012; Peters et al., 2014; Potterton et al., 2009; Ruel et al., 2012; Sadoh et al., 2007; Sherr et al., 2017; Torre et al., 2015; Van Rie et al., 2008; Whitehead et al., 2014).

Although not significant, those who reported a difficulty were slightly older (mean: six years and eight months) than those who did not report any disability (mean: six years and one month). This is reminiscent of approaches to any chronic disease where new areas of difficulty will be identified over time as the child grows and matures (Armstrong, 2006). No significant association was found between sexes and those with disability or those without disability.

5.4.3 Weight & Height

Overall Z-scores for WAZ and HAZ were skewed to the left (i.e. below average) which is consistent with other studies (McDonald et al., 2013; Potterton et al., 2016; Shead et al., 2010; Van Rie et al., 2008; Whitehead et al., 2014). In total, 10.3% were underweight (WAZ Z-score <-2), 13.8% were stunted (HAZ) and 4.7% were wasted (BAZ). This study found the same prevalence of underweight children (10.3%) as Potterton et al. (2016) which is lower than other studies (Jesson et al., 2015; Seth et al., 2017; Sherr et al., 2017; Van Rie et al., 2008). However, all the other studies were done in countries

with lower SES than South Africa (Central Africa, DRC, India, Malawi and West Africa). The prevalence of children with stunted growth in this study was much lower than other studies (Potterton et al., 2016; Shead et al., 2010). The prevalence of wasting (<-2 BAZ Z-score) was the same as McDonald et al. (2013) found in their study. Improved growth in children with HIV has been associated with health worker and caregiver nutritional training and nutrition supplementation (Sunguya et al., 2017; Vazir et al., 2013). The low prevalence of below average anthropometric data in this study may be attributed to the 33% referral rate from clinic staff to a dietician and regular nutritional information talks, that the caregivers receive in the clinic waiting room (Mwaba et al., 2015; Rose, 2017; Sunguya et al., 2014, 2017; Vazir et al., 2013).

WAZ Z-score was found to be significantly associated with the occurrence of disability ($p = 0.014$). However, WAZ Z-score was significantly associated with birth weight and birth weight was found to have no significant association when analysed in a logistical regression model. Therefore, these results need to be interpreted with care due to the low number of recorded birth weights (n=136) and differences in p-values. However, with care, a low WAZ Z-Score could be used to raise the index of suspicion of children who may be experiencing functional and developmental disability as indicated by other studies (Abubakar et al., 2009; Devendra et al., 2013; Hutchings and Potterton, 2014).

5.4.4 HIV Encephalopathy

Despite HIVE being a reliable predictor of disability (Everall et al., 2005; Mitchell, 2006; Shanbhag et al., 2005; Smith et al., 2008, 2012), very few diagnoses were made (4%). It would be hopeful to deduce that HIVE is declining with the advent of ART. However, the high prevalence of disability found in this study disagrees and researchers are more inclined to agree with Donald et al. (2015) who report, that imaging diagnosis is too expensive and clinicians tend to underdiagnose or avoid HIVE diagnosis all together. Plateau and static HIVE tend to be under-recognised, which may be an explanation for the lack of referral to support services experienced by this population (Donald et al., 2015). If HIVE diagnosis improves, children with HIVE and therefore at risk for developing a disability could be better identified with earlier and more prompt referral to support services.

5.4.5 Gestation and Mode of Delivery

Gestation and birth factors were explored to assess if there were associations between caregiver-reported disability and these features.

No significant association was found between modes of delivery (natural versus C-Section) and the occurrence of problems a child may experience. These results need to be interpreted with caution as the incidence of natural delivery was high. Furthermore, there was no significant association between gestation duration and occurrence of difficulty. The frequency of premature births as individual

groupings (34-36 weeks and <34 weeks) were too small for analysis and as a result clustered into one group (<37 weeks). This may have skewed results and hence these results should be interpreted with caution. The low prevalence of premature births is interesting as studies have shown links between maternal HIV and low gestational age (Arab et al., 2017; Uthman et al., 2017; Xiao et al., 2015; Zack et al., 2014). This study was not able to assess the association of gestation and HIV status as all children in the cohort were HIV positive. However, it appears that the low prevalence of premature births may be in line with a Malawian study that found no significant association between premature delivery and maternal HIV and ART (Chagomerana et al., 2017). More research is required to gain more insight on this matter.

5.4.6 Birth Weight

A trend of significant association (p = 0.051) between low birth weight and disability was found. However, when analysed in a logistic regression, an adjusted p-value indicated no significant relationship (p = 0.300). These results should be interpreted with caution due to the low incidence of ELBW and VLBW infants. These findings differ from other studies from developing countries, which found an association between low birth weight and disability (Hutchings and Potterton, 2014; Walker et al., 2007). Yet, children with their birth weight below 2500g and/or children born prematurely, regardless of HIV status are at high risk for developmental difficulty and should be followed up at developmental clinics (Acharya et al., 2016; Ballot et al., 2012; Bröring et al., 2017; Jarjour, 2015; Rogers and Hintz, 2016; Spittle and Treyvaud, 2016; Taylor and Clark, 2016). Moreover this population of low birth weight infants, with an additional risk factor of HIV exposure and infection, need to be monitored carefully for developmental problems and preventative intervention should be actioned.

5.4.7 ART & Clinical Factors

The overall pre-treatment and the most recent blood count data indicate that, immunologically, the children in this study are doing well on cART (86% of the sample at the time of testing were not immunosuppressed). This can be attributed to the early initiation of cART (median age of entire sample was 10.5 months) (Shiau et al., 2017). A number of ART factors were investigated to establish if there was an association between caregiver-reported disability and these elements.

5.4.7.1 Pre-treatment Blood Counts

No significant association was found between pre-treatment CD4 cell count and incidence of disability or viral load and disability. This is consistent with the findings by Devendra et al. (2013). There was a significant association (p = 0.021) between pre-treatment CD4% and the development of difficulty in a child with HIV. Therefore, there may be an increased risk of developmental problems in children with low pre-treatment CD4% (Hoare et al., 2016; Shanbhag et al., 2005).

5.4.7.2 Age of starting, duration and defaulting treatment

A trend was noted that on average, children with disabilities started ART later in life, had been on ART for longer and had defaulted treatment more often. However, no statistically significant associations were found between any of these factors and the presence of disability which is in line with findings by Devendra et al. (2013) in Malawi.

5.4.7.3 Maternal ART

No significant association was found between maternal ART during gestation and the occurrence of disability in their child. This is in contrast to other studies which have shown an association (Arab et al., 2017; Powis et al., 2016; Uthman et al., 2017; Xiao et al., 2015; Zack et al., 2014). This study agrees with results of Chagomerana et al. (2017) that found no significant association between maternal ART intake and premature birth and/or low birth. However, this study did not include HIV exposed but negative children in the sample, where studies analysing the risk of maternal ARV treatment on prematurity and/or birth weight included both, HIV exposed but negative and HIV exposed and positive children in their sample (Powis et al., 2016; Uthman et al., 2017).

5.4.8 Childhood and/or Opportunistic Infections and Hospital Admissions

Skin disorders were the most common childhood and/or opportunistic disorder/infection (53.5%). TB was the second most common (37%) followed by lower respiratory tract infections (LRTI) (24.5%) and upper respiratory tract infections (24%). There was a significant association between TB infection and the presence of disability in children with HIV ($p = 0.003$). This indicates that the TB infection can be a trigger for developmental screening (Devendra et al., 2013). This study's findings link in with previous literature, as historically, TB and HIV have always been intertwined, with up to 56% of children with TB being co-infected with HIV (Rabie et al., 2015). *Mycobacterium tuberculosis* can activate latent HIV in monocytes and drug interaction can make managing co-infection difficult (R. Govender et al., 2011). In addition studies show TB has strong connections with disability as it is the most common cause of meningitis (van Toorn and Solomons, 2014; Wolzak et al., 2012) and CNS fallout due to factors such as tuberculomas (van Toorn and Solomons, 2014).

Low pre-treatment CD4% was significantly associated with TB and disability. Therefore with earlier treatment thereby, increasing CD4% as early as possible in a child this may reduce the risk of the child developing TB and/or disability (Benki-Nugent et al., 2015). As TB is an indicator and potential risk factors, children with HIV and a history of TB should be carefully monitored for developmental difficulty.

LRTIs were the third most common opportunistic infection. A quarter of the sample had had previous or recurrent LRTIs. A significant association was found between LRTI and caregiver-reported disability.

This association may be due to the diagnosis of LRTI before TB was officially diagnosed, however, LRTI and TB were not significantly associated. Alternatively, it may be due to the nature of the chronicity of LRTI in children with HIV (Graham, 2003; Zar, 2004) and the resultant impact of a child's quality of life and developmental potential (Armstrong, 2006).

5.4.8.1 Orphanhood

Three quarters of the sample had been brought by one of their parents to the clinic and 17.3% of the sample were orphans and being cared for by grandmothers, aunts or foster parents. This is comparable to two other similar findings, Devendra et al. (2013) and Potterton et al. (2009) which found orphan status among HIV-positive children to be 14% and 16.73% respectively. Some studies conducted in sub-Saharan Africa documented orphan status, as ranging from 8.6% to 31.1% (Hrapcak et al., 2016; Lowick et al., 2012; Sherr et al., 2017; Smith et al., 2008; Van Rie et al., 2008). However, no significant association was found between orphanhood and caregiver-reported disability. Devendra et al. (2013) had similar findings. However, caregiver-reported information is a common confounding element in studies and caregivers of orphans may not be aware of their child's developmental history.

5.4.9 Socioeconomic Status

Three quarters of the sample came from households earning less than R6500 a month (Mean = R3300). A median of four people (mean: 4.5) lived in each household. This means that 92 (45.9%) children are living below the 2017 LBPL (R758pp/month) and 118 (60.2%) were living below the UBPL (R1138pp/month) (Stats SA, 2017b). This is higher than the overall 2015 South African statistics which found 55% of South Africans were living below the UBPL and 33.3% of people living in Gauteng were living below the UBPL. As the HIV clinic service at the study site is part of the public sector, it is expected that the sample will be, on average, be poorer than whole population statistics. Although this value is high, Devendra et al. (2013) found their sample to be poorer, where 57% of their HIV exposed and infected cohort had a household monthly income of less than +-R706pp/m. Sherr et al. (2017) found six household members on average while the majority of Devendra et al.'s (2013) study had 4-6 people per household. Caregivers/parents who reported difficulty in their child came from homes with lower mean household monthly income than caregivers/parents of children with no disability. Yet, there was still no significant association between household income and disability in children with HIV ($p = 0.127$).

The distribution of main caregiver education was relatively even, 22% had a Grade 7-9 education, 24% had finished matric or received vocational training and a third of the main caregivers had a Grade 10-11 level of education. However, it is interesting to note that 76% of all main caregivers never finished

school. This prevalence is similar to some studies conducted in South Africa (Baillieu and Potterton, 2008; Smith et al., 2008; Torre et al., 2015) although it is almost double than the prevalence found than other studies conducted in Malawi and Zimbabwe (33.85 – 46.57%) (Devendra et al., 2013; Hrapcak et al., 2016; Kandawasvika et al., 2011).

Overall, the caregiver/child pairs within this study's sample had similar socioeconomic backgrounds to each other and to samples from some South African studies (Baillieu and Potterton, 2008; Potterton et al., 2009; Smith et al., 2008). However, SES appears to vary when comparing this study's sample to other samples from other African countries, such as Malawi (Devendra et al., 2013; Hrapcak et al., 2016) or Zimbabwe (Hutchings and Potterton, 2014; Kandawasvika et al., 2011) as there are differences in residence location, household income and main caregiver education. .

There is no doubt that SES and consequently environment play a role in child neurodevelopment as well as HIV status (Figure 2.2) (Boivin et al., 2015; Manomano and Selebogo, 2017) and this interaction contributes to a cycle of poverty, poor development and poor health (Bachmann and Booysen, 2003; Manomano and Selebogo, 2017; Omotoso and Koch, 2017). However, Devendra et al. (2013) agreed with Simkiss et al. (Simkiss et al., 2011) that neither household income nor caregiver education had any association with disability among children living with HIV. This study found the same. A possible reason for this may be that the samples were found to have similar SES in the form of caregiver education and household income. Ultimately, in South Africa, children who are born with HIV are generally from low SES populations and therefore, whether disability and developmental difficulty are due to HIV, low SES, or a combination of the two, these children are shown to have a poor quality of life resulting in affected development and limited potential which perpetuate the poverty cycle (Manomano and Selebogo, 2017). Health and education systems need to be put in place to support these children to encourage maximum developmental potential.

5.5 Outcome Measures

Few studies in Southern Africa have looked at the disability in this age range of children with HIV. The TQSD (Appendix 7) was an appropriate tool to screen these children for disability in low resource settings (Durkin et al., 1994, 1995; Gottlieb et al., 2009; Ibrahim and Bhutta, 2013; Mung'ala-Odera et al., 2006). It has successfully been used in South African studies (Couper, 2002) and in HIV studies (Devendra et al., 2013). The TQSD was used on a once-off basis, where the parent or caregiver is used as a proxy to assist screen their child for disabilities. In ten questions, the caregiver is asked to compare their child's functional ability to his or her peers in a range of developmental domains. This is useful, as it is free, quick to administer with a high sensitivity for developmental disabilities (Durkin et al., 1994). However, it is not an assessment tool and results will not be as sensitive or specific as an

assessment tool. This is evident as studies using assessment tools have found a higher prevalence of disabilities in children with HIV than studies using caregiver/parent proxy screening tools. Despite these findings, critique of the TQSD is that it has displayed a high false positive for those on the milder spectrum of visual, hearing (Durkin et al., 1995) and cognitive impairments (Thorburn et al., 1992). As a result, findings in these areas need to be interpreted with prudence. Despite the TQSD being designed for poorly-resourced environments, more research needs to be conducted into the psychometric properties of the TQSD in South Africa.

Due to the variety of languages spoken at the clinic, a translator was employed to directly translate the TQSD, the General Additional Questionnaire and Socioeconomic Questionnaire to the caregiver in the language of their choice. This may have resulted in confounding factors, as each translation of the TQSD was not standardised. Although, as the interview was carried out on a one-on-one basis and caregivers had the opportunity to qualify any questions they did not understand.

5.6 Limitations

Every endeavour was made within the resource boundaries to ensure that the authors reduced confounding variables. However, limitations still exist. Many limitations have been discussed in the body of this chapter. Further limitations not yet, discussed include;

- A case-controlled study would have provided a more accurate comparator group.
- The TQSD has not been officially validated in South Africa and neither have the individualised verbal translations.
- Data were taken from clinic files which may not be as comprehensive in terms of medical history as hospital files.
- The TQSD is a caregiver proxy screening tool which is not as sensitive as a comprehensive developmental assessment.
- Drawing comparisons in the literature is challenging due to the inconsistencies in outcome measures used in research.

5.7 Implications

The prevalence of developmental difficulties and disabilities in children infected with HIV was more than 50% in this study. Of those children more than half of them had more than one disability however, less than half of those who reported any difficulty had been referred and/or accessed allied health profession services. With the advent of successful HIV treatment, HIV has become a chronic disease and the management of children infected with HIV needs to shift from a purely life-saving focus to a habilitative, chronic and quality-of-life focused management. Policy makers and health care

professionals need to advocate for financial and personnel resources that will allow holistic multidisciplinary management and universal developmental screening services for all children with HIV as well as early identification and appropriate intervention for those children with complications. This is vital considering the multi-systems nature of disability in children with HIV. Figures on the distribution of developmental difficulty and disability can assist with planning of service provision and TB and/or LRTI diagnosis or low pre-ART CD4% can be used as indicators for developmental assessments. Without the assistance of allied health professionals such as audiologists, dieticians, psychologists, PTs, OTs and SLTs, all children infected with HIV are likely to suffer a considerably decreased quality of life.

5.8 Recommendations

5.8.1 Clinical

- Universal screening and assessment of all children with HIV by audiologists, occupational therapists, optometrists, PT, Psychologists and speech and language therapists should be a regular part of the management of children with HIV.
- The TQSD is a time and cost effective screening tool that could be administered in a waiting room and can assist with identification for further investigation and/or referral. However, its limitations as a screening tool must be acknowledged and it cannot be used in lieu of a thorough assessment.
- Clinicians should be aware of more subtle factors that can affect development and quality of life in children infected with HIV. These elements are no less important than survival.
- Audiologists, psychologists, PTs, optometrists, OTs and SLTs need to take an active part in the multidisciplinary team approach to managing children with HIV. These professionals should be activists in;
    a. Promoting their role in the management of children living with HIV
    b. Providing education/in-house training to health care providers regarding referral requirements, distributing research regarding neurodevelopment, child development, vision and hearing difficulties that HIV-positive children may be experiencing.
    c. Providing clinic information talks and lectures aimed at caregivers/parents on awareness regarding regular vision and hearing tests as well as gross motor, fine motor, sensory, cognitive and behavioural yellow and red flags.
    d. Provide developmental screening services (including hearing & vision) at HIV clinics and PHC facilities.
    e. Provide consulting services at HIV clinics and PHC facilities.

- Better clinical diagnosis of HIVE in order to identify areas of need and predict disability.
- Some caregivers/parents are aware of services provided. Clinicians should ask caregivers/parents if they think their child needs referral to allied health professionals. Caregivers/parents need also to be empowered to request referral to these services too.

5.8.2 Research

- Due to the success of ART, children living with HIV will now become adults who need to function optimally in society. Further longitudinal studies need to be done to understand the long-wave consequences of HIV, to give a complete picture of the impact on development and the implications for a contributing and productive adult.
- The TQSD has been shown to have a high chance of false positives. However, this study found that the prevalence of disability in its sample was lower than that found in studies using assessment tools. The TQSD needs to be validated and it psychometric properties assessed with regards to the South African context.
- Research is needed into whether the incidence of HIVE is diminishing or if it is underdiagnosed is needed.
- In order to support policy makers in providing appropriate resources, longitudinal research is needed on the cost/benefit of providing appropriate early intervention in children with HIV which will enable them to become a well-functioning adult member of society which could help to break a poverty cycle.
- The effect of ART on foetal and neurodevelopment and consequent gestational age and its relation to the long term development of a child is an area where more research is required.

