THE EXTENSION OF THE INFANT GROSS MOTOR SCREENING TEST TO INCLUDE INFANTS FROM BIRTH TO FIVE MONTHS IN INFANTS WITH HIV

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DECLARATION

I, Kirsty Mae Otten, declare that this Research Report is my own, unaided work. It is being submitted for the Degree of Master of Science in Physiotherapy at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any University.

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22nd day of May 2018 in Johannesburg

ABSTRACT

The aim of this study was to extend the age range of the Infant Gross Motor Screening Test (IGMST) to make it appropriate for use in infants infected with HIV from birth to five months.

Previously completed Bayley Scales on Infant and Toddler Development (3rd Version) (BSID III) assessments, from two 2013 physiotherapy masters studies completed through the University of the Witwatersrand, were used to compile neurodevelopmental scores achieved by infants infected with HIV. These scores were used to select developmentally appropriate items for inclusion in the new section of the IGMST. These items were statistically tested against the original BSID III scores using the Pearson correlation coefficient. Following statistical testing, content validity of the new section of the IGMST was established with an expert panel using a modified nominal group technique (NGT).

The new section of the IGMST included two age bands; one to three months and four to five months. Each age band consisted of five items. Age band one to three months had a Pearson correlation coefficient of r =0.68 (p = 0.003) and 84% of the infants performed the same on both tests. Age band four to five achieved a Pearson correlation coefficient r = 0.71 (p = 0.0009) and 83% of infants performed the same on both tests. When presented to the expert panel using a modified NGT, all items

and questions raised were accepted by 100% after appropriate adjustments were made.

In conclusion, the new section of the IGMST has been developed for infants from one to five months and the content validity has been established during the course of this study. The new section must still undergo further validity and reliability testing before it can be used clinically.

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LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
AIMS	Alberta Infant Motor Scale
ART	Antiretroviral therapy
ARV	Antiretroviral
BINS	Bayley Infant Neurodevelopmental Screener
BSID II	Bayley Scales of Infant Development (2nd version)
BSID III	Bayley Scales of Infant Development (3rd version)
cART	Combination antiretroviral therapy
CHER	Children with early antiretroviral therapy
CNS	Central nervous system
DNA	Deoxyribonucleic acid
ELISA	Enzyme-linked Immunosorbent assay
GM	General movement
GMFCS	Gross Motor Function Classification System
GSMD	Griffiths Scale of Mental Development
HINT	Harris Infant Motor Scale
HIV	Human Immunodeficiency Virus
HIVE	Human Immunodeficiency Encephalopathy
IGMST	Infant Gross Motor Screening Test
NPV	Negative predictive value
NVP	Nevirapine
PCR	Polymerase chain reaction
PEDS	Parents' Evaluation of Developmental Status
PHE	Progressive HIV-1 encephalopathy
PMTCT	Prevention of mother to child transmission
PPV	Positive predictive value
RCWMST	Red Cross War Memorial Screening Tool
RTHB	Road to Health Booklet
UNAIDS	Joint United Nations Programme on HIV and AIDS
WHO	World Health Organisation

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CHAPTER ONE

1 INTRODUCTION

1.1 Introduction

Sub-Saharan Africa still faces challenges with the management of the Human Immunodeficiency Virus (HIV) epidemic despite the improved availability of antiretrovirals (ARVs). HIV has infected 36.7million people worldwide with Sub-Saharan Africa having 19.4million of those living with HIV. Women account for more than half of this number (59%) (UNAIDS, 2017). The higher percentage of women infected translates to a high number of children infected with HIV. Despite a decline in the number of infections due increased access to ARVs there were still an estimated 12000 new infections among children in South Africa in 2016 (UNAIDSa, 2017), as well as 160 000 new infections amoungst children world wide (UNAIDSb, 2017).

The infection of infants is directly linked to infection among women (UNAIDS, 2016). Mother to child transmission (vertical transmission) can occur perinatally or in the neonatal period through various pathways. The rate of HIV transmission from mother to child has been dramatically decreased since the roll out of ARVs. South Africa has achieved a 90% reduction in vertical infections (UNAIDS, 2016) and transmission rates in Gauteng are now estimated to be around 1.7% (Gauteng Department of Health, 2016/2017; Sherman et al, 2017). One factor influencing transmission of HIV is a high maternal viral load (Abubakar et al, 2008). Infants infected with HIV are

more likely to have neurodevelopmental delay and gross motor difficulties which can persist into childhood (Foster et al, 2006).

The central nervous system (CNS) may be impacted by HIV, especially when children are infected perinatally (Belman, 1992). The involvement of the CNS in HIV is common and there is a spectrum of presentations. Neurodevelopmental delay is common in infants infected with HIV (Donald et al, 2014). It has been found that a high percentage of infants with HIV exhibit global neurodevelopmental delay (Whitehead et al, 2014; Hutchings & Potterton, 2013; Potterton et al, 2009; Ballieu & Potterton, 2008; Van Rie et al, 2007). Neurodevelopmental delay is one of the first indicators of the disease and may occur before any other signs (Hilburn et al, 2011). Numerous studies have found the gross motor aspect of neurodevelopmental delay to be the most affected in young infants infected with HIV (Hilburn et al, 2011; Shead et al, 2010; Potterton et al, 2009). It has also been found that the percentage of those found to have neurodevelopmental delay increases as they age (Whitehead et al, 2014). The introduction of combination antiretroviral therapy (cART) has been found to reduce the progression of neurodevelopmental delay, but not improve the delay that was present prior to the initiation of the medication (Whitehead et al, 2014).

Gross motor delay is not only noted in infants infected with HIV. It has also been suggested that motor delays may be the first (or most easily identified) indication of a global developmental delay. As infants develop, it is expected that they acquire a

variety of motor skills early on. Those at risk for global delay may struggle to reach early motor milestones (Noritz et al, 2013).

It has been shown that early therapeutic intervention, for infants infected with HIV presenting with neurodevelopmental delay, is effective in improving their cognitive and motor development (Potterton et al, 2010). It is important to identify delay and begin treatment as early as possible, to improve a child's developmental progress and allow for a better quality of life. Numerous studies have recommended that screening and physiotherapy intervention take place in order to improve developmental outcomes (Whitehead et al, 2014; Hilburn et al, 2010; Potterton et al, 2010).

Developmental screening is used to quickly identify those that may be presenting with neurodevelopmental delay and would benefit from a more in-depth assessment (Meisels & Provence, 1988). Sub-Saharan Africa has numerous constraints that prevent in-depth assessment of each at risk individual. Once screened and identified as being at risk, infants can be referred for further assessment and, if needed, for therapeutic intervention. Hilburn et al. (2011) found that at the time of the study there was no readily available, appropriate screening tool available to use for the screening of infants infected with HIV. As gross motor skills are most often impacted by HIV infection (Hilburn et al, 2011; Shead et al, 2010; Potterton et al, 2009) it was decided a gross motor screening tool would be appropriate. The Infant Gross Motor

Screening Test (IGMST) for ages six months to eighteen months was developed and underwent preliminary validity and reliability testing (Hilburn et al, 2011). The original IGMST consists of four age bands, with five gross motor items in each. A child can be identified as 'At Risk' or 'Satisfactory' depending on the score they achieve. It is easily and freely available and simple to administer (Hilburn et al, 2011).

1.2 Problem Statement

In the South African context, there is no appropriate screening tool to detect developmental delay in infants infected with HIV from birth to five months.

1.3 Research Question

What developmentally appropriate items can be selected and included in the Infant Gross Motor Screening Test (IGMST) to make it appropriate for use in infants with HIV from birth to five months?

1.4 Aim of the Study

The aim of this study is to determine which developmentally appropriate items can be selected and included in the IGMST to make it appropriate for use in infants infected with HIV from birth to five months.

1.5 Objectives of the Study

- To identify gross motor items from the Bayley Scales of Infant and Toddler (3rd version) (BSID III) which would be suitable for inclusion in the IGMST to extend it for use in younger infants (birth to five months).
- To categorise items into age group suitability (birth to three months); (four to five months).
- Testing and refinement of the initial version of the new items to satisfy statistical criteria (Pearson's correlation coefficient r ≥0.7).
- To complete preliminary content validity.
- To design and layout the new age bands in keeping with the format of the original IGMST.

1.6 Significance of the Study

HIV infection is still a challenge in Sub-Saharan Africa (UNAIDS, 2016). Infants infected with HIV have a high incidence of neurodevelopmental delay (Potterton et al, 2009; Baillieu & Potterton, 2008). Early physiotherapy intervention has been shown to improve the developmental outcomes of these individuals (Potterton et al, 2010). Prior to the development of the IGMST there was no appropriate developmental screening tool to determine if infants infected with HIV displayed gross motor delay. This tool is currently appropriate for use on infants from six months to 18 months (Hilburn et al, 2011). HIV infection is now identified at an earlier age via Polymerase Chain Reaction (PCR) testing and it is known which infants are at an increased risk

for developmental delay. Having a screening tool that can screen for delay in younger infants will allow further intervention to occur as early as possible and improve the child's developmental outcomes and quality of life.

CHAPTER 2

2 LITERATURE REVIEW

2.1 Introduction

This chapter will discuss the epidemiology of HIV, the entry of HIV into the CNS, the pathology of Human Immunodeficiency Virus Encephalopathy (HIVE) in the paediatric population and the link between paediatric HIV and neurodevelopment. An overview of developmental screening will be discussed, as well as the process used to develop the original IGMST.

Articles discussed in this literature review were found using Science Direct, CINAHL EBSCO Host and Google Scholar search engines. Articles were also physically sourced from the Health Sciences library at the University of the Witwatersrand. Keywords in the literature search included HIV, HIV encephalopathy, neurodevelopment, CNS development, developmental surveillance and screening and Infant Gross Motor Screening Test. Only articles written in English were included in this review. There was no limit on the year of publication.

2.2 Epidemiology of the HIV/AIDS Pandemic

Globally 36.7 million people are infected with HIV. Seventeen point eight million of those are women and 2.1 million of those are children. In 2010 it was estimated that 6.1 million people in South Africa were living with HIV, it has now risen to 7.1 million. Girls and women are a particularly vulnerable group and in South Africa, women account for 59% of the HIV infected population. It is estimated that there are 257 456

pregnant women who are infected with HIV, and it is estimated that >95% (76% - >95%) of those have access to prophylaxis or treatment to prevent Mother-to-Child transmission (MTCT) (UNAIDS, 2016). In 2016 it was estimated that in South Africa there were 12 000 children between the age of 0-14 that were newly infected with HIV. The coverage for access to ARVs is 55%. (UNAIDS, 2017a; UNAIDS, 2017b).

2.3 Vertical Transmission of HIV

HIV infection in children is mainly as a result of mother to child transmission (MTCT) or vertical transmission. The infection of infants is directly linked to infection among women (UNAIDS, 2016). Vertical transmission can occur perinatally, at the time of delivery and through breast feeding, especially in mothers with a high viral load (Hilburn et al, 2010; Abubakar et al, 2008). The rate of HIV transmission from mother to child has been dramatically decreased since the roll out of ARVs. National transmission rates are estimated at 1.5% (National Department of Health 2014/2015), while transmission rates in Gauteng are estimated to be at 1.7% (Gauteng Department of Health, 2016/2017). As the access to testing and treatment with cART is increasing there is a decrease in the number of HIV infected infants, this shows that Prevention of Mother-to-Child Transmission (PMTCT) is working (Sherman & Lilian, 2011).

Infants infected with HIV via vertical transmission are more likely to have neurodevelopmental delay and gross motor difficulties that can persist into childhood

(Abubakar et al, 2008; Meyers et al, 2007; Foster et al, 2006). When compared to infants infected at a later stage, they are more likely to experience neurodevelopmental delay (Willen, 2006). Neurodevelopmental delay is due to the invasion of the CNS by HIV. This occurs early on in the infection. These infants have altered development of the brain (Boisse et al, 2008; Boivin et al, 1995). This will be discussed further in 2.7.

2.4 Infants and Children: A Priority Population

The South African Department of Health has identified infants and children as a priority population. The National HIV Testing Services policy states that infants should be diagnosed early for all HIV-exposed infants as well as any that are presenting with conditions that may be as a result of HIV infection (Department of Health, South Africa, 2016). The HIV-related mortality rate is high if the infection is left untreated. More than half of HIV infected infants will die in the first two years without appropriate ART treatment (Marinda et al, 2007). Effective PMTCT programs reduce the number of HIV infections in infants exposed to HIV (Sherman et al, 2017; Chukwuemneka et al, 2014). Early Antiretroviral Therapy (ART) has been shown to reduce the risk of death by 75% when compared to deferred ART, and can reduce mortality and progression (Cotton et al, 2013; Welch et al, 2009; Violari et al, 2008). In June 2015 routine birth testing for all HIV exposed infants was included in the South African national guidelines (National Department of Health, 2015).

2.5 HIV Testing

HIV PCR testing at birth for all HIV-exposed infants has been included in the South African National Guidelines since June 2015. (National Department of Health, 2015; Sherman, 2015). Efficient HIV testing is vital to reducing infant morbidity and mortality (Mazanderani et al, 2016).