5.8.3 Service provision

- The involvement of all allied health professionals in the multidisciplinary management of children infected with HIV should be common practice.
- Patients need better, more regular access to allied health professionals in tertiary, secondary and particularly primary facilities.
- Government and policy makers should ensure adequate financial and personnel resources to assist with this service provision.

The conclusions that may be drawn from this study will be presented in Chapter Six.

CHAPTER 6

6. CONCLUSION

"Where once our treatment aim for children with HIV was to prevent death, our focus now is on optimizing health for adulthood." (Bamford and Lyall, 2015, p.187).

With the improvement in ARV-therapy and improved immunological control, HIV has become a chronic disease. There is a plethora of research linking HIV and poor development and disability in all domains. This research, includes recommendations for holistic multidisciplinary management of children infected with HIV in order to ensure they meet their best developmental potential. The purpose of this cross-sectional study was to determine the prevalence of disability in children infected with HIV as well as to assess if these children were being referred and accessing support services and if not, why not. The presence of difficulty and disability was determined by using the Ten Question Screen for Disability.

More than half the caregivers/parents reported that their child was experiencing a difficulty in one or more domains, including development, physical, visual, auditory, speech and language, cognitive and/or behavioural. This indicates the multi-systems nature of the disabilities, children living with HIV are at risk of developing.

More than 50% of children with reported disability, had never been referred to allied health professionals. Lack of finances for transport and/or service, lack of time off work, transport difficulties and no follow-up appointment post appointment cancellation were reasons for not attending appointments if referral had been made. More than half of the sample requested referral to support services for screening or assessment of developmental concerns.

This study echoed findings of previous studies that low pre-treatment CD4%, history of TB and/or LRTI could be indicators of increased risk of developmental delay and disability but indicators of SES, household income, parental education and orphanhood found were not predictive.

This study confirms that children infected with HIV have an increased likelihood of experiencing developmental difficulty and disability but are not receiving the required support. The management of children with HIV needs to shift from purely a life-saving focus and more towards incorporating a more holistic, quality of life, multi-systems and multidisciplinary approach to care. Allied health professionals need to take an active role in the multi-disciplinary paediatric HIV management team.

Education and creating awareness among medical professionals and caregivers alike regarding the importance of neurodevelopment and child development in children infected with HIV as well as their role, as a support service, in optimising children's potentials. Early identification and intervention in all spheres of development is required for these children to achieve maximum developmental potential.

Political, social, financial, health and education sectors need concomitant commitment to enable HIV services to respond to the evolving multi-systemic and wide-ranging needs of a developing child who is infected with HIV. This amalgamated approach is vital to be able to provide these holistic services at a community, clinical and policy level.

7. BIBLIOGRAPHY

Abrams, E.J., Woldesenbet, S., Silva, J.S., Coovadia, A., Black, V., Technau, K.-G., Kuhn, L., 2016. Despite Access to Antiretrovirals for Prevention and Treatment High Rates of Mortality Persist Among HIV-infected Infants and Young Children: Pediatr. Infect. Dis. J. 1. https://doi.org/10.1097/INF.0000000000001507

Abubakar, A., Holding, P., Newton, C.R.J.C., Van Baar, A., Van De Vijver, F.J.R., 2009. The role of weight for age and disease stage in poor psychomotor outcome of HIV-infected children in Kilifi, Kenya. Dev. Med. Child Neurol. 51, 968–973. https://doi.org/10.1111/j.1469-8749.2009.03333.x

Abubakar, A., Van Baar, A., Van de Vijver, F.J.R., Holding, P., Newton, C.R.J.C., 2008. Paediatric HIV and neurodevelopment in sub-Saharan Africa: a systematic review: Paediatric HIV in SSA. Trop. Med. Int. Health 13, 880–887. https://doi.org/10.1111/j.1365-3156.2008.02079.x

Acharya, K., Pellerite, M., Lagatta, J., Andrews, B., Msall, M.E., 2016. Cerebral Palsy, Developmental Coordination Disorder, Visual and Hearing Impairments in Infants Born Preterm. NeoReviews 17, e325–e333. https://doi.org/10.1542/neo.17-6-e325

Acton, B.V., Biggs, W.S.G., Creighton, D.E., Penner, K.A.H., Switzer, H.N., Thomas, J.H.P., Joffe, A.R., Robertson, C.M.T., 2011. Overestimating Neurodevelopment Using the Bayley-III After Early Complex Cardiac Surgery. PEDIATRICS 128, e794–e800. https://doi.org/10.1542/peds.2011-0331

Adedimeji, A., Edmonds, A., Hoover, D., Shi, Q., Sinayobye, J. d'Amour, Nduwimana, M., Lelo, P., Nash, D., Anastos, K., Yotebieng, M., 2017. Characteristics of HIV-Infected Children at Enrolment into Care and at Antiretroviral Therapy Initiation in Central Africa. PLOS ONE 12, e0169871. https://doi.org/10.1371/journal.pone.0169871

Ae-Ngibise, K., Akpalu, B., Ngugi, A.K., Akpalu, A., Agbokey, F., Adjei, P., Punguyire, D., Bottomley, C., Newton, C.R., Owusu-Agyei, S., 2015. Prevalence and risk factors for Active Convulsive Epilepsy in Kintampo, Ghana. Pan Afr. Med. J. 21. https://doi.org/10.11604/pamj.2015.21.29.6084

Albers, C.A., Grieve, A.J., 2007. Test Review: Bayley, N. (2006). "Bayley Scales of Infant and Toddler Development--Third Edition". San Antonio, TX--Harcourt Assessment. J. Psychoeduc. Assess. 25, 180–190. https://doi.org/10.1177/0734282906297199

Alcock, K.J., Abubakar, A., Newton, C.R., Holding, P., 2016. The effects of prenatal HIV exposure on language functioning in Kenyan children: establishing an evaluative framework. BMC Res. Notes 9. https://doi.org/10.1186/s13104-016-2264-3

Altman, B., M., Albrecht, G., L., Seetman, K., D., Bury, M., 2001. Handbook of Disability Studies. Sage Publications Inc.

Amod, Z., Cockcroft, K., Soellaart, B., 2007. Use of the 1996 Griffiths Mental Development Scales for infants: a pilot study with a Black, South African sample. J. Child Adolesc. Ment. Health 19, 123–130. https://doi.org/10.2989/17280580709486647

Amzel, A., Toska, E., Lovich, R., Widyono, M., Patel, T., Foti, C., Dziuban, E.J., Phelps, B.R., Sugandhi, N., Mark, D., Altschuler, J., Women, T.C.S.W.G. of the I.T.T. on the P. and T. of H. in P., Children, M. and, 2013. Promoting a Combination Approach to Paediatric HIV Psychosocial Support. AIDS Lond. Engl. 27, S147. https://doi.org/10.1097/QAD.0000000000000098

Angelini, L., Zibordi, F., Triulzi, F., Cinque, P., Giudici, B., Pinzani, R., Plebani, A., 2000. Age-dependent neurologic manifestations of HIV infection in childhood. Neurol. Sci. Milano 21, 135–42. http://0-dx.doi.org.innopac.wits.ac.za/10.1007/s100720070088

Arab, K., Spence, A.R., Czuzoj-Shulman, N., Abenhaim, H.A., 2017. Pregnancy outcomes in HIV-positive women: a retrospective cohort study. Arch. Gynecol. Obstet. 295, 599–606. https://doi.org/10.1007/s00404-016-4271-y

Ardington, C., Leibbrandt, M., 2010. Orphanhood and Schooling in South Africa: Trends in the Vulnerability of Orphans between 1993 and 2005. Econ. Dev. Cult. Change 58, 507–536. https://doi.org/10.1086/650414

Armstrong, F.D., 2006. Neurodevelopment and chronic illness: Mechanisms of disease and treatment. Ment. Retard. Dev. Disabil. Res. Rev. 12, 168–173. https://doi.org/10.1002/mrdd.20114

Ataguba, J.E., Akazili, J., McIntyre, D., 2011. Socioeconomic-related health inequality in South Africa: evidence from General Household Surveys. Int. J. Equity Health 10, 48. https://doi.org/10.1186/1475-9276-10-48

Azria, E., Chougrani, Luton, Matheron, S., Mandelbrot, 2013. Safety of protease inhibitors in HIV-infected pregnant women. HIVAIDS - Res. Palliat. Care 253. https://doi.org/10.2147/HIV.S33058

Bachmann, M.O., Booysen, F.L., 2003. Health and economic impact of HIV/AIDS on South African households: a cohort study. BMC Public Health 3, 14. https://doi.org/10.1186/1471-2458-3-14

Bagenda, D., Nassali, A., Kalyesubula, I., Sherman, B., Drotar, D., Boivin, M.J., Olness, K., 2006. Health, Neurologic, and Cognitive Status of HIV-Infected, Long-Surviving, and Antiretroviral-Naive Ugandan Children. Pediatrics 117, 729–740. https://doi.org/10.1542/peds.2004-2699

Baillieu, N., Potterton, J., 2008. The Extent of Delay of Language, Motor, and Cognitive Development in HIV-Positive Infants: J. Neurol. Phys. Ther. 32, 118–121. https://doi.org/10.1097/NPT.0b013e3181846232

Ballot, D.E., Potterton, J., Chirwa, T., Hilburn, N., Cooper, P.A., 2012. Developmental outcome of very low birth weight infants in a developing country. BMC Pediatr. 12. https://doi.org/10.1186/1471-2431-12-11

Bamford, A., Lyall, H., 2015. Paediatric HIV grows up: recent advances in perinatally acquired HIV. Arch. Dis. Child. Lond. 100, 183. http://0-dx.doi.org.innopac.wits.ac.za/10.1136/archdischild-2014-306079

Banks, L.M., Kuper, H., Polack, S., 2017. Poverty and disability in low- and middle-income countries: A systematic review. PLoS ONE 12. https://doi.org/10.1371/journal.pone.0189996

Banks, L.M., Zuurmond, M., Ferrand, R., Kuper, H., 2015. The relationship between HIV and prevalence of disabilities in sub-Saharan Africa: systematic review (FA). Trop. Med. Int. Health 20, 411–429. https://doi.org/10.1111/tmi.12449

Barbarin, O.A., Khomo, N., 1997. Indicators of Economic Status and Social Capital in South African Townships: What Do They Reveal About the Material and Social Conditions in Families of Poor Children? Childhood 4, 193–222. https://doi.org/10.1177/0907568297004002005

Bardien, F., Gerber, B., Jacklin, G., Lourens, D., Pottas, L., Soer, M., Swart, S., Wilkinson, H., 2011. South African Speech-Language-Hearing Association: Guidelines: Early Communication Intervention.

Beegle, K., De Weerdt, J., Dercon, S., 2006. Orphanhood and the Long-Run Impact on Children. Am. J. Agric. Econ. 88, 1266–1272. https://doi.org/10.1111/j.1467-8276.2006.00943.x

Belmont, L., 1984. The International Pilot Study of Severe Childhood Disability. Final Report: Screening for Severe Mental Retardation in Developing Countries.

Benevides, M.L.A.C. de S. e, Filho, S.B., Debona, R., Bergamaschi, E.N.C., Nunes, J.C., 2017. Prevalence of Peripheral Neuropathy and associated factors in HIV-infected patients. J. Neurol. Sci. 375, 316–320. https://doi.org/10.1016/j.jns.2017.02.011

Benjamin, N., Potterton, J., Kamerman, P., Strehlau, R., 2015. An investigation of peripheral neuropathy in children who are infected with HIV. Physiotherapy, World Confederation for Physical Therapy Congress 2015 Abstracts, Singapore, 1-4 May 2015 101, Supplement 1, e139–e140. https://doi.org/10.1016/j.physio.2015.03.284

Benki-Nugent, S., Eshelman, C., Wamalwa, D., Langat, A., Tapia, K., Okinyi, H.M., John-Stewart, G., 2015. Correlates of Age at Attainment of Developmental Milestones in HIV-infected Infants Receiving Early Antiretroviral Therapy: Pediatr. Infect. Dis. J. 34, 55–61. https://doi.org/10.1097/INF.0000000000000526

Bobat, R., Coovadia, H., Moodley, D., Coutsoudis, A., Gouws, E., 2001. Growth in early childhood in a cohort of children born to HIV-1-infected women from Durban, South Africa. Ann. Trop. Paediatr. 21, 203–210. https://doi.org/10.1080/02724930120077772

Boivin, M.J., Kakooza, A.M., Warf, B.C., Davidson, L.L., Grigorenko, E.L., 2015. Reducing neurodevelopmental disorders and disability through research and interventions. Nature 527, nature16029. https://doi.org/10.1038/nature16029

Boraine, M., 2017. Rahima Moosa Mother and Child Hospital (Coronation Hospital) - Coronationville, Johannesburg, Gauteng, South Africa [WWW Document]. South Afr. Dr. URL http://doctors-hospitals-medical-cape-town-south-africa.blaauwberg.net/hospitals_clinics_state_hospitals/state_public_hospitals_clinics_gauteng_south_africa/rahima_moosa_mother_and_child_hospital_coronation_hospital_coronationville_johannesburg_gauteng_south_africa (accessed 4.5.18).

Boyede, G., Eley, B., Donald, K., 2016. Preliminary Validation of a New Developmental Screening Tool for Neurodevelopmental Delay in HIV-Infected South African Children. J. Child Neurol. 31, 145–152. https://doi.org/10.1177/0883073815585351

Boyede, G., Lesi, Ezeaka, C., Umeh, 2013. Impact of sociodemographic factors on cognitive function in school-aged HIV-infected Nigerian children. HIVAIDS - Res. Palliat. Care 145. https://doi.org/10.2147/HIV.S43260

Boyede, O.G., Donald, K.A., Eley, B., 2015. The validation of a new development screening tool for developmental delays among HIV-Infected South African children (Thesis). University of Cape Town.

Brackis-Cott, E., Kang, E., Dolezal, C., Abrams, E.J., Mellins, C.A., 2009. The Impact of Perinatal HIV Infection on Older School-Aged Children's and Adolescents' Receptive Language and Word Recognition Skills. AIDS Patient Care STDs 23, 415–421. https://doi.org/10.1089/apc.2008.0197

Brink, J., Pettifor, J.M., Lala, S.G., 2014. The prevalence of malnutrition in children admitted to a general paediatric ward at the Chris Hani Baragwanath Academic Hospital: A cross-sectional survey. South Afr. J. Child Health 8, 112–116.

Bröring, T., Oostrom, K.J., Lafeber, H.N., Jansma, E.P., Oosterlaan, J., 2017. Sensory modulation in preterm children: Theoretical perspective and systematic review. PLOS ONE 12, e0170828. https://doi.org/10.1371/journal.pone.0170828

Buriti, A.K.L., Oliveira, S.H. dos S., Muniz, L.F., 2013. Hearing loss in children with HIV/AIDS. CoDAS 25, 513–520. https://doi.org/10.1590/S2317-17822013.05000013

Burton, K.J., Rogathe, J., Whittaker, R., Mankad, K., Hunter, E., Burton, M.J., Todd, J., Neville, B.G.R., Walker, R., Newton, C.R.J.C., 2012. Epilepsy in Tanzanian children: Association with perinatal events and other risk factors. Epilepsia 53, 752–760. https://doi.org/10.1111/j.1528-1167.2011.03395.x

Cames, C., Pascal, L., Diack, A., Mbodj, H., Ouattara, B., Diagne, N.R., Diallo, N.F., Msellati, P., Mbaye, N., Sy Signate, H., Group, on behalf of M.C.S., 2017. Risk Factors for Growth Retardation in HIV-infected Senegalese Children on Antiretroviral Treatment: The ANRS 12279 MAGGSEN Pediatric Cohort Study. Pediatr. Infect. Dis. J. 36, e87. https://doi.org/10.1097/INF.0000000000001454

Campbell, S.K., Zawacki, L., Rankin, K.M., Yoder, J.C., Shapiro, N., Li, Z., White-Traut, R., 2013. Concurrent Validity of the TIMP and the Bayley III Scales at 6 Weeks Corrected Age: Pediatr. Phys. Ther. 25, 395–401. https://doi.org/10.1097/PEP.0b013e31829db85b

Chagomerana, M.B., Miller, W.C., Pence, B.W., Hosseinipour, M.C., Hoffman, I.F., Flick, R.J., Tweya, H., Mumba, S., Chimbwandira, F., Powers, K.A., 2017. PMTCT Option B+ Does Not Increase Preterm Birth Risk and May Prevent Extreme Prematurity: A Retrospective Cohort Study in Malawi. JAIDS J. Acquir. Immune Defic. Syndr. 74, 367–374. https://doi.org/10.1097/QAI.0000000000001253

Cherry, C.L., Affandi, J.S., Imran, D., Yunihastuti, E., Smyth, K., Vanar, S., Kamarulzaman, A., Price, P., 2009. Age and height predict neuropathy risk in patients with HIV prescribed stavudine. Neurology 73, 315–320. https://doi.org/10.1212/WNL.0b013e3181af7a22

Chetty, V., Hanass-Hancock, J., 2016. A rehabilitation model as key to comprehensive care in the era of HIV as a chronic disease in South Africa. AIDS Care 28, 132–139. https://doi.org/10.1080/09540121.2016.1146204

Chetty, V., Hanass-Hancock, J., 2015. The need for a Rehabilitation Model to address the disparities of public healthcare for people living with HIV in South Africa. Afr. J. Disabil. 4. https://doi.org/10.4102/ajod.v4i1.137

Chetty, V., Hanass-Hancock, J., 2014. Development of a Model of Care for Rehabilitation of People Living With HIV in a Semirural Setting in South Africa. JMIR Res. Protoc. 3. https://doi.org/10.2196/resprot.3580

Chetty, V., Maharaj, S.S., 2013. Collaboration Between Health Professionals in the Era of Antiretroviral Therapy. J. Assoc. Nurses AIDS Care 24, 166–175. https://doi.org/10.1016/j.jana.2012.04.005

Christianson, A.L., Zwane, M.E., Manga, P., Rosen, E., Venter, A., Downs, D., Kromberg, J.G.R., 2002. Children with intellectual disability in rural South Africa: prevalence and associated disability. J. Intellect. Disabil. Res. 46, 179–186. https://doi.org/10.1046/j.1365-2788.2002.00390.x

Christopher, N., Edward, T., Sabrina, B.-K., Agnes, N., 2013. The prevalence of hearing impairment in the 6 months – 5 years HIV/AIDS-positive patients attending paediatric infectious disease clinic at Mulago Hospital. Int. J. Pediatr. Otorhinolaryngol. 77, 262–265. https://doi.org/10.1016/j.ijporl.2012.11.013

Cloete, I., Daniels, L., Jordaan, J., Derbyshire, C., Volmink, L., Schubl, C., 2013. Knowledge and perceptions of nursing staff on the new Road to Health Booklet growth charts in primary healthcare clinics in the Tygerberg subdistrict of the Cape Town metropole district. South Afr. J. Clin. Nutr. 26, 141–146.

Cobbing, S., Chetty, V., Hanass-Hancock, J., Jelsma, J., Myezwa, H., Nixon, S.A., 2013. The essential role of physiotherapists in providing rehabilitation services to people living with HIV in South Africa. South Afr. J. Physiother. 69, 22–25. https://doi.org/10.4102/sajp.v69i1.368

Cobbing, S., Hanass-Hancock, J., Deane, M., 2014. Physiotherapy rehabilitation in the context of HIV and disability in KwaZulu-Natal, South Africa. Disabil. Rehabil. 36, 1687–1694. https://doi.org/10.3109/09638288.2013.872199

Cobbing, S., Hanass-Hancock, J., Myezwa, H., 2017. Assessing home-based rehabilitation within the development of an integrated model of care for people living with HIV in a resource-poor community. Afr. J. Prim. Health Care Fam. Med. 9. https://doi.org/10.4102/phcfm.v9i1.1374

Connolly, A.M., Florence, J.M., Cradock, M.M., Malkus, E.C., Schierbecker, J.R., Siener, C.A., Wulf, C.O., Anand, P., Golumbek, P.T., Zaidman, C.M., Philip Miller, J., Lowes, L.P., Alfano, L.N., Viollet-Callendret, L., Flanigan, K.M., Mendell, J.R., McDonald, C.M., Goude, E., Johnson, L., Nicorici, A., Karachunski, P.I., Day, J.W., Dalton, J.C., Farber, J.M., Buser, K.K., Darras, B.T., Kang, P.B., Riley, S.O., Shriber, E., Parad, R., Bushby, K., Eagle, M., 2013. Motor and cognitive assessment of infants and young boys with

Duchenne Muscular Dystrophy: results from the Muscular Dystrophy Association DMD Clinical Research Network. Neuromuscul. Disord. 23, 529–539. https://doi.org/10.1016/j.nmd.2013.04.005

Couper, J., 2016. The Precious Years : A guide to early child development - birth to three years. Struik Lifestyle: Penguin Random House South Africa, South Africa.

Couper, J., 2002. Prevalence of childhood disability in rural KwaZulu-Natal. South Afr. Med. J. Suid-Afr. Tydskr. Vir Geneeskd. 92, 549–552.

Cromwell, E.A., Dube, Q., Cole, S.R., Chirambo, C., Dow, A.E., Heyderman, R.S., Van Rie, A., 2014. Validity of US norms for the Bayley Scales of Infant Development-III in Malawian children. Eur. J. Paediatr. Neurol. 18, 223–230. https://doi.org/10.1016/j.ejpn.2013.11.011

Crowell, C.S., Huo, Y., Tassiopoulos, K., Malee, K.M., Yogev, R., Hazra, R., Rutstein, R.M., Nichols, S.L., Smith, R.A., Williams, P.L., Oleske, J., Muller, W.J., 2015. Early viral suppression improves neurocognitive outcomes in HIV-infected children: AIDS 29, 295–304. https://doi.org/10.1097/QAD.0000000000000528

Danaei, G., Andrews, K.G., Sudfeld, C.R., Fink, G., McCoy, D.C., Peet, E., Sania, A., Fawzi, M.C.S., Ezzati, M., Fawzi, W.W., 2016. Risk Factors for Childhood Stunting in 137 Developing Countries: A Comparative Risk Assessment Analysis at Global, Regional, and Country Levels. PLOS Med. 13, e1002164. https://doi.org/10.1371/journal.pmed.1002164

Deininger, K., Garcia, M., Subbarao, K., 2003. AIDS-Induced Orphanhood as a Systemic Shock: Magnitude, Impact, and Program Interventions in Africa. World Dev. 31, 1201–1220. https://doi.org/10.1016/S0305-750X(03)00061-5

Department of Health, 2015. B-Wise Mobi-Site [WWW Document]. URL https://bwisehealth.com/ (accessed 11.28.17).

Department of Social Development, Department of Women, Children and People with Disabilities, UNICEF, 2012. Children with Disabilities in South Africa: A Situation Analysis 2001 - 2011 [WWW Document]. URL https://www.health-e.org.za/wp-content/uploads/2013/10/Integrated_School_Health_Policy.pdf (accessed 24.10.17)

Devendra, A., Makawa, A., Kazembe, P.N., Calles, N.R., Kuper, H., 2013. HIV and Childhood Disability: A Case-Controlled Study at a Paediatric Antiretroviral Therapy Centre in Lilongwe, Malawi. PLoS ONE 8, e84024. https://doi.org/10.1371/journal.pone.0084024

DOH, DOBE, 2013. Department of Health and Department of Basic Education: Integrated School Health Policy [WWW Document]. URL https://www.health-e.org.za/wp-content/uploads/2013/10/Integrated_School_Health_Policy.pdf (accessed 24.10.17)

Donald, K.A., Hoare, J., Eley, B., Wilmshurst, J.M., 2014. Neurologic Complications of Pediatric Human Immunodeficiency Virus: Implications for Clinical Practice and Management Challenges in the African Setting. Semin. Pediatr. Neurol. 21, 3–11. https://doi.org/10.1016/j.spen.2014.01.004

Donald, K.A., Walker, K.G., Kilborn, T., Carrara, H., Langerak, N.G., Eley, B., Wilmshurst, J.M., 2015. HIV Encephalopathy: pediatric case series description and insights from the clinic coalface. AIDS Res. Ther. 12, 2. https://doi.org/10.1186/s12981-014-0042-7

Durkin, M.S., Davidson, L.L., Desai, P., Hasan, Z.M., Khan, N., Shrout, P.E., Thorburn, M.J., Wang, W., Zaman, S.S., 1994. Validity of the ten questions screened for childhood disability: results from population-based studies in Bangladesh, Jamaica, and Pakistan. Epidemiol. Camb. Mass 5, 283–289.

Durkin, M.S., Wang, W., Shrout, P.E., Zaman, S.S., Hasan, Z.M., Desai, P., Davidson, L.L., 1995. Evaluating a ten questions screen for childhood disability: reliability and internal structure in different cultures. J. Clin. Epidemiol. 48, 657–666.

Egeraat, L. van, Hanass-Hancock, J., Myezwa, H., 2015. HIV-related disabilities: an extra burden to HIV and AIDS healthcare workers? Afr. J. AIDS Res. 14, 285–294. https://doi.org/10.2989/16085906.2015.1084938

Eley, B., Nuttall, J., 2007. Antiretroviral therapy for children: challenges and opportunities. Ann. Trop. Paediatr. 27, 1–10. https://doi.org/10.1179/146532807X170448

ESRU, 2018a. Empilweni Services and Research Unit (ESRU) Let's Help Each Other Live [WWW Document]. Empilweni Serv. Res. Unit ESRU. URL http://www.esru.co.za/Home.aspx (accessed 12.10.17).

ESRU, 2018b. ESRU Publications [WWW Document]. Empilweni Serv. Res. Unit ESRU. URL http://www.esru.co.za/Publications.aspx (accessed 4.6.18).

Esteban, P., Zunt, J.R., Torres, S., Bravo, J., Roca, L., Quispe, N., 2008. Distal peripheral neuropathy in HIV-infected children. BMC Proc. 2, P37. https://doi.org/10.1186/1753-6561-2-s1-p37

Everall, I.P., Hansen, L.A., Masliah, E., 2005. The shifting patterns of HIV encephalitis neuropathology. Neurotox. Res. 8, 51–61. https://doi.org/10.1007/BF03033819

Fick, C., 2017. SAHR 2017. 20th Edition. Twenty years of IMCI implementation in South Africa: accelerating impact for the next decade.

Fois, A.F., Brew, B.J., 2015. The Potential of the CNS as a Reservoir for HIV-1 Infection: Implications for HIV Eradication. Curr. HIV/AIDS Rep. 12, 299–303. https://doi.org/10.1007/s11904-015-0257-9

Fortuin-de Smidt, M., de Waal, R., Cohen, K., Technau, K.-G., Stinson, K., Maartens, G., Boulle, A., Igumbor, E.U., Davies, M.-A., 2017. First-line antiretroviral drug discontinuations in children. PloS One 12, e0169762. https://doi.org/10.1371/journal.pone.0169762

Foster, C.J., Biggs, R.L., Melvin, D., Walters, M.D.S., Tudor-Williams, G., Lyall, E.G.H., 2006. Neurodevelopmental outcomes in children with HIV infection under 3 years of age. Dev. Med. Child Neurol. 48, 677–682. https://doi.org/10.1111/j.1469-8749.2006.tb01339.x

Gauteng Provincial Government, 2017a. Rahima Moosa Hospital [WWW Document]. Gauteng Prov. Gov. Website. URL http://www.gauteng.gov.za/government/departments/health/services/hospitals/Pages/Rahima-Moosa-Hospital.aspx (accessed 1.10.18).

Gauteng Provincial Government, 2017b. Helen Joseph Hospital [WWW Document]. Helen Joseph Hosp. URL http://www.gauteng.gov.za/government/departments/health/services/hospitals/Pages/Helen-Joseph-Hospital.aspx (accessed 4.6.18).

Gavin, P., Yogev, R., 1999. Central Nervous System Abnormalities in Pediatric Human Immunodeficiency Virus Infection. Pediatr. Neurosurg. Basel 31, 115–23.

Gay, C.L., Armstrong, F.D., Cohen, D., Lai, S., Hardy, M.D., Swales, T.P., Morrow, C.J., Scott, G.B., 1995. The effects of HIV on cognitive and motor development in children born to HIV-seropositive women with no reported drug use: birth to 24 months. Pediatrics 96, 1078–1082.

Gilbert, L., Walker, L., 2002. Treading the path of least resistance: HIV/AIDS and social inequalities—a South African case study. Soc. Sci. Med. 54, 1093–1110. https://doi.org/10.1016/S0277-9536(01)00083-1

Gladstone, M., 2010. A review of the incidence and prevalence, types and aetiology of childhood cerebral palsy in resource-poor settings. Ann. Trop. Paediatr. 30, 181–196. https://doi.org/10.1179/146532810X12786388978481

Glascoe, F.P., 1994. It's Not What It Seems: The Relationship between Parents' Concerns and Children with Global Delays. Clin. Pediatr. (Phila.) 33, 292–296. https://doi.org/10.1177/000992289403300507

Gorry, P.R., Ong, C., Thorpe, J., Bannwarth, S., Thompson, K.A., Gatignol, A., Vesselingh, S.L., Purcell, D.F.J., 2003. Astrocyte infection by HIV-1: mechanisms of restricted virus replication, and role in the pathogenesis of HIV-1-associated dementia. Curr. HIV Res. 1, 463–473.

Gottlieb, C.A., Maenner, M.J., Cappa, C., Durkin, M.S., 2009. Child disability screening, nutrition, and early learning in 18 countries with low and middle incomes: data from the third round of UNICEF's Multiple Indicator Cluster Survey (2005–06). The Lancet 374, 1831–1839.

Govender, P., Hansraj, R., Naidoo, K.S., Visser, L., 2011. Ocular manifestations of HIV/AIDS: A literature review (Part 2)*. Afr. Vis. Eye Health 70. https://doi.org/10.4102/aveh.v70i2.97

Govender, P., Hansraj, R., Naidoo, K.S., Visser, L., 2010. Ocular manifestations of HIV/AIDS: A literature review* (Part 1). Afr. Vis. Eye Health 69. https://doi.org/10.4102/aveh.v69i4.141

Govender, R., Eley, B., Walker, K., Petersen, R., Wilmshurst, J.M., 2011. Neurologic and Neurobehavioral Sequelae in Children with Human Immunodeficiency Virus (HIV-1) Infection. J. Child Neurol. 26, 1355–1364. https://doi.org/10.1177/0883073811405203

Govender, S., Latiff, N., Asmal, N., Ramsaroop, S., Mbele, T., 2015. Evaluating the Outcomes of a Hearing Screening Service for Grade One Learners in Urban Areas at Durban, South Africa. J. Public Health Afr. 6. https://doi.org/10.4081/jphia.2015.529

Graham, S.M., 2003. HIV and respiratory infections in children. Curr. Opin. Pulm. Med. 9, 215.

Gray, L.R., Brew, B.J., Churchill, M.J., 2016. Strategies to target HIV-1 in the central nervous system: Curr. Opin. HIV AIDS 11, 371–375. https://doi.org/10.1097/COH.0000000000000278

Gray, L.R., Roche, M., Flynn, J.K., Wesselingh, S.L., Gorry, P.R., Churchill, M.J., 2014. Is the central nervous system a reservoir of HIV-1?: Curr. Opin. HIV AIDS 9, 552–558. https://doi.org/10.1097/COH.0000000000000108

Grover, G., Pensi, T., Banerjee, T., 2007. Behavioural disorders in 6–11-year-old, HIV-infected Indian children. Ann. Trop. Paediatr. 27, 215–224. https://doi.org/10.1179/146532807X220334

Hackman, D.A., Farah, M.J., 2009. Socioeconomic status and the developing brain. Trends Cogn. Sci. 13, 65–73. https://doi.org/10.1016/j.tics.2008.11.003

Hallbauer, U.M., Atkins, M.D., Tiedt, N.J., Butler, I.R.T., Pieters, M., Elliott, E., Joubert, G., Seedat, R.Y., 2014. Co-morbidities in Children Presenting with Chronic Suppurative Otitis Media--A South African Study. J. Trop. Pediatr. 60, 198–202. https://doi.org/10.1093/tropej/fmt107

Hanass-Hancock, J., Alli, F., 2015. Closing the gap: training for healthcare workers and people with disabilities on the interrelationship of HIV and disability. Disabil. Rehabil. 37, 2012–2021. https://doi.org/10.3109/09638288.2014.991455

Hanass-Hancock, J., Nixon, S.A., 2009. The fields of HIV and disability: past, present and future. J. Int. AIDS Soc. 12, 28. https://doi.org/10.1186/1758-2652-12-28

Harris, T., Peer, S., Fagan, J.J., 2012. Audiological monitoring for ototoxic tuberculosis, human immunodeficiency virus and cancer therapies in a developing world setting. J. Laryngol. Otol. 126, 548–551. https://doi.org/10.1017/S0022215112000357

Hattam, M., Louw, B., Geertsema, S., 2014. Communication characteristics of young children with HIV in South Africa as reported by some physicians. Afr. J. AIDS Res. 13, 371–382. https://doi.org/10.2989/16085906.2014.985236

Heaton, T.B., Crookston, B., Pierce, H., Amoateng, A.Y., 2016. Social inequality and children's health in Africa: a cross sectional study. Int. J. Equity Health 15. https://doi.org/10.1186/s12939-016-0372-2

Hellmuth, J., Valcour, V., Spudich, S., 2015. CNS reservoirs for HIV: implications for eradication. J. Virus Erad. 1, 67.

Hilburn, N., Potterton, J., Stewart, A., 2010. Paediatric HIV encephalopathy in sub-Saharan Africa. Phys. Ther. Rev. 15, 410–417. https://doi.org/10.1179/1743288X10Y.0000000013

Hilburn, N., Potterton, J., Stewart, A., Becker, P., 2011. The development of a screening tool to evaluate gross motor function in HIV-infected infants. AIDS Care 23, 1619–1625. https://doi.org/10.1080/09540121.2011.579942

Hilburn, N., Potterton, J., Strehlau, R., 2015. The neurodevelopmental profile of HIV-infected pre-school aged children receiving highly active antiretroviral therapy (HAART) in Johannesburg, South Africa. Physiotherapy, World Confederation for Physical Therapy Congress 2015 Abstracts, Singapore, 1-4 May 2015 101, Supplement 1, e561–e562. https://doi.org/10.1016/j.physio.2015.03.3378

Hoare, J., Phillips, N., Joska, J.A., Paul, R., Donald, K.A., Stein, D.J., Thomas, K.G.F., 2016. Applying the HIV-associated neurocognitive disorder diagnostic criteria to HIV-infected youth. Neurology 87, 86–93. https://doi.org/10.1212/WNL.0000000000002669

Howe, L.D., Galobardes, B., Matijasevich, A., Gordon, D., Johnston, D., Onwujekwe, O., Patel, R., Webb, E.A., Lawlor, D.A., Hargreaves, J.R., 2012. Measuring socio-economic position for epidemiological studies in low- and middle-income countries: a methods of measurement in epidemiology paper. Int. J. Epidemiol. 41, 871–886. https://doi.org/10.1093/ije/dys037

Howe, L.D., Hargreaves, J.R., Ploubidis, G.B., De Stavola, B.L., Huttly, S.R.A., 2011. Subjective measures of socio-economic position and the wealth index: a comparative analysis. Health Policy Plan. 26, 223–232. https://doi.org/10.1093/heapol/czq043

HPCSA, 2017. Health Professions Council of South Africa: Minimum Standards for Child Vision Care [WWW Document]. URL http://www.hpcsa.co.za/Uploads/editor/UserFiles/downloads/optometry/childrens_vision_minimum_standards.pdf (accessed 5.6.17).