2.5.1 Enzyme-linked immunosorbent assay (ELISA)

In 1985 the first assay tests developed for HIV were designed to screen blood products rather than diagnosing HIV. First generation HIV testing could only detect Immunoglobin G (IgG) antibodies six to twelve weeks after infection had occurred and were not always accurate and a second test was needed. A false positive could be detected if the patient was pregnant, had an auto-immune disease or infections. By the fifth-generation assay tests for HIV, antigen and antibodies results and infection can be detected two weeks post-exposure (Alexander, 2016). Maternal antibodies circulate in an infant's body for up to 15 months after birth and the recommendation is that ELISA is not done in children younger than 18 months (Fearon, 2005). The ELISA would identify maternal antibodies rather than the infants own antibodies up to 15 months (Fearon, 2005). This makes it ineffective in correctly identifying HIV infection in infants.

2.5.2 Polymerase chain reaction (PCR)

PCR testing for HIV amplifies viral nucleic acid so that it may be detected in the patient's sample. It is a very sensitive test and can pick up a small amount of viral

particles. It is the test of choice for infants as it detects viral particles rather than the maternal antibodies that can circulate in an infant's body up to the age of 15 months (Alexander, 2016; WHO, 2007; Fearon, 2005). PCR testing is considered the gold standard of testing for HIV in infants (Mazanderani et al, 2015).

PCR testing in South Africa was introduced in 2004 in infants from six weeks of age (Meyers et al, 2007). The test, done at six weeks, was done in conjunction with the scheduled vaccinations. Testing at six weeks was, however, too late to detect *in utero* and intrapartum HIV infections and did not support the PMTCT program. It did not detect HIV infections that caused infants to die before the age of six weeks, and was too early to detect HIV infections that were supressed by NVP (Nevirapine) or maternal prophylaxis that crossed the placenta or in breastmilk. The PCR test done at six weeks had decreased sensitivity due to the neonates increased duration of exposure to preventative drugs (Sherman, 2015).

PCR testing is now done on HIV exposed infants at birth, and then follow-up testing is done at ten weeks of age as well as six weeks after stopping breastfeeding if the child is under 18 months (Sherman, 2015; Department of Health, South Africa, 2016). Lilian et al. (2013) demonstrated that 76% of all early HIV infections were detectable at birth, and because of this PCR testing at birth is an appropriate way of detecting infection early and initiating early ART. This will reduce the early morbidity and mortality of infants infected with HIV.

2.6 Central Nervous System Involvement in HIV

2.6.1 Entry of HIV into the CNS

The CNS is commonly affected by HIV and there is a diverse spectrum of presentations (Boisse et al, 2008). Children infected perinatally are especially at risk for CNS involvement (Belman, 1992).

Invasion of the CNS (brain and cerebrospinal fluid) occurs early after infection when the virus crosses the blood brain barrier (Puthanakit et al, 2013; Nozyce et al, 2006; Blumberg et al, 1994; Sharer, 1992). A study has shown HIV infection present in the CNS as early as eight days after infection (Valcour et al, 2012). HIV infects CD4+ T lymphocytes and macrophages. It is these macrophages that are involved in the changes that damage the CNS (Zayyad & Spudich, 2015; Ellis et al, 2009; An et al, 1999; Blumberg et al, 1994; Johnson, 1993).

There are two pathways that cause neuronal damage in HIV. Large numbers of astrocytes are actively or latently infected with HIV-1. This leads to neuronal dysfunction through loss of supporting growth factors, excitotoxicity due to dysregulation of neurotransmitter reuptake and loosening of the blood-brain barrier, which allows further infection of the CNS with HIV-1. In addition, macrophages infected with HIV-1 begin an inflammatory process. Macrophages and astrocytes interact, producing neurotoxic cytokines, viral proteins and nitric oxide. These two factors combined can result in widespread tissue disease and severe neurological

impairments (Gannon et al, 2011; Boisse et al, 2008; Blumberg et al, 1994; Gendelman et al, 1994).

2.6.2 CNS changes and HIV Encephalopathy

The most common clinical feature of HIV-related CNS disease is HIVE. HIVE is defined as the disease, damage or malfunction of the brain caused by HIV-1 (Donald et al, 2015). It is the failure to achieve, or the loss of previously achieved cognitive and motor milestones (Hilburn et al, 2010). HIVE is an AIDS-defining illness (Patel et al, 2009).

As HIV invades the central nervous system, there is an increased risk of brain damage. This presents as intracerebral calcifications and microcephaly, as well as global neurodevelopmental delay (Walker et al, 2013; Hilburn et al, 2010).
HIV affects the motor centres of the brain early on in the infection, causing tremor, ataxia and spasticity (Boisse et al, 2008; Boivin et al, 1995). HIV can cause damage to the CNS in two ways: disease can be primarily caused by HIV (HIVE) and secondarily there can be CNS disease caused by opportunistic infections (such as meningitis) (Ellis et al, 2009). The use of ART decreased the number of opportunistic diseases of the CNS, and the most commonly seen dysfunction in the CNS has changed to primary HIV disease (Ellis et al, 2009; Boisse et al, 2008; Langford et al, 2003).

Infiltration of CNS by HIV occurs at a very early age, and the initial infiltration causes subtle changes in the structure of the white matter (Donald et al, 2015; Mann et al, 2015). The severity of the condition depends on the age of the child when infected. Children that experienced perinatal infection have more severe signs when compared to those infected postnatally. The developing brain is severely impacted by HIV, these infants experience more severe infections than adults (Donald et al, 2015). It is thought that HIV infection reduces the growth of brain cells in-utero (Mann et al, 2015; Tardieu et al, 2000). When HIV-1 encephalopathy is present there is myelin pallor, reactive astrogliosis, reduced neuronal density and changes to the neocortical dendritic processes (Blumberg et al, 1994; Gendelman et al, 1994; Wiley et al, 1991).

The most common symptom of HIVE is motor disturbances (Ojukwa & Epstein, 1998). This is first picked up as gross motor disturbance or delay in infants (Hilburn et al, 2011; Shead et al, 2010; Potterton et al, 2009). Some of these children then develop hypertonia in the lower limbs (Mann et al, 2015). HIVE can either be static (unchanging) or progressive (Donald et al, 2015). Progressive HIV-1 encephalopathy (PHE) presents with microcephaly, delay or regression of developmental milestones as well as pyramidal deficits (Belman et al, 1988). It was found in a study done in Cape Town, South Africa, that as many as 63% of the children with HIVE presented with spastic diplegia or long tract signs (Donald et al, 2015).

2.7 Paediatric HIV and Neurodevelopment

Neurodevelopment in children with HIV can be impacted by numerous factors. These include the impact of the virus itself, ART regiment as well as environmental factors (Sherr et al, 2014). Sherr et al. (2014) found in a systematic review that 81% of studies done on children with HIV, found that they presented with some form of neurodevelopmental delay when compared with control groups.

Neurodevelopmental delay is common in infants infected with HIV (Donald et al, 2014; Abubakar et al, 2008) and occurs early in the infection due to the early invasion of the CNS by the virus (Puthanakit et al, 2013). The motor centres are affected (Boisse et al, 2008; Boivin et al, 1995). Many studies have found that a high percentage of infants with HIV exhibit global neurodevelopmental delay before their first birthday. All developmental domains have been shown to be affected, these include gross motor, cognitive and language delay (Hutchings & Potterton, 2013; Whitehead et al, 2013; Strehlau, 2013; Potterton et al, 2009; Sherr et al, 2009; Abubakar et al, 2008; Ballieu & Potterton, 2008; Van Rie et al, 2007). As described earlier in this review, HIV invades the CNS which causes structural changes to the brain which alters neurodevelopment (Donald et al, 2015; Tardieu et al, 2000; Gendelman et al, 1994; Blumberg et al, 1994; Wiley et al, 1991).

2.7.1 Motor delay

Motor delay includes both fine and gross motor delay. It is the most commonly measured developmental domain in HIV, and this is the area that is most consistently

found to be delayed (Laughton et al, 2012; Hilburn et al, 2011; Shead et al, 2010; Potterton et al, 2009; Van Rie et al, 2009; Abubakar et al, 2008; McGrath et al, 2006). It has also been found that the percentage of infants found to have neurodevelopmental delay increases as they age (Whitehead et al, 2014; Abubakar et al, 2008). Ferguson and Jelsma (2009) found that two-thirds of children infected with HIV displayed a significant gross motor delay. This was compared to a 5.7% delay in a healthy age matched sample.

Whitehead et al. (2014) found that infants as young as four months demonstrated varying degrees of developmental delay. Numerous studies have shown that there is gross motor impairment (McGrath et al, 2006; Boivin et al, 1995; Msellati et al, 1993). It has also been noted that motor delay is seen early in the disease (Boivin et al, 1995). This changes from a moderate impairment at six months to a severe impairment at eighteen months (Abubakar et al, 2008).

Abubakar et al. (2008) concluded that motor development was the most frequently measured area and provided consistent evidence of delay in children infected with HIV.

Gross motor delay is caused by changes in the CNS, caused by the virus (Donald et al, 2015). There is also loss of body protein, as well as abnormal metabolism of protein during HIV infection (Hsu et al, 2005). Abnormal protein metabolism can

cause reduced muscle leading to weakness and it has been suggested that gross motor delay could also be as a result of decreased muscle strength (Baillieu & Potterton, 2008). A recent South African study found that functional participants infected with HIV, were weaker than their uninfected peers, this suggests a link between HIV and muscle weakness (Naik & Potterton, 2017).

2.7.2 Cognitive delay

There were discrepancies between the degrees of cognitive impairment reported in children infected with HIV. Bagenda et al. (2006) reported no significant difference in the performance of HIV infected children and the controls, whereas Boivin et al. (1995) reported severe levels of impairment, but only between the ages of three to six years. In younger children (three months to eighteen months) it was found that social development was impacted in children with HIV (Boivin et al, 1995). A South African study showed a significant delay in the cognitive development of HIV positive infants (Baillieu & Potterton, 2008).

A recent South African study used the Griffiths Scale of Mental Development (GSMD) to ascertain the developmental status of preschool children receiving cART. It showed that the children were delayed in all facets of development except person-social development. It showed that at preschool age the most affected facet of development related to cognition and perceptual abilities. This relates to poor performance at school (Potterton et al, 2016).

The reasons for cognitive delay have not been well explored. A 2017 study used MRI imaging to investigate the structure of the brain in paediatric patients with HIV. This study found altered cortical and subcortical structures in the study participants when compared to healthy controls. The participants also had significantly lower cognitive performance (Yadav et al, 2017). This suggests that the cognitive delay is, at least in part, due to structural changes in the brain.

2.7.3 Language delay

There are different findings in the extent of language delay in HIV infection. Msellati et al. (1993) and Boivin et al. (1995) reported no significant delay in language scores achieved in infants between six to eighteen months, but by 24 months Msellati et al. (1993) reported severe impairment. A 2008 study reported 77% delay in language comprehension and 85% delay in language expression in children with HIV between the ages of 18 months to 72 months (Van Rie et al, 2008). Le Doaré (2012) reported subtle delays in language scores of older children with HIV who were receiving ART; while Baillieu and Potterton (2008) studied children with HIV from 18 months to 30 months. This study reported language delay in 82.5% of the study participants (Beillieu & Potterton, 2008).

Potterton et al. (2016) reported significant delay in the GSMD hearing/speech scores of preschool children receiving cART. These children showed a twelve month delay when compared with the normed population (Potterton et al, 2016).

Language delay can be related to motor difficulties due to difficulties with co-ordination and control of oral muscles. It can also be attributed to cognitive delays causing delayed language development (Baillieu & Potterton, 2008; Wolters et al, 1995).

2.7.4 Gross motor delay as an early identifier of global delay

Gross motor delay is not only noted in infants infected with HIV. It has also been suggested that motor delays may be the first (or most easily identified) indication of a global developmental delay. As infants develop it is expected that they acquire a variety of motor skills early on. Those at risk for global delay may struggle to reach early motor milestones (Noritz et al, 2013). Numerous studies have identified gross motor skills as the area most commonly impacted by HIV infection (Laughton et al, 2012; Hilburn et al, 2011; Potterton et al, 2009; Shead et al, 2010; Van Rie et al, 2009; Abubakar et al, 2008; McGrath et al, 2006).

In addition, gross motor delay has been found as early as four months (Whitehead et al, 2014; Abubakar et al, 2008; Boivin et al, 1995). In order to assess an infant and pick up delay early on, a tool that can identify gross motor delay early would be most appropriate.

2.8 Impact of Timing of HIV Infection on Neurodevelopment

McGrath et al. (2006) investigated children infected with HIV before 21 days old. They scored significantly lower on the cognitive scales than those infected after 21 days. There was a small delay at the age of six months, and by eighteen months a larger delay. Infants who present with the most severe neurodevelopmental delay are those that are diagnosed before the age of three months, and were exposed to the disease very early (Le Doaré et al, 2012), therefore, the earlier the infant is infected, the more severe the extent of neurodevelopmental delay.