HPCSA, 2008. Health Professions Council of South Africa: Booklet 13: Ethical Guidelines for Health Researchers [WWW Document]. URL http://www.hpcsa.co.za/Conduct/Ethics (accessed 12.12.17)

HPCSA, 2007. Health Professions Council of South Africa: Early Hearing Detection and Intervention Programmes in South Africa: Position Statement [WWW Document]. URL http://www.hpcsa.co.za/Uploads/editor/UserFiles/downloads/speech/early_hearing_detection_statement.pdf (accessed 6.16.17).

Hrapcak, S., Kuper, H., Bartlett, P., Devendra, A., Makawa, A., Kim, M., Kazembe, P., Ahmed, S., 2016. Hearing Loss in HIV-Infected Children in Lilongwe, Malawi. PLOS ONE 11, e0161421. https://doi.org/10.1371/journal.pone.0161421

HREC, 2016. Human Research Ethics Committee Memorandum for Protocol M160450.

Hutchings, J., Potterton, J., 2014. Developmental delay in HIV-exposed infants in Harare, Zimbabwe. Vulnerable Child. Youth Stud. 9, 43–55. https://doi.org/10.1080/17450128.2013.778440

Ibrahim, S.H., Bhutta, Z.A., 2013. Prevalence of early childhood disability in a rural district of Sind, Pakistan. Dev. Med. Child Neurol. 55, 357–363. https://doi.org/10.1111/dmcn.12103

Ikoona, E., Kalyesubula, I., Kawuma, M., 2003. Ocular manifestations in paediatric HIV/AIDS patients in Mulago Hospital, Uganda. Afr. Health Sci. 3, 83–86.

Innes, S., Lazarus, E., Otwombe, K., Liberty, A., Germanus, R., Van Rensburg, A.J., Grobbelaar, N., Hurter, T., Eley, B., Violari, A., Cotton, M.F., 2014. Early severe HIV disease precedes early antiretroviral therapy in infants: Are we too late? J. Int. AIDS Soc. 17, 18914.

Isanaka, S., Duggan, C., Fawzi, W.W., 2009. Patterns of postnatal growth in HIV-infected and HIV-exposed children. Nutr. Rev. 67, 343–359. https://doi.org/10.1111/j.1753-4887.2009.00207.x

Jacobs, Z., 2016. Applicability of the Griffiths Mental Development Scales-Extended Revised to the South African Context: A Systematic Review. Department of Psychology; University of Fort Hare.

Jankiewicz, M., Holmes, M.J., Taylor, P.A., Cotton, M.F., Laughton, B., van der Kouwe, A.J.W., Meintjes, E.M., 2017. White Matter Abnormalities in Children with HIV Infection and Exposure. Front. Neuroanat. 11. https://doi.org/10.3389/fnana.2017.00088

Jarjour, I.T., 2015. Neurodevelopmental Outcome after Extreme Prematurity: A Review of the Literature. Pediatr. Neurol. 52, 143–152. https://doi.org/10.1016/j.pediatrneurol.2014.10.027

Jelsma, J., Davids, N., Ferguson, G., 2011. The motor development of orphaned children with and without HIV: Pilot exploration of foster care and residential placement. BMC Pediatr. 11. https://doi.org/10.1186/1471-2431-11-11

Jesson, J., Masson, D., Adonon, A., Tran, C., Habarugira, C., Zio, R., Nicimpaye, L., Desmonde, S., Serurakuba, G., Kwayep, R., Sare, E., Konate, T., Nimaga, A., Saina, P., Kpade, A., Bassuka, A., Gougouyor, G., Leroy, V., 2015. Prevalence of malnutrition among HIV-infected children in Central and West-African HIV-care programmes supported by the Growing Up Programme in 2011: a cross-sectional study. BMC Infect. Dis. 15, 216. https://doi.org/10.1186/s12879-015-0952-6

Johnson, L., Budlender, D., 2002. HIV Risk Factors: A review of Demographic, Socio-economic, Biomedical and Behavioural Determinants of HIV Prevalence in South Africa.

Jonker, L., Stellenberg, E.L., 2014. Missed opportunities in child healthcare. Afr. J. Prim. Health Care Fam. Med. 6. https://doi.org/10.4102/phcfm.v6i1.537

Joubert, R., 2010. Exploring the history of occupational therapy's development in South Africa to reveal the flaws in our knowledge base. South Afr. J. Occup. Ther. 40, 21–26.

Joubert, R., Motala, N., Motta, N., Christopher, C., 2008. Occupational Therapy and its potentially positive influence upon the CD4 count of individuals with HIV: A single case study. South Afr. J. Occup. Ther. 38, 14–18.

Kandawasvika, G.Q., Kuona, P., Chandiwana, P., Masanganise, M., Gumbo, F.Z., Mapingure, M.P., Nathoo, K., Stray-Pedersen, B., 2015. The burden and predictors of cognitive impairment among 6- to 8-year-old children infected and uninfected with HIV from Harare, Zimbabwe: A cross-sectional study. Child Neuropsychol. 21, 106–120. https://doi.org/10.1080/09297049.2013.876493

Kandawasvika, G.Q., Ogundipe, E., Gumbo, F.Z., Kurewa, E.N., Mapingure, M.P., Stray-Pedersen, B., 2011. Neurodevelopmental impairment among infants born to mothers infected with human immunodeficiency virus and uninfected mothers from three peri-urban primary care clinics in Harare, Zimbabwe: Neurodevelopmental Impairment in HIV-exposed Infants. Dev. Med. Child Neurol. 53, 1046–1052. https://doi.org/10.1111/j.1469-8749.2011.04126.x

Kanji, A., Kara, R., 2013. Pediatric physicians' referral of children aged 0-3 years for audiological evaluation in the public health care sector. Audiol. Res. 3, 7. https://doi.org/10.4081/audiores.2013.e7

Kathard, H., Ramma, L., Pascoe, M., Jordaan, H., Moonsamy, S., Wium, A.-M., du Plessis, S., Pottas, L., Khan, N.B., 2011. How can speech-language therapists and audiologists enhance language and literacy outcomes in South Africa? (And why we urgently need to). S. Afr. J. Commun. Disord. 58, 59. https://doi.org/10.4102/sajcd.v58i2.27

Keino, S., Plasqui, G., Ettyang, G., van den Borne, B., 2014. Determinants of Stunting and Overweight among Young Children and Adolescents in Sub-Saharan Africa. Food Nutr. Bull. 35, 167–178. https://doi.org/10.1177/156482651403500203

Kelly, D., Coutts, A.G.P., 2000. Early nutrition and the development of immune function in the neonate. Proc. Nutr. Soc. 59, 177–185. https://doi.org/10.1017/S0029665100000197

Kestelyn, P., Lepage, P., Karita, E., Van de Perre, P., 2000. Ocular manifestations of infection with the human immunodeficiency virus in an African pediatric population. Ocul. Immunol. Inflamm. 8, 263–273.

Khoza-Shangase, K., 2013. Ototoxicity in tuberculosis treatment in South Africa: Exploring the current status. Afr. J. Pharm. Pharmacol. 7, 2140–2145.

Khoza-Shangase, K., 2011. Highly active antiretroviral therapy: Does it Sound toxic? J. Pharm. Bioallied Sci. 3, 142. https://doi.org/10.4103/0975-7406.76494

Khoza-Shangase, K., Barratt, J., Jonosky, J., 2010. Protocols for early audiology intervention services: Views from early intervention practitioners in a developing country. South Afr. J. Child Health 4, 100. https://doi.org/10.7196/SAJCH.271

Khoza-Shangase, K., Jina, K., 2013. Ototoxicity monitoring in general medical practice: Exploring perceptions and practices of general practitioners about drug-induced auditory symptoms. Innov. Pharm. Pharmacother. 1, 250–259.

Khoza-Shangase, K., Turnbull, T., 2009. HEARING SCREENING IN A GROUP OF PAEDIATRIC PATIENTS ATTENDING AN HIV/AIDS CLINIC: A PILOT STUDY. Afr. J. Infect. Dis. AJID 3, 57–68.

Kitahata, M.M., Gange, S.J., Abraham, A.G., Merriman, B., Saag, M.S., Justice, A.C., Hogg, R.S., Deeks, S.G., Eron, J.J., Brooks, J.T., Rourke, S.B., Gill, M.J., Bosch, R.J., Martin, J.N., Klein, M.B., Jacobson, L.P., Rodriguez, B., Sterling, T.R., Kirk, G.D., Napravnik, S., Rachlis, A.R., Calzavara, L.M., Horberg, M.A., Silverberg, M.J., Gebo, K.A., Goedert, J.J., Benson, C.A., Collier, A.C., Van Rompaey, S.E., Crane, H.M.,

McKaig, R.G., Lau, B., Freeman, A.M., Moore, R.D., NA-ACCORD Investigators, 2009. Effect of early versus deferred antiretroviral therapy for HIV on survival. N. Engl. J. Med. 360, 1815–1826. https://doi.org/10.1056/NEJMoa0807252

Koekkoek, S., de Sonneville, L.M.J., Wolfs, T.F.W., Licht, R., Geelen, S.P.M., 2008. Neurocognitive function profile in HIV-infected school-age children. Eur. J. Paediatr. Neurol. EJPN Off. J. Eur. Paediatr. Neurol. Soc. 12, 290–297. https://doi.org/10.1016/j.ejpn.2007.09.002

Koenig, L.J., Nesheim, S., Abramowitz, S., 2011. Adolescents with perinatally acquired HIV: emerging behavioral and health needs for long-term survivors. Curr. Opin. Obstet. Gynecol. 23, 321–327. https://doi.org/10.1097/GCO.0b013e32834a581b

Kuhn, L., Hunt, G., Technau, K.-G., Coovadia, A., Ledwaba, J., Pickerill, S., Penazzato, M., Bertagnolio, S., Mellins, C.A., Black, V., Morris, L., Abrams, E.J., 2014. Drug resistance among newly diagnosed HIV-infected children in the era of more efficacious antiretroviral prophylaxis. AIDS Lond. Engl. 28, 1673–1678. https://doi.org/10.1097/QAD.0000000000000261

Kurtz, L.A., 2006. Visual Perception Problems in Children with AD/HD, Autism, and Other Learning Disabilities: A Guide for Parents and Professionals. Jessica Kingsley Publishers.

Laughton, B., Cornell, M., Boivin, M., Van Rie, A., 2013. Neurodevelopment in perinatally HIV-infected children: a concern for adolescence. J. Int. AIDS Soc. 16. https://doi.org/10.7448/IAS.16.1.18603

Laughton, B., Springer, P., Grove, D., Seedat, S., Cornell, M., Kidd, M., Madhi, S., Cotton, M., 2010. Longitudinal developmental profile of children from low socio-economic circumstances in Cape Town, using the 1996 Griffiths Mental Development Scales. SAJCH South Afr. J. Child Health 4, 106–111.

Lazarus, J.R., Rutstein, R., Lowenthal, E., 2015. Treatment initiation factors and cognitive outcome in youth with perinatally acquired HIV infection: Cognitive outcome in HIV-infected youth. HIV Med. 16, 355–361. https://doi.org/10.1111/hiv.12220

Lecuona, R.E., Jaarsveld, A. van, Heerden, R. van, Raubenheimer, J., 2016. The developmental status and prevalence of sensory integration difficulties in premature infants in a tertiary hospital in Bloemfontein, South Africa. South Afr. J. Occup. Ther. Johannesbg. 46. http://0-dx.doi.org.innopac.wits.ac.za/10.17159/23110-3833/2016/v46n1a5

Lennon, E., Gardner, J., Karmel, B., Flory, M., 2008. Encyclopedia of Infant & Early Childhood Development: Bayley Scales of Infant Development, 1st ed. Academic Press.

Lilian, R.R., Mutasa, B., Railton, J., Mongwe, W., McIntyre, J.A., Struthers, H.E., Peters, R.P.H., 2017. A 10-year cohort analysis of routine paediatric ART data in a rural South African setting. Epidemiol. Infect. 145, 170–180. https://doi.org/10.1017/S0950268816001916

Lindsey, J.C., Malee, K.M., Brouwers, P., Hughes, M.D., for the PACTG 219C Study Team, 2007. Neurodevelopmental Functioning in HIV-Infected Infants and Young Children Before and After the Introduction of Protease Inhibitor-Based Highly Active Antiretroviral Therapy. PEDIATRICS 119, e681–e693. https://doi.org/10.1542/peds.2006-1145

Linhar, L.S., Traebert, J., Galato, D., da Silva, R.M., Schuelter-Trevisol, F., Rovaris, N.S., da Silva, J., 2014. Allergic diseases in subjects under 18 years living with HIV. Allergy Asthma Clin. Immunol. Off. J. Can. Soc. Allergy Clin. Immunol. 10, 35. https://doi.org/10.1186/1710-1492-10-35

Locks, L.M., Manji, K.P., Kupka, R., Liu, E., Kisenge, R., McDonald, C.M., Aboud, S., Wang, M., Fawzi, W.W., Duggan, C.P., 2017. High Burden of Morbidity and Mortality but Not Growth Failure in Infants Exposed to but Uninfected with Human Immunodeficiency Virus in Tanzania. J. Pediatr. 180, 191-199.e2. https://doi.org/10.1016/j.jpeds.2016.09.040

Lowenthal, E.D., Bakeera-Kitaka, S., Marukutira, T., Chapman, J., Goldrath, K., Ferrand, R.A., 2014. Perinatally acquired HIV infection in adolescents from sub-Saharan Africa: a review of emerging challenges. Lancet Infect. Dis. 14, 627–639. https://doi.org/10.1016/S1473-3099(13)70363-3

Lowick, S., Sawry, S., Meyers, T., 2012. Neurodevelopmental delay among HIV-infected preschool children receiving antiretroviral therapy and healthy preschool children in Soweto, South Africa. Psychol. Health Med. 17, 599–610. https://doi.org/10.1080/13548506.2011.648201

Luiz, D.M., Foxcroft, C.D., Stewart, R., 2001. The construct validity of the Griffiths Scales of Mental Development. Child Care Health Dev. 27, 73–83.

Lyman, W.D., Kress, Y., Chiu, F.-C., Raine, C.S., Bbornstein, M.B., Ruvinstein, A., 1988. Human Foetal Neural Tissue Organotypic Cultures.: A Model for Perinatal AIDS Neuropathology. Ann. N. Y. Acad. Sci. 546, 225–226. https://doi.org/10.1111/j.1749-6632.1988.tb21647.x

Lyman, W.D., Kress, Y., Kure, K., Rashbaum, W.K., Rubinstein, A., Soeiro, R., 1990. Detection of HIV in fetal central nervous system tissue. AIDS Lond. Engl. 4, 917–920.

Maddocks, S., Chetty, V., Maghoo, A., Mhlongo, N., Mthembu, N., Khanyile, S., Chiliza, S., Munsamy, T., Gamede, Z., Mazibukoc, S., 2018. 'Treating a patient should be approached in a holistic manner': collaboration of doctors and physiotherapists in the rehabilitation of people living with HIV. South Afr. Fam. Pract. 60, 53–57. https://doi.org/10.1080/20786190.2017.1382969

Maenner, M.J., Global Partnership for the Epidemiology of Developmental Disabilities, Early Childhood Development Task Force, 2013. Ten Question Screen for Disabilities [WWW Document]. Disabilitymeasures.org. URL http://disabilitymeasures.org/tenquestions/TQ_MICS3_Child_Disablity_Module_English_2013-04-14.pdf (accessed 9.25.15).

Maes, J.-P., 2016. Movement Analysis and Education Strategies for the treatment of children with Cerebral Palsy and similar neurological conditions, Specialist Course Hand-outs.

Makar, S.K., Dhara, S., Sinha, A.K., Chatterjee, I., Dutta, P., 2012. Nature and onset of communication disorder in pediatrics with HIV. Int. J. Pediatr. Otorhinolaryngol. 76, 1065–1066. https://doi.org/10.1016/j.ijporl.2012.04.001

Manomano, T., Selebogo, M.M., 2017. Children in Difficult Circumstances: A South African Perspective. J. Soc. Sci. 51, 87–95. https://doi.org/10.1080/09718923.2017.1317960

Martin, S.C., Wolters, P.L., Toledo-Tamula, M.A., Zeichner, S.L., Hazra, R., Civitello, L., 2006. Cognitive functioning in school-aged children with vertically acquired HIV infection being treated with highly active antiretroviral therapy (HAART). Dev. Neuropsychol. 30, 633–657. https://doi.org/10.1207/s15326942dn3002_1

Martínez-Bonet, M., Puertas, M.C., Fortuny, C., Ouchi, D., Mellado, M.J., Rojo, P., Noguera-Julian, A., Muñoz-Fernández, M.A., Martinez-Picado, J., 2015. Establishment and Replenishment of the Viral Reservoir in Perinatally HIV-1-infected Children Initiating Very Early Antiretroviral Therapy. Clin. Infect. Dis. Off. Publ. Infect. Dis. Soc. Am. 61, 1169–1178. https://doi.org/10.1093/cid/civ456

M'bongo Zindamoyen, A.., Masinde, S., Njuguna, M., Kollmann, M., Schaller, U., Gichuhi, S., Ilako, D., 2013. Ocular findings in children with HIV/AIDS at Mbagathi District Hospital Nairobi, Kenya. JOECSA 14.