A study done on the neurodevelopment of infants with early and late HIV infections was done by Smith et al. (2000). Early infected infants received a positive diagnosis within the first 48 hours of life, whereas the late infected group were diagnosed after 48 hours. The Bayley Scales of Infant Development (1st Version) was used to assess the infants in this study. It was found that infants infected early had significantly lower scores on the mental and motor scales by the age of 24 months (Smith et al, 2000).

2.9 Impact of ART on Neurodevelopment

The early introduction of ART has been found to improve neurodevelopmental outcomes and reduce the incidence of HIVE (Whitehead et al, 2014; Puthanakit et al, 2013; Strehlau, 2013; Natchman et al, 2012; Thomaidis et al, 2010; Chiriboga et al, 2005; Epstein et al, 1986). South Africa has implemented the early introduction of ART for infants with HIV, which will combat the infection early, reducing the extent of CNS damage (Lilian, 2013). It has been observed that ART medications must be

able to cross the blood-brain-barrier in order to combat the infection in the brain (Letendre et al, 2008). A 2009 study showed a 50% reduction in HIVE when ART included medication that could cross the blood-brain-barrier when compared to patients receiving regimes that did not (Patel et al, 2009). After commencement of ART, the sequelae of HIVE may improve, but the damage that was done prior to initiation persists (Langerak et al, 2014; Walker et al, 2013).

The Children with Early Antiretroviral Therapy (CHER) trial, was a randomised control trial in asymptomatic HIV positive infants younger than 12 weeks in South Africa. It included a group that received immediate ART for 40 weeks or received immediate ART for 96 weeks; these infants received ART at the time of diagnosis. The deferred ART group received ART when their CD4% was less than 25% in infancy, or CD4% less than 20%, or Centres for Disease Control and Prevention severe stage B or stage C disease. The trial found that the group that received deferred ART had a higher incidence of HIVE when compared to the groups that received early ART. It has been suggested that early ART could be neuroprotective (Cotton et al, 2013; Puthanakit et al, 2013).

In a cross-sectional sub-study of the CHER trial, Laughton et al. (2012), described the neurodevelopmental outcomes in infants receiving deferred ART compared to early ART (as described in the previous paragraph). The infants receiving deferred ART scored lower on the GMDS then those receiving early ART. Those receiving

early ART had GMDS scores similar to those HIV-uninfected infants except in the locomotor subscale (Laughton et al, 2012).

The PREDICT trial concluded that the ideal time for initiation of ART was in early infancy (Puthanakit et al, 2013). In a literature review Le Doaré et al. (2012) found that infants who received ART prior to 12 weeks of age had improved scores on standardised developmental tests. It was also noted that older children who were treated with ART had scores that were near to normal global developmental scores (Le Doaré et al, 2012).

2.10 Developmental Screening

It has been estimated that worldwide 200 million children under the age of five fail to meet their developmental potential (Grantham-McGregor et al, 2007). There has been an increasing emphasis on early identification of developmental disorders. By conducting developmental surveillance, screening and assessment where appropriate, developmental outcomes can be improved (Engle et al, 2011; Council on Children with Disabilities, 2006; Blackman, 2002).

A certain set of skills is expected to be attained in infancy and early childhood. There are multiple factors that can have a negative impact on a child's development. These include poverty, malnutrition, recurrent or chronic infections as well as inadequate cognitive stimulation (Sabanathan et al, 2015; Engle et al, 2011). In developing countries children are at a greater risk of these factors influencing their development,

and adequate identification and intervention in these cases is vital. When an individual fails to attain these expected domains, developmental delay is diagnosed (Al Notal & Schwenk, 2013).

In order to accurately assess developmental domains, standardized tools should be used. Numerous screening tools have been developed worldwide. Western screening tools are often inappropriate for the developing world. Western tools can either be adapted to make them appropriate for use, or new tools can be created to suit a specific population (Kammerer et al, 2013).

Screening is a “brief assessment procedure designed to identify children who should receive more intensive diagnosis or assessment” (Meisels, 1988 pg 527). Screening tools need to be administered quickly and have a limited sample of items that represent a domain and have a definite cut-off point. They are used to identify infants and children that may have neurodevelopmental delay, and further in-depth assessment should be done to determine the exact nature and extent of the delay. Screening tools can miss subtle neurodevelopmental delays which can impact on development later in life. They are found to be especially useful as part of a developmental surveillance program where infants and children can be monitored over time (Sabanathan et al, 2015).

2.10.1 Methods of assessment

The methods employed by various screening tools include:

1. Direct assessment. Standardised activities are done with a trained assessor in a clinical environment.
2. Indirect assessment. This includes verbal reporting or completion of a questionnaire by a parent, teacher or guardian as well as structured observations.
3. Unstructured observations. A trained assessor observes a child in a familiar environment.

Tools can use one or a combination of the above methods in order to assess a child (Sabanathan et al, 2015; Kammerer et al, 2013). Developmental screening is often in the form of an indirect assessment and are advantageous, as they take a short period of time to administer (Kammerer et al, 2013). Sub-Saharan Africa has numerous constraints that prevent in-depth assessment of each at-risk individual. This makes a reliable screening tool vital in this setting. Once screened and identified as being at-risk, children can be referred for further assessment and, if needed, therapeutic intervention.

2.10.2 Developmental domains

There are numerous developmental domains that can be assessed by a screening tool, namely: cognitive, language (expressive and receptive), motor (fine and gross), socio-emotional and adaptive behaviour (Sabanathan et al, 2015; Kammerer et al, 2013).

A tool can either focus on one, or include numerous domains. For example the IGMST is a screening tool that screens for gross motor delay in infants that are infected with HIV (Hilburn et al, 2011) whereas, the Bayley Infant Neurodevelopmental Screener (BINS) includes four different developmental areas (basic neurological functions, expressive functions, receptive functions and cognitive functions) (Aylward & Verhulst, 2000). Historically, tests of global neurodevelopment have been employed in the African setting, as more tests are created and adapted, single domain tests are being used (Kammerer et al, 2013).

2.11 Development of a Screening Tool

2.11.1 Content validity

A screening tool should undergo testing before it is used. Initially its content validity should be examined. According to Lynn, 1985; validity "is the extent to which that instrument measures what it is intended to measure'' (Lynn, 1986, pg 382). Validity includes content, criterion and construct validity. Content validity should be looked at as a two-stage process, namely development and judgement. The developmental phase should include domain identification (identifying which domain is being assessed), item generation (which items should be included) and instrument formation (placing items together in a usable form). These steps can vary slightly depending on the context in which they are being used (Lynn, 1986).

Following this, the tool must undergo judgement. This can be by a predetermined group of experts. This should be done for each individual item as well as for the instrument as a whole. These experts should achieve agreement for content validity to be established. (Lynn, 1986).The Nominal Group Technique (NGT) and the Delphi survey are the most commonly used formal methods for determining consensus agreement (Harvey & Holmes, 2012).

2.11.2 Nominal group technique

The Nominal Group Technique (NGT) is a structured, face to face meeting to determine content validity. It is a tool to generate information and determine consensus agreement. It follows a set process, and on completion of the meeting, members of the panel have reached consensus (Harvey & Holmes, 2012).

Between five to nine experts should be included in the discussion. A consensus of 80% should be reached (Potter et al, 2004). Experts should be invited to participate in the panel discussion and the following steps should be followed:

1) Introduction and explanation: The meeting should begin with introduction and an explanation and the participants given the purpose and procedure of the meeting.
2) Silent Idea Generation: The participants are provided with a sheet of paper and asked to write down all the ideas that came to mind when thinking about

the questions presented during the discussion. During this time the participants are asked not to speak or share ideas.

3) Idea Sharing: Participants are invited to share their ideas. Each participant is given time to present their ideas. Any new ideas generated by any participants are written down. This allows all participants to contribute equally and provides a written record. There is no debate or discussion at this point in the meeting.
4) Group discussion and clarifying: Participants are asked to comment, or ask their colleagues for further detail on any of the ideas produced.
5) Voting and ranking: The ideas are then prioritised in relation to the original question asked. Results are immediately available to the participants. When the meeting is concluded the results were available to the participants. (Harvey & Holmes, 2012).

A nominal group technique was used to successfully establish the content validity of the Gross Motor Function Classification System (GMFCS) (Palisano et al, 1997) as well as the expanded and revised version of the same tool (Palisano et al, 2008). It was also used successfully during the development of the original IGMST (Hilburn et al, 2011).

2.11.3 Requirements of a screening tool in a resource poor area

In a developing country a screening tool should meet certain criteria. It should identify those children who are experiencing developmental problems in order for them to be referred for additional assessment. The tool should be sensitive enough to

distinguish between children who have developmental delay and those who do not. Time constraints should be considered. It should be quick and easy to administer, both to reduce the time taken for the assessor to get through a large volume of patients, but also to reduce the assessment time for a young child. Specific training on administration of the tool should not be required. Nurses or counsellors could administer it, if need be. Budget should be taken into consideration. The tool should be inexpensive and should not require any specialised equipment or forms (Kammerer et al, 2013; Hilburn et al, 2011).

2.12. Infant Gross Motor Screening Test

2.12.1 Purpose and administration

The Infant Gross Motor Screening Test (IGMST) (Appendix IV) was developed to screen for gross motor delay in infants infected with HIV. It is a valid and reliable tool that can be used to screen for gross motor delay in infants from six to eighteen months. The IGMST requires no specific training to administer. It was created after it was found that the Bayley Infant Neurodevelopmental Screener (BINS) was an inappropriate tool for South African HIV infected infants (Hilburn et al, 2011).

2.12.2 IGMST development

The IGMST was developed by selecting six gross motor items per age group from the Bayley Scales of Infant Development (3rd version) (BSID III) which distinguished

an infant scoring in the At-Risk, Emerging or Competent categories. These items were then statistically tested using a Kappa statistic to assess agreement. The items selection was adjusted and refined until excellent agreeability was achieved in statistical testing (Hilburn et al, 2011).

2.12.3 Statistical properties

Content validity was carried out by a panel of experts in the field of paediatrics using a modified Nominal Group Technique (NGT), and agreement of 80% was required. Concurrent validity was carried out on 60 infants using the gross motor section of the BSID III, and excellent agreement was found (Kappa 0.85). Preliminary statistical testing showed it to have high sensitivity (97.4%) and specificity (85.7%). It also has a high positive predictive value (PPV) of 92.7% and negative predictive value (NPD) of 94.7%. Reliability testing was carried out using 30 infants and found excellent inter-rater, test-retest and intra-rater reliability. The diagnostic properties were found to be excellent and preliminary testing showed it to be a valid and reliable tool to screen for gross motor delay in infants infected with HIV (Hilburn et al, 2011).

2.12.4 The need for expansion of the original IGMST

The number of assessment tools for young children and infants is very limited when compared to the number available for school-going children. Thus, tools that can be used on this population are needed (Kammerer et al, 2013). In order to appropriately plan for interventions for children with HIV, developmental milestones must be

understood in this group (Le Doaré et al, 2012). At the time of Hilburn et al's. 2011; study PCR testing was carried out at 6 weeks, and infants were not always identified early enough to prevent morbidity and mortality (Lilian et al, 2013). Infants are now identified as HIV positive at an earlier age due to PCR testing at birth. Early identification of this high-risk population means that developmental surveillance, and where required, therapeutic intervention, can begin earlier.

McGrath et al. (2006) suggested that as there is an increased survival of children receiving ART, it is important to set up services that promote the neurodevelopment of these children. It was also suggested in another unpublished study, that early identification and referral needs to be done in order to improve the neurodevelopmental outcomes of children with HIV (Strehlau, 2013).

2.13 Other Locally Developed Screening Tools

2.13.1 Red Cross War Memorial Screening Tool (RCWMST)

The Red Cross War Memorial Screening Tool (RCWMST) was developed in 2014 to screen for neurodevelopmental delay in children infected with HIV in South Africa. It can be used on children from nine to thirty-six months with moderate to severe developmental delay. The nine and eighteen months items were adapted from the Western Cape Developmental Screening Tool and the twenty-four and thirty-six month items were selected from the Denver Developmental Tool, the Molteno Adapted Scales and clinical experience (Boyede et al, 2015).

The age categories were selected to coincide with the vaccination schedule, and can only be used at these points time. It is a multi-domain screening tool and tests for delay in motor (gross and fine), communication and social behaviours. It also includes a list of warning signs for each age, as well as the action to be taken should the test be failed. It consists of six sections with tick boxes for each item. It requires a short time to administer and no specific equipment which makes it useful in the South African clinic setting (Boyede et al, 2015).

Concurrent validity was carried out against the BSID III and it was found that the tool has a sensitivity of 78.5%, which is acceptable. It has a specificity of 54.6%, which was deemed moderate, authors suggest this is due to the emphasis of the tool being on sensitivity. Its PPV is 42.3%, which is low, and NPV is 85.7% (Boyede et al, 2015). The statistical properties of this tool indicate that there may be over referral, which can lead to too many assessments being done and leading to time being wasted.