McAuley, J.B., 2014. Congenital Toxoplasmosis. J. Pediatr. Infect. Dis. Soc. 3, S30–S35. https://doi.org/10.1093/jpids/piu077

McDonald, C.M., Manji, K.P., Kupka, R., Bellinger, D.C., Spiegelman, D., Kisenge, R., Msamanga, G., Fawzi, W.W., Duggan, C.P., 2013. Stunting and Wasting Are Associated with Poorer Psychomotor and Mental Development in HIV-Exposed Tanzanian Infants. J. Nutr. 143, 204–214. https://doi.org/10.3945/jn.112.168682

McGrath, C.J., Nduati, R., Richardson, B.A., Kristal, A.R., Mbori-Ngacha, D., Farquhar, C., John-Stewart, G.C., 2012. The Prevalence of Stunting Is High in HIV-1–Exposed Uninfected Infants in Kenya. J. Nutr. 142, 757–763. https://doi.org/10.3945/jn.111.148874

Meltzer, E.O., 2001. Quality of life in adults and children with allergic rhinitis. J. Allergy Clin. Immunol. 108, S45–S53. https://doi.org/10.1067/mai.2001.115566

Merrian-Webster, 2017. Merriam-Webster Medical Dictionary [WWW Document]. URL https://www.merriam-webster.com/medical/neurodevelopment (accessed 11.29.17).

Mitchell, C.D., 2006. HIV-1 encephalopathy among perinatally infected children: Neuropathogenesis and response to highly active antiretroviral therapy. Ment. Retard. Dev. Disabil. Res. Rev. 12, 216–222. https://doi.org/10.1002/mrdd.20111

Mofenson, L.M., 2016. Antiretroviral Therapy and Adverse Pregnancy Outcome: The Elephant in the Room? J. Infect. Dis. 213, 1051–1054. https://doi.org/10.1093/infdis/jiv390

Monasch, R., Boerma, J.T., 2004. Orphanhood and childcare patterns in sub-Saharan Africa: an analysis of national surveys from 40 countries. AIDS Lond. Engl. 18 Suppl 2, S55-65.

Moschos, M.M., Mostrou, G., Psimenidou, E., Spoulou, V., Theodoridou, M., 2007. Objective Analysis of Retinal Function in HIV-positive Children Without Retinitis Using Optical Coherence Tomography. Ocul. Immunol. Inflamm. 15, 319–323. https://doi.org/10.1080/09273940701375154

Moutquin, J.-M., 2003. Classification and heterogeneity of preterm birth. BJOG Int. J. Obstet. Gynaecol. 110 Suppl 20, 30–33.

Muga, E., 2003. Screening for disability in a community: the “ten questions” screen for children, in Bondo, Kenya. Afr. Health Sci. 3, 33–39.

Mung’ala-Odera, V., Meehan, R., Njuguna, P., Mturi, N., Alcock, K.J., Newton, C., 2006. Prevalence and risk factors of neurological disability and impairment in children living in rural Kenya. Int. J. Epidemiol. 35, 683–688. https://doi.org/10.1093/ije/dyl023

Muri, L., Gamell, A., Ntamatungiro, A.J., Glass, T.R., Luwanda, L.B., Battegay, M., Furrer, H., Hatz, C., Tanner, M., Felger, I., Klimkait, T., Letang, E., 2017. Development of HIV drug resistance and therapeutic failure in children and adolescents in rural Tanzania: an emerging public health concern. AIDS 31, 61–70. https://doi.org/10.1097/QAD.0000000000001273

Mwaba, S., Ms, N., T, K., Ja, M., 2015. The Effect of HIV on Developmental Milestones in Children. J. AIDS Clin. Res. 6, 1–6. https://doi.org/10.4172/2155-6113.1000482

Myezwa, H., Buchalla, C.M., Jelsma, J., Stewart, A., 2011. HIV/AIDS: use of the ICF in Brazil and South Africa – comparative data from four cross-sectional studies. Physiotherapy 97, 17–25. https://doi.org/10.1016/j.physio.2010.08.015

Myezwa, H., Stewart, A., Musenge, E., Nesara, P., 2009. Assessment of HIV-positive in-patients using the International Classification of Functioning, Disability and Health (ICF) at Chris Hani Baragwanath Hospital, Johannesburg. Afr. J. AIDS Res. 8, 93–105. https://doi.org/10.2989/AJAR.2009.8.1.10.723

Newman, D., K., Hitchcock, A., McCarthy, H., Keast-Butler, J., Moore, A.T., 1996. Preschool vision screening: outcome of children referred to the hospital eye service. Br. J. Ophthalmol. 80, 1077–1082.

Nixon, S.A., Hanass-Hancock, J., Whiteside, A., Barnett, T., 2011. The increasing chronicity of HIV in sub-Saharan Africa: Re-thinking "HIV as a long-wave event" in the era of widespread access to ART. Glob. Health 7, 41. https://doi.org/10.1186/1744-8603-7-41

Nkonki, L.L., Chopra, M., Doherty, T.M., Jackson, D., Robberstad, B., 2011. Explaining household socio-economic related child health inequalities using multiple methods in three diverse settings in South Africa. Int. J. Equity Health 10, 13. https://doi.org/10.1186/1475-9276-10-13

Nozyce, M.L., Lee, S.S., Wiznia, A., Nachman, S., Mofenson, L.M., Smith, M.E., Yogev, R., McIntosh, K., Stanley, K., Pelton, S., 2006. A Behavioral and Cognitive Profile of Clinically Stable HIV-Infected Children. Pediatrics 117, 763–770. https://doi.org/10.1542/peds.2005-0451

Omoni, A.O., Ntozini, R., Evans, C., Prendergast, A.J., Moulton, L.H., Christian, P.S., Humphrey, J.H., 2017. Child Growth According to Maternal and Child HIV Status in Zimbabwe: Pediatr. Infect. Dis. J. 36, 869–876. https://doi.org/10.1097/INF.0000000000001574

Omotoso, K.., Koch, S.., 2017. Exploring Child Poverty and Inequality in Post-Apartheid South Africa: A Multidimensional Perspective.

O'Toole, M.T., 2003. Miller-Keane Encyclopedia and Dictionary of Medicine, Nursing, and Allied Health, Seventh. ed. Saunders, Elsevier, Inc.

Padhani, D.H., Manji, K.P., Mtanda, A.T., 2000. Ocular manifestations in children with HIV infection in Dar es Salaam, Tanzania. J. Trop. Pediatr. 46, 145–148.

Palacios, G.C., Montalvo, M.S., Fraire, M.I., Leon, E., Alvarez, M.T., Solorzano, F., 2008. Audiologic and vestibular findings in a sample of Human Immunodeficiency Virus type-1-infected Mexican children under Highly Active Antiretroviral Therapy. Int. J. Pediatr. Otorhinolaryngol. 72, 1671–1681. https://doi.org/10.1016/j.ijporl.2008.08.002

Paranjpe, R.R., Maheshgauri, R.D., Yadav, S.R., Kotadia, B.J., Nagdev, N.G., Jethwa, K.G., 2016. A study of visual problems in children scoring low grades and those with lack of concentration at school in Pune city. Natl. J. Med. Res. 6, 87–88.

Penazzato, M., Prendergast, A.J., Muhe, L.M., Tindyebwa, D., Abrams, E.J., 2014. Optimization of antiretroviral therapy in HIV-infected children under 3 years of age: a systematic review. AIDS 28, S137–S146. https://doi.org/10.1097/QAD.0000000000000240

Peters, R., Ramshorst, M., Struthers, H., McIntyre, J., 2014. Clinical assessment of peripheral neuropathy in HIV-infected children on antiretroviral therapy in rural South Africa. Eur. J. Pediatr. 173, 1245–1248. https://doi.org/10.1007/s00431-014-2303-9

Petrocchi-Bartal, L., Khoza-Shangase, K., 2016. Infant hearing screening at primary healthcare immunisation clinics in South Africa: The current status. South Afr. J. Child Health 10, 139. https://doi.org/10.7196/SAJCH.2016.v10i2.1114

Phillips, N., Amos, T., Kuo, C., Hoare, J., Ipser, J., Thomas, K.G.F., Stein, D.J., 2016. HIV-Associated Cognitive Impairment in Perinatally Infected Children: A Meta-analysis. Pediatrics 138, e20160893. https://doi.org/10.1542/peds.2016-0893

Pollack, H., Kuchuk, A., Cowan, L., Hacimamutoglu, S., Glasberg, H., David, R., Krasinski, K., Borkowsky, W., Oberfield, S., 1996. Neurodevelopment, Growth, and Viral Load in HIV-Infected Infants. Brain. Behav. Immun. 10, 298–312. https://doi.org/10.1006/brbi.1996.0026

Pons-Duran, C., González, R., Quintó, L., Munguambe, K., Tallada, J., Naniche, D., Sacoor, C., Sicuri, E., 2016. Association between HIV infection and socio-economic status: evidence from a semirural area of southern Mozambique. Trop. Med. Int. Health 21, 1513–1521. https://doi.org/10.1111/tmi.12789

Portney, L., Watkins, M., 2009. Foundations of Clinical Research Applications to Practice, Third. ed. Pearson Prentice Hall.

Potterton, J., Hilburn, N., Strehlau, R., 2016. Developmental status of preschool children receiving cART: a descriptive cohort study: Development of preschool children on cART. Child Care Health Dev. 42, 410–414. https://doi.org/10.1111/cch.12321

Potterton, J., Stewart, A., Cooper, P., Goldberg, L., Gajdosik, C., Baillieu, N., 2009. Neurodevelopmental delay in children infected with human immunodeficiency virus in Soweto, South Africa. Vulnerable Child. Youth Stud. 4, 48–57. https://doi.org/10.1080/17450120802183728

Powis, K.M., Smeaton, L., Hughes, M.D., Tumbare, E.A., Souda, S., Jao, J., Wirth, K.E., Makhema, J., Lockman, S., Fawzi, W., Essex, M., Shapiro, R.L., 2016. In-utero triple antiretroviral exposure associated with decreased growth among HIV-exposed uninfected infants in Botswana: AIDS 30, 211–220. https://doi.org/10.1097/QAD.0000000000000895

Rabie, H., Frigati, L., Hesseling, A.C., Garcia-Prats, A.J., 2015. Tuberculosis: opportunities and challenges for the 90–90–90 targets in HIV-infected children. J. Int. AIDS Soc. 18. https://doi.org/10.7448/IAS.18.7.20236

Rademeyer, V., Jacklin, L., 2013. A study to evaluate the performance of black South African urban infants on the Bayley Scales of Infant Development III. South Afr. J. Child Health 7, 54–59.

Reuner, G., Fields, A.C., Wittke, A., Löpprich, M., Pietz, J., 2013. Comparison of the developmental tests Bayley-III and Bayley-II in 7-month-old infants born preterm. Eur. J. Pediatr. 172, 393–400. https://doi.org/10.1007/s00431-012-1902-6

Rice, M.L., Zeldow, B., Siberry, G.K., Purswani, M., Malee, K., Hoffman, H.J., Frederick, T., Buchanan, A., Sirois, P.A., Allison, S.M., Williams, P.L., 2013. Evaluation of Risk for Late Language Emergence after In-Utero Antiretroviral Drug Exposure in HIV-exposed Uninfected Infants: Pediatr. Infect. Dis. J. 32, e406–e413. https://doi.org/10.1097/INF.0b013e31829b80ee

Right to Care, T., Mwanandimai, O., 2015. Flipsters Support Club Tool for Adolescents: Right to Care | Resources [WWW Document]. URL http://www.righttocare.org/resources/ (accessed 11.28.17).

Rogers, E.E., Hintz, S.R., 2016. Early neurodevelopmental outcomes of extremely preterm infants. Semin. Perinatol. 40, 497–509. https://doi.org/10.1053/j.semperi.2016.09.002

Rose, L., 2017. ESRU Support Services & Talks.

Ruel, T.D., Boivin, M.J., Boal, H.E., Bangirana, P., Charlebois, E., Havlir, D.V., Rosenthal, P.J., Dorsey, G., Achan, J., Akello, C., Kamya, M.R., Wong, J.K., 2012. Neurocognitive and Motor Deficits in HIV-Infected Ugandan Children with High CD4 Cell Counts. Clin. Infect. Dis. 54, 1001–1009. https://doi.org/10.1093/cid/cir1037

Rutar, T., Youm, J., Porco, T., Tilton, N., Muskat, M., McNamara, N., Wara, D., 2015. Ophthalmic manifestations of perinatally acquired HIV in a US cohort of long-term survivors: Table 1. Br. J. Ophthalmol. 99, 650–653. https://doi.org/10.1136/bjophthalmol-2014-305557

Sadoh, W.E., Okunola, O.P., Oviawe, O., 2007. Neurologic manifestations of childhood AIDS in Benin City, Nigeria. J. Pediatr. Neurol. JPN Van 5, 21–25.

Said-Mohamed, R., Micklesfield, L.K., Pettifor, J.M., Norris, S.A., 2015. Has the prevalence of stunting in South African children changed in 40 years? A systematic review. BMC Public Health 15, 534. https://doi.org/10.1186/s12889-015-1844-9

Saloojee, G., Phohole, M., Saloojee, H., IJsselmuiden, C., 2007. Unmet health, welfare and educational needs of disabled children in an impoverished South African peri-urban township. Child Care Health Dev. 33, 230–235. https://doi.org/10.1111/j.1365-2214.2006.00645.x

Saloojee, H., Bamford, L., 2006. South African Health Review: Key childhood health promotion and disease prevention programmes. Durb. Health Syst. Trust 181–202.

Saloojee, H., De Maayer, T., Garenne, M.L., Kahn, K., 2007. What's new? Investigating risk factors for severe childhood malnutrition in a high HIV prevalence South African setting1. Scand. J. Public Health 35, 96–106. https://doi.org/10.1080/14034950701356435

Samia, P., Petersen, R., Walker, K.G., Eley, B., Wilmshurst, J.M., 2013. Prevalence of Seizures in Children Infected With Human Immunodeficiency Virus. J. Child Neurol. 28, 297–302. https://doi.org/10.1177/0883073812446161

Sankhyan, N., Lodha, R., Sharma, S., Menon, P.R., Choudhary, A., Kabra, S.K., Gulati, S., 2015. Peripheral Neuropathy in Children on Stavudine Therapy. Indian J. Pediatr. 82, 136–139. https://doi.org/10.1007/s12098-014-1477-5

Schwartz, L., Civitello, L., Dunn-Pirio, A., Ryschkewitsch, S., Berry, E., Cavert, W., Kinzel, N., Lawrence, D.M.P., Hazra, R., Major, E.O., 2007. Evidence of human immunodeficiency virus type 1 infection of nestin-positive neural progenitors in archival pediatric brain tissue. J. Neurovirol. 13, 274–283. https://doi.org/10.1080/13550280701344975

Seth, A., Malhotra, R.K., Gupta, R., Chandra, J., Kumar, P., Singh, S., Sharma, G., 2017. Effect of Anti-Retroviral Therapy on Growth Parameters of Children with HIV Infection. Pediatr. Infect. Dis. J. Publish Ahead of Print. https://doi.org/10.1097/INF.0000000000001719

Seth, P., Major, E.O., 2005. Human brain derived cell culture models of HIV-1 infection. Neurotox. Res. 8, 83–89.

Shanbhag, M.C., Rutstein, R.M., Zaoutis, T., Zhao, H., Chao, D., Radcliffe, J., 2005. Neurocognitive Functioning in Pediatric Human Immunodeficiency Virus Infection: Effects of Combined Therapy. Arch. Pediatr. Adolesc. Med. 159, 651–656. https://doi.org/10.1001/archpedi.159.7.651

Sharp, C., Jardin, C., Marais, L., Boivin, M., 2015. Orphanhood by AIDS-Related Causes and Child Mental Health: A Developmental Psychopathology Approach. J. HIV AIDS 1.

Shead, G.M., Potterton, J., Stewart, A., 2010. Neurodevelopment and growth of institutionalized children with vertically transmitted human immunodeficiency virus. Vulnerable Child. Youth Stud. 5, 33–43.

Sheppard, J.D., Comstock, T.L., Cavet, M.E., 2016. Impact of the Topical Ophthalmic Corticosteroid Loteprednol Etabonate on Intraocular Pressure. Adv. Ther. 33, 532–552. https://doi.org/10.1007/s12325-016-0315-8

Sherman, G.G., Galpin, J.S., Patel, J.M., Mendelow, B.V., Glencross, D.K., 1999. CD4+ T cell enumeration in HIV infection with limited resources. J. Immunol. Methods 222, 209–217. https://doi.org/10.1016/S0022-1759(98)00172-0

Sherr, L., Cluver, L.D., Betancourt, T.S., Kellerman, S.E., Richter, L.M., Desmond, C., 2014a. Evidence of impact: health, psychological and social effects of adult HIV on children. AIDS 28, S251. https://doi.org/10.1097/QAD.0000000000000327

Sherr, L., Croome, N., Parra Castaneda, K., Bradshaw, K., Herrero Romero, R., 2014b. Developmental challenges in HIV infected children—An updated systematic review. Child. Youth Serv. Rev., Children and Youth Growing Up with HIV Infection in Sub-Saharan Africa: Implications for Health Service Delivery 45, 74–89. https://doi.org/10.1016/j.childyouth.2014.03.040

Sherr, L., Hensels, I.S., Tomlinson, M., Skeen, S., Macedo, A., 2017. Cognitive and physical development in HIV-positive children in South Africa and Malawi: A community-based follow-up comparison study. Child Care Health Dev. 1–10. https://doi.org/10.1111/cch.12533

Sherr, L., Mueller, J., Varrall, R., 2009. A systematic review of cognitive development and child human immunodeficiency virus infection. Psychol. Health Med. 14, 387–404. https://doi.org/10.1080/13548500903012897

Shiau, S., Strehlau, R., Technau, K.-G., Patel, F., Arpadi, S.M., Coovadia, A., Abrams, E.J., Kuhn, L., 2017. Early age at start of antiretroviral therapy associated with better virologic control after initial suppression in HIV-infected infants: AIDS 31, 355–364. https://doi.org/10.1097/QAD.0000000000001312

Sibanda, A., Doctor, H.V., 2013. Measuring health gaps between the rich and the poor: a review of the literature and its implications for health research in Africa. J. Public Health Afr. 4, 3. https://doi.org/10.4081/jphia.2013.e3

Siberry, G., Tindyebwa, D., 2014. Commentary: When to start and what to use in children – recommendations and rationale. AIDS 28, S133–S135. https://doi.org/10.1097/QAD.0000000000000241

Siberry, G.K., Joyner, M., Hutton, N., 2008. Growing Up with Perinatal HIV Infection: Time for a HAART to Heart. J. Pediatr. 153, 456–457. https://doi.org/10.1016/j.jpeds.2008.05.049

Simkiss, D.E., Blackburn, C.M., Mukoro, F.O., Read, J.M., Spencer, N.J., 2011. Childhood disability and socio-economic circumstances in low and middle income countries: systematic review. BMC Pediatr. 11, 1–15. https://doi.org/10.1186/1471-2431-11-119

Singhi, P., Kumar, M., Malhi, P., Kumar, R., 2007. Utility of the WHO Ten Questions Screen for disability detection in a rural community the North Indian experience. J. Trop. Pediatr. 53, 383–387. https://doi.org/10.1093/tropej/fmm047

Slyker, J.A., 2016. Cytomegalovirus and paediatric HIV infection. J. Virus Erad. 2, 208–214.