2.13.2 The Road to Health Booklet

This locally developed tool is not specific to the HIV population. The Road to Health Booklet (RTHB) was introduced in October 2010 as part of the South African Department of Health's plan to improve service delivery to infants and young

children. It should be distributed to all infants in the private and state sectors. It contains a developmental screener that consists of three questions that should be asked at each visit and specific questions for each age group. It aims to screen for delays in vision and adaptive behaviour, hearing and communication and motor development (South African Department of Health, 2017).

Van der Linde et al. (2015) conducted a study to compare the RTHB with Parents' Evaluation of Developmental Status (PEDS). It was found to have poor correlation with the PEDS. Sensitivity was found to be 25% and specificity 91%. It was found to be ineffective at identifying delay, and should be adapted or replaced to ensure adequate identification of infants with neurodevelopmental delay (Van der Linde et al, 2015).

In an unpublished dissertation, the use of the RTHB screening test was investigated. It compared the use of the screening section in the RTHB, to parental report and paediatrician assessment. This study found that primary care nurses using the tool reported 13% delay, compared to parent report which indicated 25% of the population presenting with delay. In this case the examining paediatrician found 28% delay. It was concluded that the RTHB screening test is not used optimally in the primary care setting to detect developmental delay (Naborn, 2016).

2.14 Early Intervention

Early intervention is based on the concept of brain plasticity. Plasticity involves the brain's ability to form new synaptic connections and remove excessive ones. This allows the brain to change and learn from new experiences (Sullivan et al, 2014; Johnston et al, 2000). In order to allow early intervention to take place, the infants at risk of delay need to be identified as soon as possible. With the improved prevention and treatment of HIV in sub-Saharan Africa there must be adequate screening, neurodevelopmental assessment and identification of those in need of intervention. (Whitehead et al, 2014; Kammerer et al, 2013; Potterton et al, 2011; Hilburn, 2010; Grantham-McGregor et al, 2007).

A systematic review on early intervention on motor development, concluded that early intervention, using general developmental programs, is effective in improving the motor outcomes in full term high-risk infants (Blauw-Hospers & Hadders-Algra, 2005). Other studies have also shown that early intervention and stimulation programs can improve the presentation of neurodevelopmental delay (Potterton et al, 2010; Blackman, 2002). The goal of early therapeutic intervention should be to address existing developmental issues as well as minimising any further physical, cognitive and emotional delay.

2.15 Conclusion

In order to improve the developmental outcomes and quality of life of infants infected by HIV, it is vital to offer them the intervention and support that they need. Infants with HIV need additional care to allow them to thrive. By identifying those requiring assessment and physiotherapy intervention as early as possible, it will offer them the best chance of giving them the support they need.

There is no developmental screening tool available to screen for gross motor delay in infants under the age of six months, which has been developed and validated for this population.

CHAPTER 3

3 PHASE ONE – SCREENING TOOL DEVELOPMENT- METHODOLOGY & RESULTS

3.1 Development of a New Section of the IGMST

This study was based on the study which developed the initial IGMST by Dr Nicole Hilburn titled '' The development of a screening tool to evaluate gross motor function in HIV-infected infants'' (Hilburn et al, 2011). In order to create an addition to the exisiting screening tool, the original methods were replicated.

This chapter will present the first phase in the development of the new section of the IGMST.

3.2 Objectives

The objectives of phase one were as follows:

- To identify gross motor items from the BSID III which would be suitable for inclusion in the IGMST to extend it for use in younger infants (one to five months).

- To categorise items into age group suitability (one to three months); (four to five months).

- Testing and refinement of the initial version of the new items to satisfy statistical criteria (Pearson's correlation ≥0.7).

3.3 Ethical Considerations

Ethical clearance was obtained from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand prior to starting the data collection process (clearance certificate number M160503, see appendix II).

Permission was obtained from the author of the IGMST (see appendix IV) to extend the screening tool (see appendix III). Permission was also obtained from the holder of the data sets to access the data and extract the relevant information (see appendix V).

3.4 Study Design

Phase one of the study was a retrospective record analysis.

3.5 Study Population

Two 2013 physiotherapy masters studies, completed through the University of the Witwatersrand, investigated the neurodevelopment of infants infected with HIV using the BSID III. The completed BSID III from Whitehead et al. (2014) study titled "The neurodevelopment of HIV-infected infants on HAART compared to HIV-exposed but

uninfected infants" (Ethical clearance certificate M10535) and Hutchings et al. (2013) study titled ''Developmental delay in HIV-exposed infants in Harare, Zimbabwe" (Ethical clearance certificate M110484) were analysed in this study. BSID III assessments meeting the inclusion criteria below were selected for analysis.

3.6 Sample Size

The sample size was based on an expected success proportion of 0.8 with significance set at 0.05 (Hilburn et al, 2011). In order to have a Pearson's Correlation of 0.70, a sample of at least thirteen infants per age band is required. A sample of twenty five (n=25) infants for age band one to three months and eighteen (n=18) for age band four to five months was used. In total forty three (n=43) infants were used in this study.

3.7 Inclusion Criteria

BSID III forms of infants confirmed HIV positive from birth to five months from the available data sets.

3.8 Exclusion Criteria

BSID III with any missing data were excluded.

3.9 Measurement Tools – BSID III

The Bayley Scales of Infant Development III (BSID III) is an instrument which assesses developmental functioning of infants and young children aged between one and forty-two months which is administered on an individual basis. The BSID III is reliable and valid, and is predictive of later developmental outcome (Bayley, 2006). The BSID III has been considered the 'gold standard' in infant developmental assessment, which is why it was chosen (Harris et al, 2005). Studies have been conducted using the BSID III on typical black African infants (zero to eighteen months) in Johannesburg, who have socioeconomic backgrounds similar to the study population. Results of this study showed the infants did well to above average in the BSID III. This makes it a suitable tool to base the new section of the screening tool (Rademeyer, 2010; Brown, 2009).

3.10 Procedure

The procedure is as out-lined in the Figure 3.1 below:

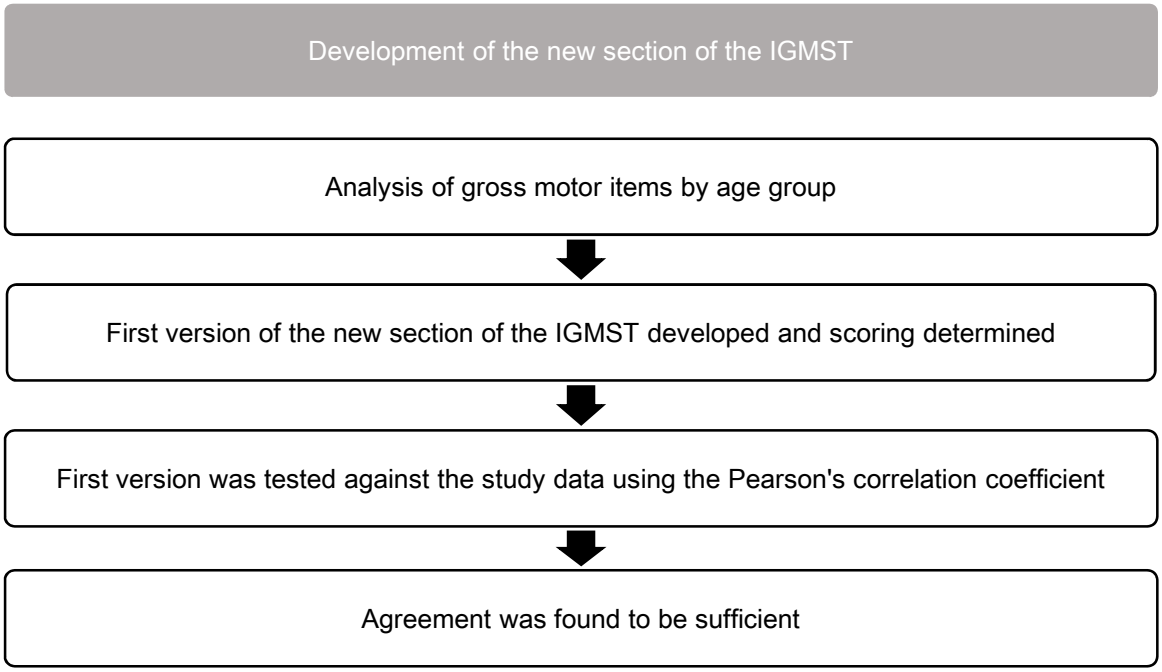


Figure 3.1 Process of development for the new section of the IGMST

3.10.1 Analysis of gross motor items by age group

Completed BSID III were sorted and those fulfilling the inclusion and exclusion criteria were selected for further analysis. The analysis determined which gross motor items from the original BSID III should be included in the IGMST. The item analysis was performed by entering scores into an Excel spreadsheet.

Each item received a score; namely:

1=credit

0=no credit

2= finish the test (i.e. after obtaining five zero's in a row)

The data were then entered according to age group and grouped according to the score obtained on the BSID-III; namely: ‘At-Risk’, ‘Emerging’, and ‘Competent’ (See appendix VI for example).

Percentages of the number of infants that completed an item were then obtained. Items were selected for each age group according to the percentages obtained.

The items selected for the new section of the IGMST were those that discriminate between the ‘At-Risk’ and ‘Emerging’ and ‘Competent’ groups. Five items were selected for each age band (one to three months and four to five months). The first two items should be achieved by the majority of the infants (≥70%, or as close to 100% as possible), the second two items done by some of the infants (30% - 69%) and the final item by few of the infants (≤29%). This selection ensured that the most advanced infants were able to do all the selected items, while those experiencing neurodevelopmental delay scored as ‘At Risk’ and were identified for further assessment. Table 3.1 illustrates the selection.

Table 3.1 Item selection	
Item	**Percentage of Infants able to complete item**
One	≥70%,
Two	≥70%,
Three	30% - 69%
Four	30% - 69%
Five	≤29%

The items selected needed to fulfil the following criteria, namely:

1) The items needed to be observational (the infant should require minimal handling).

2) The items must reflect a movement rather than the quality of movement.

Selection of items was done in conjunction with a literature search to determine which items would be most indicative of delay (Bly, 2011; Bayley, 2006; Harris & Daniels,1996; Aylward, 1995; Piper, et al., 1992). During the item selection there were two versions of the four to five age band developed. Version one included items which the literature deemed more appropriate and indicated early abdominal activation, while version II was the best fit and would most likely perform well statistically.

The items that were selected were grouped according to age bands (one to three months and four to five months). Scoring was determined according to the following: the oldest infants should be able to obtain credit for most/all items to be competent. The younger infants should have been able to obtain one less credit to be considered competent. The selection and scoring was done in conjunction with a literature search to determine which items were appropriate for each age band (Bly, 2011; Bayley, 2006; Harris & Daniels,1996; Aylward, 1995; Piper, et al., 1992). Table 3.2 illustrates the scoring for one to three months age band.

Table 3.2 Scoring

Age	**Score to be obtained to be placed in the Satisfactory category**	**Score to be placed in the At-Risk category**
1 months	1-5	0
2 months	3-5	0-2
3 months	4-5	0-3

The first draft of the new items for the screening tool was statistically tested against the initial BSID III data to determine the agreeability of the new test and the BSID III. Correlations between the new items and the items on the BSID III were carried out using the Pearson's correlation. Results were then analysed.

3.10.2 Testing of the first version of the new items for the IGMST

After the items had been selected and scoring assigned, the new section of the IGMST was ready for testing against the original BSID III data. The comparison was

using only the gross motor scale. The comparison was with the scaled scores on the BSID III. Forty three BSID III assessments where compared to the new section of the screening tool in the selected age groups. The age groups and number of infants is outlined below in Table 3.3

Table 3.3 Age groups for testing according to the new items of the IGMST (n = 43)	
Age	**Number**
1-3 months	25
4-5 months	18

3.10.2.1 Statistical analysis

The data were entered into an Excel spreadsheet, and the statistical analysis done in consultation with a statistician from the National Institute for Occupational Health.

Correlations between the new items and the items on the BSID III were carried out using the Pearson's correlation coefficient (using STATA Version 14.2) Pearson ≥ 0.70 indicates good agreement. The results are presented in Table 3.4 below:

Table 3.4 Agreement between the BSID III and the new section of the IGMST (n=45)			
Age Group	**Pearson's correlation(r)**	**P Value**	**Percentage of Children whose Scores Correlated on both Tools**
1-3 months	0.68	0.003	84%
4-5 months (Version I)	0.71	0.0009	83%
4-5 months (Version II)	0.76	0.0002	88%

Agreement was good in both tested versions of the four to five month group where Pearson's correlation ≥ 0.7 indicates good agreement. The data for the one to three month group were found to have a modest correlation, but at 0.68 were very close to good correlation of 0.7 (Jogi et al, 2011).