Smith, L., Adnams, C., Eley, B., 2008. Neurological and neurocognitive function of HIV-infected children commenced on antiretroviral therapy. South Afr. J. Child Health 2, 108–113.

Smith, R., Chernoff, M., Williams, P.L., Malee, K.M., Sirois, P.A., Kammerer, B., Wilkins, M., Nichols, S., Mellins, C., Usitalo, A., Garvie, P., Rutstein, R., 2012. Impact of HIV Severity on Cognitive and Adaptive Functioning During Childhood and Adolescence: Pediatr. Infect. Dis. J. 31, 592–598. https://doi.org/10.1097/INF.0b013e318253844b

South African National Department of Health, 2015. National Consolidated Guidelines for the preventions of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults.

Spittle, A., Treyvaud, K., 2016. The role of early developmental intervention to influence neurobehavioral outcomes of children born preterm. Semin. Perinatol. 40, 542–548. https://doi.org/10.1053/j.semperi.2016.09.006

Spittle, A.J., Doyle, L.W., Boyd, R.N., 2008. A systematic review of the clinometric properties of neuromotor assessments for preterm infants during the first year of life. Dev. Med. Child Neurol. 50, 254–266. https://doi.org/10.1111/j.1469-8749.2008.02025.x

Stats SA, 2017a. Mid-Year Population Estimates: P0302 [WWW Document]. URL http://www.statssa.gov.za/publications/P0302/P03022017.pdf (accessed 04/12/17)

Stats SA, 2017b. Poverty Trends in South Africa: An examination of absolute poverty between 2006 and 2015. [WWW Document]. URL http://www.statssa.gov.za/publications/Report-03-10-06/Report-03-10-062015.pdf (accessed 19.12.17)

Stats SA, Lehohla, P., 2011. Census 2011: Profile of Persons with Disabilities in South Africa [WWW Document]. URL http://www.statssa.gov.za/publications/Report-03-01-59/Report-03-01-592011.pdf (accessed 04.11.17)

Stats SA, Lehohla, P., 2005. Census 2001: Prevalence of Disability in South Africa. [WWW Document]. URL http://www.statssa.gov.za/census/census_2001/disability/Disability.pdf (accessed 30.05.17)

Stein, Z., Durkin, M., Belmont, L., 1986. "Serious" Mental Retardation in Developing Countries: An Epidemiologic Approach. Ann. N. Y. Acad. Sci. 477, 8–21. https://doi.org/10.1111/j.1749-6632.1986.tb40316.x

Stokes, S.C., Tankersley, M.S., 2011. HIV: practical implications for the practicing allergist-immunologist. Ann. Allergy Asthma Immunol. Off. Publ. Am. Coll. Allergy Asthma Immunol. 107, 1–9; quiz 9–11. https://doi.org/10.1016/j.anai.2011.05.004

Sunguya, B.F., Mlunde, L.B., Urassa, D.P., Poudel, K.C., Ubuguyu, O.S., Mkopi, N.P., Leyna, G.H., Kessy, A.T., Nanishi, K., Shibanuma, A., Yasuoka, J., Jimba, M., 2017. Improving feeding and growth of HIV-positive children through nutrition training of frontline health workers in Tanga, Tanzania. BMC Pediatr. 17, 94. https://doi.org/10.1186/s12887-017-0840-x

Sunguya, B.F., Poudel, K.C., Mlunde, L.B., Shakya, P., Urassa, D.P., Jimba, M., Yasuoka, J., 2013a. Effectiveness of nutrition training of health workers toward improving caregivers' feeding practices for children aged six months to two years: a systematic review. Nutr. J. 12, 66. https://doi.org/10.1186/1475-2891-12-66

Sunguya, B.F., Poudel, K.C., Mlunde, L.B., Urassa, D.P., Yasuoka, J., Jimba, M., 2014. Poor Nutrition Status and Associated Feeding Practices among HIV-Positive Children in a Food Secure Region in Tanzania: A Call for Tailored Nutrition Training. PLoS ONE 9. https://doi.org/10.1371/journal.pone.0098308

Sunguya, B.F., Poudel, K.C., Mlunde, L.B., Urassa, D.P., Yasuoka, J., Jimba, M., 2013b. Nutrition Training Improves Health Workers' Nutrition Knowledge and Competence to Manage Child Undernutrition: A Systematic Review. Front. Public Health 1. https://doi.org/10.3389/fpubh.2013.00037

Tarwa, C., De Villiers, F.P.R., 2007. The Use of the Road to Health Card in Monitoring Child Health. South Afr. Fam. Pract. 49, 15.

Taylor, H.G., Clark, C.A.C., 2016. Executive function in children born preterm: Risk factors and implications for outcome. Semin. Perinatol. 40, 520–529. https://doi.org/10.1053/j.semperi.2016.09.004

Technau, K.-G., Kuhn, L., Coovadia, A., Carmona, S., Sherman, G., 2017a. Improving early identification of HIV-infected neonates with birth PCR testing in a large urban hospital in Johannesburg, South Africa: successes and challenges. J. Int. AIDS Soc. 20. https://doi.org/10.7448/IAS.20.01/21436

Technau, K.-G., Kuhn, L., Coovadia, A., Murnane, P.M., Sherman, G., 2017b. Xpert HIV-1 point-of-care test for neonatal diagnosis of HIV in the birth testing programme of a maternity hospital: a field evaluation study. Lancet HIV 4, e442–e448. https://doi.org/10.1016/S2352-3018(17)30097-8

Technau, K.-G., Mazanderani, A.H., Kuhn, L., Hans, L., Strehlau, R., Abrams, E.J., Conradie, M., Coovadia, A., Mbete, N., Murnane, P.M., Patel, F., Shiau, S., Tiemessen, C.T., Sherman, G.G., 2017c. Prevalence and outcomes of HIV-1 diagnostic challenges during universal birth testing - an urban South African observational cohort. J. Int. AIDS Soc. 20, 21761. https://doi.org/10.7448/IAS.20.7.21761

The DHS Programme, 2015. UNICEF: The Demographic and Health Surveys Model Questionnaire - DHSQ7, Household Survey [WWW Document]. URL http://dhsprogram.com/publications/publication-dhsq7-dhs-questionnaires-and-manuals.cfm (accessed 1.16.17).

The Teddy Bear Clinic, 2018. Welcome to The Teddy Bear Foundation [WWW Document]. Teddy Bear Clin. URL http://ttbc.org.za/ (accessed 4.6.18).

Thein, P., Kalinec, G.M., Park, C., Kalinec, F., 2014. In vitro assessment of antiretroviral drugs demonstrates potential for ototoxicity. Hear. Res. 310, 27–35. https://doi.org/10.1016/j.heares.2014.01.005

Thelen, E., 1995. Motor development: A new synthesis. Am. Psychol. 50, 79–95. https://doi.org/10.1037/0003-066X.50.2.79

Thorburn, M., Desai, P., Paul, T.J., Malcolm, L., Durkin, M., Davidson, L., 1992. Identification of childhood disability in Jamaica: the ten question screen. Int. J. Rehabil. Res. Int. Z. Rehabil. Rev. Int. Rech. Readaptation 15, 115–127.

Tiedt, N.J., Butler, I.R., Hallbauer, U.M., Atkins, M.D., Elliott, E., Pieters, M., Joubert, G., Seedat, R.Y., 2013. Paediatric chronic suppurative otitis media in the Free State Province: Clinical and audiological features. S. Afr. Med. J. 103, 467. https://doi.org/10.7196/SAMJ.6636

Tieman, B.L., Palisano, R.J., Sutlive, A.C., 2005. Assessment of motor development and function in preschool children. Ment. Retard. Dev. Disabil. Res. Rev. 11, 189–96. https://doi.org/10.1002/mrdd.20074

Tladi, L.S., 2006. Poverty and HIV/AIDS in South Africa: an empirical contribution. SAHARA-J J. Soc. Asp. HIVAIDS 3, 369–381. https://doi.org/10.1080/17290376.2006.9724863

Torre, P., Cook, A., Elliott, H., Dawood, G., Laughton, B., 2016. Middle Ear Function in Human Immunodeficiency Virus (HIV)-Infected South African Children. J.Paedi.Care.Inol 1, 13–17.

Torre, P., Cook, A., Elliott, H., Dawood, G., Laughton, B., 2015. Hearing assessment data in HIV-infected and uninfected children of Cape Town, South Africa. AIDS Care 27, 1037–1041. https://doi.org/10.1080/09540121.2015.1021746

Torre, P., Zeldow, B., Hoffman, H.J., Buchanan, A., Siberry, G.K., Rice, M., Sirois, P.A., Williams, P.L., 2012. Hearing Loss in Perinatally HIV-infected and HIV-exposed but Uninfected Children and Adolescents: Pediatr. Infect. Dis. J. 31, 835–841. https://doi.org/10.1097/INF.0b013e31825b9524

Tumusiime, D.K., Stewart, A., Venter, F.W., 2015. Effect of physiotherapeutic exercises on peripheral neuropathy, functional limitations of lower extremity and quality of life in people with HIV. Physiotherapy 101, e1547–e1548. https://doi.org/10.1016/j.physio.2015.03.1542

UNAIDS, 2017. UNAIDS: South Africa: Overview [WWW Document]. UNAIDS South Afr. Overv. URL http://www.unaids.org/en/regionscountries/countries/southafrica (accessed 4.11.17).

University of the Witwatersrand, 2017. Rahima Moosa Mother and Child Hospital [WWW Document]. URL https://www.wits.ac.za/clinicalmed/departments/paediatrics/contact-us/rahima-moosa-mother-and-child-hospital/ (accessed 4.6.18).

Uthman, O.A., Nachega, J.B., Anderson, J., Kanters, S., Mills, E.J., Renaud, F., Essajee, S., Doherty, M.C., Mofenson, L.M., 2017. Timing of initiation of antiretroviral therapy and adverse pregnancy outcomes: a systematic review and meta-analysis. Lancet HIV 4, e21–e30. https://doi.org/10.1016/S2352-3018(16)30195-3

Van den Hof, M., Blokhuis, C., Cohen, S., Scherpbier, H.J., Wit, F.W.N.M., Pistorius, M.C.M., Kootstra, N.A., Teunissen, C.E., Mathot, R.A.A., Pajkrt, D., 2017. CNS penetration of ART in HIV-infected children. J. Antimicrob. Chemother. https://doi.org/10.1093/jac/dkx396

van der Linde, J., Swanepoel, D.W., Glascoe, F.P., Louw, E., Vinck, B., 2015. Developmental screening in South Africa: comparing the national developmental checklist to a standardized tool. Afr. Health Sci. 15, 188–196. https://doi.org/10.4314/ahs.v15i1.25

van Jaarsveld, A., 2014. Patterns of sensory integration dysfunction in children from South Africa. South Afr. J. Occup. Ther. Johannesbg. 44.

Van Rie, A., Harrington, P.R., Dow, A., Robertson, K., 2007. Neurologic and neurodevelopmental manifestations of pediatric HIV/AIDS: A global perspective. Eur. J. Paediatr. Neurol. 11, 1–9. https://doi.org/10.1016/j.ejpn.2006.10.006

Van Rie, A., Mupuala, A., Dow, A., 2008. Impact of the HIV/AIDS Epidemic on the Neurodevelopment of Preschool-Aged Children in Kinshasa, Democratic Republic of the Congo. PEDIATRICS 122, e123–e128. https://doi.org/10.1542/peds.2007-2558

van Toorn, R., Solomons, R., 2014. Update on the Diagnosis and Management of Tuberculosis Meningitis in Children. Semin. Pediatr. Neurol. 21, 12–18. https://doi.org/10.1016/j.spen.2014.01.006

Vazeux, R., Lacroix-Ciaudo, C., Blanche, S., Cumont, M.C., Henin, D., Gray, F., Boccon-Gibod, L., Tardieu, M., 1992. Low levels of human immunodeficiency virus replication in the brain tissue of children with severe acquired immunodeficiency syndrome encephalopathy. Am. J. Pathol. 140, 137–144.

Vazir, S., Engle, P., Balakrishna, N., Griffiths, P.L., Johnson, S.L., Creed-Kanashiro, H., Rao, S.F., Shroff, M.R., Bentley, M.E., 2013. Cluster-randomized trial on complementary and responsive feeding education to caregivers found improved dietary intake, growth, and development among rural Indian toddlers. Matern. Child. Nutr. 9, 99–117. https://doi.org/10.1111/j.1740-8709.2012.00413.x

Violari, A., Cotton, M.F., Gibb, D.M., Babiker, A.G., Steyn, J., Madhi, S.A., Jean-Philippe, P., McIntyre, J.A., 2008. Early Antiretroviral Therapy and Mortality among HIV-Infected Infants. N. Engl. J. Med. 359, 2233–2244. https://doi.org/10.1056/NEJMoa0800971

Wabiri, N., Taffa, N., 2013. Socio-economic inequality and HIV in South Africa. BMC Public Health 13. https://doi.org/10.1186/1471-2458-13-1037

Wagner, R.G., Ngugi, A.K., Twine, R., Bottomley, C., Kamuyu, G., Gómez-Olivé, F.X., Connor, M.D., Collinson, M.A., Kahn, K., Tollman, S., Newton, C.R., 2014. Prevalence and risk factors for active convulsive epilepsy in rural northeast South Africa. Epilepsy Res. 108, 782–791. https://doi.org/10.1016/j.eplepsyres.2014.01.004

Walker, S.P., Wachs, T.D., Meeks Gardner, J., Lozoff, B., Wasserman, G.A., Pollitt, E., Carter, J.A., 2007. Child development: risk factors for adverse outcomes in developing countries. The Lancet 369, 145–157. https://doi.org/10.1016/S0140-6736(07)60076-2

Walker, S.Y., Pierre, R.B., Christie, C.D.C., Chang, S.M., 2013. Neurocognitive function in HIV-positive children in a developing country. Int. J. Infect. Dis. IJID Off. Publ. Int. Soc. Infect. Dis. 17, e862-867. https://doi.org/10.1016/j.ijid.2013.02.014

Wamani, H., Tylleskär, T., Astrøm, A.N., Tumwine, J.K., Peterson, S., 2004. Mothers' education but not fathers' education, household assets or land ownership is the best predictor of child health inequalities in rural Uganda. Int. J. Equity Health 3, 9. https://doi.org/10.1186/1475-9276-3-9

Wang, I.-C., Tsai, J.-D., Shen, T.-C., Lin, C.-L., Li, T.-C., Wei, C.-C., 2016. Allergic Conjunctivitis and the Associated Risk of Migraine among Children: A Nationwide Population-based Cohort Study. Ocul. Immunol. Inflamm. 0, 1–9. https://doi.org/10.1080/09273948.2016.1178303

Whitehead, N., Potterton, J., Coovadia, A., 2014. The neurodevelopment of HIV-infected infants on HAART compared to HIV-exposed but uninfected infants. AIDS Care 26, 497–504. https://doi.org/10.1080/09540121.2013.841828

WHO, 2011. World Report on Disability [WWW Document]. URL http://www.who.int/disabilities/ world_report/ 2011/report.pdf (accessed 11.04.17)

WHO, 2007. WHO Case definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-Related Disease in Adults and Children [WWW Document]. (accessed 11.12.17)

Wigdahl, B., Guyton, R.A., Sarin, P.S., 1987. Human immunodeficiency virus infection of the developing human nervous system. Virology 159, 440–445.

Wikipedia, Conlinp, 2018. Rahima Moosa Mother and Child Hospital [WWW Document]. Wikipedia Free Encylopedia. URL https://en.wikipedia.org/w/index.php?title=Rahima_Moosa_Mother_ and_Child_Hospital&oldid=820551133 (accessed 4.6.18).

Willen, E.J., 2006. Neurocognitive outcomes in pediatric HIV. Ment. Retard. Dev. Disabil. Res. Rev. 12, 223–228. https://doi.org/10.1002/mrdd.20112

Wium, A.M., Louw, B., 2013. Revisiting the roles and responsibilities of speech-language therapists in South African schools. S. Afr. J. Commun. Disord. 60, 31–37. https://doi.org/10.4102/sajcd.v60i1.8

Wolzak, N.K., Cooke, M.L., Orth, H., van Toorn, R., 2012. The Changing Profile of Pediatric Meningitis at a Referral Centre in Cape Town, South Africa. J. Trop. Pediatr. 58, 491–495. https://doi.org/10.1093/tropej/fms031

Xiao, P.-L., Zhou, Y.-B., Chen, Y., Yang, M.-X., Song, X.-X., Shi, Y., Jiang, Q.-W., 2015. Association between maternal HIV infection and low birth weight and prematurity: a meta-analysis of cohort studies. BMC Pregnancy Childbirth 15. https://doi.org/10.1186/s12884-015-0684-z

Yan, J., 2015. Epigenetics and Immunotherapy: New Perspective for Breaking Chronic Viral Infection. Immunother. Open Access 2. https://doi.org/10.4172/2471-9552.1000106

Zack, R.M., Golan, J., Aboud, S., Msamanga, G., Spiegelman, D., Fawzi, W., 2014. Risk Factors for Preterm Birth among HIV-Infected Tanzanian Women: A Prospective Study. Obstet. Gynecol. Int. 2014, 1–9. https://doi.org/10.1155/2014/261689

Zaman, S.S., Khan, N.Z., Islam, S., Banu, S., Dixit, S., Shrout, P., Durkin, M., 1990. Validity of the "Ten Questions" for screening serious childhood disability: results from urban Bangladesh. Int. J. Epidemiol. 19, 613–620.

Zar, H.J., 2004. Pneumonia in HIV-infected and HIV-uninfected children in developing countries: epidemiology, clinical features, and management. Curr. Opin. Pulm. Med. 10, 176.

8. APPENDICES

Appendix 1:

Table 8.1: Table of definitions

Term	Definition
Neurodevelopment	Growth and development of the neuronal networks and pathways (Boivin et al., 2015; Maes, 2016; Merrian-Webster, 2017).
Child Development	The simultaneous development of motor (gross and fine), sensory, speech, language, emotional, behaviour and cognitive processes (Boivin et al., 2015; Couper, 2016).
Developmental Delay	Below norm scores on developmental measurement tools and perceptions of the parent/caregiver that their child is not achieving milestones within universal and family norms
Disability	An umbrella term, covering impairments, activity limitations, and participation restrictions. An impairment is a problem in body function or structure; an activity limitation is a difficulty encountered by an individual in executing a task or action; while a participation restriction is a problem experienced by an individual in involvement in life situations (WHO, 2011). "Disability" is on a spectrum of mild to severe.
Habilitation	"Assisting of a child with achieving developmental skills when impairments have caused delaying or blocking of initial acquisition of the skills. Habilitation can include cognitive, social, fine motor, gross motor, or other skills that contribute to mobility, communication, and performance of activities of daily living and enhance quality of life." (O'Toole, 2003)
Rehabilitation	"The process of restoring a person's ability to live and work as normally as possible after a disabling injury or illness. It aims to help the patient achieve maximum possible physical and psychological fitness and regain the ability to be independent. It offers assistance with the learning or relearning of skills needed in everyday activities, with occupational training and guidance and with psychological readjustment." (O'Toole, 2003)

Appendix 2:

Table 8.2: Outcome measurement tools used in studies on children infected with HIV.

Measurement Tool	Study where tool is used
Aberrant Behaviour Checklist	R. Govender et al., 2011
Ages & Stages Questionnaire	Rice et al., 2013;
Bayley Infant Neurodevelopmental Screener	Kandawasvika et al; 2011
Bayley Scales of Infant Development I, II and III (BSID)	Gay et al., 1995; Foster et al., 2006; Drotar et al., 1997 and Petersen 1999 as cited in Abubakar et al., 2008; Van Rie et al., 2008; Baillieu and Potterton., 2008; Potterton et al., 2009; Alimenti et al.,2010; Shead et al., 2010; Hillburn et al., 2011; Kandawasvika et al., 2011; Hutchings and Potterton., 2013; Whitehead et al., 2014;
Beery-Butkenica Developmental Test of Visual-Motor Integration	Smith at al 2008
Bruininks-Oseretsky Test of Motor Proficiency (BOTMP)	Ruel et al., 2012
Buffalo-III Informal Voice Rating Scale	Makar et al., 2012;
Child Behaviour Checklist	Grover et al., 2007;
Child Depression Inventory	Sherr et al., 2017
Child Status Index Tool	Sherr et al., 2017
Clinical Evaluation of Language Functioning -IV edition	Rice et al., 2012
Clinical Neurological Examination	Foster et al., 2006; R.Govender et al., 2011; Samia et al., 2012;
Corsi Block Test	Walker et al., 2013;
Denver II Developmental Screening tool	Boivin et al., 1995 as cited in Abubakar et al., 2008; R.Govender et al., 2011;
Draw-a-Person test	Sherr et al., 2017
Early Childhood Screening Profiles	Ruel et al., 2012
Fagan test of infant development	Ruel et al., 2012
Frenchay Dysarthria Assessment	Makar et al., 2012;
Griffiths Scales of Mental Development	Angelini et al., 2000; Smith et al., 2008; Laughton et al., 2012; Lowick et al., 2012; Potterton et al., 2016
Gross Motor Function Classification System (GMFCS)	Foster et al., 2006;
Infant Gross Motor Screening Test	Hilburn et al., 2015
International Classification of Functioning, Disability & Health (ICF)	Myezwa et al., 2009;
Kauffman Assessment Battery for Children (K-ABC)	Boivin et al., (1995) as cited in Abubakar et al., 2008, Bagenda et al., 2006; Ruel et al., 2012
MacArthur-Bates Communicative Development Inventory - Local Adaptation	Rice et al., 2013; Alcock et al., 2016
McCarthy Scales of Children's Abilities	Kandawasvika et al., 2015
Molteno Scale	Samia et al., 2012
Movement-ABC-2	Benjamin et al., 2015
Neuropathy Symptom Score	Peters et al., 2014;

Peabody Developmental Motor scales	Jelsma et al., 2011; A. Van Rie et al., 2008
Pediatric Quality of Life Inventory	Devendra et al., 2013; Hrapcak et al., 2016; Sherr et al., 2017
Photo Articulation Test II	Makar et al., 2012;
Raven Progressive Coloured Matrices	Smith at al., 2008; Walker et al., 2013;
Raven's Standard Progressive Matrices	Boyede et al., 2013
Receptive-Expressive Emergent Language Scale	Makar et al., 2012;
Scale for Early Communication Skills	Makar et al., 2012;
Self-developed measures	Msellati et al., (1993) as cited in Abubakar et al., 2008; Walker et al., 2013; Benki-Nugent et al., 2014; Sherr et al., 2017
Snijders-Oomen Non-verbal Intelligence test for Children and Adolescents	Koekkoek et al., 2008;
Strengths and Difficulties Questionnaire	Sherr et al., 2017
Ten Question Screen for Disability	Devendra et al., 2013
Test of Everyday Attention for Children (TEACh)	Walker et al., 2013;
Test of the Reception of Grammar	Smith at al 2008
Test of Variables of Attention	Ruel et al., 2012
The Adaptive Behaviour Assessment System	Smith et al., 2012
The Harris-Goodenough-Draw-A-Person	Smith at al., 2008
Vineland Adaptive Behaviour Scales	Alimenti et al., 2010
Wechsler Intelligence Scale for Children (WISC) III & IV edition	Angelini et al., 2000; Martin et al., 2006; Smith et al., 2012; Walker et al., 2013; Crowell el al., 2015; Lazerus et al., 2015;
Wechsler Preschool and Primary Scale of Intelligence	Angelini et al., 2000; Lazarus et al., 2015

Appendix 3:

Human Research Ethics Committee Clearance Certificate

R14/49 Ms Shane Hodges

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160450

NAME: (Principal Investigator)	Ms Shane Hodges
DEPARTMENT:	Physiotherapy Rahima Moosa Mother and Child Hospital
PROJECT TITLE:	Prevalence of Disability in a Cohort of HIV-Infected Children Attending an Urban Paediatric HIV Clinic in Johannesburg, South Africa
DATE CONSIDERED:	06/05/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof Joanne Potterton
APPROVED BY:	Professor P. Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	22/06/2016

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004,10th floor, Senate House/2nd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. I/We fully understand the the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated,from the research protocol as approved, I/we undertake to resubmit to the Committee **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially review in April and will therefore be due in the month of April each year.

Principal Investigator Signature

Date 30/06/2016

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 4:

RMMCH and ESRU Permission letters for conducting this study at ESRU clinic

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

RAHIMA MOOSA MOTHER AND CHILD HOSPITAL

Enquiries : Dr Edward Hank
Tel : (011) 470 9030/1
Fax : (011) 477 4117
Email : Edward.Hank@gauteng.gov.za

Faculty of Health Sciences
University of the Witwatersrand

Dear Ms. Hodges

RE: PREVALANCE OF DISABILITY IN A COHORT OF HIV-INFECTED CHILDREN ATTENDING AN URBAN PAEDIATRICS HIV CLINIC IN JOHANNESBURG, SOUTH AFRICA

Permission is granted for you to conduct the research as indicated in the title above.

The terms under which this permission is granted is contained in the Researcher Declaration form that you have signed. Failure to comply with these conditions will result in the withdrawal of such permission.

It is crucial for you to inform the Research Coordinator, Karen Marshall of the actual start and end dates of your study. This could be done by e-mail.

Should the study commence more than 12 months after receipt of this approval letter you will have to go through the process of applying again.

You are strongly advised to keep a signed copy of the declaration form so as to ensure that the terms of this agreement are complied with at all times.

Yours sincerely,

DR EDWARD HANK
Clinical Manager
2016:06:13

ADDRESS: Cnr. FUEL & OUDSTHOORN STREET CORONATIONVILLE 2093 / PRIVATE BAG X20 NEWCLARE 2112 JHB

Shane Hodges <shanehodges55@yahoo.com>
Reply-To: Shane Hodges <shanehodges55@yahoo.com>
To: Shane Brassell <shanebrassell@gmail.com>

From: Lesley Rose <Lesley.Rose@wits.ac.za>
To: "shanehodges55@yahoo.com" <shanehodges55@yahoo.com>; "Karen.Marshall@wits.ac.za" <Karen.Marshall@wits.ac.za>; "Joanne.Potterton@wits.ac.za" <Joanne.Potterton@wits.ac.za>
Cc: "Renate.Strehlau@wits.ac.za" <Renate.Strehlau@wits.ac.za>; "karltechnau@gmail.com" <karltechnau@gmail.com>
Sent: Tuesday, May 24, 2016, 1:16:21 PM GMT+2
Subject: RE: Requested Documents for Permission to conduct dada collection

Good day Shane

Permission is granted from Empilweni Clinic for the research and access to records.

Karen will you check whether additional permission is required from the hospital please. If so will you please forward the details to Shane.

Thank you

Kind Regards

Lesley Rose

Assistant Manager

Empilweni Clinic

Rahima Moosa Mother and Child Unit

Tel: 011470 9424

Cell:0829340446

Email:Lesley.Rose@wits.ac.za

Appendix 5:

Information Sheet

Prevalence of Disability in a Cohort of HIV-Infected Children attending an urban paediatric HIV clinic in Johannesburg, South Africa

Dear Parent/Caregiver/ Guardian

My name is Shane Hodges. I am currently conducting my Masters research at Rahima Moosa Mother and Child Hospital. In this study, I would like to find out how many children living with HIV have any difficulties or disabilities and whether they are able to access rehabilitation services.

What is involved?

If you are willing, I would like to interview you about your child and your home. The first survey is a set of 10 questions, called the TQSD, with Yes/No answers followed by a questionnaire about your child's history and about your home. If any of the questions on the TQSD are answered with "Yes," an additional questionnaire will be added which askes about any difficulties your child may be experiencing. The questionnaires should take about 20minutes or less to fill in.

Participation is voluntary and participants will receive no compensation for their time.

Confidentiality

Information about you, your child and your family will be kept safe and confidential. All information obtained will be used for the study purposes only. No names will be put on any of the study sheets or results.

Participation & Withdrawal

You or your child has the right to decline participation in this study. You or your child may withdraw from this study at any time. Choosing not to participate or withdrawing will not affect the clinical care you receive at Rahima Moosa Hospital.

If you and your child are willing to participate in this study please sign the consent form provided. If your child is over 5 years old, he/she will also be required to sign an assent form.

Thank you for taking the time to read this.

If you have any further questions or worries, please ask me at any point during the interview.

Thank you,

Kind Regards

Shane Hodges (Physiotherapist)

Joanne Potterton (Supervisor)

Appendix 6:

Parental/Caregiver Consent Form

Research Title: Prevalence of Disability in a Cohort of HIV-Infected Children attending an urban paediatric HIV clinic in Johannesburg, South Africa

I _____(Name) have read the information sheet and understand the purpose of the study. All my questions have been answered regarding this study.

I give/ do not give (please circle your choice) consent to participate in an interview for this study. I am aware that I or my child may withdraw at any time without any consequences.

Child's folder number: _____

_____ _____

(Parent/ Guardian Signature) Date

_____ _____

Researcher Signature Date

Appendix 7:

Prevalence of Disability in a Cohort of HIV-Infected Children attending an urban paediatric HIV clinic in Johannesburg, South Africa

QUESTIONNAIRES

Date: _____/_____/2016

Child's Folder number:

Child's date of birth: Child's age:

Relationship of caregiver at the clinic to the child:

TEN QUESTION SCREEN FOR DISABILITY

	Screen	**Yes**	**No**
S1	Compared with other children, does or did your child have any serious delay in sitting, standing or walking?		
S2	Compared with other children, does or did your child have any difficulty seeing in the daytime or at night?		
S3	Does your child appear to have any difficulty hearing? (uses hearing aid, hears with difficulty or completely deaf)		
S4	When you tell your child to do something, does he/she seem to understand what you are saying?		
S5	Does your child have difficulty in walking or moving his/her arms or does he she have weakness or stiffness in the arms or legs?		
S6	Does the child sometimes have fits, become rigid or lose consciousness?		
S7	Does your child learn to do things like other children his/her age?		
S8	Does your child speak at all? (Can he/she make him or herself understood in words? Can they say any recognisable words?)		
S9	**For 3-9 years olds:** Is the child's speech in any way different from normal (not clear enough to be understood by people other than the immediate family?)		
S10	**For 2 year olds:** Can your child name at least one object (e.g. an animal, a toy, a cup, a spoon)		
S11	Compared with other children of the same age does your child appear in any way mentally backward, dull or slow?		

http://disabilitymeasures.org/tenquestions/(Belmont, 1984; Maenner et al., 2013; Stein et al., 1986)

Appendix 8:

GENERAL ADDITIONAL QUESTIONNAIRE

PRENATAL HISTORY:

Were you on ARVs during pregnancy? Yes / No

Were there any problems during pregnancy, such as illness, fainting, bleeding, anaemia or operations? If yes please describe:
_____
_____
_____
_____

DELIVERY & BIRTH:

Was the pregnancy full term? If not what was the child's gestation age:_____

Was the delivery normal? (Breech, Caesarean)_____

Were there any problems at birth? _____

SCHOOL:

Is your child at school? Yes / No

What class/grade are they in?_____

Have they passed every year? Yes / No

If no; how many years have they repeated? _____

CLINICAL FACTORS
(Information gathered from the child's clinical file & Road to Health Chart)

Age of diagnosis with HIV: _____

Does the child have a previous diagnosed clinical encephalopathy? Yes / No

What age was HAART started?_____

What was the CD4 count before implementation of HAART: _____
Growth parameters before treatment started:

- Weight
  - At Birth:_____
  - Growth percentile: _____

- Height
  - At Birth:_____
  - Growth percentile: _____

- Head circumference
  - At Birth:_____
  - Growth percentile: _____

How many times has the child been hospitalised? _____

What type of treatment adherence is followed?

☐ Good

☐ Poor/sporadic

☐ Failed

Opportunistic Infections/diseases experienced by the child.

☐ Meningitis

☐ Tuberculosis

☐ Toxoplasmosis

☐ Cytomegalovirus

☐ Otitis Media

☐ Other:_____

Have the doctors told you that your child has any other diagnosis/ problems apart from HIV?

☐ Cerebral Palsy

☐ Developmental delay

☐ Cognitive delay

☐ Peripheral Neuropathy

☐ Epilepsy

☐ ADHD

☐ Other:_____

Vision

Has the doctor ever told you to have your child's vision tested? Yes / No

Has your child's vision ever been tested? Yes / No

If yes;

When was it last tested?

☐ < 3months ago

☐ 3-6months ago

☐ 6-12 months ago

☐ >12 months ago

How easy is it to get your child's vision tested?

☐ Very easy

☐ Somewhat easy

☐ Difficult

☐ Very difficult

Why?_____
_____
_____

Hearing

Has the doctor ever told you to have your child's hearing tested? Yes / No

Has your child's hearing ever been tested? Yes / No

If yes;

When was it last tested?

☐ < 3months ago

☐ 3-6months ago

☐ 6-12 months ago

☐ >12 months ago

How easy is it to get your child's hearing tested?

☐ Very easy

☐ Somewhat easy

☐ Difficult

☐ Very difficult

Why?_____
_____
_____

Physiotherapy

Have the doctors ever told you to see a Physiotherapist?
Yes / No

Has your child ever been seen/assessed by a Physiotherapist?
Yes / No

If Yes;

What do you think Physiotherapy is? What has Physiotherapy done for your child?

_____
_____
_____

Does your child currently receive therapy?
Yes / No

If No; Why did you stop?

☐ Difficult to get to the therapist

- ☐ Transport
- ☐ Cost

☐ Discharged

☐ Forgot follow up date

☐ Not helping

☐ Other:_____

How often does your child see the Physio?

☐ 1x week

☐ 1x month

☐ Every 6 months

☐ 1x a year

Where do you receive therapy?

☐ At Home

☐ At the clinic

☐ At the hospital

☐ Other:_____

How easy is it to get to Physiotherapy?

☐ Very easy

☐ Somewhat easy

☐ Difficult

☐ Very difficult

How long does it take you to take your child to therapy and come back? _____

Do you think the Physiotherapy is helping your child?

☐ Yes

☐ No

☐ I don't know

What do you think would make it easier for you to see the Physiotherapist?

☐ Physiotherapist closer to my home

☐ Transport available

☐ SMS reminder of appointment date

☐ Speaking the same language at the therapist

☐ Other:_____

Occupational Therapy

Have the doctors ever told you to see an Occupational Therapist?
Yes / No

Has your child ever been seen/assessed by an Occupational Therapist?
Yes / No

If Yes;

What do you think Occupational Therapy is? What has Occupational therapy done for your child? _____
_____
_____

Does your child currently receive therapy?
Yes / No

If No; why did you stop?