3.10.2.2 Analysis of results

The data for the one to three month age group were analysed to determine if these scores could be improved. It was decided that other possible combinations would only weaken the statistical performance of the test and the final decision of the items would be left to the expert panel to make. The new section of the screening tool was then ready to be presented to an expert panel in the field of paediatrics. Figure 3.2 illustrates the first version of the items for the new section of the IGMST.

1 – 3 months

1. Turns head to sides (object of interest): Child turns head from one side to the other by raising his or her head off the supporting surface enough to clear the nose. Child must be able to turn to both sides.
2. Attempts to bring hand to mouth: Child purposely attempts to place his or her hand in mouth.
3. Controls head while prone: 45° (object of interest): Child maintains raised head at least 45° from exam surface for at least 2 seconds.
4. Controls head while upright (15 seconds): Child holds head erect and steady for at least 15 seconds
5. Rolls from side to back: Child actively from both sides to his or her back.

Scoring:

1 month: 0 At Risk

1-5 Satisfactory

2 months: 0-2 At Risk

3-5 Satisfactory

3 months: 0-3 At Risk

4-5 Satisfactory

4-5 months (I)

1. Holds head in midline (object of interest): Child holds head in midline for at least 5 seconds.
2. Controls head while prone: 45° (object of interest): Child maintains raised head at least 45° from exam surface for at least 2 seconds.
3. Sits with support: 30 seconds: Child sits with slight support for 30 seconds.
4. Rolls from back to sides (object of interest): Child turns from back to both right and left sides.
5. Grasps foot with hands: Child brings one or both feet up to hands (above the hips) and grasps a foot.

Scoring:

4 months: 0-2 At Risk

3-5 Satisfactory

5 months: 0-3 At Risk

4-5 Satisfactory

4-5 months (II)

1. Holds head in midline (object of interest): Child holds head in midline for at least 5 seconds.
2. Controls head while prone: 45° (object of interest): Child maintains raised head at least 45° from exam surface for at least 2 seconds.
3. Rolls from side to back: Child actively from both sides to his or her back.
4. Sits with support: 30 seconds: Child sits with slight support for 30 seconds.
5. Rolls from back to sides (object of interest): Child turns from back to both right and left sides.

Scoring:

4 months: 0-2 At Risk

3-5 Satisfactory

5 months: 0-4 At Risk

5 Satisfactory

Figure 3.2 First version of the Items for the new section of the IGMST

The first phase of the study was completed and the test was ready for scrutiny by an expert panel. A modified nominal group technique was chosen to complete content validity. Phase two of this study will be presented in Chapter Four.

CHAPTER 4

4 PHASE TWO – CONTENT VALIDITY – METHODOLOGY & RESULTS

4.1 Content Validity of the New Section of the IGMST

This chapter will present phase two of the study. A NGT was chosen to examine the content validity of the new section of the IGMST.

4.2 Objectives

The objectives for phase two were as follows:

- To complete preliminary content validity through an expert panel examining the tool and making adjustments accordingly.
- To design and layout the new age bands in keeping with the format of the IGMST.

4.3 Ethical Considerations

Written invitations, including an information sheet, were sent to the expert panel to request their participation in the panel discussion (see appendix VII).

4.4 Study Design

Phase two made use of a panel meeting using a modified NGT (Potter et al, 2004).

4.5 Study Population

An expert panel was invited to examine the content validity of the new section of the screening tool. Ten experts in the field of paediatrics were invited to attend the panel with the requirements being that between five and nine members attend the meeting. These experts included various disciplines with knowledge of early development. Written invitations (Appendix VII) were sent to each person describing the study and outlining the proposed meeting, as well as enquiring whether they would like to participate in the meeting.

4.6 Inclusion Criteria

- A minimum of five years of experience in the field of paediatrics
- A medical, physiotherapy or occupational therapy degree
- Currently practicing in the field of paediatrics
- Preferably involved in research
- Familiar with the administration of standardised assessment tools (Hilburn et al, 2011).

4.7 Sample Size

Potter et al. (2004) states that the five to nine experts should attend the meeting in order to fulfil the criteria for a modified NGT. Five experts attended the expert panel discussion.

4.8 Procedure

A modified NGT (Potter et al, 2004) was followed to facilitate the panel discussion. The session was held in the physiotherapy department at the University of the Witwatersrand.

The following steps were followed, as dictated by the NGT protocol:

1) Introduction and explanation: The meeting began with an introduction and an explanation and the participants were welcomed. The participants were given an explanation of the purpose and procedure of the meeting.
2) Idea Generation: The participants were provided with a sheet of paper and asked to write down all the ideas that came to mind when thinking about the questions presented. During this time the participants were asked not to speak or share ideas.
3) Idea Sharing: After this the participants were then invited to share their ideas. Each participant was given time to present their ideas. Any new ideas generated by any participants during the idea sharing were written down. This allowed all participants to contribute equally and provided a written record. There was no debate or discussion at this point in the meeting.
4) Group Discussion: Participants were asked to comment or ask their colleagues for further detail on any of the ideas produced.
5) Voting and Ranking: The ideas were prioritised in relation to the original question asked. Results were immediately available to the participants. When the meeting was concluded the results were available to the participants.

The meeting was held with five experts in the field of paediatrics who fulfilled the inclusion criteria. The panel consisted of four physiotherapists and one medical doctor, all of whom were currently working in the field of paediatrics. All had more than 5 years' experience, were involved in research and familiar with the administration of standardised assessments.

On arrival the participants were provided with a copy of the original IGMST, new section of the screening tool and a copy of the proposal, which included the methodology used. They were asked to look through the documents provided to familiarise themselves with the tool. They were welcomed and introduced to one another. They were then given a verbal explanation of the development of the new section of the screening tool. An outline of the meeting and objectives for the session were given. Participants were asked to sign informed consent (Appendix VIII) after the introduction and explanation.

The above protocol was followed, and the group was asked to comment on the following:

1) Whether the age band two to three months could be expanded to one to three months without compromising the results of the tool.

2) Whether the four to five (I) or four to five (II) was a more appropriate for the new section of the screening tool.

3) Appropriateness of each selected item (the item itself, and item wording).

4) Appropriateness of the age groups which had been selected.

5) Appropriateness of the items for the age-group in which they fell.

6) Appropriateness of scoring.

4.9 Statistical Analysis

Consensus of 80% for each of the items discussed indicates agreement. Any issues arising during the discussion were addressed and adjustments to the screening tool were made when necessary.

There was 100% consensus for items one, two, four, five and six. Item three had a consensus of 40%. Once discussion and appropriate changes were made, the agreement was 100%. Once all items received consensus of ≥80% the meeting was complete. Table 4.1 shows the agreement between participants for each question:

Table 4.1 Agreement between Participants for Each Question		
Question	**Agreement**	**Agreement after suggested changes**
Whether the age band 2-3 months can be expanded to 1-3 months without compromising the results of the tool.	100%	n/a
Whether the 4-5 (I) or 4-5(II) is a more appropriate tool.	Option I 100%	n/a
Appropriateness of each item selected (the item itself, and item wording)	40%	100%
Appropriateness of the age groups which had been selected.	100%	n/a
Appropriateness of the items for the age-group in which they fell	100%	n/a
Appropriateness of scoring.	100%	n/a

The issues brought up at the panel discussion are outlined below:

4.9.1 Issues brought up at the panel discussion

It was raised at the discussion that the wording of the items was directly from the BSID III, and should be adjusted to original wording that is more easily understood, as well as to be more specific, regarding the starting position of each item. A starting position for each item was included in the description.

4.9.1.1 Age band one to three months

Item one: ‘Attempts’ to bring hand to mouth was changed to ‘brings’ hand to mouth. It was specified that it could be either one or both hands. Item three: ‘raised head’ was changed to ‘lifts head’. Item five: Included ‘this should be voluntary, and initiate by turning the head’.

4.9.1.2 Age band four to five months

The literature indicated that acquiring abdominal control in supine is important for further development an important for further gross motor development (Bly, 2011). This can be demonstrated by the ability of an infant to lift their legs and grasp their feet. However from the sample in the study including this item would not produce the most statistically significant tool. For this reason two versions of the four to five age band were developed and scored. The decision as to which is more appropriate for the screening tool was left to the expert panel to make.

- Item one was too easy for a four month old. It was suggested that the time be increased from five seconds to ten seconds.
- Item two was too easy for the age group. The time was increased from two seconds to ten seconds. A description of the starting position of the shoulder was included, ‘the elbow must be in-line or in front of the shoulders’.
- Item three needed clarity on ‘slight’ support. This was changed to ‘support by the hips on a flat surface’.

- Item five was too difficult. ‘Grasps’ foot was changed to ‘touches’ foot to make it easier.
- In addition, the panel suggested that two items be added to the existing instructions for use of the IGMST. These were:
    - The child should be dressed in light clothing or nappy during administration.
    - A small toy can be used to attract the child’s attention if needed.

The revisions for both age bands are presented in figure 4.1 below:

FIRST VERSION	SECOND VERSION
1– 3 months 1. Turns head to sides (object of interest): Child turns head from one side to the other by raising his or her head off the supporting surface enough to clear the nose. Child must be able to turn to both sides. 2. Attempts to bring hand to mouth: Child purposely attempts to place his or her hand in mouth. 3. Controls head while prone: 45° (object of interest): Child maintains raised head at least 45° from exam surface for at least 2 seconds. 4. Controls head while upright (15 seconds): Child holds head erect and steady for at least 15 seconds **5.** Rolls from side to back: Child actively from both sides to his or her back. **Scoring: 1 month:** 0 At Risk; 1-5 Satisfactory **2 months**: 0-2 At Risk; 3-5 Satisfactory **3 months:** 0-3 At Risk; 4-5 Satisfactory	**1-3 months** 1. Turns head to both sides while lying on stomach: Child lies on stomach, and turns head from one side to the other by raising head off surface enough to clear the nose. (Must be able to turn to both sides) 2. Brings hands to mouth: Lying on the back, the child brings either one or both hands to the mouth. 3. Controls head at 45 degrees: Child lies on stomach, and lifts head to 45 degrees for at least 2 seconds. 4. Controls head: Child supported at the hips in a sitting position can hold head up for at least 15 seconds 5. Rolls from side to back: When placed on side, the child can roll onto back from both sides. This should be voluntary, and initiated by turning the head. **Scoring: 1 month:** 0 At Risk; 1-5 Satisfactory **2 months**: 0-2 At Risk; 3-5 Satisfactory **2 months:** 0-3 At Risk; 4-5 Satisfactory

FIRST VERSION	SECOND VERSION
4-5 months 1. Holds head in midline (object of interest): Child holds head in midline for at least 5 seconds. 2. Controls head while prone: 45° (object of interest): Child maintains raised head at least 45° from exam surface for at least 2 seconds. 3. Sits with support: 30 seconds: Child sits with slight support for 30 seconds. 4. Rolls from back to sides (object of interest): Child turns from back to both right and left sides. 5. Grasps foot with hands: Child brings one or both feet up to hands (above the hips) and grasps a foot. **Scoring:** **4 months:** 0-2 At Risk; 3-5 Satisfactory **5 months:** 0-3 At Risk; 4-5 Satisfactory	**4-5 months** 1. Keeps head in midline: Child supported at the hips in a sitting position keeps head in midline for at least 10 seconds. 2. Controls head at 45 degrees: Child lies on stomach, and lifts head to 45 degrees for at least 10 seconds. The elbows must be in-line or in front of the shoulders. 3. Sits with support: Child sits with support at the hips on a flat surface for at least 30 seconds. 4. Rolls from back to sides. Child can do this to both sides. This should be voluntary, and initiated by lifting the head. 5. Touches foot with hands: Child brings one or both feet up to hands to touch them **Scoring:** **4 months:** 0-2 At Risk; 3-5 Satisfactory **5 months:** 0-3 At Risk; 4-5 Satisfactory

Figure 4.1 Items for the new section of the IGMST

After the appropriate changes were made following the discussion, the final version of the new section of the screening tool was ready to be compiled and the layout done.

4.10 Compilation and Layout

The completed IGMST (one to three months) (four to five months) was then compiled and an illustrator employed to insert appropriate images and ensure the layout matches the original IGMST. This section of the IGMST is now ready for further validity and reliability testing in future studies.

CHAPTER FIVE

5 DISCUSSION

The results of this study will be discussed in this chapter. The outcomes will be discussed as well as the data collected. Suggestions for future research will be given.

The original IGMST was developed to screen for gross motor delay in infants between six and eighteen months. The new section of the tool was developed to screen for gross motor delay in infants from one month to five months. This will allow for earlier identification of infants with gross motor delay.

Gross motor delay has been shown to be indicative of cognitive delay (including cognition, memory and processing speed) as the child gets older (Piek et al, 2008). Preschool age children receiving cART have been shown to be at risk for developmental delay across several developmental facets (Potterton et al, 2016). Early identification of gross motor delay allows for prompt referral for comprehensive assessments and access to early intervention services if needed. This addition to the screening tool is important as it allows for early identification of infants. Early referral and therapeutic intervention will give the infants experiencing delay the best possible outcome. As life expectancy of babies with medically managed HIV is increasing, this population is now likely to reach adulthood. They must be managed in all aspects

including neurodevelopment. This will give them the best quality of life in infancy and going into adulthood.