☐ Difficult to get to the therapist

☐ Discharged

☐ Forgot follow up date

☐ Not helping

☐ Other:_____

How often does your child see the OT?

- 1x week
- 1x month
- Every 6 months
- 1x a year

Where do you receive therapy?

- At Home
- At the clinic
- At the hospital
- Other:_____

How easy is it to get to Occupational therapy?

- Very easy
- Somewhat easy
- Difficult
- Very difficult

How long does it take you to take your child to therapy and come back? _____

Do you think the Occupational therapy is helping your child?

- Yes
- No
- I don't know

What do you think would make it easier for you to see the Occupational Therapist?

☐ I don't know

☐ Therapist closer to my home

☐ Transport available

☐ SMS reminder of appointment date

☐ Speaking the same language at the therapist

☐ Other:_____

Speech Therapy

Have the doctors ever told you to see a Speech Therapist? Yes / No

Has your child ever been seen/assessed by a Speech Therapist? Yes / No

If Yes;

What do you think Speech Therapy is? What has Speech Therapy done for your child? _____
_____
_____

Does your child currently receive therapy?
Yes / No

If No; why did you stop?

☐ Difficult to get to the therapist

☐ Discharged

☐ Forgot follow up date

☐ Not helping

☐ Other:_____

How often does your child see the ST?

☐ 1x week

☐ 1x month

☐ Every 6 months

☐ 1x a year

Where do you receive therapy?

☐ At Home

☐ At the clinic

☐ At the hospital

☐ Other:_____

How easy is it to get to ST?

☐ Very easy

☐ Somewhat easy

☐ Difficult

☐ Very difficult

How long does it take you to take your child to therapy and come back? _____

Do you think Speech Therapy is helping your child?

☐ Yes

☐ No
☐ I don't know

What do you think would make it easier for you to see the Occupational Therapist?
☐ I don't know
☐ Therapist closer to my home
☐ Transport available
☐ SMS reminder of appointment date
☐ Speaking the same language at the therapist
☐ Other:_____

Medication

Is your child on any medication other than ARV?
☐ Yes
☐ No
☐ I don't know

If Yes;

Where do you get the medication?
☐ At a local pharmacy
☐ At the clinic
☐ At the hospital
☐ Other:_____

How easy is it to get the medication?
☐ Very easy
☐ Somewhat easy
☐ Difficult
☐ Very difficult

How long does it take you to fetch the medication? _____

Other
Have you as the parent/carer ever been offered any counselling services because of your child's difficulty? Yes / No

Are there any other services you have used in the past?
☐ Dentist
☐ Psychologist
☐ Counsellor
☐ Traditional healer/Sangoma
☐ Other;_____

Are there any services that you would like to be made available to you and/or your child?

☐ Dentist
☐ Psychologist
☐ Counsellor
☐ Play Therapist
☐ Traditional healer/Sangoma
☐ Other;_____
_____

If Yes to S1 &/or S5: Gross/Fine Motor skills

Please describe your child's difficulty:

_____
_____
_____

GMFCS level (if applicable): Level 1, 2, 3, 4, 5

Does your child need anything to help them move?

☐ Crutches
☐ Walking frame
☐ Wheelchair/pram
☐ Splints

If Yes to S2: Vision

Please describe your child's difficulty:

☐ Visually Impaired
☐ Blind
☐ Eye movement difficulties (e.g. strabismus)

_____
_____

Has your child been told to wear glasses? Yes / No

If yes, does your child wear glasses? Yes / No

If No; Why not? _____
_____

If Yes to S3, S4, S8 and/or S9/S10: Hearing, Speech and Language

Please describe your child's delay or difficulty:

Hearing:

☐ Child is completely deaf
☐ Child wears a hearing aid
☐ Child can hear with difficulty

☐ The child can hear but he doesn't understand what I am saying

☐ Other:_____

Speech & Language

☐ Child cannot speak

☐ Child cannot speak but uses some sounds and hand movements to communicate.

☐ The child speaks but I don't understand what he/she is saying

☐ The child speaks but only the family can understand him/her. Other people find it difficult to understand them.

☐ Child can speak a little bit

☐ Child speaks, but not as good as his peers.

☐ Other:_____

<u>If Yes to S6: Epilepsy</u>

"Does your child sometimes have fits, becomes rigid or lose consciousness?"

How often does this happen

☐ >1x a day

☐ 1x a day

☐ 1x week

☐ 1x month

☐ 1x a year

Is your child on medication for these episodes? Yes / No

If Yes

Do you feel the medication helps? Yes / No

<u>If Yes to S4, S7 and/or S11: Cognitive ability</u>

Please describe your child's delay or difficulty:

_____

_____

Appendix 9:

Socioeconomic Questionnaire

Child's Folder number: _____

Where is the household located? _____

1. Family Structure/ Household Composition

1a Mother's Marital Status

1. Never married, not currently living with partner
2. Married, but not living with partner now
3. Divorced
4. Widowed
5. Never married but currently living with partner
6. Married and currently living with partner

1b Household Membership. How many people currently reside in the household?
Number: _____

1c What is their relationship to the child? How old are they?

	Relationship	Age	>18y	6-18y	<6y
1.					
2.					
3.					
4.					
5.					
6.					
7.					
8.					
9.					
10.					

2. Social Status

2a. Mother's education: What is the highest level of education attained by the mother

1. Less than Grade 5
2. Primary School: Grade 5-6
3. Junior school: Grade 7-9
4. Senior School: Grade 9-11
5. Matric/Vocational training diploma
6. 1-2yr College/Technikon
6. 3-4years University

8. Ph.D., M.D., any other doctoral degree

2b Mother's partners education: What is the highest level of education attained by the mother's partner?

1. Less than Grade 5
2. Primary School: Grade 5-6
3. Junior school: Grade 7-9
4. Senior School: Grade 9-11
5. Matric/Vocational training diploma
6. 1-2yr College/Technikon
7. 3-4years University
8. Ph.D., M.D., any other doctoral degree

2c What are the occupation and industry of the primary wage earners and their relationship to the child? *Use the numbers from Q: 1c.

No.	Occupation	Industry

3 Housing/Accommodation

3a In what type of housing do you live?

0. None: Homeless
1. Shack
2. Hostel
3. Room/Garage/Wendy house
4. Flat, cottage
5. Home shared with other family (ies)
6. Home that is not shared with other families

3b In your home how many separate rooms are there just for sleeping? (1, 2, 3, 4, >4) _____

3c Do you have running water inside your home? 0. No 1. Yes

3d Do you have electricity in your home? 0. No 1. Yes

3e Do you or your immediate family own or rent your home?

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

3f Does your household have a;

		Yes	No	>1?
1.	Car			
2.	Motorbike			
3.	Bicycle			
4.	Television			
5.	Refrigerator			
6.	Cell phone			
7.	Computer/Laptop			
8.	Tablet (iPad, Samsung etc.)			
9.	Electric oven			
10.	Microwave oven			
11.	Washing Machine			
12.	DVD machine			
13.	DSTV			
14.	Internet			
15.	Radio			
16.	CD Player			
17.	Heaters			
18.	Fan			
19.	Generator			
20.	camera			

4 Approximately how much does the household earn on a monthly basis?

R_____

Appendix 10

Table 8.3: Summary of results for associated factors to disability in HIV children

Variable	Total	With Disability	Without Disability	P-Value
Individual Factors				
Total N	**200**	**101**	**99**	
AGE (Months)	Range: 24-107			
Mean	76.78	79.87	73.63	0.071
Sex (male), n (%)	101 (50.5)	54 (53.5)	47 (46.5)	0.480
Anthropometric Data				
WAZ Z-score				
Total N	**194**	**100**	**94**	
Mean	-1.16	-0.78	-0.42	0.014
WAZ Z-score <-2	20 (10.3)	12 (12)	8 (8.5)	
HAZ Z-score				
Total N	**196**	**100**	**96**	
Mean	-1.66	-0.88	-0.60	0.064
HAZ Z-score <-2	24 (13.8)	17 (17)	7 (7.3)	
BAZ Z-score				
Total N	**193**	**100**	**93**	
Mean	-0.05	-0.37	-0.08	0.058
BAZ Z-Score <-2, n (%)	9 (4.7)	5 (5)	4 (4.3)	
Birth Factors				
Mode of Delivery, n (%)				
Total N	**197**	**99**	**98**	
Normal	152 (77.2)	70 (70.7)	82 (83.7)	0.292
C-Section	45 (22.8)	29 (29.3)	16 (16.3)	
Prematurity, n (%)				
Total N	**195**	**99**	**96**	
>37 weeks	172 (88.2)	83 (83.8)	89 (92.7)	0.075
<37 weeks	23 (11.9)	16 (16.2)	7 (7.3)	
Birth Weight				
Total N	**136**	**64**	**72**	
Mean (kg)	3,03	2.92	3.12	0.051
Distribution of Birth weight, n (%)				
ELBW	1 (0.7)	1 (1.6)	0 (0)	
VLBW	2 (1.4)	0 (0)	2 (2.8)	
LBW	18 (13.2)	13 (20.3)	5 (6.9)	
Typical BW	115 (84.6)	50 (78.1)	65 (90.3)	
Clinical Factors				
No. Of Admissions, n (%)				
Total N	**154**	**78**	**76**	
Never	44 (28.6)	17 (21.8)	27(35.5)	0.368
Once	75 (48.7)	40 (51.3)	35 (46.1)	
> Once	35 (17.5)	21 (26.9)	14 (18.4)	

Variable	Total	With Disability	Without Disability	P-Value
Pre-Treatment Blood Count Data				
CD4 Count				
Total N	**156**	**76**	**80**	
Mean CD4 Count 10*6/1 cells/mm3	1064.83 SD: 814.44	975.66 SD: 840.02 Std. Err. Mean: 96.36	1149.54 SD: 785.24 Std. Err. Mean: 87.79	0.183
CD4 %				
Total N	**150**	**76**	**74**	
Mean CD4%	21.44 SD: 11.25	19.15 SD: 10.96 Std. Err. Mean: 1.27	23.43 SD: 11.47 Std. err. Mean: 1.33	0.021
CD4% Thresholds, n (%)				
<15%	48 (32.2%)	31 (40.8)	17 (23)	
15-25%	66 (44.3)	33 (43.4)	33 (44.6)	
>25%	36 (24.2)	12 (15.8)	24 (32.4)	
Viral Load, cells/mL				
Total N	**144**	**68**	**76**	
Mean Viral Load, cells/mL	10187879 SD: 70489049	19130134 SD:100669931	1961005 SD: 2955962	0.689
Viral Load Thresholds, n (%)				
<50	0	0	0	
50 - 1000	3 (2.1)	1 (1.5)	2 (2.6)	
1000 - 10 000	8 (5.6)	1 (1.5)	7 (9.2)	
10 000 - 50 000	11 (7.6)	3 (4.4)	8 (10.5)	
>50 000	122 (84.7)	63 (92.6)	59 (77.6)	
Treatment Factors				
Age of starting cART (Months)				
Total N	**189**	**93**	**96**	
Mean	20.27	20.53	18.47	0.578
Duration on cART (Months)				
Total N	**183**	**94**	**89**	
Mean	57.2	58.4	56	0.556
Treatment Defaulting, n (%)				
Total N	**139**	**73**	**66**	
Ever defaulted treatment	51 (36.7)	28 (38.4)	23 (34.8)	0.726
Maternal ART, n (%)				
Total N	**188**	**95**	**93**	
Maternal ART, n (%)	52 (27.7)	22 (23.2)	30 (32.3)	0.193

Variable	Total	With Disability	Without Disability	P-Value
Opportunistic Infections, n (%)				
Total N	**200**	**101**	**99**	
1 or more Infection	149 (74.5)	85 (84.2)	64 (64.4)	0.007
AGE	27 (14.5)	16 (15.8)	11 (11.1)	0.409
CMV	7 (3.5)	3 (3)	4 (4)	Too small
Conjunctivitis	34 (17)	17 (16.8)	17 (17.2)	0.949
LRTI	49 (24.5)	31 (30.7)	18 (18.2)	0.049
Meningitis	7 (3.5)	5 (5)	2 (2)	Too small
Otitis Media	38 (19)	20 (19.8)	18 (18.2)	0.858
Oral Thrush	29 (14.5)	18 (17.8)	11 (11.1)	0.229
Skin infection	107 (53.5)	60 (59.4)	57 (57.6)	0.886
TB	74 (37)	49 (48.5)	25 (25.3)	0.003
URTI	48 (24)	25 (24.8)	23 (23.2)	0.063
SES Factors				
Household Income				
Total N	**196**	**99**	**97**	
Mean Monthly Household Income (Rands)	5235 SD: 5813 SE: 436	4653 SD: 4829 SE: 725	6337 SD: 7110 SE: 485	0.127
Mean Rands/person/month	1342.17 SD: 1513.02	1205.31 SD: 1402.15	1486.34 SD: 1613.29	0.194
Rand/person/month thresholds, n (%)				
< R531 (FPL)	60 (30.6)	33 (33.3)	27 (27.8)	
R532- R758 (LBPL)	32 (16.3)	17 (17.2)	15 (15.5)	
R759 - R1138 (UBPL)	26 (13.3)	15 (15.2)	11 (11.3)	
R1139 – R2000	46 (23.5)	19 (19.2)	27 (27.9)	
R2001 – R5000	24 (12.2)	12 (12.1)	12 (12.4)	
>R5001	8 (4.1)	3 (3)	5 (5.2)	
> R5000	8 (4.1)	3 (3)	5 (5.2)	
Orphan Status, n (%)				
Total N	**191**	**94**	**97**	
No. of orphans	33 (17.3)	18 (19.1)	15 (15.5)	0.568
Main Caregiver Education, n (%)				
Total N	**195**	**100**	**95**	
No School	6 (3.1)	3 (3)	3 (3.2)	0.226
< Grade 7	10 (5.1)	6 (6)	4 (4.2)	
Grade 7-9	42 (21.5)	27 (27)	15 (15.8)	
Grade 10-11	57 (29.2)	28 (28)	29 (30.5)	
Matric/Vocational training	47 (24.1)	22 (22)	25 (26.3)	
1-2y college/technikon	29 (14.9)	13 (13)	16 (16.8)	
>3y University	4 (2.1)	1 (1)	3 (3.2)	

Appendix 11:

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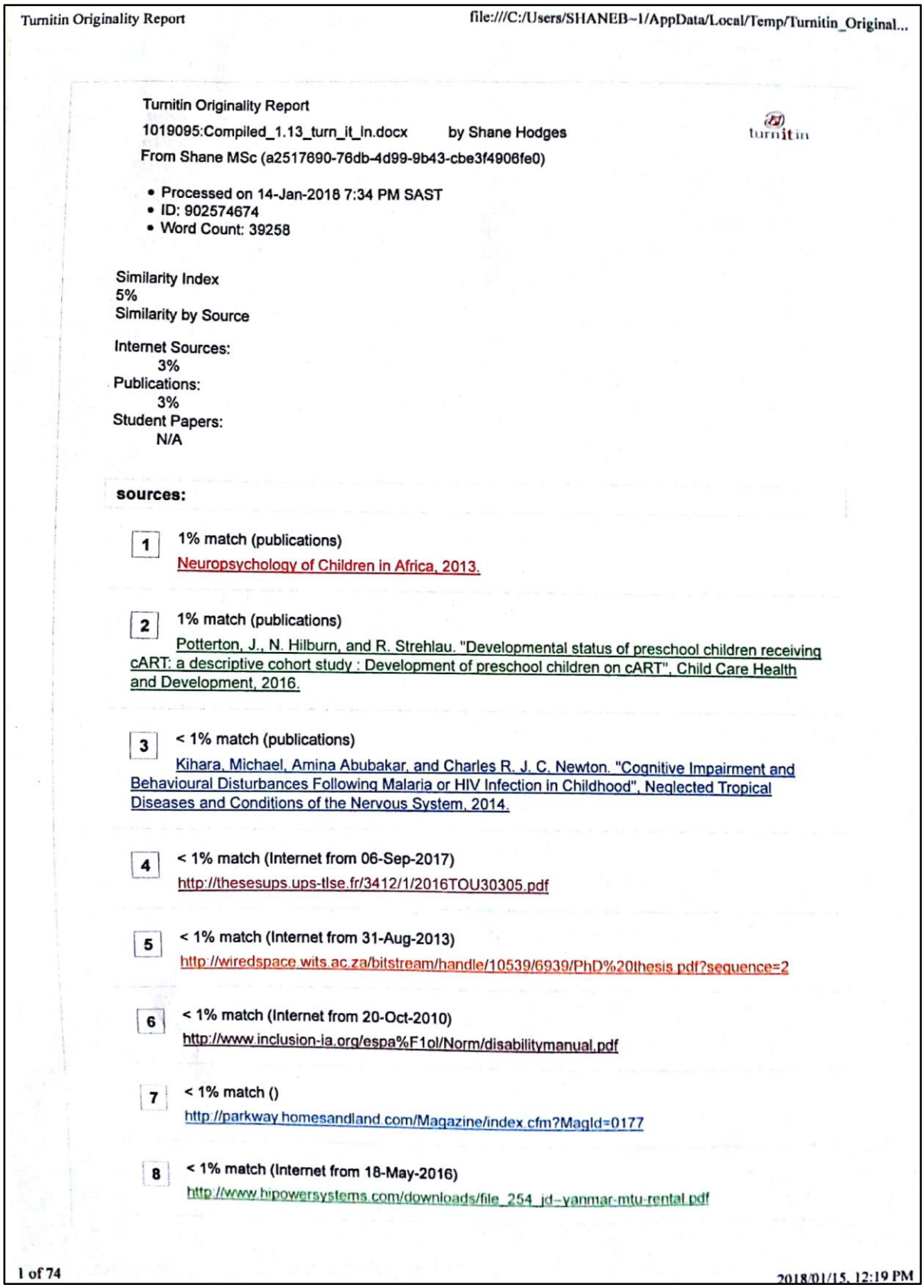

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