The screening tool is easily accessible and reproducible. It can be administer without and specific training. This makes it a valuable resource in busy South African HIV clinics where time and staff are limited.

5.1 Identification of Appropriate Items

One of the objectives of the study was to identify gross motor items from the BSID III which were suitable for inclusion in the new section of the IGMST to include infants from one month to five months. This process will be discussed below:

5.1.1 Selection of items from the BSID III

The BSID III is a developmental assessment tool. It is used on infants and young children aged between one and forty-two months, and is administered on an individual basis. It is used to assess infants who may be presenting with developmental delay. The BSID III is reliable and valid, and is predictive of later developmental outcome (Bayley, 2006). The BSID III is considered the gold standard in infant development (Harris et al, 2005; Tieman et al, 2005). Its use on typical black African infants (0-18 months) in Johannesburg, who have socioeconomic

backgrounds similar to the study population, has been studied and it was found to be appropriate (Rademeyer, 2010; Brown, 2009).

In this study, the BSID III was the starting point for the selection of items used to develop the new section of the IGMST. As this tool is considered the gold standard in infant development, and has proven validity, it was appropriate to begin the process of screening development using this tool.

In addition, gross motor function is a set of skills that are achieved by all typically developing infants, making it universal. There is a limited number of items that can be assessed when examining gross motor function, especially in infants, this leads to similar items being used in a range of developmental assessment tools (Harris et al, 2003; Aylward, 1995; Frankenburg et al, 1992; Piper et al, 1992).

5.2 Requirements of the New Section of a Screening Tool

Chapter two outlined the requirements for a screening tool in a resource-poor setting. It should identify those children who are experiencing developmental problems in order for them to be referred for additional assessment. The tool should be sensitive enough to distinguish between children who have developmental delay, and those who do not. Time-constraints should be considered. It should be quick and easy to administer, both to reduce the time taken for the assessor to get through a large volume of patients, but also to reduce the assessment time for a young child. Specific

training on administration of the tool should not be required. Nurses or counsellors could administer it, if need be. Budget should be taken into consideration. The tool should be inexpensive and should not require any specialised equipment or forms (Kammerer et al, 2013; Hilburn et al, 2011).

South African HIV clinics are busy and experience many challenges. It is, therefore, important that the new section of the screening tool follow the guidelines above.

The new section of the screening tool consists of two age bands (one to three months and four to five months). Each age band has five items that can be either achieved or not achieved. Along with this is the scoring. The tool is quick and simple to use and does not require specific training. Once further validity and reliability testing is completed, it will be uploaded along with the original IGMST, and will be available for free access online. It can also be freely distributed and copied which makes it an inexpensive tool. It also does not require any specialised equipment.

The layout of the screening tool was based on the format and layout of the original version of the IGMST. This tool has been available since July 2011 for free download (Hilburn et al, 2011).

5.3 Single Domain Screening Test

As outlined in Chapter Two, developmental assessments can either focus on a single domain or include numerous domains (Sabanathan et al, 2015; Kammerer et al, 2013). The original IGMST used gross motor delay to identify infants at risk of global neurodevelopmental delay (Hilburn et al, 2011).

5.3.1 Gross motor delay as an early identifier of global delay

Gross motor items were chosen to make up the items of the new section of the IGMST. Numerous studies have demonstrated the existence of motor delay in infants infected with HIV (Laughton et al, 2012; Hilburn et al, 2011; Shead et al, 2010; Potterton et al, 2009; Van Rie et al, 2009; Abubakar et al, 2008; McGrath et al, 2006). It has been shown that gross motor delay can be seen as early as four months (Whitehead et al, 2014). It has also been suggested that gross motor delay is the first indicator of global neurodevelopmental delay (Noritz et al, 2013). Testing for a single domain (gross motor) will likely identify an infant who is experiencing global delay now, or who may have global neurodevelopmental delay in the future.

The new section of the IGMST will screen a single developmental domain (namely, gross motor) to identify infants who require a global neurodevelopmental assessment which may indicate a global neurodevelopmental delay.

5.4 Screening Tool Development

The development of a screening tool was discussed in more detail in 2.9. According to the literature there are various means of screening tool development.

The original IGMST was developed by analysing the available literature. Items were taken from an existing tool, namely the BSID III. Expert opinion was also used to formulate the items (Hilburn et al, 2011).

Another locally developed screening tool, the RCWMST, was developed in 2014 to screen for nuerodevelopmental delay in infants with HIV. This tool adapted items from the Western Cape Developmental Screening Tool, the Denver Developmental Tools and the Molteno Adapted Scales. Clinical experience was also used to form the screening tool (Boyede et al, 2015).

International tools such as the HINT (Harris et al, 2003) and Malawian Developmental Assessment Tool (Gladstone et al, 2008), have also sucessfully adapted items from exisiting tools to form a stand-alone tool.

The process followed in the creation of the original IGMST produced a screening tool with excellent statistical properties. These methods are similar to the development of other local and international tools. The success of this original IGMST warrants replicating the methods to create an addition to the tool.

5.5 Age Band One to Three Months

Initially, the study aimed to extend the IGMST from birth to five months, however, when the sample was analysed, the youngest infant was 2.0 months old. From the sample available, the age band could not be extended from birth. The evaluation of neonates is complex, this is explained in more detail in 5.5.1. It was, therefore, decided to exclude the first month due to the technical skill involved.

5.5.1 Evaluation of neonates

The evaluation of neonates primarily consists of eliciting responses to specific stimuli or handling techniques. This evaluation of reflexes and analysis of the movements repertoire requires specific training of professionals (Majnemer & Snider, 2005).

Prechtl's Assessment of General Movements is a frequently used method of assessing the integrity of the young nervous system. When used by a trained professional they are 83% in agreement (Valentin et al, 2005). General Movement (GM) assessment have been shown to be predictive of later scores on the BSID (those having atypical GM assessments scored poorly on the BSID) (Kodric et al, 2010).

GMs are a set of spontaneous movements shown by the young infant. They involve whole body movements and sequences, and an individual, specifically trained to do so, can analyse the quality of these movements. A child with an impaired nervous system has changes in the quality of their GMs. To perform these assessments

specific basic and advanced training must be done. Doctors or therapists usually undergo this training (Einspieler & Prechtl, 2005).

Identification of early neurodevelopmental delay is difficult, and to be effective may rely on specific identification of the quality of movement done by profesionals with intensive training. According to the requirements for the screening tool (as outlined in 5.2) the first month of life would be very difficult to include successfully.

For this reason it was decided to not include the first month of life in this screening tool as it would be too difficult for individuals without specific training to assess these early movements.

5.5.2 Overlap of fine and gross motor skills

During the selection of items the second item, of the one to three month age band, was selected from the fine motor section of the BSID III. The item ‘brings hands to mouth’ was deemed to fit the criteria of a gross motor item. The movement involves whole limb movement which fits the criteria for inclusion in a gross motor screening tool. It was specified that two items in the age band should be completed by ≥70% of the infants, an additional two by 30% - 69% of the infants and one item completed by ≤29%. In the age band one to three months, items one and three had 72% of infants completing this activity. Items two and four were completed by 68% of infants and item five completed by 28% of the infants. This selection ensured that the most

advanced infants were able to do all the selected items, while those experiencing neurodevelopmental delay scored as ‘At Risk’ and were identified for further assessment. This age band satisfies the criteria set for the items. In the second part of the study the item, ‘brings hands to mouth’, was accepted by 100% of the panel once wording had been adjusted.

5.6 Scoring of the New Section of the IGMST

For consistency, two scoring groups were used, as was done in the original IGMST. This also makes a decision based on the score easier. These categories are “At-risk” and “Satisfactory” (Hilburn et al, 2011).

The final scoring is shown in the table 5.1 below:

Table 5.1 Final Scoring

Age	Score to be obtained to be considered ‘Satisfactory’	Score to be obtained to be considered ‘At-Risk’
1 month	1-5	0
2 months	3-5	0-2
3 months	4-5	0-3
4 months	3-5	0-2
5 months	4-5	0-3

As outlined in chapter three; scoring was determined according to the following: the oldest infants should be able to obtain credit for most/all items to be competent. The younger infants should have been able to obtain one less credit to be considered

competent. These guidelines were followed by Hilburn et al. (2011) in order to successfully create the original IGMST.

5.7 Statistical Testing of the Items

In this study, Pearson's correlation coefficient was calculated in order to determine the relationship between the scores of the original BSID III scores and the reduced selection of items to be included in the IGMST. This was done in the initial development prior to presenting it to the expert panel. Pearson's correlation has been used successfully to measure concurrent validity during the development of the Harris Infant Neuromotor Test (HINT) (Harris & Daniels, 1996), BINS (Aylward, 1995) and the AIMS (Piper et al, 1992).

There were no reported values for Pearson's correlation coefficient at this point in tool development on the above-mentioned tools.

The Pearson's correlation coefficient is interpreted as presented in Table 5.2 below (Jogi et al, 2011).

Table 5.2 Interpretation of the Pearson's correlation coefficient (r)	
R value	**Interpretation**
0.90 - 1.0	Excellent
0.70 – 0.89	Good
0.40 – 0.69	Modest
0.20 – 0.39	Low
<0.20	Slight

The minimally acceptable level for Pearson's correlation co-efficient is 0.6 (Palisano et al, 2008; Meyer, 1974).

The study aimed for a good correlation between the new section of the IGMST (Pearson's correlation ≥0.7) and the scores achieved in gross motor section of the BSID III. The age band one to three months achieved r= 0.68 (p=0.003). The one to three age band had a modest correlation. Although it does not satisfy the initial goal, it was very close to 0.7 and well above the 0.6 minimally accepted level (Palisano et al, 2008; Meyer, 1974). In addition the p value indicates that this is a significant correlation. The four to five age band had a Pearson's correlation of 0.71 (p=0.0009). This is a good correlation and satisfied the initial goal for the screening tool, p=0.0009 indicates a significant correlation. The one to three month age band scored lower on the Pearson's correlation, it however had a greater percentage (84%) of children who score the same on both tests than the four to five month age band (83%).

Pearson's correlation was used to assess the concurrent validity in the development of the Harris Infant Neuromotor Test (HINT). This study found a Pearson's correlation of r = - 0.89 (good correlation) between the motor scale of Bayley Scales of Infant development (2nd version) and the HINT and in the mental scale of BSID II r= -0.73 (good correlation) (Harris & Daniels, 2001).

In a Columbian study to develop and validate a scale for assessing the difficulties of daily care of children with severe cerebral palsy, Pearson's correlation coefficient of 0.71 (good correlation) was obtained when compared to the Gross Motor Function Classification System (GMFCS) (Carreno-Mora et al, 2015).

Both the studies described above, reported a good Pearson's correlation during the development of tools. This study achieved a good correlation (r=0.71; p=0.0009) for the four to five month age band and a modest correlation (r=0.68; p=0.003) for the one to three month age band. This is, however, very close to a good correlation and 84% of the infants achieved the same score on both tests. This is also above the minimally acceptable level of 0.60 (Meyer, 1974; Palisano, 1986). When compared to the correlations achieved in other screening tools; the results achieved can be interpreted as acceptable.

5.8 Content Validity

Validity is a measure of whether or not a tool measures what it is intended to. Validity encompasses content, criterion-related and construct validity. This study examined the content validity of the new section of the IGMST. Content validity specifically looks at whether the items in the tool are relevant to what they are intending to measure (Lynn, 1986).

Establishing content validity is the first step in examining the validity of a new tool (McEwan et al, 2003). The same method of establishing content validity was done as in Hilburn et al. (2011). This was done using a panel of experts who obtained consensus on each item and commented on whether it was an appropriate tool or not (Harris & Daniels, 1996).

Content validity can be considered a matter of expert judgement. There should be two phases, namely, careful development and expert assessment (Lynn, 1986). For development of a screening tool, there should first be identification of which domain is being assessed. For the development of the new items of the IGMST, gross motor items were chosen from the BSID III. Secondly, item generation should be completed. The items chosen from the gross motor section of the BSID III would assess gross motor performance. As discussed earlier in this chapter, the BSID III is considered the gold standard in infant development and has undergone thorough testing. The motor items selected from the BSID III are appropriate for inclusion in a

gross motor screening tool. This was completed in the development of the new section of the IGMST.

Following this, the items must go through judgement by experts in the field of paediatrics. In this study a modified NGT was used to determine the content validity of the new section of the screening tool. It was shown to be a reliable method to establish content validity (Dobbie et al, 2004; Hyrkas et al, 2003).

The NGT has successfully been used to establish content validity in development of the original IGMST. In this case, after appropriate changes, there was 100% agreement (Hilburn et al, 2011). A NGT was used sucessfully to establish the content validity of the original version of the GMFCS and the expanded and revised version of the GMFCS. In both of these studies 80% consenus was also used to establish agreement (Palisano et al, 2008; Palisano et al, 1997). The new section of the tool went through the appropriate steps in establishing content validity.

As discussed in chapter four, this study had an expert panel consisting of five experts in the field of paediatrics. They were asked to examine and comment on five different questions relating to the content of new section of the screening tool.

The concerns of the participants were discussed, and appropriate changes made to the tool. Once the appropriate changes had been made, there was 100% consensus

on all questions raised. Literature states that in order to reach agreement during a NGT discussion, 80% consensus must be reached (Potter et al, 2004). Having 100% agreement for all items meets this criteria.

The expert panel was asked whether the age band two to three months could be expanded to one to three months without compromising the results of the tool. This was agreed upon by 100% of the expert panel.

During the development of the HINT a group of experts was used to examine the content validity of the tool. When consensus was less than 80% revisions were made prior to the further validation of the tool. These revisions included changes to the wording of items and background information (Harris & Daniels, 1996).

Changes were made at this point in the development of the original version of the IGMST. There were changes to items themselves, as well as the wording of items (Hilburn et al, 2011).

5.9 Limitations

- The available data sets did not include infants younger than 2.0 months. Expert opinion was used to expand the age band to one to three months, but the tool cannot be used on infants in the first month of life.

- The tool, as it stands, needs to undergo further validity and reliability testing before it can be used clinically.
- The tool has only been standardised for use in infants with HIV.

5.10 Implications of the Study

- As access to cART increases, there is an increase in children living with HIV. These children have been shown to be at risk of severe neurodevelopmental delay. Once this tool has undergone further validity and reliability testing, it will be able to identify those infants at risk of neurodevelopmental delay and facilitate early referral of those infants a risk of delay.
- The IGMST screens for gross motor delay. Gross motor function has been shown be the most affected developmental domain in infants with HIV. It has also been shown to be a predictor of global neurodevelopmental delay. Once infants are identified at risk of delay on this screening tool, they can undergo a full neurodevelopmental assessment which will test language and cognitive domains.

5.11 Recommendations for Further Research

5.11.1 Validity and reliability testing

The new section of the IGMST has been developed during the course of this study. It has undergone preliminary testing. Before it can be used to test for developmental

delay in infants with HIV, it must undergo further validity and reliability testing. Criterion validity and concurrent validity must be established.

The criteria for screening tool in a resource poor setting were outlined earlier in this chapter. After undergoing further testing, it will be known whether the tool properly identifies those who are experiencing delay and those who are not.

Screening tests must also be tested to give information on the sensitivity, specificity, Positive Predictive Value and Negative Predictive Value. Further testing to establish these values should be undertaken to provide users of this test with more information on how it functions.

Reliability testing should also be undertaken, this must include inter-rater reliability, test-retest reliability as well as intra-rater reliability.

5.11.2 Standardisation of the IGMST in other high risk populations

The original Infant Gross Motor Screening Test, and the new section created during this study, was developed to screen for gross motor delay in infants with HIV. The tool is standardised for this population. Standardisation testing on typically developing children as well as other high-risk populations (such as premature infants) should be done.

CHAPTER SIX

6 CONCLUSIONS

With early infant diagnosis of HIV and the improved access to cART, there is an increasing population of infants with HIV living into their childhood and adolescent years. These infants are at risk of neurodevelopmental delay. The key to offering appropriate therapeutic intervention in these cases is early identification of neurodevelopmental delay. Gross motor skills have been found to be consistently delayed in infants with HIV. In addition, gross motor skills have been shown to be predictive of global neurodevelopmental delay. Early gross motor screening, as in the IGMST, will allow for early referral for global neurodevelopmental assessments.

To our knowledge, this is the first gross motor screening tool to be developed for infants with HIV from one month to five months. With this addition to the original IGMST, the tool as a whole, provides a way to screening for gross motor delay from one month to eighteen months.

This study has created the new section of the screening tool by taking items from the motor section of the BSID III. Statistical testing of the new age bands was significant. The one to three month age band achieved a modest Pearson's correlation of r=0.68 (p=0.003). The four to five month age band achieved a good Pearson's correlation of r=0.71 (p=0.009). These items have undergone content validity testing through a modified nominal group technique. The response of the panel was favourable.

The tool is now ready for further validity and reliability testing before it can be used in the clinical setting. The new age bands for the IGMST are shown in Figure 6.1 below:

The Infant Gross Motor Screening Test

Instructions for use

Purpose

The Infant Gross Motor Screening Test was developed to assess the gross motor function of HIV positive infants between the ages of 1 and 18 months.

User Qualifications

The Infant Gross Motor Screening Test was designed to be used by those working in a paediatric HIV setting, and does not require profession specific training. Potential users should be trained in the administration of the items, and the observation of responses from the child.

Administration time

The Infant Gross Motor Screening Test takes 5 – 10 minutes to administer,

Administration procedure

- The child's exact age in months should be calculated, and correction for prematurity should be made.
- The correct age group should be selected from the test score sheet.
- Items should be administered in a quiet child-friendly environment. The child should be dressed in light clothing or nappy during administration. The child's caregiver may be used to place the child in the necessary position should the child be upset by the administrator handing him/her. A small toy can be used to attract the child's attention if needed.

- Items do not need to be administered in sequential order, but responses need to be observed in order to be credited, the administrator may not give credit based on parent-report.
- All items should be completed for the age group.

Scoring

- For each item that the child achieves, a score of '1'should be given.
- If the child does not achieve the item, a score of '0'should be given.
- Once all the items have been completed, the child's total score should be obtained by adding up the '1's and '0's.
- The child's corresponding developmental category can be found at the bottom of the page.

The Infant Gross Motor Screening Test

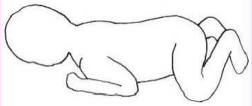
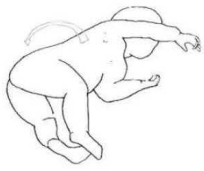
1-3 months

Child's name _____

Date of Birth ____/____/____

Date of Assessment ____/____/____

Age _____ months

		Score
	**Turns head to both sides while lying on stomach** Child lies on stomach, and turns head from one side to the other by raising head off surface enough to clear the nose. (Must be able to turn to both sides)	☐
	**Brings hands to mouth** Lying on the back, the child brings either one or both hands to the mouth	☐
	**Controls head at 45 degrees** Child lies on stomach, and lifts head to 45 degrees for about 2 seconds	☐
	**Controls head** Child supported at the hips in a sitting position can hold head up for about 15 seconds	☐
	**Rolls from side to back** When placed on side, the child can roll onto back from both sides. This should be voluntary, and initiated by turning the head	☐

1 month	2 months	3 months
☐ 1-5 Satisfactory	☐ 3-5 Satisfactory	☐ 4-5 Satisfactory
☐ 0 At Risk	☐ 0-2 At Risk	☐ 0-3 At Risk

The Infant Gross Motor Screening Test

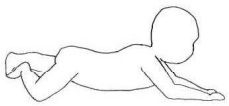
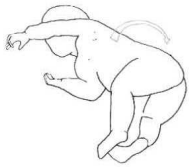
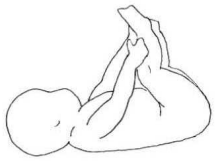
4-5 months

Date of Assessment ____/____/____

Child's name _____

Date of Birth ____/____/____

Age _____ months

		Score
	**Keeps head in midline** Child supported at the hips in a sitting position keeps head in midline for about 10 seconds	☐
	**Controls head at 45 degrees** Child lies on stomach, and lifts head to 45 degrees for about 10 seconds. The elbows must be in-line or in front of the shoulders	☐
	**Sits with support** Child sits with support at the hips on a flat surface for about 30 seconds	☐
	**Rolls from back to sides** Child can do this to both sides. This should be voluntary, and initiated by lifting the head	☐
	**Touches foot with hands** Child brings one or both feet up to hands to touch them	☐

4 months	5 months
☐ 3-5 Satisfactory	☐ 4-5 Satisfactory
☐ 0-2 At Risk	☐ 0-3 At Risk

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APPENDIX I: APPROVAL OF TITLE

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
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Reference: Mrs Sandra Benn
E-mail: sandra.benn@wits.ac.za

29 June 2016
Person No: 0402953Y
PAG

Mrs KM Otten
1237 Pluimbal Avenue
Weltevredenpark
1709
South Africa

Dear Mrs Otten

Master of Science in Physiotherapy: Approval of Title

We have pleasure in advising that your proposal entitled *The extension of the infant gross motor screening test to include infants from birth to five months in infants with HIV* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

APPENDIX II: ETHICAL CLEARANCE

R14/49 Mrs Kirsty Mae Otten

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160503

NAME: (Principal Investigator)	Mrs Kirsty Mae Otten
DEPARTMENT:	Therapeutic Sciences - Physiotherapy University of the Witwatersrand
PROJECT TITLE:	The Extension of the Infant Gross Motor Screening Test to Include Infants from Birth to Five Months in Infants with HIV
DATE CONSIDERED:	27/05/2016
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 May and will therefore be due in the month of May each year.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX III: LETTER OF PERMISSION

22nd February 2016

To whom it may concern

I give Kirsty Otten permission to use the study design from my PhD entitled The Evaluation of a Screening tool to assess gross motor development in HIV Infected Infants.

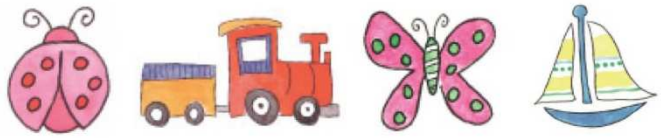
I also give her permission to extend the age range of the Infant Gross Motor Screening Test (IGMST) which I developed as part of the PhD study

Kind regards

Nicole Hilburn

APPENDIX IV: INFANT GROSS MOTOR SCREENING TEST

The Infant Gross Motor Screening Test



Instructions for use

Purpose

The Infant Gross Motor Screening Test was developed to assess the gross motor function of HIV positive Infants between the ages of 6 and 18 months.

User Qualifications

The Infant Gross Motor Screening Test was designed to be used by those working in a paediatric HIV setting, and does not require profession specific training. Potential users should be trained in the administration of the items, and the observation of responses from the child.

Administration time

The Infant Gross Motor Screening Test takes 5 - 10 minutes to administer.

Administration procedure

- The child's exact age in months should be calculated, and correction for prematurity should be made.
- The correct age group should be selected from the test score sheet
- Items should be administered in a quiet child-friendly environment. The child's caregiver may be used to place the child in the necessary position should the child be upset by the administrator handling him/her
- Items do not need to be administered in sequential order, but responses need to be observed in order to be credited, the administrator may not give credit based on parent-report.
- All items should be completed for the age group

Nicole Hilburn 2010 • nicolehilburn@gmail.com

Scoring

- For each item that the child achieves, a score of '1' should be given
- If the child does not achieve the item, a score of '0' should be given
- Once all the items have been completed, the child's total score should be obtained by adding up the '1's and '0's.
- The child's corresponding developmental category can be found at the bottom of the page.

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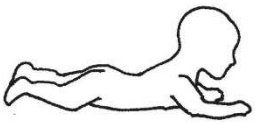
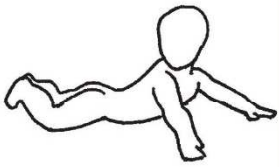
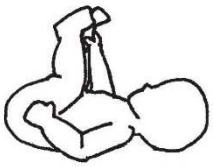
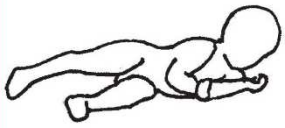
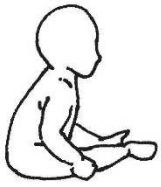
The Infant Gross Motor Screening Test 6-8 months

Date of Assessment____/____/_____

Child's name_____

Date of Birth____/____/_____

Age_____ months

		Score
	**Controls head at 90 degrees while lying on stomach** Child lies on stomach, and should be able to lift head up to 90 degrees for about 5 seconds	☐
	**Elevates chest whilst lying on stomach (with extended arms)** Child supports weight on both hands, whilst keeping arms straight, and lifting head at 90 degrees	☐
	**Plays with feet** Child should bring one or both feet to hands (above the hips), and be able to maintain this position whilst playing with feet	☐
	**Rolls from back to stomach** Child can do this to both or one side. This should be voluntary, and initiated by lifting the head	☐
	**Sits alone** The child should be able to sit alone for about 30 seconds without using arms for support	☐

6-7 months	8 months
☐ 4-5 Satisfactory	☐ 5 Satisfactory
☐ 0-3 At risk	☐ 0-4 At risk

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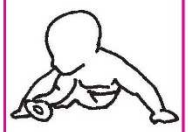
The Infant Gross Motor Screening Test 9-12 months

Child's name_____

Date of Birth____/____/_____

Date of Assessment____/____/_____

Age_____ months

		Score
	**Turns body while seated** Child turns his or her trunk and reaches for object	☐
	**Makes stepping movements** Child makes at least two stepping movements that move him/herself forward whilst hands are held	☐
	**Moves from sitting to being on hands and knees** Child uses rotation to move from sitting to being on hands and knees	☐
	**Crawls/moves forward at least 1½ metres** Child uses crawling/moving on stomach and pulling with hands to move forwards at least 1 ½ metres	☐
	**Pulls up to standing position** Child uses an object such as a table in order to pull him/herself into a standing position, or pushes up on the floor without support	☐

9-10 months	11-12 months
☐ 4-5 Satisfactory	☐ 5 Satisfactory
☐ 0-3 At risk	☐ 0-4 At risk

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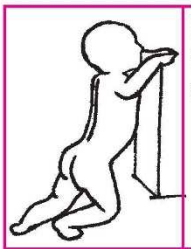
The Infant Gross Motor Screening Test 13-16 months

Child's name_____

Date of Birth____/____/_____

Date of Assessment____/____/_____

Age_____ months

		Score
	**Pulls up to standing position** Child uses an object such as a table in order to pull him/herself into a standing position, or pushes up on the floor without support	☐
	**Sits down from supported standing in a controlled manner** Child sits down from a standing position using good control e.g. by using a controlled squat	☐
	**Stands independently** Child is able to stand without support for at least 20 seconds	☐
	**Walks alone with coordination** Child should be able to walk a reasonable distance (such as 20 steps) with good control and coordination	☐
	**Squats without support** The child should be able to squat down with good control, and maintain this position for play. The child's bottom should not be resting on the floor	☐

13 months	14 months	15-16 months
☐ 3-5 Satisfactory	☐ 4-5 Satisfactory	☐ 5 Satisfactory
☐ 0-2 At risk	☐ 0-3 At risk	☐ 0-4 At risk

Nicole Hilburn 2010 • nicolehilburn@gmail.com

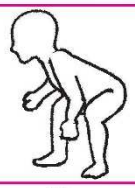
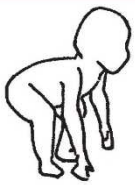
The Infant Gross Motor Screening Test 17-18 months

Child's name_____

Date of Birth____/____/_____

Date of Assessment____/____/_____

Age_____ months

		Score
	**Sits down from supported standing in a controlled manner** Child sits down from a standing position using good control e.g. by using a controlled squat	☐
	**Stands independently** Child is able to stand without support for at least 1 minute	☐
	**Stands up with no assistance** Child moves into a standing position without using an object to pull on. The child may push up on the floor in order to stand up	☐
	**Walks alone with coordination** Child should be able to walk a reasonable distance (such as 40 steps) with good control and coordination	☐
	**Squats without support** The child should be able to squat down with good control, and maintain this position for play. The child's bottom should not be resting on the floor	☐
	**Runs with coordination** The child should be able to run without falling over	☐

17-18 months
☐ 6 Satisfactory
☐ 0-5 At risk

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APPENDIX V: ACCESS TO DATA

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

DEPARTMENT OF PHYSIOTHERAPY

5 April 2016

The Chairperson Human research Ethics Committee

I hereby give permission for Ms Kirsty Otten to access my database to extract data on developmental assessments of HIV positive infants using the Bayley Scales of Infant and Toddler Development. Ms Otten may extract data on age and BSID composite scores for infants aged between one and six months of age. This data was collected for two research projects between 2011-2013 and is anonymised.

Kind regards

Prof Joanne Potterton

Physiotherapy Department
School of Therapeutic Sciences, Private Bag 3, Wits, 2050, South Africa
T +27 11 717 3702 | F +27 11 717 3719 | E joanne.potterton@wits.ac.za | W www.wits.ac.za/staff/joanne.potterton.htm

APPENDIX VI: EXAMPLE OF DATA CARPTURING FOR ITEM ANALYSIS

Age	Scaled	Score	Gross 1	Gross 2	Gross 3	Gross 4	Gross 5	Gross 6	Gross 7	Gross 8	Gross 9	Gross 10	Gross 11	Gross 12	Gross 13	Gross 14
5.04	4	55	1	1	1	1	1	0	1	0	1	1	1	1	0	0
5.17	2	49	1	1	1	1	1	0	1	0	1	1	0	1	0	1
			2	2	2	2	2	0	2	0	2	2	1	2	0	1
			100%	100%	100%	100%	100%	0%	100%	0%	100%	100%	50%	100%	0%	50%
4.02	5	76	0	0	1	1	1	1	1	1	0	1	0	1	0	0
4.08	6	77	1	1	1	1	1	1	1	0	0	1	0	1	0	0
5.12	6	70	1	1	1	1	1	1	1	1	1	1	1	1	0	0
5.19	6	70	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5.28	6	61	1	1	1	1	1	1	1	1	1	1	1	1	1	1
			4	4	5	5	5	5	5	4	3	5	3	5	2	2
			80%	80%	100%	100%	100%	100%	100%	80%	60%	100%	60%	100%	40%	40%
4.07	10	88	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4.11	10	82	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4.04	12	100	1	1	1	1	1	1	1	0	1	1	1	1	0	1
4.07	8	107	1	1	1	1	1	1	1	1	1	1	1	1	1	0
4.02	11	91	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4.09	9	85	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4.09	11	112	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4.0	11	103	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5.27	12	110	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5.19	11	107	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5.02	9	91	1	1	1	1	1	1	1	1	1	1	1	1	1	1
			11	11	11	11	11	11	11	10	11	11	11	11	10	10
			100%	100%	100%	100%	100%	100%	100%	91%	100%	100%	100%	100%	91%	91%

APPENDIX VII: INFORMATION SHEET

Good day.

My name is Kirsty Otten, I am a Physiotherapist studying at the University of the Witwatersrand. I would like to invite you to consider participating in an expert panel discussion for the research study, entitled "The extension of the Infant Gross Motor Screening Test to include infants from birth to five months in infants with HIV."

I would like you to be a member of an expert panel that will evaluate the content validity of an addition to the Infant Gross Motor Screening Test (IGMST). The original IGMST is a valid and reliable tool to screen for gross motor delay in infants with Human Immunodeficiency Virus (HIV) between the ages of 6-18 months. A need was seen to identify infants as early as possible in order to begin early therapeutic intervention. Thus it was decided to extend the tool to include infants from birth to 5 months. The addition was created based on the gross motor portion of the Bayley Scales of Infant development (BSID-III). BSID-III items were selected and evaluated and those items which were most predictive of a gross motor delay were selected. These items were statistically analysed to assess agreement.

In order to evaluate the content validity of this new portion of the screening tool an expert panel will be assembled and a modified Nominal Group Technique will be used to evaluate the new portion of the tool.

The meeting will take place at the Physiotherapy Department of the University of the Witwatersrand. It should take approximately 2 hours. Please note that for record keeping the meeting will be recorded with a Dictaphone.

On arrival at the meeting you will be given a copy of the proposal, methodology and the new screening tool. The meeting will have the following step:

Step 1: Welcome and explanation. The meeting will begin with an introduction and an explanation of the meeting. The purpose and procedure of the meeting will be discussed. You will be required to comment on the following ideas:

1) Appropriateness of each item selected (the item itself, and item wording, the appropriateness of the age groups which had been selected
2) Appropriateness of the items for the age-group in which they fell and the appropriateness of scoring.

Step 2: There will then be 10 minutes allocated for the generation of ideas. Each participant will be provided with a sheet of paper with the question to be addressed and will be asked to write down any ideas that come to mind. During this time, participants are asked not to discuss their ideas with the other participants.

Step 3: After this the participants will be invited to share their ideas. Each participant will be given time to present their ideas. Any new ideas generated by any participants during the idea sharing will be written down. This is to allow all participants to contribute equally and provided a written record.

Step 4: There will then be a group discussion. Participants will then be invited to ask for any further explanation about the ideas generated from the other participants.

Step 5: Voting and ranking will then take place to prioritise the recorded ideas. Results will be available immediately to participants so that the outcomes of the meeting are reached by the time the meeting is finished.

I hope that you will consider participating in this discussion.

Regards

Kirsty Otten
083 297 2100

APPENDIX VIII: INFORMED CONSENT

Informed Consent

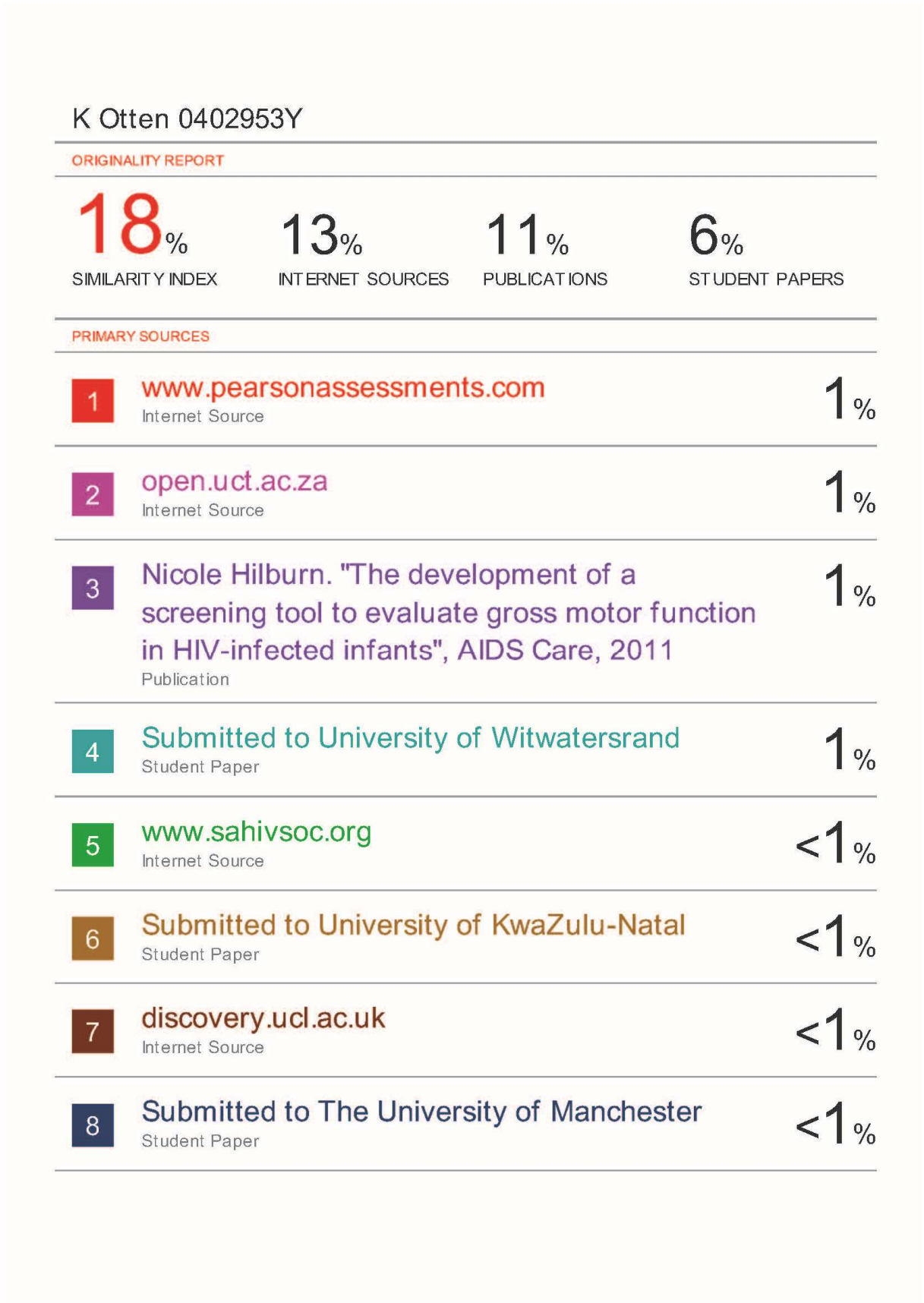
If you would like to take part in this panel discussion, please sign below

I, _____,

agree to take part in this study. I understand that I may withdraw from the study at any time. I have read the information sheet provided. I understand that notes on the discussion will be taken and securely stored, but that there is no guarantee of confidentiality for the notes.

Signed: _____ Date: _____

APPENDIX IX: TURN IT IN ORIGINALITY REPORT



K Otten 0402953Y

ORIGINALITY REPORT

18%	13%	11%	6%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	www.pearsonassessments.com Internet Source	1%
2	open.uct.ac.za Internet Source	1%
3	Nicole Hilburn. "The development of a screening tool to evaluate gross motor function in HIV-infected infants", AIDS Care, 2011 Publication	1%
4	Submitted to University of Witwatersrand Student Paper	1%
5	www.sahivsoc.org Internet Source	<1%
6	Submitted to University of KwaZulu-Natal Student Paper	<1%
7	discovery.ucl.ac.uk Internet Source	<1%
8	Submitted to The University of Manchester Student Paper	<1%

APPENDIX X: PLAGARISM DECLARATION

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

I Kirsty Mae Otten (Student number: 0402953Y) am a student registered for the degree of Masters of Physiotherapy in the academic year 2018.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: KOtten Date: 01/02/2018

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